

Effect of increasing central venous pressure during passive heating on skin blood flow

C. G. CRANDALL,^{1,2} B. D. LEVINE,^{1,2} AND R. A. ETZEL¹

¹*Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, Dallas 75231; and* ²*Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas 75235*

Crandall, C. G., B. D. Levine, and R. A. Etzel. Effect of increasing central venous pressure during passive heating on skin blood flow. *J. Appl. Physiol.* 86(2): 605–610, 1999.—Whole body heating in humans increases skin blood flow (SkBF) and decreases central venous pressure (CVP). This study sought to identify whether elevations in SkBF are augmented during passive heating if CVP is increased during the heat stress. Seven subjects were exposed to passive heating. Once SkBF was substantially elevated, 15 ml/kg warm saline were rapidly infused intravenously. Whole body heating significantly increased cutaneous vascular conductance and decreased CVP from 7.7 ± 0.6 to 4.9 ± 0.5 mmHg ($P < 0.05$). Saline infusion returned CVP to pre-heat-stress pressures (7.9 ± 0.6 mmHg; $P > 0.05$) and significantly increased cutaneous vascular conductance relative to the period before saline administration. Moreover, saline infusion did not alter mean arterial pressure, pulse pressure, or esophageal temperature (all $P > 0.05$). To serve as a volume control, 15 ml/kg saline were rapidly infused intravenously in normothermic subjects. Saline infusion increased CVP ($P < 0.05$) without affecting mean arterial pressure, pulse pressure, or cutaneous vascular conductance (all $P > 0.05$). These data suggest that cardiopulmonary baroreceptor unloading during passive heating may attenuate the elevation in SkBF in humans, whereas loading cardiopulmonary baroreceptors in normothermia has no effect on SkBF.

cutaneous vascular conductance; baroreflex; cardiopulmonary baroreceptors; human; temperature regulation; peripheral circulation

WHEN A HUMAN is exposed to an increased heat load, skin blood flow (SkBF) increases secondary to increases in internal temperature and skin temperature (T_{sk}). This elevation in SkBF is accomplished through a combination of increases in cutaneous vascular conductance and cardiac output. These adjustments, coupled with relaxation of cutaneous veins, result in central venous pressure (CVP) decreasing 2–6 mmHg and mean arterial pressure (MAP) decreasing 5–10 mmHg (26). Decreases in blood pressure of this magnitude likely unload cardiopulmonary and sinoaortic baroreceptors, respectively.

In addition to thermoregulatory reflexes, nonthermoregulatory reflexes such as baroreflexes also modulate SkBF. For example, application of lower body negative pressure (LBNP) in both normothermia and heat stress reduced cutaneous vascular conductance (5, 10, 11, 15,

18, 27, 31). Given the aforementioned unloading of baroreceptors during passive heating (26), coupled with evidence that SkBF can be modulated by baroreceptors (5, 10, 11, 15, 18, 27, 31), is it possible that baroreceptors serve to modulate the elevation in SkBF during a thermal challenge? Data from studies investigating the control of SkBF during dynamic exercise support this hypothesis. During exercise in the heat, SkBF tends to plateau when internal temperature approaches 38°C (2). However, if procedures are performed to maintain or increase CVP during the exercise bout (21–23), SkBF does not plateau but continues to increase as internal temperature increases. In these studies, arterial blood pressure was either not changed (22) or was slightly reduced (21) by the procedure used to alter CVP. Thus it is likely that either the maintenance or increase of cardiopulmonary baroreceptor tension was the primary mechanism responsible for continued elevation of SkBF during the exercise bout.

An important question that remains unanswered is whether the aforementioned reduction in CVP, and accompanying cardiopulmonary baroreceptor unloading, during passive heating similarly affects the elevation in SkBF. That is, if CVP, and thus cardiopulmonary baroreceptor loading, were increased during passive heating, would the elevation in SkBF be augmented during the heat stress? Thus the purpose of this study was to identify whether increases in SkBF during passive heating would be accentuated if CVP were increased via rapid saline infusion.

METHODS

Subjects

Seven subjects (4 men, 3 women) participated in *protocol 1*, and ten subjects (4 men, 6 women) participated in *protocol 2*. The subjects' ages were between 20 and 42 yr, and all were of normal height (172 ± 2 cm), weight (74 ± 19 kg), and health. A written informed consent from each subject was obtained before participation in this institutionally approved study.

Protocol 1

Each subject was instrumented for the measurement of esophageal temperature (T_{es}) with a thermocouple at the level of the atria and mean T_{sk} from the electrical average of six thermocouples placed on the skin. MAP was continuously recorded from the electrical integration of the pulsatile blood pressure signal from a finger (Finapres) referenced to heart level. Heart rate (HR) was obtained from the electrocardiogram. Forearm SkBF was monitored by laser-Doppler flowmetry (Perimed). An index of cutaneous vascular conductance was calculated from the ratio of laser-Doppler flux to MAP. CVP was measured from a catheter inserted in the subject's

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

basilic vein, with the tip of the catheter being advanced to the superior vena cava. The CVP catheter was connected to a sterile disposable pressure transducer. Zero reference for this transducer was set at the subject's midaxillary line. The pressure transducer was calibrated before and after each experiment.

The subject was placed in a tube-lined suit that permitted the control of T_{sk} by changing the temperature of the water perfusing the suit. The suit covered the entire body surface with the exception of the head, feet, and the forearm where SkBF was monitored. A plastic garment was placed over this suit to impede sweat evaporation.

With the subject in the supine position, neutral ($\sim 34^{\circ}\text{C}$) water was perfused through the tube-lined suit. After ~ 10 min, baseline data were collected. After this baseline period, T_{sk} was increased to 38.5°C by perfusing the tube-lined suit with warm water. Once cutaneous vascular conductance was elevated and stable, CVP was returned to pre-heat-stress levels via rapid (7- to 10-min) infusion of 15 ml/kg warmed (37°C) isotonic saline through a different catheter placed in an antecubital vein (Fig. 1). After the infusion, T_{sk} was returned to pre-heat-stress levels by perfusing the suit with cool water. A heater surrounding the laser Doppler flow probe was used to raise local skin temperature to 42°C . Local temperature was held at this level for 30 min to elicit maximal cutaneous vasodilation. Values for cutaneous vascular conductance were then converted to percentages of maximum for that site.

Protocol 2

The intent of this protocol was to assess cutaneous vascular effects of loading cardiopulmonary baroreceptors in normothermia via saline infusion. This procedure served as a volume control for *protocol 1*. Each subject was instrumented as outlined in *protocol 1* with the exception of the tube-lined suit and T_{sk} probes. Moreover, rather than T_{es} , blood temperature (T_b) was obtained from a thermistor at the tip of a Swan-Ganz catheter advanced to the pulmonary artery. After a period of baseline data collection, 15 ml/kg warm saline were infused over a period of 7–10 min through a catheter placed in the antecubital vein. Data were continuously collected throughout baseline and saline infusion periods.

Data Collection and Statistics

Protocol 1. Data were sampled at 1 Hz and reduced to the following 2-min periods: immediately before whole body heating (pre-heat stress), immediately before the onset of saline infusion (heat stress), and during *minutes 5–7* of the saline infusion. These data were statistically analyzed by using one-way repeated-measures analysis of variance followed by a Student-Newman-Keuls multiple-comparison test when significant main-factor differences were identified. The rates of rise in cutaneous vascular conductance and T_{es} were identified from the slope of the linear regression equation during the 5-min period immediately before the onset of saline infusion and during the first 5 min of saline infusion. Nonaveraged data (i.e., 1 Hz) were used for slope determination. A paired *t*-test was used to identify differences in the slope between these periods.

Protocol 2. Data were sampled at 1 Hz and reduced to a 2-min period immediately before the onset of saline infusion and a 2-min period during *minutes 5–7* of the saline infusion. These data were statistically analyzed by using a paired *t*-test. All data for both protocols are expressed as means \pm SE. The level of statistical significance was set at $P = 0.05$.

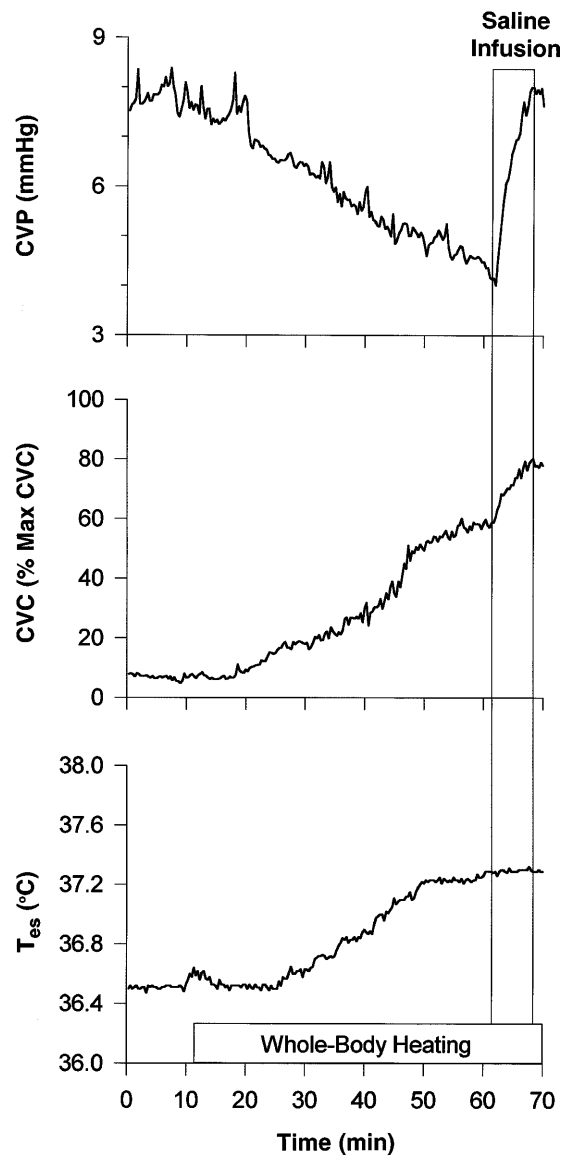


Fig. 1. Effects of whole body heating and saline infusion on central venous pressure (CVP), cutaneous vascular conductance (CVC), and esophageal temperature (T_{es}) for 1 subject. Whole body heating increased T_{es} and CVC while reducing CVP. Rapid infusion of saline (15 ml/kg) returned CVP and presumably cardiopulmonary baroreceptor loading to pre-heat-stress levels without affecting mean arterial pressure or pulse pressure (see text). Returning CVP to pre-heat-stress levels significantly increased rate of rise of CVC without affecting rate of rise of T_{es} . Max, maximum.

RESULTS

In *protocol 1*, whole body heating significantly increased T_{es} , HR, and cutaneous vascular conductance while decreasing CVP and MAP (Table 1). Saline infusion returned CVP to pre-heat-stress pressures without significantly changing MAP, pulse pressure, or T_{es} . Interestingly, HR was ~ 10 beats/min higher during saline infusion than during the period immediately before saline infusion. SkBF before saline infusion was significantly less than SkBF after 5 min of saline infusion (57 ± 3 vs. $75 \pm 6\%$ maximum cutaneous vascular conductance units; $P < 0.001$). This difference

Table 1. Responses to passive heating and saline infusion

	Pre-Heat Stress	Heat Stress	Saline Infusion
CVC, units	13 ± 2	54 ± 5*	70 ± 8*†
CVP, mmHg	7.7 ± 0.6	4.9 ± 0.5*	7.9 ± 0.6†
MAP, mmHg	88 ± 4	75 ± 4*	73 ± 4*
Heart rate, beats/min	66 ± 4	89 ± 4*	98 ± 4*†
Pulse pressure, mmHg		47 ± 2.2	47 ± 2.0
T _{es} , °C	36.5 ± 0.1	37.2 ± 0.1*	37.3 ± 0.1*
Osmol _p , mosmol/kgH ₂ O	286 ± 1.5	286 ± 0.9	291 ± 1.8*†

Values are means ± SE. CVC, cutaneous vascular conductance; CVP, central venous pressure; MAP, mean arterial pressure; T_{es}, esophageal temperature; Osmol_p, plasma osmolality. CVC is expressed as (laser-Doppler flux/mmHg) · 100. *Significantly different from pre-heat-stress stage, $P < 0.05$. †Significantly different from heat-stress stage, $P < 0.05$.

was primarily due to an increased rate of elevation in cutaneous vascular conductance during the first 5 min of saline infusion when compared with the period just before saline infusion (0.5 ± 0.2 to $2.8 \pm 0.4\%$ maximum cutaneous vascular conductance units/min; $P < 0.001$; see Fig. 1). If the rate of increase in cutaneous vascular conductance had not increased as a result of saline infusion (i.e., remained at 0.5% maximum cutaneous vascular conductance units/min), the predicted cutaneous vascular conductance after 5 min of saline infusion would be $59 \pm 4\%$ maximum cutaneous vascular conductance units. This predicted value was significantly less than the value achieved after 5 min of saline infusion (i.e., $75 \pm 6\%$ maximum cutaneous vascular conductance units; $P < 0.001$). The profound increase in cutaneous vascular conductance during saline infusion was not due to an increase in internal temperature because neither the rate of elevation in T_{es} (0.03 ± 0.01 to $0.02 \pm 0.01^\circ\text{C}/\text{min}$; $P = 0.12$) nor absolute T_{es} (37.0 ± 0.1 to $37.1 \pm 0.1^\circ\text{C}$; $P > 0.05$) changed during saline administration. Plasma osmolality did not change significantly during whole body heating but increased significantly after saline infusion (see Table 1). This increase was likely due to the administration of saline that had an osmolality slightly greater than the subjects' plasma osmolality.

In protocol 2, saline infusion in normothermia significantly increased CVP without affecting MAP, pulse pressure, or T_{bl} (Table 2). Despite the increase in CVP, cutaneous vascular conductance was not significantly altered. Because there were no changes in cutaneous vascular conductance or T_{bl} during saline infusion, no

Table 2. Responses to saline infusion in normothermia

	Preinfusion	Saline Infusion	P Value
CVC, units	12.2 ± 2.0	11.9 ± 2.0	0.34
CVP, mmHg	7.5 ± 0.5	11.6 ± 0.7	<0.001
MAP, mmHg	90 ± 3	91 ± 4	0.13
Pulse pressure, mmHg	53 ± 2	55 ± 2	0.34
Heart rate, beats/min	70 ± 2	77 ± 3	0.02
T _{bl} , °C	36.7 ± 0.1	36.6 ± 0.1	0.19

Values are means ± SE. T_{bl}, pulmonary artery blood temperature. CVC is expressed as (laser-Doppler flux/mmHg) × 100.

assessment was performed on the rate of increase of these variables.

DISCUSSION

The primary finding from these experiments suggests that increasing CVP during passive heating significantly increases the rate of elevation of cutaneous vascular conductance. This conclusion was obtained after the return of CVP to pre-heat-stress levels with rapid isotonic saline administration while SkBF was simultaneously measured. During saline infusion, the rate of elevation in cutaneous vascular conductance increased greater than fivefold, which increased absolute cutaneous vascular conductance to a level greater than that predicted had the rate of increase in cutaneous vascular conductance not changed.

As shown in this and other studies, passive heating substantially increases SkBF (11). Depending on the thermal status before heating, an initial small increase in SkBF may be due to withdrawal of cutaneous vasoconstrictor activity. As the heat stress progresses, the cutaneous active vasodilator system is then activated and mediates the majority of the elevation in SkBF during the heat stress (11). Because the sympathetic vasoconstrictor system is withdrawn during heat stress (11, 14), increases in the rate of elevation in cutaneous vascular conductance observed in the present study during saline infusion were most probably due to increases in cutaneous active vasodilator activity. However, data from the present study do not rule out the possibility that some of the elevation in cutaneous vascular conductance during saline infusion may have been due to withdrawal of cutaneous vasoconstrictor activity. It is likely that the cardiopulmonary baroreceptors were the baroreceptor population mediating this response because saline infusion did not change MAP or pulse pressure.

The primary determinants governing cutaneous vascular conductance are internal temperature and T_{sk}. However, nonthermoregulatory factors, including baroreceptors, also modulate cutaneous vascular conductance (5, 10, 15, 18, 27, 31). For example, during passive heating, moderate to high levels of LBNP significantly reduced cutaneous vascular conductance (5, 10, 15, 18), and this reduction was due to withdrawal of active vasodilator activity (5, 15). Because these levels of LBNP likely unload both cardiopulmonary and arterial baroreceptor populations (12, 34), it is unknown which baroreceptor population was responsible for the reduction in active vasodilator activity.

We recently found that cardiopulmonary baroreceptor unloading during passive heating with 5 and 10 mmHg LBNP did not change cutaneous vascular conductance, MAP, or HR but significantly reduced forearm vascular conductance (5). The fact that forearm vascular conductance was reduced by this stimulus implies that the cardiopulmonary baroreflex was engaged. Taken together, the present findings, coupled with the aforementioned finding (5), suggest that during passive heating individuals are functioning at, or close to, threshold on the cardiopulmonary-cutaneous

active vasodilator baroreflex curve. Such a hypothesis dictates that cardiopulmonary baroreceptor unloading in this environment would not reduce cutaneous vascular conductance, whereas cardiopulmonary baroreceptor loading would elevate cutaneous vascular conductance through increased cutaneous active vasodilator activity. Alternatively, it could be that the magnitude of cardiopulmonary baroreceptor unloading during passive heating with -5 and -10 mmHg LBNP did not unload the cardiopulmonary baroreceptors sufficiently to evoke measurable responses in the cardiopulmonary-cutaneous active vasodilator baroreflex curve, even though changes in muscle vascular conductance were identified (5).

Previous studies provide evidence of the importance of the cardiopulmonary baroreceptors in governing the elevation in SkBF during exercise (21–23). During dynamic exercise in the heat, SkBF tends to plateau when internal temperature approaches 38°C (2). However, if CVP is either maintained or increased during the exercise bout, SkBF continues to increase beyond an internal temperature of 38°C . Given that cutaneous vasoconstrictor activity is not fully withdrawn during exercise in the heat (13), it is unknown whether the aforementioned responses in SkBF were due to withdrawal of cutaneous active vasoconstrictor activity and/or increased cutaneous active vasodilator activity.

No change in cutaneous vascular conductance was observed during saline infusion in normothermia. This finding is consistent with previous findings of a lack of change in hand blood flow (the hand being primarily skin) during elevations in CVP induced by passive leg raises (25) or negative-pressure breathing (1). In normothermia, SkBF is governed exclusively by cutaneous vasoconstrictor activity without influences from cutaneous active vasodilator activity (11). In light of this fact, two theories may explain the lack of change in cutaneous vascular conductance during saline infusion in normothermia. The first theory suggests that cardiopulmonary baroreceptors do not have an efferent limb governing the cutaneous vasoconstrictor system. Data supporting such a conclusion are equivocal. For example, low levels of LBNP in normothermia, which primarily unload cardiopulmonary baroreceptors (12, 34), evoke cutaneous vasoconstriction in some (31) but not all studies (32). This issue is further clouded by recent data that suggest these levels of LBNP may not selectively unload the cardiopulmonary baroreceptors (17, 30).

The second theory suggests that cardiopulmonary baroreflexes modulate the cutaneous vasoconstrictor system; however, in the thermal environment of the present study (room temperature 25°C), the operating point is located near the saturated portion of the cardiopulmonary-cutaneous vasoconstrictor baroreflex curve. Such a hypothesis dictates that in thermoneutral environments tonic cutaneous vasoconstrictor tone is low or absent but can increase during baroreceptor unloading. Evidence from the literature supporting such a hypothesis has shown that cutaneous nerve block does not increase forearm SkBF in thermoneutral

subjects (6). Taken together, decreases in SkBF during cardiopulmonary baroreceptor unloading with low levels of LBNP in normothermia (31), coupled with the present findings of a lack of change in cutaneous vascular conductance during volume loading, support this second hypothesis. However, for such a hypothesis to be correct, unloading of arterial baroreceptors during low levels of LBNP must be inconsequential with respect to efferent responses to the skin.

Potential Limitations of the Interpretation of the Results

Increases in blood flow cause vasodilation via flow-mediated nitric oxide release (28). Is it possible that the increased rate of elevation in SkBF after the return of CVP to pre-heat-stress levels was due to nitric oxide-mediated vasodilation? To address this possibility, in four hyperthermic subjects cutaneous vascular conductance was calculated during intravenous saline infusion (15 ml/kg) from skin in which nitric oxide production was inhibited by local administration of 145 mM N^{G} -monomethyl-L-arginine via intradermal microdialysis. The rate of increase in cutaneous vascular conductance remained elevated at these sites during saline infusion (pre-saline infusion: $0.26 \pm 0.15\%$ maximum cutaneous vascular conductance units/min; saline infusion: $1.44 \pm 0.55\%$ maximum cutaneous vascular conductance units/min; $P = 0.04$). Thus it is unlikely that increases in the rate of elevation in cutaneous vascular conductance during saline infusion were due to flow-mediated nitric oxide release and subsequent vasodilation.

The basic premise of the present findings is that returning CVP to pre-heat-stress pressures also returns cardiopulmonary baroreceptor loading to pre-heat-stress levels. However, our data do not permit us to confirm this hypothesis. Previous studies report that decreases in CVP do not always follow decreases in central blood volume (19, 24). To our knowledge, no studies have been performed to identify whether increasing central blood volume causes a proportional increase in CVP in normothermia or during heat stress. Although we are unable to conclude whether saline infusion returned cardiopulmonary baroreceptor loading to pre-heat-stress levels, we are confident that some degree of cardiopulmonary baroreceptor loading occurred as a result of saline infusion.

Saline infusion in normothermia and during passive heating did not change pulse pressure or MAP. Thus we concluded that this perturbation primarily loaded cardiopulmonary baroreceptors. However, recent studies demonstrate that low-levels of LBNP, which previously were thought to unload only the cardiopulmonary baroreceptors, may also unload sinoaortic baroreceptors (17, 30). Little is known regarding the effects of rapid central blood volume expansion on sinoaortic baroreceptor tensions. Thus the possibility cannot be excluded that some degree of sinoaortic baroreceptor loading occurred during volume infusion during the heat stress despite a lack of change in MAP or arterial pulse pressure.

Along this line of thinking, the Finapres may not have detected subtle increases in arterial pressure during saline infusion. This possibility exists despite data demonstrating that the Finapres accurately tracks radial artery blood pressure during progressive increases in blood pressure (29). Nevertheless, if volume infusion slightly increased arterial and/or pulse pressures, it is unlikely those small changes in pressure perturbed the sinoaortic baroreceptors sufficiently to increase cutaneous vascular conductance. This conclusion is drawn from the observation that substantial changes in effective pulse pressure and MAP at the carotid sinus via neck pressure (5) or neck suction (unpublished observations), or electrical stimulation of the carotid sinus nerve (33), were insufficient to alter cutaneous vascular conductance or skin sympathetic nerve activity, respectively.

Implications of the Findings

Elevations in SkBF during a heat stress is attenuated in dehydrated subjects (9, 20). Similar findings have been observed after actual (8) and simulated microgravity exposure (4), which also decrease plasma volume (7). In each of these conditions, CVP is reduced before the onset of heating (3, 16). What remains unknown is whether the nadir of CVP during passive heating is lower in dehydrated subjects or after actual or simulated microgravity exposure when compared with the nadir of CVP during passive heating in euhydrated subjects. If this is the case, attenuated elevations in SkBF during a heat stress in dehydrated subjects (9, 20) or after microgravity exposure (4, 8) may be a consequence of augmented cardiopulmonary baroreceptor unloading during the thermal challenge.

Conclusion

These data provide evidence that support the hypothesis that cardiopulmonary baroreceptor unloading coincident with passive heating attenuates the elevation in cutaneous vascular conductance. Moreover, loading cardiopulmonary baroreceptors with saline infusion in normothermia does not alter cutaneous vascular tone. These data provide a possible explanation for attenuated thermoregulatory responses in dehydrated subjects (9, 20) or in subjects exposed to simulated or actual microgravity (4, 8).

The authors express their appreciation to Michael Avenshine for assistance with the collection and reduction of the data and to the subjects for willing participation in this project.

This research project was funded in part by American Heart Association, Texas Affiliate, Grant 96G380 and by National Aeronautics and Space Administration Grants NAGW 3582 and NAG9-1033.

Address for reprint requests: C. G. Crandall, Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, 7232 Greenville Ave., Dallas, TX 75231 (E-mail: crandall@email.swmed.edu).

Received 6 April 1998; accepted in final form 14 October 1998.

REFERENCES

1. Blair, D. A., W. E. Gover, A. D. M. Breenfield, and I. C. Roddie. The effect of continuous positive and negative pressure breathing upon the resistance and capacity blood vessels of the human forearm and hand. *Clin. Sci. (Colch.)* 18: 9–16, 1959.
2. Brengelmann, G. L., J. M. Johnson, L. Hermansen, and L. B. Rowell. Altered control of skin blood flow during exercise at high internal temperatures. *J. Appl. Physiol.* 43: 790–794, 1977.
3. Crandall, C. G., K. A. Engelke, V. A. Convertino, and P. B. Raven. Aortic baroreflex control of heart rate following 15 days simulated microgravity exposure. *J. Appl. Physiol.* 77: 2134–2139, 1994.
4. Crandall, C. G., J. M. Johnson, V. A. Convertino, P. B. Raven, and K. A. Engelke. Altered thermoregulatory responses after 15 days of head-down tilt. *J. Appl. Physiol.* 77: 1863–1867, 1994.
5. Crandall, C. G., J. M. Johnson, W. A. Kosiba, and D. L. Kellogg, Jr. Baroreceptor control of the cutaneous active vasodilator system. *J. Appl. Physiol.* 81: 2192–2198, 1996.
6. Edholm, O. G., R. H. Fox, and R. K. Macpherson. Vasomotor control of the cutaneous blood vessels in the human forearm. *J. Physiol. (Lond.)* 139: 455–465, 1957.
7. Fortney, S. M., K. H. Hyatt, J. E. Davis, and J. M. Vogel. Changes in body fluid compartments during 28-day bed rest. *Aviat. Space Environ. Med.* 62: 97–104, 1991.
8. Fortney, S. M., V. Mikhaylov, S. M. C. Lee, Y. Kobzev, R. R. Gonzalez, and J. E. Greenleaf. Body temperature and thermoregulation during submaximal exercise after 115-day spaceflight. *Aviat. Space Environ. Med.* 69: 137–141, 1998.
9. Horstman, D. H., and S. M. Horvath. Cardiovascular and temperature regulatory changes during progressive dehydration and euhydration. *J. Appl. Physiol.* 33: 446–450, 1972.
10. Johnson, J. M., M. Niederberger, L. B. Rowell, M. M. Eisman, and G. L. Brengelmann. Competition between cutaneous vasodilator and vasoconstrictor reflexes in man. *J. Appl. Physiol.* 35: 798–803, 1973.
11. Johnson, J. M., and D. W. Proppe. Cardiovascular adjustments to heat stress. In: *Handbook of Physiology. Environmental Physiology*. Bethesda, MD: Am. Physiol. Soc., 1996, sect. 4, vol. II, chapt. 11, p. 215–243.
12. Johnson, J. M., L. B. Rowell, M. Niederberger, and M. M. Eisman. Human splanchnic and forearm vasoconstrictor responses to reduction of right atrial and aortic pressures. *Circ. Res.* 34: 515–524, 1974.
13. Kellogg, D. L., Jr., J. M. Johnson, W. L. Kenney, P. E. Pergola, and W. A. Kosiba. Mechanisms of control of skin blood flow during prolonged exercise in humans. *Am. J. Physiol.* 265 (*Heart Circ. Physiol.* 34): H562–H568, 1993.
14. Kellogg, D. L., Jr., J. M. Johnson, and W. A. Kosiba. Selective abolition of adrenergic vasoconstrictor responses in skin by local iontophoresis of bretylium. *Am. J. Physiol.* 257 (*Heart Circ. Physiol.* 26): H1599–H1606, 1989.
15. Kellogg, D. L., Jr., J. M. Johnson, and W. A. Kosiba. Baroreflex control of the cutaneous active vasodilator system in humans. *Circ. Res.* 66: 1420–1426, 1990.
16. Kirsch, K. A., L. Rocker, H. V. Ameln, and K. Hrynyschyn. The cardiac filling pressure following exercise and thermal stress. *Yale J. Biol. Med.* 59: 257–265, 1986.
17. Lacolley, P. J., B. M. Pannier, M. A. Slama, J. L. Cuche, A. P. G. Hoeks, S. Laurent, G. M. London, and M. E. Safar. Carotid arterial haemodynamics after mild degrees of lower-body negative pressure in man. *Clin. Sci. (Colch.)* 83: 535–540, 1992.
18. Mack, G. W., T. Nishiyasu, and X. Shi. Baroreceptor modulation of cutaneous vasodilator and sudomotor responses to thermal stress in humans. *J. Physiol. (Lond.)* 483: 537–547, 1994.
19. Murray, R. H., L. J. Thompson, J. A. Bowers, and C. D. Albricht. Hemodynamic effects of graded hypovolemia and vasodepressor syncope induced by lower body negative pressure. *Am. Heart J.* 76: 799–811, 1968.
20. Nadel, E. R., S. M. Fortney, and C. B. Wenger. Effect of hydration state on circulatory and thermal regulations. *J. Appl. Physiol.* 49: 715–721, 1980.
21. Nagashima, K., H. Nose, A. Takamata, and T. Morimoto. Effect of continuous negative-pressure breathing on skin blood flow during exercise in a hot environment. *J. Appl. Physiol.* 84: 1845–1851, 1998.
22. Nielsen, B., L. B. Rowell, and F. Bonde-Petersen. Cardiovascular responses to heat stress and blood volume displacements during exercise in man. *Eur. J. Appl. Physiol.* 52: 370–374, 1984.

23. **Nose, H., G. W. Mack, X. Shi, K. Morimoto, and E. R. Nadel.** Effect of saline infusion during exercise on thermal and circulatory regulations. *J. Appl. Physiol.* 69: 609–616, 1990.
24. **Pawelczyk, J. A., R. A. Pawelczyk, S. Matzen, and N. H. Secher.** Thoracic impedance, not central venous pressure, predict changes in central blood volume during orthostatism (Abstract). *FASEB J.* 6: A1771, 1992.
25. **Roddie, I. C., and J. T. Shepherd.** The reflex nervous control of human skeletal muscle blood vessels. *Clin. Sci. (Colch.)* 15: 433–440, 1956.
26. **Rowell, L. B., G. L. Brengelmann, and J. A. Murray.** Cardiovascular responses to sustained high skin temperature in resting man. *J. Appl. Physiol.* 27: 673–680, 1969.
27. **Rowell, L. B., C. R. Wyss, and G. L. Brengelmann.** Sustained human skin and muscle vasoconstriction with reduced baroreceptor activity. *J. Appl. Physiol.* 34: 639–643, 1973.
28. **Rubanyi, G. M., J. C. Romero, and P. M. Vanhoutte.** Flow-induced release of endothelium-derived relaxing factor. *Am. J. Physiol.* 250 (*Heart Circ. Physiol.* 19): H1145–H1149, 1986.
29. **Shi, X., J. M. Andresen, J. T. Potts, B. H. Foresman, S. A. Stern, and P. B. Raven.** Aortic baroreflex control of heart rate during hypertensive stimuli: effects of fitness. *J. Appl. Physiol.* 74: 1555–1562, 1993.
30. **Taylor, J. A., J. R. Halliwill, T. E. Brown, J. Hayano, and D. L. Eckberg.** 'Non-hypotensive' hypovolaemia reduces ascending aortic dimensions in humans. *J. Physiol. (Lond.)* 483: 289–298, 1995.
31. **Tripathi, A., and E. R. Nadel.** Forearm skin and muscle vasoconstriction during lower body negative pressure. *J. Appl. Physiol.* 60: 1535–1541, 1986.
32. **Vissing, S. F., U. Scherrer, and R. G. Victor.** Increase of sympathetic discharge to skeletal muscle but not to skin during mild lower body negative pressure in humans. *J. Physiol. (Lond.)* 481: 233–241, 1994.
33. **Wallin, B. G., G. Sundlof, and W. Delius.** The effect of carotid sinus nerve stimulation on muscle and skin nerve sympathetic activity in man. *Pflügers Arch.* 358: 101–110, 1975.
34. **Zoller, R. P., A. L. Mark, F. M. Abboud, P. G. Schmid, and D. D. Heistad.** The role of low pressure baroreceptors in reflex vasoconstrictor responses in man. *J. Clin. Invest.* 51: 2967–2972, 1972.

