Is Cardiac Filling Pressure the Limiting Factor in Adjusting to Heat Stress?

PETER B. RAVEN, Ph.D.

Department of Physiology, Texas College of Osteopathic Medicine, Fort Worth, Texas

Received September 13, 1985

The concept that a specific level of central venous pressure (CVP) limits man's adjustment to heat stress has been debated. Evidence was presented that identifies a true limit of adjustment as being more related to factors affecting evaporative cooling, such as level of hydration, release of active vasodilation substance (AVS), and sweat gland fatigue. However, it was conceded that decreases in CVP and subsequent low-pressure baroreceptor activation modify cutaneous blood flow and subsequently reduce conductance of heat from the core to the periphery. It was suggested that CVP merely reflects a downstream pressure, which must be allowed to reach a pressure lower than that observed in the peripheral venous bed during active cutaneous vasodilation, to insure adequate venous return. However, a loss of evaporative cooling has been observed during prolonged progressive dehydration of subjects in the supine position, resulting in 3 to 4 percent loss of total body weight. This loss of evaporative cooling was not apparent when euhydration was maintained. As it was unlikely that CVP was reduced in these experiments in the supine position, it was concluded that CVP was not the limiting factor in man's adjustment to heat stress.

In an attempt to lay the foundation for a scientific debate with respect to the role of central venous pressure (CVP), or cardiac filling pressure, as a limiting factor in adjusting to heat stress, we need to keep in mind a basic tenet of Huxley's, this being:

Next to being right in this world, the best of all things is to be clearly and definitely wrong [Thomas Henry Huxley].

To date, no investigation has been attempted whereby cardiac filling pressures [i.e., CVP or right atrial mean pressures (Ra-MP)] have been singularly manipulated during which no adaptation to heat stress has occurred. Therefore, we may note that the question raised is one to which there are no data to support the issue and therefore does not require an opposite view in a Socratic debate. However, in order not to dismiss the issue entirely, it should be noted that when CVP or Ra-MP has been altered, using, for example, hypo- and hypervolemia [1–3], lower body negative pressure (LBNP) [4], or upright exercise while submerged to the neck [5], with comparisons against representative control conditions during heat stress, that many relationships between effector responses and assumed driving signals have been altered (see Fig. 1).

The problem with these experiments lies in the concept that these experimental manipulations do not singularly alter CVP, especially LBNP and hypo- or hypervolemia. Furthermore, in all of the experiments where CVP has been altered and/or measured, it was apparent that the primary concern of the cardiovascular system, or the hierarchic decision made, was to protect the brain blood flow. This was
FIG. 1. (Upper left panel): An example of an alteration in effected response (FBF) for a given core temperature ($T_a$) using hyper- and hypovolemic subjects. Reprinted with permission from E.R. Nadel et al. and the American Physiological Society [3]. (Upper right panel): An example of an alteration in effected response (FBF) for a given core temperature ($T_a$) using upright exercise while submerged to the neck in water temperature at 38°C compared to air temperature of 45°C. Reprinted with permission from B. Nielsen and the Eur J Appl Physiol [5]. (Lower panel): An example of the use of LBNP in determining the role of high- and low-pressure baroreceptors on the effected response (FBF) to a given core temperature ($T_a$). Reprinted with permission from J.M. Johnson et al. and the American Physiological Society [4].
accomplished by maintaining an adequate cardiac output to support brain blood flow while the CVP was not protected [6]. It will be seen later, and, as documented by Professor Kirsch, that it was imperative that CVP be allowed to fall in order to insure that the pressure gradient from the periphery to the heart favored venous return.

In summary, the changes in perfusion pressure necessary to maintain adequate brain blood flow were sensed by the high-pressure baroreceptors of the carotid and aortic arch [7], while integration of many other peripheral and central command afferent inputs must serve to modulate the effector responses emanating from the cardiovascular center (see Fig. 2). Unfortunately, in those experiments which have used LBNP, the primary challenge was to alter systemic arterial pressure, and secondarily a change in CVP was produced. Hence, we must question the extrapolation of data documenting a change in the relationship of forearm blood flow (FBF) to esophageal temperature (T_e) (see Fig. 3) as being solely related to CVP. Further to this argument, the concept that a change in this relationship provides evidence of a limitation to the human's adjustment to heat stress must be questioned.

FIG. 2. H.L. Stone's concept of the central and peripheral neural control of arterial blood pressure. Reprinted with permission from the American Physiological Society [7].

FIG. 3. Four representative individual patterns of FBF per °C (T_e) during moderate upright exercise (86–147 W) while T_e was maintained at 38°C by a whole-body heating suit. Note that the break point in the relationship FBF vs. T_e occurs at 38°C. Reprinted with permission from G.L. Brengelmann et al. and the American Physiological Society [12].
We could propose that the limit, or the boundary, to the adjustments to heat stress of the human can be determined when the balance between heat loss mechanisms and heat gained is no longer in equilibrium (see Fig. 4). An example of this concept was clearly demonstrated by Lind [8] in his description of the prescriptive zone, whereby environmental temperature and metabolic rate are interrelated to present conditions of heat gain which override the cooling provided by the evaporation of sweat (see Fig. 5). Subsequently, in 1973, Horstman and Horvath [9] described the cardiovascular adjustments of ten subjects undergoing progressive dehydration. Each subject was exposed, in the resting supine position on a metabolic balance (Potter scale), to 48°C and 7.0 mm Hg vapor pressure for seven hours. Throughout the seven hours of exposure, cardiac output remained elevated at 10 l/minute, a value double that observed during a seven-hour control exposure of 28°C and 7.0 mm Hg vapor pressure. The increase in cardiac output was brought about by increases in heart rate (31 percent) and stroke volume (59 percent) (refer to Table 1), which was maintained over

![Diagram of heat production and loss mechanisms.](image)

**FIG. 4.** A conceptual balance between mechanisms of heat loss and heat gain first proposed by E.F. DuBois in 1937 at the Lane Medical Lectures of Stanford, California. Reprinted by permission from W.S. Hoar and Prentice-Hall Publishing Co.

![Graph of effective temperatures.](image)

**FIG. 5.** Levels of the equilibrium and break-point temperatures for one subject working at 180 (●), 300 (▲); and 420 (△) Kcal/hour in a wide range of climatic conditions. Note the inverse relationship between effective temperatures and the work load-related break point in T_{re}. Reprinted with permission from A.R. Lind and the American Physiological Society [8].
TABLE 1
Ventilation Rate, Oxygen Uptake, Cardiac Output, Stroke Volume, and Arterial-Venous Oxygen Difference During Seven Hours of Exposure to 48°C, WVP 7 mm Hg, Without Fluid Replacement*

| Time (minutes) | \( \dot{V}_{BTPS} \) (l/minute) | \( \dot{V}_{O_2} \) (l/minute) | \( \dot{Q} \) (l/minute) | HR (beats/minute) | SV (ml/beat) | (a-v) O\(_2\) Difference (ml/l) |
|----------------|----------------------------------|--------------------------------|--------------------------|-------------------|--------------|-------------------|
| Control (28°C) | 7.4 ± 0.4                        | 0.22 ± 0.02                    | 5.1 ± 0.2                | 65 ± 3            | 87 ± 7       | 43 ± 3            |
| 20             | 10.0 ± 0.5                       | 0.34 ± 0.02                    | 10.4 ± 0.3              | 82 ± 6            | 127 ± 12     | 33 ± 3            |
| 40             | 9.7 ± 0.4                        | 0.33 ± 0.02                    | 10.0 ± 0.5              | 82 ± 5            | 122 ± 12     | 33 ± 3            |
| 60             | 9.7 ± 0.5                        | 0.33 ± 0.02                    | 9.8 ± 0.5               | 85 ± 3            | 115 ± 9      | 34 ± 3            |
| 80             | 9.9 ± 0.5                        | 0.32 ± 0.02                    | 9.8 ± 0.6               | 86 ± 3            | 114 ± 8      | 33 ± 2            |
| 120            | 9.3 ± 0.4                        | 0.31 ± 0.02                    | 10.0 ± 0.3              | 85 ± 5            | 118 ± 8      | 31 ± 2            |
| 180            | 9.4 ± 0.5                        | 0.31 ± 0.02                    | 10.1 ± 0.4              | 81 ± 5            | 124 ± 10     | 31 ± 3            |
| 240            | 9.6 ± 0.4                        | 0.31 ± 0.02                    | 10.1 ± 0.4              | 81 ± 4            | 124 ± 8      | 31 ± 3            |
| 300            | 9.6 ± 0.5                        | 0.33 ± 0.03                    | 9.8 ± 0.5               | 87 ± 4            | 112 ± 8      | 34 ± 3            |
| 360            | 10.0 ± 0.6                       | 0.36 ± 0.04                    | 10.1 ± 0.5              | 89 ± 4            | 113 ± 8      | 36 ± 4            |
| 420            | 10.0 ± 0.9                       | 0.36 ± 0.05                    | 10.1 ± 0.5              | 94 ± 4            | 107 ± 7      | 36 ± 5            |

*Values are means ± SE.

four hours. After four hours, when dehydration approached a mean of 2.36 percent of body weight, the heart rate progressively increased to 44 percent above resting control value, and stroke volume decreased from 51 percent to 33 percent above resting control values at seven hours of exposure. However, as can be seen from Fig. 6, peripheral blood flow monitored in both the forearm (FBF) and calf (CBF) peaked during the first hour of exposure and subsequently progressively declined over the remainder of the exposure. These reductions in FBF and CBF were significant after four hours of exposure and correlated well with a significant decline in evaporative cooling. This decline in evaporative cooling and peripheral blood flow was reflected by an acceleration in the rate of increase of tympanic temperature (Ty) from a 0.3°C rise in the initial two hours to a 0.6°C rise in the final two hours of exposure. These data suggest that a limit in the cooling mechanism had been reached, which in some way was interrelated to sweat rate peripheral blood flow and the subjects’ level of hydration. Furthermore, as the subjects were in the supine position, it was highly unlikely that CVP was significantly altered. In support of this argument, the imbalance between heat gain and heat loss was not apparent when hydration was maintained throughout the exposure [10].

It has been apparent since the historical work of Pitts et al. [11] that thermal equilibrium was affected by the level of hydration (see Fig. 7). In Pitts et al.’s study, core temperature reached equilibrium and was maintained during prolonged exercise in the heat as long as the pre-exercise level of hydration was maintained. Hence, it would appear that the relationship between level of hydration, sweating capacity, and delivery of heat from the core to the skin surface (i.e., peripheral blood flow) becomes the limiting factor in man’s ability to adapt to heat stress. This limitation would be apparent regardless of whether the heat stress exposure is combined with rest or exercise. However, it is this integration and the subsequent hierarchic decision to be made that become more evident during exercise in the heat. An example of such hierarchy is observed many times in competitive distance running. Many instances
FIG. 6. The time course of evaporative cooling, tympanic temperature $T_{ty}$, FBF, and CBF of ten subjects exposed to 48°C and 7.0 mm Hg water vapor pressure. Note the close relationship to decreases in FBF, CBF, and evaporative cooling and the greatest increase in $T_{ty}$ during the final hours of exposure. Reprinted with permission from D.H. Horstman and the American Physiological Society [9].

have been reported in which the runner appears to have lost temperature regulation, in that core temperature has been allowed to achieve near fatal levels, and yet the competitor maintains an upright exercising posture, suggesting adequate mean arterial pressure and brain perfusion.

The link between peripheral blood flow and sweating, or sudomotor activity, becomes important in determining the role of CVP in adjusting to heat stress. Many of the investigations attempting to discover this link have recently been critically reviewed by Rowell [12]. Since the time of Bernard [13] it has been repeatedly demonstrated that cutaneous blood flow (SkBF) in humans was affected by the sympathetic vasoconstrictor nerves, which have a baseline tonicity during thermoneutral environments [14]. Redirection of flow to the skin during exercise in the heat must occur in the face of a generalized increase in vasoconstrictor tone. The degree of the exercise-induced increase in vasoconstrictor tone has been demonstrated to be directly proportional to core temperature [15] (see Fig. 8) and absolute work level of exercise [16] (see Fig. 9). It would appear that, in the heat, increases in SkBF were closely related to the release of an active vasodilator substance (AVS) produced during increases in sudomotor activity [17] (see Fig. 10). This is analogous to the situation in
working skeletal muscle, where localized vasodilation occurs and overrides a sympathetically mediated generalized vasoconstriction being produced within the working muscle [18]. One such substance, bradykinin, is thought to be the candidate for the AVS [19]. Regardless of the specifics of the mechanism, it appears that SkBF in the heat is regulated by local vasodilator mechanisms overriding the generalized vasoconstrictor tone. However, many factors can play a part in modifying this competitive balance between vasoconstriction and vasodilation at any given thermal stress. Indeed, from the data of Horstman and Horvath [9, 10] it could be postulated that sudomotor activity fatigues, thereby reducing local metabolite accumulation and consequently

FIG. 7. The time course of rectal temperature ($T_r$) of one subject walking at 5 km/hour on a 2.5 percent grade at 39°C DB and 35% rh. (- - -) indicates water loss not replaced; (---O---) indicates water drunk ad libitum; and (- - -) indicates water loss replaced following hourly weighing. Note that thermal balance was only achieved if sweating capacity was optimized by maintaining the subjects normovolemic. Reprinted with permission from G.E. Pitts et al. and the American Physiological Society [11].

FIG. 8. The time course of changes in splanchnic vascular resistance (SVR, $\Delta$) and splanchnic blood flow (SBF, $\bullet$) as related to rise in arterial blood temperature ($T_a$) during prolonged whole-body heating. Note the close relationship between increasing resistance and decreasing flow in response to generalized vasoconstriction and increased core temperature ($T_c$). Reprinted with permission from L.B. Rowell and the American Physiological Society [15].
The linear relationship between SBF as a percentage of resting SBF and the heart rate (HR) during exercise in hot and neutral environments (O—O). Also note that the regression line for SBF versus HR in resting humans during heat stress is displaced to the left. However, the linear relationship between HR and percentage of resting SBF remains and confirms the generalized vasoconstriction associated with either heat stress (increasing core temperature) or exercise stress. Reprinted with permission from L.B. Rowell and the American Physiological Society [12].

reducing the degree of vasodilation competing against active vasoconstriction, culminating in a reduction of SkBF. However, more pertinent to the question is the role that CVP plays in this modification. For example, it could be proposed that, as dehydration progressed and core temperature increased, cutaneous blood volume increased, resulting in a reduced CVP. Subsequently, low-pressure baroreceptor activation in response to the reduced CVP resulted in a stronger central vasoconstrictor drive, reducing SkBF and reducing the delivery of heat from the core to the surface.

The fact that CVP has a role to play in the human’s adaptation to heat stress has been succinctly reviewed by Rowell [12]. In a classic demonstration, Johnson et al. [20] utilizing a -1 mm Hg/minute ramp of LBNP clearly demonstrated the low-pressure baroreceptor involvement in regional vasoconstrictor responses, (see Fig. 11). Such involvement would clearly provide an explanation for the modification of the relationship between FBF and $T_{c}$ which occurs when $T_{c}$ is above 38°C (see Fig. 3). In

![Graph showing the linear relationship between SBF and heart rate](image)

**Fig. 10.** Right and left forearm blood flows in one subject with congenital absence of sweat glands (anhidrotic ectodermal dysplasia) during direct whole-body heating (forearms were not heated). Forearm blood flows showed almost no increase in response to a 1.5°C increase in $T_{c}$. In normal skin, this would raise blood flow to 20–30 ml· min$^{-1}·100$ ml$^{-1}$ in the forearm, the increment being confined to the skin. This provides a classic example of the link between sudomotor activity and active cutaneous vasodilation. Reprinted with permission from L.B. Rowell and the American Physiological Society [12].
the conceptual model described by Rowell [12], one notes that primary to heat stress adaptation was the divergence of the central blood volume toward the periphery (see Fig. 12), which by reason of the non-linearity of the flow volume relationship in a highly compliant vascular bed [21], i.e., the venous system, and the differential pressures between the venules and the great veins [12], a sequestration of volume within the periphery occurs. Subsequently, venous return to the heart would be reduced, and this reduced venous return would be augmented by the increasing dehydration, the resultant of which would be a reduction in CVP. Thus, the reduced CVP, which would be indicative of the unloading of atrial stretch receptors, appeared manifest at $T_{es} > 38^\circ C$ and resulted in a greater vasoconstrictive drive, thereby further reducing peripheral blood flow. In addition, low-pressure baroreceptor activation would result in a significant peripheral and central vasoconstriction in an attempt to maintain venous return [22] in opposition to the heat-related increased greater pooling of blood in the cutaneous bed.

Despite the reduced CVP and the modification of FBF to $T_{es}$ relationship above a $T_{es}$ of 38°C, it is apparent from many investigations [12] that there is no identifiable absolute CVP at which adaptation to thermal stress becomes limited (see Fig. 13). If
FIG. 12. A schematic illustration of the relationship between skin vasodilatation-increased sequestration of volume in the venous side and the decrease in CVP and CBV. Reprinted with permission from L.B. Rowell and the American Physiological Society [12].

FIG. 13. A representative subject's circulatory responses to whole-body heating to limits of thermal tolerance. Note the time courses of aortic (Ao BP) and Ra-MP. Also, note Ao BP is maintained throughout the exposure, whereas Ra-MP, a measure of CVP, is allowed to fall toward zero while HR and cardiac output only achieve submaximal levels. Despite circulatory conditions being submaximal, Tᵣ₀ achieves intolerable limits. Reprinted with permission from L.B. Rowell and the American Physiological Society [12].
we view CVP as merely a measurement of the downstream pressure within the venous system, then obviously CVP must be allowed to fall toward zero, or as measured by Tripathi et al. during LBNP (quoted by Nadel [22]) to values less than zero (see Fig. 14), in order to insure a venous-sided pressure gradient from the cutaneous bed toward the heart in order to enable venous return to continue and maintain cardiac output and mean arterial pressure (see Fig. 13). However, the establishment of an interaction between the decreases in CVP and the reduction in FBF above a $T_{\alpha}$ of 38°C does not in itself identify a limit of the adaptation to heat stress.

A more plausible link to identify a limit in adaptation to heat stress is provided by Johnson et al. [4] (see Fig. 15). In these experiments, subjects were exposed to five minutes of −50 mm Hg LBNP at intervals prior to, during, and following whole-body

---

FIG. 14. Changes in forearm venous volume and heart rate as a result of decreasing CVP from +5 cm H$_2$O to −2.5 cm H$_2$O induced by LBNP. Reprinted with permission from E.R. Nadel and the American Physiological Society [22].

FIG. 15. Skin vasoconstrictive response (forearm vascular conductance [FVC] to five minutes of −50 mm Hg LBNP during periods of whole-body heating and cooling. Note that the arrow denotes the time at which the subject was unable to produce sufficient high- and low-pressure baroreceptor-mediated skin vasoconstriction to oppose thermally induced vasodilation. Reprinted with permission from J.M. Johnson et al. and the American Physiological Society [4].
surface heating. During the cool period [mean skin temperatures ($\bar{T}_{sk}$) $\approx$ 33.5°C and rectal temperatures ($T_r$) $\approx$ 37.2°C], activation of high-pressure baroreceptors enabled mean arterial pressure to be maintained by reflex tachycardia and vasoconstriction. However, during heating, where $\bar{T}_{sk}$ $\approx$ 37°C and $T_r$ increased to 37.6°C, a point was reached at which baroreceptor-mediated cutaneous vasoconstriction could not prevent a fall in blood pressure. These data would indicate that local vasodilation was overriding both the low-pressure and high-pressure baroreceptor-mediated cutaneous vasoconstriction. However, a corollary to Johnson et al.'s experiment, in which they have identified a situation in which sudomotor-mediated vasodilation overrides CVP and baroreceptor-mediated reflex cutaneous vasoconstriction could be proposed. This corollary would support the previously described work of Horstman and Horvath [9, 10] and the early work of Pitts et al. [11]. The scheme for the corollary situation of Johnson's experiment would suggest that sudomotor activity itself was depressed (which may be strongly linked to the level of hydration), and the subsequent release of AVS was reduced (or AVS production became minimal by interruption of the synthesis pathways), resulting in FBF being restricted by low-pressure baroreceptor vasoconstrictor activity surpassing vasodilatory activity. Hence, the central-to-peripheral conductance of heat would have been reduced, along with evaporative cooling, thereby producing an imbalance in heat gained to heat lost.

In summary, it is incorrect to attempt to establish an absolute value of CVP as limiting to the human's adaptation to heat stress. Such a discussion may be identifying a semantic difference; however, despite Huxley's precaution, it appears that CVP is purely a measure of the central volume which provides the central controller information concerning the state of hydration. In addition, CVP reflects the balance between peripheral and central blood volumes. Furthermore, it would appear that the human's limit of adaptation to heat stress appears to lie in those mechanisms that promote cooling and not those that support the maintenance of blood pressure.

REFERENCES

1. Fortney SM, Nadel ER, Wenger CB, Bove JR: Effect of blood volume on sweating rate and body fluids in exercising humans. J Appl Physiol 51:1594–1600, 1981
2. Fortney SM, Wenger CB, Bove JR, Nadel ER: Effect of blood volume on forearm venous and cardiac stroke volume during exercise. J Appl Physiol 55:884–890, 1983
3. Nadel ER, Fortney SM, Wenger CR: Effect of hydration state on circulatory and thermal regulations. J Appl Physiol 49:715–721, 1980
4. Johnson JM, Niederberger M, Rowell LB, Eisman MM, Brengelmann GL: Competition between cutaneous vasodilator and vasoconstrictor reflexes in man. J Appl Physiol 35:798–803, 1973
5. Nielsen B, Rowell LB, Bonde-Petersen F: Cardiovascular responses to heat stress and blood volume displacements during exercise in man. Eur J Appl Physiol 52:370–374, 1984
6. Tripathi A, Shi X, Wenger CB, Nadel ER: Effect of temperature and baroreceptor stimulation on reflex venomotor responses. J Appl Physiol 57:1384–1392, 1984
7. Stone HL, Dormer KJ, Forman RD, Theis R, Blair RW: Neural regulation of the cardiovascular system during exercise. Fed Proc 44:2271–2278, 1985
8. Lind AR: A physiological criterion for setting thermal environmental limits for everyday work. J Appl Physiol 18:51–56, 1963
9. Horstman DH, Horvath SM: Cardiovascular adjustments to progressive dehydration. J Appl Physiol 35:501–504, 1973
10. Horstman DH, Horvath SM: Cardiovascular and temperature regulatory changes during progressive dehydration and euhydration. J Appl Physiol 33:446–450, 1972
11. Pitts GC, Johnson RE, Consolazio FC: Work in the heat as affected by intake of water, salt and glucose. Amer J Physiol 142:253–257, 1944
12. Rowell LB: Cardiovascular adjustments to thermal stress. In Handbook of Physiology, Volume III, Section 2. The Cardiovascular System: Peripheral Circulation, Part 2. Edited by JT Shephard, FM Abboud, SR Geiger. Bethesda, MD, American Physiological Society, 1983, pp 967–1023
13. Bernard C: Influence du grand sympathique sur la sensibilite et sur la calorification. CR Soc Biol Paris 3:163–164, 1851; cited as reference 31 in [12]
14. Roddie IC: Circulation to skin and adipose tissue. In Handbook of Physiology, Volume III, Section 2. The Cardiovascular System: Peripheral Circulation, Part 2. Edited by JT Shephard, FM Abboud, SR Geiger. Bethesda, MD, American Physiological Society, 1983, pp 285–318
15. Rowell LB: Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev 54:75–159, 1974
16. Rowell LB: The splanchnic circulation. In The Peripheral Circulations. Edited by R Zelis. New York. Grune & Stratton, 1975, Chapter 8, pp 163–192
17. Bevegard BS, Shepherd JT: Regulation of the circulation during exercise in man. Physiol Rev 47:178–191, 1967
18. Edholm OG, Fox RH, MacPherson RK: Vasomotor control of the cutaneous blood vessels in the human forearm. J Physiol (Lond) 139:455–465, 1957
19. Fox RH, Hilton SM: Bradykinin formation in human skin as a factor in heat vasodilatation. J Physiol (Lond) 142:219–232, 1958
20. Johnson JM, Rowell LB, Neiderberger M, Eisman M: Human splanchnic and forearm vasoconstrictor responses to reductions of right atrial and aortic pressure. Circ Res 34:515–524, 1974
21. Kirsch KA, Mercke J, Hinghofer-Szalkay H, Barnkow M, Wicke HJ: A new miniature plethysmograph to measure volume changes in small circumscribed tissue areas. Pfluegers Arch 383:189–194, 1980
22. Nadel ER: Recent advances in temperature regulation during exercise in humans. Fed Proc 44:2286–2292, 1985