

## The Role of Low Pressure Baroreceptors in Reflex Vasoconstrictor Responses in Man

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**ABSTRACT** Studies were performed on 11 healthy men to evaluate the role of low pressure baroreceptors in the reflex forearm vasoconstrictor responses (plethysmography) to venous pooling produced by lower body negative pressure. Lower body negative pressure (LBNP) at  $-5$ ,  $-10$ ,  $-20$ , and  $-40$  mm Hg lowered central venous pressure by 42, 59, 74, and 93%, respectively, and decreased forearm vascular conductance by 24, 29, 34, and 40%, respectively. The decreases in forearm blood flow and conductance during the low levels of venous pooling (LBNP  $-5$  and  $-10$  mm Hg) occurred without significant changes in arterial pressure, arterial  $dP/dt$ , and heart rate. These results with the low levels indicate that maneuvers which decrease venous return and central venous pressure in man can influence forearm vascular tone without significant changes in the determinants of carotid and aortic baroreceptor activity. During high levels of venous pooling (LBNP  $-20$  and  $-40$  mm Hg), significant decreases in arterial pressure and  $dP/dt$  and significant increases in heart rate accompanied the further reductions in cen-

tral venous pressure, forearm blood flow, and forearm vascular conductance. About 73% of the decrease in conductance during venous pooling at LBNP  $-40$  mm Hg, which was sufficient to decrease arterial pressure and activate high pressure baroreceptor reflexes, occurred during low levels of venous pooling at LBNP  $-10$  mm Hg without changes in arterial pressure. This suggests that much of the forearm vasoconstriction with the high levels of venous pooling, which were sufficient to decrease arterial pressure, may be accounted for by reflexes originating in areas other than high pressure baroreceptors. The results of these studies suggest that low pressure baroreceptors exert an important influence on forearm vascular tone during decreases in venous return and central venous pressure in man.

### INTRODUCTION

Reflex vasoconstriction occurring during venous pooling produced by upright tilting or lower body negative pressure has been attributed to changes in arterial pressure which activate reflexes mediated through high pressure baroreceptors. In preliminary observations we noted that vasoconstriction occurred in the forearm during lower body negative pressure before or in the absence of an obvious fall in arterial pressure. This suggested that low pressure baroreceptors might play a role in vasoconstrictor responses to venous pooling. Roddie, Shepherd, and Whelan (1) observed that dilator

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TABLE I  
Responses to Lower Body Negative Pressure in 11 Normal Subjects\*

	Control	LBNP			Recovery
		-10	-20	-40	
Central venous pressure, <i>mm Hg</i>	7.3 ±0.7	3.0‡ ±0.6	1.9‡ ±0.6	0.5‡ ±0.6	7.6 ±0.6
Forearm blood flow, $\frac{\text{ml/min}}{100 \text{ ml}}$	6.24 ±0.96	4.44‡ ±0.93	4.08‡ ±0.72	3.53‡ ±0.66	6.15 ±0.99
Forearm vascular conductance, $\frac{\text{ml/min} \times 100 \text{ ml}}{\text{mm Hg}} \times 1000$	68.73 ±9.36	48.87‡ ±9.20	45.05‡ ±6.99	41.41‡ ±6.81	67.35 ±9.71
Systolic arterial pressure, <i>mm Hg</i>	115.0 ±3.4	114.4 ±3.5	113.5 ±3.5	110.4‡ ±4.0	115.6 ±3.4
Mean arterial pressure, <i>mm Hg</i>	90.0 ±2.7	90.3 ±3.2	89.6 ±2.7	87.6‡ ±3.4	90.3 ±2.8
Arterial pulse pressure, <i>mm Hg</i>	40.7 ±2.0	38.6 ±2.0	38.4‡ ±2.0	32.9‡ ±2.0	40.3 ±1.7
Arterial dP/dt, <i>mm Hg/sec</i>	752 ±83	745 ±100	727 ±82	652‡ ±77	744 ±85
Heart rate, <i>beats/min</i>	62.2 ±2.2	64.7 ±2.5	66.1 ±3.1	76.0‡ ±4.3	62.6 ±2.1

\* Entries represent mean  $\pm$ SE of the average of all the runs (2 to 3) of LBNP in each subject. Values for arterial pressure for each run were the average of two determinations approximately 15 and 45 sec after onset of each level of LBNP.

‡ Indicates values which are significantly different from control observations ( $P < 0.05$ ).

responses to increases in venous return did not correlate with the magnitude of the increases in arterial pressure and heart rate and suggested that low pressure baroreceptors mediate these reflex vasodilator responses. The contribution of low pressure baroreceptors to the reflex vasoconstrictor response to decreases in venous return and central venous pressure has not been studied. The present experiments were done to evaluate the amount of reflex forearm vasoconstriction which occurs during venous pooling in the absence of changes in the determinants of high pressure baroreceptor activity.

## METHODS

11 healthy men, age 21-39 yr, were studied. These studies were performed with the subjects supine in a warm room (26-27° C). Forearm blood flow was measured with a mercury-in-silastic strain-gauge plethysmograph (2). The forearm was elevated and supported so that the proximal part of the forearm was approximately 10 cm above the anterior chest wall. The strain-gauge was applied to the arm 4-8 cm distal to the elbow to measure changes in forearm volume. A pneumatic cuff placed around the arm proximal to the elbow was inflated intermittently above venous pressure for 6-10 sec to produce venous occlusion. A second cuff applied to the wrist was inflated to suprasystolic pressures during measurements to exclude the hand circulation from the measurements. Forearm blood flow was calculated from the

rate of increase of forearm volume during venous occlusion and expressed as ml/min per 100 ml forearm volume. Forearm vascular conductance, expressed in arbitrary units, was calculated by dividing blood flow in ml/min per 100 ml by mean arterial pressure in mm Hg and multiplying by 1000. After minimal superficial local anesthesia, a polyethylene cannula (PE 90; o.d. 1.3 mm and i.d. 0.9 mm) was inserted percutaneously into the brachial artery and advanced so that the tip was 10-20 cm proximal to the antecubital area. Systemic arterial pressure was measured with the cannula and a P23Db Statham pressure transducer (Statham Instruments, Inc., Oxnard, Calif.). In preliminary studies on two patients undergoing cardiac catheterization, changes in brachial arterial pressure accurately reflected changes in aortic pressure during a Valsalva maneuver. Changes in arterial pressure of 1 mm Hg were detectable using these methods. Arterial dP/dt was obtained using an RC differentiating circuit with a time constant of 0.5 msec. Heart rate was obtained from the arterial pressure recordings. Central venous pressure was measured with a cannula (60 cm long; i.d. 0.7 mm) inserted into an antecubital vein and advanced into an intrathoracic vein.

We obtained measurements of central venous pressure, forearm blood flow, mean arterial pressure, pulse pressure, arterial dP/dt, and heart rate during the control state, during lower body negative pressure (LBNP)<sup>1</sup> at -10, -20, and -40 mm Hg for 1 min each and during a re-

<sup>1</sup> Abbreviation used in this paper: LBNP, low body negative pressure.

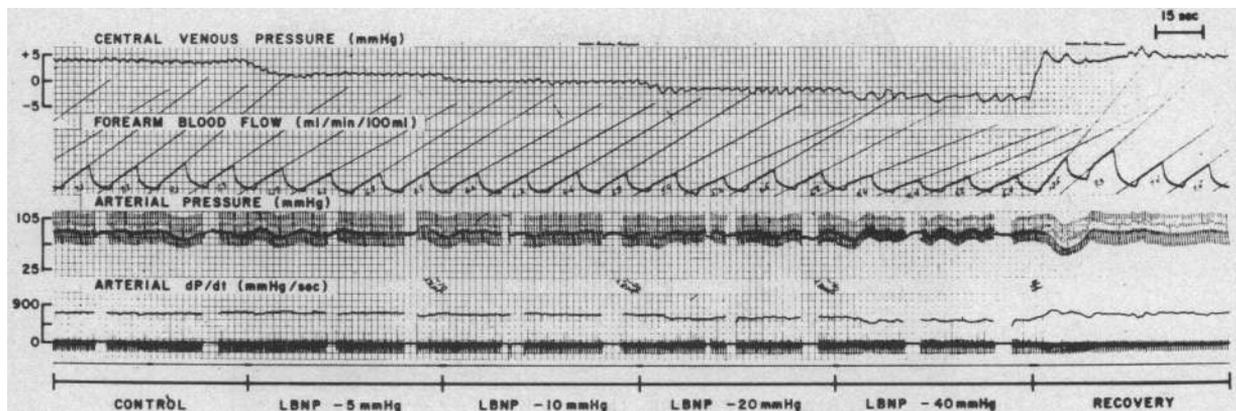


FIGURE 1 (Subject F. V.) Responses to graded LBNP in one of these subjects. Because the tracing for arterial dP/dt was faint, a horizontal line indicating peak dP/dt was drawn on the record. Forearm blood flow averaged 8.0 ml/min per 100 ml during the control period, 6.6 during LBNP -5 mm Hg, 6.3 during -10 mm Hg, 5.9 during -20 mm Hg, and 4.8 during -40 mm Hg.

covery period. This sequence was repeated two to three times in each subject. In four subjects, responses to LBNP at -5 mm Hg also were obtained.

Statistical comparisons were performed with analysis of variance and Dunnett's test (3).

## RESULTS

**Responses to low levels of venous pooling.** LBNP at -5 and -10 mm Hg produced significant decreases in forearm blood flow and conductance (Table I and Figs. 1-5). These reflex vasoconstrictor responses were associated with striking decreases in central venous pressure in the absence of significant changes in systolic and mean arterial pressures, pulse pressure, arterial dP/dt, and heart rate (Table I and Fig. 2). Systolic arterial pressures averaged  $113.4 \pm 4.1$  (SE),  $114.3 \pm 4.7$ ,  $113.4 \pm 5.0$ , and  $113.8 \pm 4.6$  mm Hg at 48, 32, 16, and 0 sec before the start of LBNP and  $113.9 \pm 4.5$ ,  $113.3 \pm 3.9$ ,  $114.0 \pm 4.1$ ,  $113.1 \pm 4.8$ ,  $113.5 \pm 4.2$ ,  $115.0 \pm 4.2$ ,  $113.3 \pm 4.4$ ,  $115.6 \pm 4.6$ , and  $115.4 \pm 4.9$  mm Hg at 4, 8, 12, 16, 20, 24, 32, 40, and 48 sec after the onset of negative pressure at -10 mm Hg.

**Responses to high levels of venous pooling.** During LBNP at -20 mm Hg, forearm blood flow and central venous pressure decreased further without significant changes in systolic and mean arterial pressure, arterial dP/dt, and heart rate (Table I and Fig. 2). There was a slight but statistically significant decrease in arterial pulse pressure at -20 mm Hg (Table I). During LBNP at -40 mm Hg, there were additional decreases in forearm blood flow and conductance and in central venous pressure. These decreases were accompanied by significant reductions in systolic and mean arterial pressure, pulse pressure, and dP/dt averaging -4, -3, -19, and -13%, respectively, and significant increases in heart rate averaging +22% (Table I).

## DISCUSSION

These studies suggest that reflexes originating in low pressure baroreceptors play an important role in the forearm vasoconstrictor responses to decreases in venous return in man.

The reflex vasoconstrictor response to LBNP at -5 and -10 mm Hg was associated with decreases in central venous pressure without significant changes in the determinants of high pressure baroreceptor activity, such as systolic and mean arterial pressures, pulse pressure,

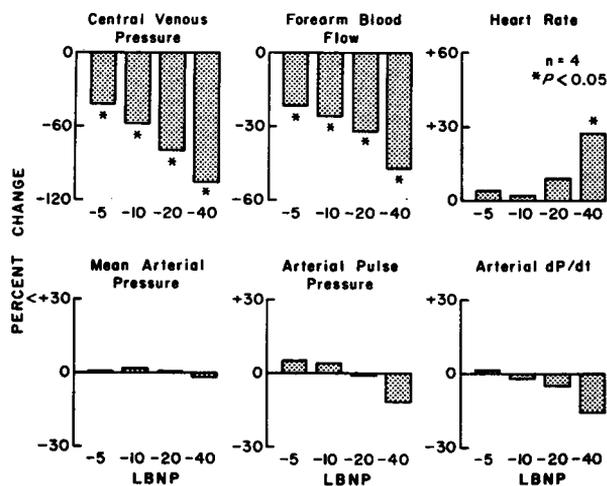


FIGURE 2 Per cent change from control during LBNP in the four subjects in whom responses to -5 mm Hg as well as -10, -20, and -40 mm Hg were obtained. Control values were as follows: central venous pressure  $6.6 \pm 1.2$  (mean  $\pm$  SE) mm Hg, forearm blood flow  $8.1 \pm 1.8$  ml/min per 100 ml, heart rate  $67.5 \pm 5.1$  beats/min, mean arterial pressure  $89.3 \pm 6.5$  mm Hg, arterial pulse pressure  $37.0 \pm 3.7$  mm Hg, and arterial dP/dt  $614 \pm 144$  mm Hg/sec.

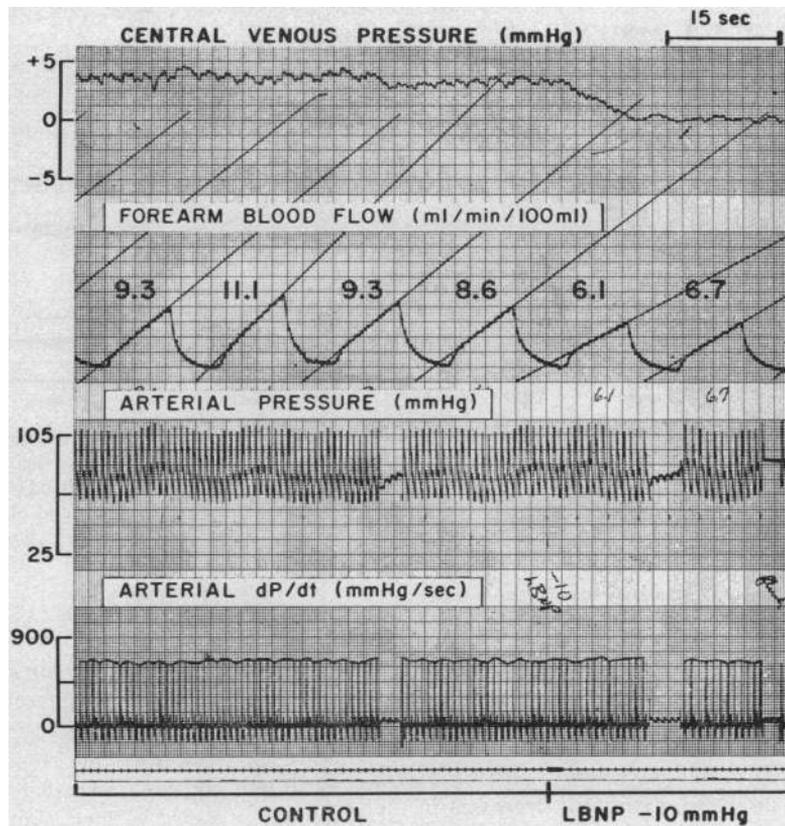


FIGURE 3 (Subject F. V.) Responses to LBNP at  $-10$  mm Hg in same study shown in Fig. 1.

arterial  $dP/dt$ , and heart rate (4). These observations suggest that low pressure baroreceptors mediate the reflex forearm vasoconstrictor response to low levels of venous pooling.

We cannot from the data in this study separate the contribution of low and high pressure baroreceptor reflexes to the forearm vascular responses during high levels of venous pooling (LBNP  $-40$  mm Hg). However, several observations suggest that much of the forearm vasoconstriction with the high level of venous pooling (LBNP  $-40$  mm Hg), which was sufficient to decrease arterial pressure and activate arterial baroreceptor reflexes, can be accounted for by reflexes originating in low pressure baroreceptors. First, a large fraction of the total decrease in flow and conductance during LBNP at  $-40$  mm Hg was observed at lower levels of venous pooling, e.g., if the decrease in conductance at  $-40$  mm Hg is considered as 100% of the vasoconstrictor response, then 73% of the vasoconstriction occurred at  $-10$  mm Hg (Table I). Second, the additional decreases in blood flow and conductance at  $-40$  mm Hg were accompanied by further reductions in central venous pressure suggesting that there could have been further activation of reflexes arising from low pressure

baroreceptors. And third, Roddie and Shepherd (5) demonstrated previously that a fall in carotid sinus pressure of 40–60 mm Hg produced by compressing the common carotid artery at the base of the neck in man increased rather than decreased forearm blood flow and tended to increase forearm conductance. The absence of forearm vasoconstriction during carotid sinus hypotension in the experiments of Roddie and Shepherd cannot be explained by manual distortion of carotid baroreceptors since the increases in forearm flow and conductance occurred when the carotid sinus reflex was activated as indicated by increases in heart rate and systemic arterial pressure (5). Their experiments suggest that decreases in carotid sinus pressure which are greater than any observed in our experiments do not produce significant vasoconstriction in the forearm of man. Recent experiments in dogs indicate that aortic baroreceptors are less sensitive to changes in pressure than carotid baroreceptors and do not contribute appreciably to vasoconstrictor responses to decreases in arterial pressure (6–8). These observations raise the possibility that reflexes originating in low pressure baroreceptors may exert the dominant influence on forearm vascular tone at even high levels of venous pooling which are

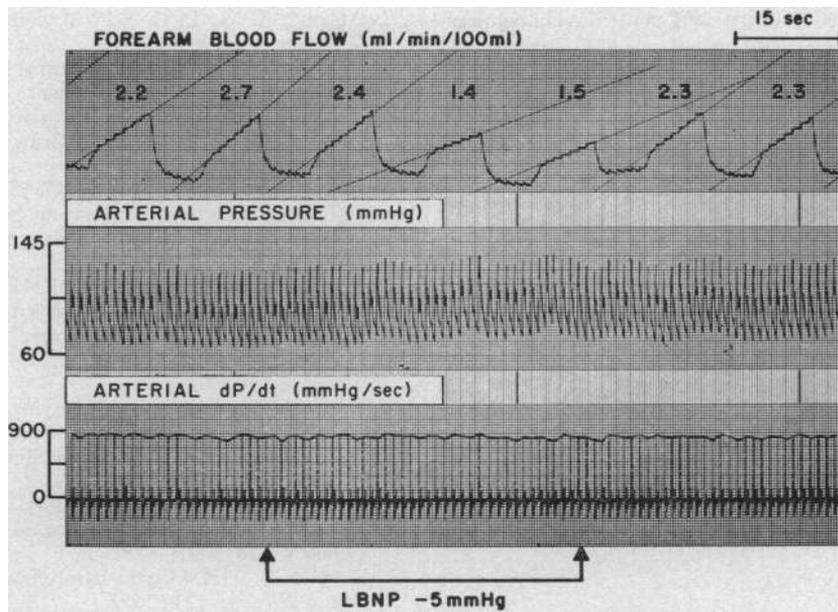


FIGURE 4 (Subject C. V.) Responses to LBNP at  $-5$  mm Hg.

associated with decreases in arterial pressure and activation of high pressure baroreceptor reflexes.

The precise location of the receptors mediating these responses cannot be determined from these experiments, but previous studies in animals have suggested that there are baroreceptors in the pulmonary vessels (9) and right and left atria (10).

The role of reflexes originating from low pressure baroreceptors in clinical states, such as hypovolemia and hypotension, is speculative. Changes in atrial or pulmonary arterial pressures may contribute significantly to reflex alterations in forearm vascular tone during hypovolemia or during tilting to the upright position.

In conclusion, these studies indicate that maneuvers

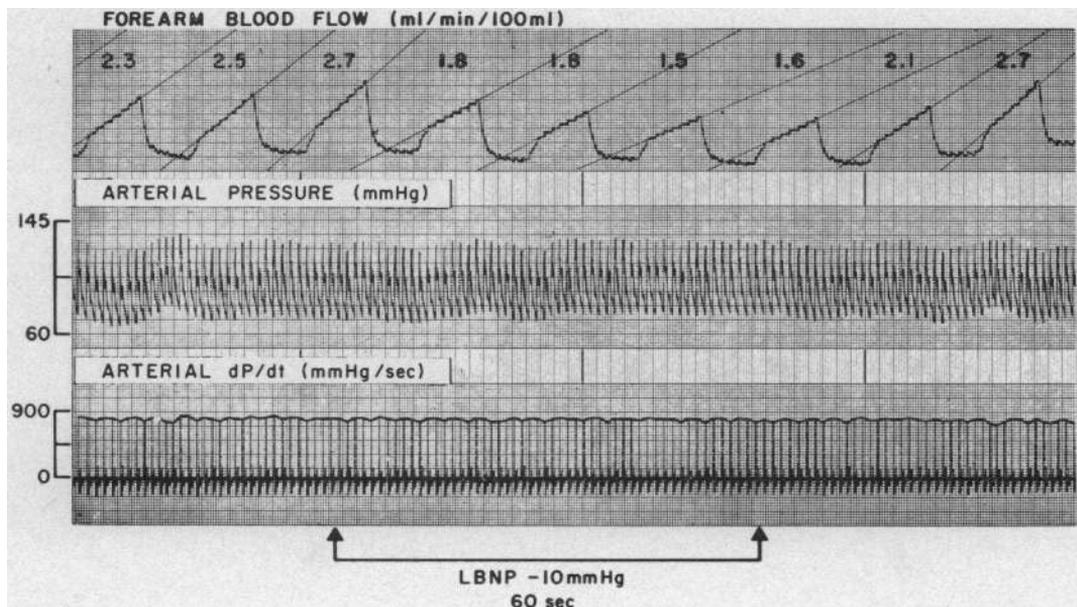


FIGURE 5 Responses to LBNP at  $-10$  mm Hg. The reflex vasoconstrictor response to this low level of LBNP occurred without appreciable changes in arterial pressure or  $dP/dt$ .

which decrease venous return and central venous pressure can influence forearm vascular tone without significant changes in the determinants of carotid and aortic baroreceptor activity. The results suggest that low pressure baroreceptors exert an important influence on forearm vascular tone during venous pooling in man.

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