Defense reaction alters the response to blood loss in the conscious rabbit

JAMES C. SCHADT AND EILEEN M. HASSER

Dalton Cardiovascular Research Center and Department of Veterinary Biomedical Sciences, University of Missouri, Columbia, Missouri 65211

Received 18 July 2000; accepted in final form 30 November 2000

Schadt, James C., and Eileen M. Hasser. Defense reaction alters the response to blood loss in the conscious rabbit. Am J Physiol Regulatory Integrative Comp Physiol 280: R985–R993, 2001.—The interaction of sensory stressors with the cardiovascular response to blood loss has not been studied. The cardiovascular response to a stressor (i.e., the defense reaction) includes increased skeletal muscle blood flow and perhaps a reduction in arterial baroreflex function. Arterial pressure maintenance during blood loss requires baroreflex-mediated skeletal muscle vasoconstriction. Therefore, we hypothesized that the defense reaction would limit arterial pressure maintenance during blood loss. Male, New Zealand White rabbits were chronically prepared with arterial and venous catheters and Doppler flow probes. We removed venous blood in conscious rabbits until mean arterial pressure decreased to <40 mmHg. We repeated the experiment with (air) and without (sham) simultaneous exposure to an air jet stressor. Air resulted in a defense reaction (e.g., mean arterial pressure = 94 ± 1 and 67 ± 1 mmHg for air and sham, respectively). Contrary to our hypothesis, air increased the blood loss necessary to produce hypotension (19.3 ± 0.2 vs. 16.9 ± 0.2 ml/kg for sham). Air did not reduce skeletal muscle vasoconstriction during normotensive hemorrhage. However, air did enhance renal vasoconstriction (97 ± 3 and 59 ± 3% of baseline for sham and air, respectively) during the normotensive phase. Thus the defense reaction did not limit but rather extended defense of arterial pressure during hemorrhage.

METHODS

Preparation. These studies were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, National Institutes of Health 85–23, revised 1985, and were approved by the University of Missouri-Columbia Animal Care and Use Committee. Male, New Zealand White rabbits (n = 31), weighing 2.5–3.1 kg (2.77 ± 0.03 kg) were anesthetized with halothane, and a midline laparotomy was performed. Arterial and venous catheters were implanted in the abdominal aorta and vena cava (3) for recording arterial pressure and withdrawing blood or injecting drugs, respectively. In seven rabbits, a second vena caval catheter (tip in the thoracic cavity) was implanted for measurement of central venous pressure (n = 7). Doppler flow probes were placed at one or more of the following locations (19): the abdominal aorta near the iliac bifurcation (n = 13); the cranial mesenteric artery near the aorta (n = 13); or the left renal artery (n = 10). For cardiac output measurement (n = 7), a flow probe was placed on the ascending aorta (19) during another surgical procedure (pentobarbital sodium anesthesia and artificial ventilation) 2 wk prior to the abdominal surgery. Flow probe wires and catheters were exteriorized in the dorsal cervical region. Antibiotics (60,000 IU im; Pen BP-48, Pfizer).

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.
were given the day before and the day after surgery. Animals recovered for a minimum of 10 days before the first experiment, and experiments in the same animal were separated by at least 4 days. We varied the order of experiments among rabbits to produce a balanced design.

General. During experiments, the arterial catheter was connected to a pressure transducer (Statham P23 Dc), and flow probe wires were connected to pulsed Doppler flowmeters (Triton model 100). Blood was withdrawn through the abdominal venous catheter into a sterile 60-ml syringe driven by a syringe pump (Sage Instruments model 351). Heart rate (triggered by arterial pressure), pulsatile and mean arterial blood pressure, and pulsatile and mean blood flow velocities were monitored on a chart recorder (Gould model 3800). Arterial pressure and pulsatile blood flow velocity were also recorded (Neuro-Data model DR-886) on VCR tape and analyzed on- or off-line using a microcomputer and commercially available data acquisition and analysis hardware and software (RC Electronics). Animals were fasted 15–23 h before experimentation. During experiments, animals were placed in a box (33 × 15 × 18 cm, inside dimensions) with a 6-cm diameter hole in the front. The rabbits were acclimated to the box prior to experiments. For air jet exposure (air), a continuous stream of room air from a polyvinyl chloride tube (OD, 9 mm; ID, 5 mm) was directed at the rabbit’s nose (17).

Experimental protocol. Rabbits were heparinized (Lilly; sodium heparin; 2,000 U iv) and allowed 10–30 min to reach a stable baseline in terms of hemodynamic parameters. Once stable, we recorded prestimulus baseline data for 1 min. Next, we started the sensory stimulation (either air or no stimulation, sham) and this continued for the remainder of the experiment. Two minutes after the start of stimulation, we began removing blood from the abdominal venous catheter at a rate of 8–9 ml/min. The end point of the hemorrhage was 5 ml after mean arterial pressure reached 40 mmHg. At the conclusion of the experiment, we reinfused the withdrawn blood. Hemodynamic data were monitored throughout the experiment.

Analysis of data. The blood loss required to reduce arterial pressure varies among rabbits (19). Therefore, hemorrhage data were normalized to the percentage of total blood loss to allow statistical comparisons at similar points. Total blood loss was defined as that necessary to decrease mean arterial pressure to 40 mmHg and was set at 100%. All other percentage points were calculated from the 100% value. Because 5 ml of blood were removed after mean arterial pressure reached 40 mmHg, we could compare the response to hemorrhage from 0–105% of total blood loss. For example, the 105% value was calculated by multiplying the blood loss required to reduce mean arterial pressure to 40 mmHg (i.e., the 100% value) by 1.05. Because cardiovascular changes during blood loss are biphasic, the statistical analysis was performed separately on the normotensive and hypotensive phases (8). The steep decline in arterial blood pressure begins at 80–85% of the total blood loss. Thus the normotensive phase extended from the start of the hemorrhage through 80% of total blood loss and the hypotensive phase from 85 through 105% of total blood loss.

The hemodynamic effects of blood loss were analyzed by two-way repeated measures analysis of variance (ANOVA). The independent variables were treatment (i.e., air or sham) and blood loss (percentage of total). When the ANOVA demonstrated a significant primary effect of treatment or a significant interaction of treatment and blood loss, differences between individual means were assessed by a least-significant difference (LSD) test (20). Significant differences were determined at \( P < 0.05 \). The dashed lines on either side of the sham stimulation data (see Figs. 4–6) are \( \pm \) LSD (\( \alpha = 0.05 \)). If the ANOVA demonstrated significant effects, points during air that are outside the dashed lines differ significantly from sham stimulation values. Data in the text and representative points in the figures and tables are shown as means \( \pm \) SE. The SE was computed from the pooled estimate of the sample variance calculated in the associated ANOVA. Regional blood flows and vascular conductances were normalized to pre-stressor levels to facilitate regional comparisons.

We attempted to identify factors associated with the enhanced defense of arterial pressure during air. To do this we examined the relationship between changes in the measured or calculated cardiovascular parameters due to air and the associated increase in hypotensive blood loss. We calculated changes in hemodynamic parameters and blood loss by subtracting values during sham stimulation from values during air. We then performed simple linear regression analysis on the resultant blood loss and hemodynamic difference values. A one-way ANOVA was used to determine the significance of the correlation.

A decrease in hindquarters conductance is a prominent feature of the normotensive phase of the response to hemorrhage. It is essential for maintenance of arterial pressure (2, 9, 13, 18, 19). Thus hindquarters vasoconstriction is a measure of an animal’s ability to compensate for blood loss. We evaluated the effects of air on this measure of compensation. We calculated linear regression equations for the relationship between hindquarters conductance and blood loss over the normotensive phase of the response (0–80% of total blood loss) for each experiment. We then tested for effects of treatment (air or sham) on the slope and intercept of this relationship (one-way repeated measures ANOVA).

RESULTS

Figures 1 and 2 show examples of the hemodynamic response to hemorrhage in two different rabbits during air (Fig. 1B and 2B) and sham (Fig. 1A and 2A) stimulation. These rabbits were implanted to measure hindquarters and mesenteric blood flows (Fig. 1) or renal flow and cardiac output (Fig. 2). Air increased arterial pressure and heart rate in both rabbits. In Fig. 1, the pressor response was accompanied by an increase in hindquarters blood flow and a decrease in mesenteric blood flow. In the experiment shown in Fig. 1, there was a biphasic (decrease followed by increase) change in renal flow and an increase in cardiac output on exposure to air. The arterial pressure and heart rate changes during blood loss were qualitatively similar in both experiments in the presence and absence of air, although the blood loss required to produce hypotension was increased by air. With or without air, mean arterial pressure was initially well maintained (normotensive phase) and heart rate increased. Once the critical blood loss was reached, mean arterial blood pressure declined precipitously (hypotensive phase), and heart rate decreased toward prehemorrhage levels. Some of the regional flow changes during hemorrhage were altered by air exposure (e.g., renal flow in Fig. 2), whereas others were not. These are discussed below. In the presence of air, rabbits were better able to defend arterial pressure (Fig. 3). A greater blood loss was necessary to produce the simultaneous decrease in...
mean arterial pressure and heart rate characteristic of the hypotensive phase (Fig. 3A). The total blood loss (i.e., that required to reduce mean arterial pressure to 40 mmHg) was 19.3 ± 0.2 and 16.9 ± 0.2 ml/kg for air and sham, respectively (Fig. 3B). Thus whereas air did not appear to qualitatively change the arterial pressure or heart rate response to blood loss, air did extend the phase of arterial pressure maintenance.

The normalized (to total blood loss, see METHODS) hemodynamic changes during hemorrhage are shown in Figs. 4–6. Air increased mean arterial pressure before hemorrhage (94 ± 1 mmHg) compared with sham stimulation (67 ± 1 mmHg; Figs. 3A and 4). The normotensive phase (i.e., first 80% of total blood loss) was prolonged by air (15.4 ± 0.2 ml/kg) compared with sham (13.5 ± 0.2 ml/kg). This phase is characterized by relatively good maintenance of arterial pressure (i.e., compared with the hypotensive phase). However, whereas mean arterial pressure during the normotensive phase did not change during sham stimulation (65 ± 1 mmHg), it had significantly decreased at the end of this phase during air (81 ± 1 mmHg). Thus whereas the period before the precipitous decline in arterial pressure was extended (Figs. 3 and 4), there was a significant decrease in arterial pressure during this period. During the hypotensive phase (85–105% of the total blood loss) there was a rapid decrease in mean arterial pressure to 31 ± 1 mmHg in both sham and air experiments. However, the absolute change in arterial pressure during the hypotensive phase was increased during air because arterial pressure at the onset of this phase was higher (Figs. 3A and 4).

Prehemorrhage heart rate was increased by air (190 ± 2 beats/min) compared with sham stimulation (149 ± 2 beats/min) (Figs. 3A and 4). Heart rate began to increase as soon as we started to draw blood in either condition (Figs. 3A and 4). At the end of the normotensive phase, heart rates were 217 ± 2 and 293 ± 2 beats/min in the sham stimulation and air experiments, respectively. The maximum heart rate during hemorrhage occurred near the beginning of the hypotensive phase (90% of the total blood loss) and was greater during air than during sham stimulation (300 ± 2 and 237 ± 2 beats/min, respectively). After the maximum was reached, heart rate decreased. Heart rate was greater during air than during sham
stimulation at the end of the hypotensive phase (251 ± 2 and 212 ± 2 beats/min, respectively). The heart rate changes during both phases of the response to blood loss were modified by air.

Central venous pressure was increased by air (2.6 ± 0.3 mmHg) compared with sham stimulation (0.8 ± 0.3 mmHg; Fig. 4). However, the decrease in central venous pressure during the normotensive phase was greater during air than during sham. Thus central venous pressure was not statistically different between the experiments after 10% of the total blood loss (Fig. 4). Although the changes in central venous pressure during normotensive blood loss were affected by air, the changes during the hypotensive phase were not.

Before hemorrhage, cardiac output (Figs. 2 and 5) was greater during air (120 ± 4% of baseline) than during sham stimulation (96 ± 4% of baseline). In both experiments there was a statistically similar, steady decline in cardiac output over both phases of the response to hemorrhage. Air significantly decreased total peripheral conductance (Fig. 6) compared with sham stimulation (85 ± 2 and 97 ± 5% of baseline, respectively). This relative vasoconstriction was maintained throughout the normotensive phase. During the hypotensive phase, total peripheral conductance increased in either experiment, reflecting the global vasodilation associated with this phase. However, this increase in total peripheral conductance was greater in the presence of air.

Hindquarters blood flow was increased by air compared with sham stimulation (130 ± 3 and 98 ± 3% of

Fig. 3. Effects of air or sham (n = 31) on the MAP and HR response to hypotensive hemorrhage (A) and on the blood loss required to reduce MAP to 40 mmHg (B). Values are means. The pooled estimates of the SE (from the ANOVA) are plotted on the ends of the curves in A (not visible) and on each bar in B. Air increased the blood loss necessary to reduce MAP to 40 mmHg [F(1,30) = 26.1]. Other abbreviations defined in Fig. 1. bpm, Beats/min. *P < 0.05.

Fig. 4. MAP (n = 31), HR (n = 31), and central venous pressure (CVP; n = 7) responses to hemorrhage during air or sham. Blood loss (x-axis) is normalized (%total) with 100% equal to the volume loss required to reduce MAP to 40 mmHg (see METHODS). Blood removal began at 0 on the x-axis, and sensory stimulation began 2 min earlier. Values are means. An individual ANOVA was done on the normotensive and hypotensive phases of the response to blood loss (see METHODS). The pooled estimate of the SE (from the ANOVA) was calculated separately for each phase and is plotted on the ends of the curves (not visible for HR and MAP). Dashed lines are the values during sham ± least significant difference (LSD; α = 0.05). During the normotensive phase, there was a significant interaction effect of blood loss and treatment on MAP [F(4,120) = 18.2], HR [F(4,120) = 13.5], and CVP [F(4,48) = 2.8]. During the hypotensive phase, there was a significant interaction effect of blood loss and treatment on MAP [F(4,120) = 32.5] and HR [F(4,120) = 23.2], but not CVP [F(4,24) = 0.6]. Only the main effect of blood loss significantly affected CVP [F(4,24) = 4.9].
HEMORRHAGE DURING ACUTE STRESS

During air or sham stimulation. Blood loss renal flow during air or sham stimulation. Blood loss renal flow appeared to be passive (i.e., driven by the increase in perfusion pressure) and was not associated with an increase in conductance (Fig. 6). During the normotensive phase, there was vasoconstriction in the hindquarters in both experiments as indicated by the simultaneous decrease in flow and vascular conductance (Figs. 5 and 6). During the hypotensive phase in either air or sham experiments, hindquarters blood flow continued to decrease (Fig. 5) but the decrease was limited by the simultaneous vasodilation (Fig. 6).

Our initial hypothesis was that blood pressure maintenance during hemorrhage would be compromised by air exposure due in part to skeletal muscle vasodilation. Whereas the group results indicated no change in hindquarters conductance with air, individual responses to air ranged from 66 to 161% of control. However, there was no correlation between the stressor-induced change in blood loss and the stressor-induced increase in either hindquarters blood flow or hindquarters vascular conductance (P < 0.67 and P < 0.62, respectively; Table 1).

Before blood removal, mesenteric flow was not consistently affected by air (range, 52–154% of baseline). Thus while Fig. 1 illustrates a rabbit that showed a clear decrease in mesenteric flow during air, the mean values (Fig. 5) for air and sham (101 ± 3 and 103 ± 3% of baseline, respectively) before hemorrhage were not different. However, exposure to air did result in mesenteric vasoconstriction as evidenced by the significant decrease in vascular conductance during air compared with sham (76 ± 3 and 104 ± 3% of baseline, respectively) (Fig. 6). Once blood loss commenced, mesenteric blood flow (Fig. 5) and conductance (Fig. 6) did not decrease during the normotensive phase under either stimulation condition. During the hypotensive phase, while mesenteric conductance increased (Fig. 6), there was a substantial decrease in mesenteric blood flow with air or sham (Fig. 5).

Compared with sham, air significantly increased renal blood flow (86 ± 3 and 121 ± 4% of baseline, respectively) but decreased renal conductance (98 ± 3 and 85 ± 3% of baseline, respectively) (Figs. 2, 5, and 6). During normotensive blood loss with sham stimulation, renal blood flow and vascular conductance were well maintained. However, both renal flow and conductance decreased steadily and significantly during the same phase in the presence of air. That is to say, the presence of air changed the renal response to normotensive blood loss from maintenance of flow to vasoconstriction (Figs. 2, 5, and 6). During the hypotensive phase, renal blood flow appeared to follow the change in arterial pressure. This is supported by the relative constancy of renal conductance during the hypotensive phase. Thus in these experiments, vasodilation associated with hypotensive hemorrhage was not obvious in the kidneys (Fig. 6).

To identify factors associated with the air-induced increase in total blood loss, we examined the relationship between the changes in measured or calculated cardiovascular parameters and the associated changes in blood loss. We performed linear regression analyses on the change (air or sham) in blood loss vs. the prehemorrhage change in each parameter (Table 1). Air-induced changes in blood loss were significantly corre-
The decrease in hindquarters conductance is an important compensatory response to blood loss (Fig. 6), which is essential to maintenance of arterial pressure (2, 9, 13, 18). In 13 rabbits prepared for measurement of hindquarters blood flow, air had no effect on the slope or intercept of the relationship between hindquarters conductance and blood loss (Fig. 7). Thus air did not alter this compensatory response.

**DISCUSSION**

The purpose of this study was to evaluate the effects of a stressor-induced cardiovascular defense reaction on the hemodynamic response to blood loss in the conscious rabbit. The stressor we chose, air jet, increased arterial blood pressure, heart rate, cardiac output, and hindquarters blood flow and caused visceral vasoconstriction. That is, air jet resulted in hemodynamic changes characteristic of the defense reaction (6, 17). Our initial hypothesis was that air jet stimulation would decrease the animal’s ability to defend arterial pressure during blood loss. The major finding of this study was that, contrary to our hypothesis, air jet stimulation extended defense of arterial blood pressure.

The virtual absence of studies examining the response to blood loss in the presence of stressful sensory stimuli is surprising for several reasons. First, blood loss under natural conditions normally occurs coincident with an uncontrolled increase in stressful sensory stimulation. Second, stressors and blood loss appear to activate the same efferent systems. Third, proposed stressor-induced decreases in arterial baroreflex function would surely compromise arterial pressure maintenance during blood loss. Finally, the cardiovascular and neurohumoral responses to hemorrhage or sensory stressors are similar in a variety of mammalian species suggesting an important biological value in terms of survival.

In the present study, the air jet-induced defense reaction included an increase in skeletal muscle blood flow. Maintenance of arterial pressure early in blood loss is dependent on sympathetic vasoconstriction in skeletal muscle (2, 9, 13, 18, 19). Therefore, we predicted that the air jet-induced increase in skeletal muscle blood flow would oppose the hemorrhage-induced vasoconstriction. However, despite the increase in skeletal muscle blood flow and contrary to our hypothesis, air jet exposure improved maintenance of arterial pressure during blood loss.

The cardiovascular response to stressful sensory stimulation, the defense reaction, should support the somatic response (6, 17). If the somatic response is active (i.e., defense or escape), the cardiovascular response might include skeletal muscle vasodilation. Consistent with this idea, anesthetized rabbits exhibit cholinergic, skeletal muscle vasodilation following electrical stimulation of the hypothalamic defense area (10). Indeed, some animals in our study showed hindquarters vasodilation in response to air jet exposure. However, for the group, the increase in skeletal muscle blood flow during air jet was a passive result of the
increase in arterial pressure and not due to vasodilation. The overall absence of muscle vasodilation may have been due to our experimental paradigm, which did not encourage an active response. In cats, the pattern of skeletal muscle blood flow changes associated with the defense reaction is strongly influenced by the nature of the somatic response (1). That is to say, a more active response is accompanied by a greater degree of muscle vasodilation.

If air jet exposure had resulted in skeletal muscle vasodilation and a larger increase in blood flow (1), this might have compromised defense of arterial pressure during blood loss. We recently recorded results in one rabbit that were consistent with this possibility (unpublished observations). During the first experiment, the rabbit pawed at the front of the box during the air jet exposure until mean arterial pressure reached 40 mmHg. The blood loss required to reduce arterial pressure to this level was 15 ml/kg. During additional experiments in this rabbit, the requisite blood losses were 17 ml/kg during sham stimulation and 21 ml/kg during a second air jet experiment (in which the rabbit did not move). The smallest blood loss (i.e., the poorest defense of arterial pressure) was during the first air jet experiment when motor activity increased and a large hindquarters vasodilation accompanied air jet exposure.

Although the results described were consistent with our hypothesis, the group results were not. Individual rabbit responses to air jet ranged from vasoconstriction to vasodilation. However, the group response failed to demonstrate any change in hindquarters vascular conductance. In addition, the correlation between the stressor-induced change in hindquarters conductance and the increase in blood loss was not significant (Table 1). If air jet-induced muscle vasodilation had limited defense of arterial pressure, there should have been a negative correlation between these two changes.

The mechanism(s) by which stressful sensory stimulation increased defense of arterial pressure is not clear. We attempted to identify potential mechanisms by examining the correlation between the air jet-associated increase in blood loss and changes in the hemodynamic parameters (Table 1). The only significant correlation was between the change in blood loss and the changes in either renal blood flow or renal vascular conductance. This correlation was positive. At first glance, it seems unlikely that increases in renal flow or conductance would increase the hypotensive blood loss. However, whereas renal flow and conductance were maintained during the normotensive phase in sham-stimulated rabbits, air jet stimulation changed this response to vasoconstriction (Figs. 2, 4, and 5). Thus although renal flow initially increased, it decreased steadily during hemorrhage in the presence of air jet. As a result, renal flow was lower with air jet than with sham stimulation at the end of both the normotensive and hypotensive phase. Thus enhanced renal vasoconstriction is a potential mechanism for the air jet-induced improvement in defense of arterial blood pressure during blood loss.

Critical changes in regional volumes might also account for the air jet-induced increase in hypotensive blood loss. Exposure to air jet produces mesenteric vasoconstriction, which might increase central blood volume. An increase in central blood volume and/or central venous pressure could delay (in terms of blood loss) stimulation of left ventricular receptors. This paradoxical activation of left ventricular receptors is pro-

Table 1. Relationship of air jet-induced changes in hemodynamic parameters to air jet-induced changes in total blood loss (i.e., blood loss to MAP = 40 mmHg)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Slope</th>
<th>Intercept</th>
<th>$r$</th>
<th>$F$ ($df$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>0.03</td>
<td>1.67</td>
<td>0.09</td>
<td>0.23(1,29)</td>
<td>&lt;0.64</td>
</tr>
<tr>
<td>HR</td>
<td>0.002</td>
<td>2.33</td>
<td>0.03</td>
<td>0.03(1,29)</td>
<td>&lt;0.86</td>
</tr>
<tr>
<td>CVP</td>
<td>0.75</td>
<td>2.65</td>
<td>0.49</td>
<td>1.62(1,5)</td>
<td>&lt;0.26</td>
</tr>
<tr>
<td>HQ flow</td>
<td>-0.01</td>
<td>1.67</td>
<td>0.13</td>
<td>0.20(1,11)</td>
<td>&lt;0.67</td>
</tr>
<tr>
<td>HQ con</td>
<td>-0.04</td>
<td>2.17</td>
<td>0.13</td>
<td>0.26(1,11)</td>
<td>&lt;0.62</td>
</tr>
<tr>
<td>CM flow</td>
<td>-0.03</td>
<td>0.25</td>
<td>0.33</td>
<td>1.38(1,11)</td>
<td>&lt;0.27</td>
</tr>
<tr>
<td>Renal flow</td>
<td>0.04</td>
<td>1.78</td>
<td>0.67</td>
<td>6.42(1,8)</td>
<td>&lt;0.035*</td>
</tr>
<tr>
<td>Renal con</td>
<td>0.05</td>
<td>3.26</td>
<td>0.67</td>
<td>6.63(1,8)</td>
<td>&lt;0.033*</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>0.01</td>
<td>2.21</td>
<td>0.35</td>
<td>0.70(1,5)</td>
<td>&lt;0.44</td>
</tr>
<tr>
<td>TP con</td>
<td>0.02</td>
<td>2.77</td>
<td>0.43</td>
<td>1.13(1,5)</td>
<td>&lt;0.34</td>
</tr>
</tbody>
</table>

MAP, mean arterial pressure; HR, heart rate; CVP, central venous pressure; HQ, hindquarter; CM, cranial mesenteric; con, conductance; TP, total peripheral. *Significant correlation.
posed to occur during situations involving decreased cardiac filling and increased sympathetic stimulation. It is one suggested cause of the sympathoinhibitory phase of the response to acute blood loss (11). However, although air jet exposure increased central venous pressure, the increase was not correlated with the increase in blood loss.

Arterial pressure decreased to virtually the same level with or without stressful stimulation. This suggests that the pressor system(s) activated by air jet exposure prior to hemorrhage had to be turned off or ineffective during the hypotensive phase. For example, air jet exposure might have increased arterial pressure by activating the sympathetic nervous system. In that case the sympathoinhibition associated with the hypotensive phase (4, 12) had to be equally effective at inhibiting the stressor- and blood loss-induced increases in sympathetic activity. If a humoral agent were responsible, release of that compound would have to decrease at the onset of hypotension. However, release of renin, epinephrine, and vasopressin increase dramatically at the onset of hypotension (14–16). An additional possibility is a humoral mechanism, such as the renin-angiotensin system, which facilitates sympathetic nervous system activity and actions (7, 21–23). Such a system would become less effective in the absence of peripheral sympathetic nerve activity as occurs during the hypotensive phase.

It has been suggested that arterial baroreflex function is significantly compromised during stressful sensory stimulation (6). Indeed, baroreflex control of heart rate in conscious rats (5) and rabbits (17) is altered by air jet. The result is a relative tachycardia at any arterial pressure with no change in reflex gain. This allows normal control of heart rate, but in a different arterial pressure range (5, 17). This type of information is not available for baroreflex control of the vasculature in conscious animals. However, in the present study, there was probably not a significant loss of baroreflex control of the vasculature during air jet exposure. The arterial baroreflex-mediated, hindquarters vasoconstriction during blood loss is essential for normal blood pressure maintenance (2, 9, 13, 18). The negative relationship between blood pressure and hindquarters conductance was not affected by air jet. In addition, any significant loss of baroreflex function would certainly have compromised defense of arterial blood pressure (2, 9, 13). We found that this defense was enhanced by air jet stimulation.

In conclusion, air jet stimulation produced hemodynamic changes characteristic of the defense reaction and enhanced defense of arterial blood pressure during hemorrhage in conscious rabbits. This enhanced defense of arterial pressure may have been due in part to enhanced renal vasoconstriction. Functional indexes of baroreflex-mediated compensation during acute blood loss (i.e., skeletal muscle vasoconstriction and defense of arterial pressure) were not significantly compromised during air jet. The enhanced ability to defend arterial blood pressure may be due to increased sympathetic activation and/or the sympathoexcitatory effects of a humoral system such as the renin-angiotensin system.

**Perspectives**

The hemodynamic response to blood loss is biphasic and is similar across a wide range of species. Arterial blood pressure is initially well maintained by regional vasoconstriction. However, once blood loss exceeds 25–35% of total blood volume, blood pressure decreases dramatically due to sympathoinhibition and the resultant vasodilation. The similarity in this response across species suggests a process fundamental to survival. Potential advantages of such a response include decreased blood loss due to the decrease in arterial pressure and enhanced hemostasis as well as decreased cardiac work. However, the biological relevance of the response could be questioned because it always has been observed under conditions of limited sensory input. Although easily achieved in the laboratory, this situation rarely occurs in nature where blood loss is normally associated with a relatively uncontrolled increase in sensory input. Some of this input is painful and most is probably stressful (e.g., a predator). Thus while a sudden and profound decrease in blood pressure might make sense in a quiet laboratory, it might be more difficult to understand in the presence of a stressful stimulus, which produces a defense reaction.

In this study, we examined the effects of sensory input that resulted in a defense reaction on the hemodynamic response to blood loss. One of the cardiovascular effects of air jet exposure is increased skeletal muscle blood flow. This vascular bed is an important site of vasoconstriction during the normotensive phase of the response to blood loss. Therefore, our initial hypothesis was that air jet exposure would decrease the blood loss necessary to produce hypotension. Contrary to our hypothesis, we found that air jet extended the rabbits’ ability to maintain arterial blood pressure during blood loss. Despite this difference, the basic biphasic nature of the response was preserved. In other words, whereas the transition from sympathoexcitation to sympathoinhibition still occurred in the presence of air jet, it occurred after a significantly greater blood loss. In a teleological sense, perhaps the biological advantage of escape from a stressful stimulus can at least temporarily exceed the advantage of limiting blood loss.

A major limitation of this finding is that the experiments did not encourage an active response to stress. That is to say, movement (e.g., defense or flight) in response to stressful stimuli was limited by the experimental paradigm. This may have accounted for our inability to demonstrate active vasodilation in skeletal muscle and also for the stress-induced improvement in arterial blood pressure maintenance during hemorrhage.
We thank Jack Taylor and Michael McKown for technical assistance with this study.

This study was supported in part by the National Heart, Lung, and Blood Institute Grant HL-31218 and grants from the American Heart Association (National and Missouri Affiliate).

REFERENCES