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John W. Eckstein, … , William K. Hamilton, John M. McCammond

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Research Article

PRESSURE–VOLUME CHANGES IN THE FOREARM VEINS OF MAN DURING HYPERVENTILATION [1, 2]

By JOHN W. ECKSTEIN, WILLIAM K. HAMILTON, AND JOHN M. McCAMMOND [3]

(From the Hemodynamic Laboratory, Cardiovascular Research Laboratories, Department of Internal Medicine and the Division of Anesthesiology, Department of Surgery, State University of Iowa College of Medicine, Iowa City, Iowa)

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Peripheral venous pressure is known to fall during voluntary hyperventilation (2). Méan (3) found this pressure reduction to be accompanied by a decrease in the volume of small segments of superficial forearm veins. He regarded the volume change as a mechanical phenomenon secondary to the fall in venous pressure and the aspirating effect of the ventilatory efforts. In more recent studies (4, 5) the pressure in temporarily isolated forearm veins was found to rise during overbreathing, indicating an increase in venous tone. From these reports it is evident that the forearm venous volume may decrease during hyperventilation and that the change may be attributed to two factors—a fall in intraluminal pressure and active venous constriction. The experiments reported here were designed to assess the importance of each of these factors in the intact human forearm and to determine if the venous responses to hyperventilation with associated hypocapnia are different from the responses to hyperventilation when carbon dioxide is added to the inspired air.

METHOD AND PROCEDURE

Forearm venous pressure-volume curves were obtained by the plethysmographic method of Litter, Wood, and Wilkins (6, 7). In this procedure the forearm is enclosed in a tall plethysmograph and water is added to a level such that the external pressure on the arm is greater than venous pressure but less than diastolic arterial pressure. The arterial inflow continues and drives venous pressure in the segment of limb within the plethysmograph to a height greater than that of the water column. The difference between the pressure within the veins and the pressure surrounding the veins is the *effective* venous pressure. Under these conditions it is a small positive reproducible value ranging from 0.5 to 1.0 mm. Hg (8). For practical purposes it is regarded as zero pressure. The volume of blood in the veins at this effective pressure is small and constant (9). After the limb is fixed, a pneumatic cuff about the arm proximal to the plethysmograph is inflated by 1.0 mm. Hg increments until the first perceptible increase in limb volume occurs. From this point of "zero" effective pressure an additional pressure of 30.0 mm. Hg is applied to the arm in 5.0 mm. increments. This raises *effective* pressure in the veins of the forearm segment within the plethysmograph from 0 to 30 mm. Hg by the same increments of 5.0 mm. Hg. The increase in forearm venous volume caused by each pressure increment is recorded. The pressure-volume curve is constructed by plotting each volume level achieved at inflow-outflow equilibrium, expressed in ml. per 100 ml. of forearm tissue, against the corresponding level of effective venous pressure (Figure 1). The curve so obtained is convex toward the volume axis. If the veins become less distensible (Figure 1), a subsequent curve will fall below the control curve, nearer the pressure axis. Conversely, if the veins become more distensible, the subsequent curve falls above the control curve, nearer the volume axis. The final point on the curve is the venous volume which exists at an effective venous pressure of 30 mm. Hg. This volume value in a sense represents the venous distensibility since a high value would be associated with a curve of increased slope and a low value with a curve of decreased slope. For the sake of simplicity the venous volume at an effective pressure of 30 mm. Hg is termed arbitrarily the *venous distensibility.* A high value indicates relative venous dilatation and a low value relative venous constriction.

The pressure-volume curve obtained in this fashion expresses the volume to which the forearm venous system is distended by any level of effective venous pressure between 0 and 30 mm. Hg. Assuming that the venous pressure-volume characteristics are the same in both arms, the naturally occurring venous volume of the forearm segment is the volume coordinate of that point on the curve which corresponds to the natural venous pressure (equals effective venous pressure) in the opposite forearm. If a stimulus such as hyperventilation produces venous constriction and also a fall in venous pressure, the decrease

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[3] Undergraduate Research Fellow of the National Science Foundation.

in volume caused by each of these factors alone may be determined. The volume coordinate of the point on the hyperventilation curve which corresponds to the resting venous pressure is the venous volume which would have existed had the total volume reduction been caused by venous constriction alone (Figure 1). The difference between this value and the venous volume which actually existed during the stimulus represents the reduction in venous volume caused by the fall in pressure alone.

Twenty experiments were performed on 16 healthy men 21 to 34 years of age. Room temperature was maintained at 78° to 80° F. and plethysmographic water temperature at 89° F. Venous pressure was measured in the dependent left antecubital vein and venous distensibility in the right forearm as previously described (10) with minor execptions. Forearm volume changes were measured by means of two partially immersed electrodes [4] (11) which sensed changes in the height of the water in a vertical cylinder attached to the top of the plethysmograph. The diameter of the cylinder was such that maximal volume increases within the plethysmograph raised the water level only a few millimeters. This increase in the height of the water was not great enough to produce a measurable error in effective venous pressure. The tandem plethysmograph previously described (8) was not used. Instead a plethysmograph was employed which contained a very long segment of forearm. With such an instrument volume changes in the incompletely pressurized cone of tissue near the proximal end of the plethysmograph represent only negligible fractions of the total volume change within the apparatus unless the diameter of the forearm is unusually large.

During control periods venous distensibility and pressure were measured intermittently. In 11 experiments end-expiratory CO_2 concentration was monitored with a Liston-Becker CO_2 analyzer. Venous pressure was measured with a Statham 0 to 5 cm. Hg pressure transducer. Volume, pressure and CO_2 concentration were recorded simultaneously using a Sanborn direct-writing oscillograph. Respiratory minute-volume was measured using the gas meter method (12).

After values for venous distensibility and pressure became stable the subject was asked to hyperventilate. In the first 9 experiments the subject was instructed to overbreathe to the point of symptoms by means of maximal inspiratory efforts with passive expirations. In the final 11 experiments the subjects overbreathed in the same way with prompting in an effort to maintain a reduction in end-expiratory CO_2 tension of about 15 mm. Hg. The baseline venous volume of the forearm was recorded continuously during the initial portion of the hyperventilation period and no significant changes were observed. After two to three minutes of hyperventilation or after stabilization of respiratory rate and depth or end-expiratory CO_2 tension, one or two measurements of venous distensibility were made. The overbreathing was then stopped and observations were continued until control values returned. In the final 11 experiments hyperventilation was repeated with 5 or 7 per cent CO_2 and 21 per cent oxygen in the inspired gas. An effort was made to reproduce the same quality and volume of overbreathing which prevailed during the first part of the experiment. After one or two observations on venous distensibility and pressure the hyperventilation was stopped and the measurements were continued until control values returned.

After the experiment venous pressure-volume curves were constructed. The venous volume which existed during each measurement of distensibility was obtained by drawing a line perpendicular to the pressure axis from the natural venous pressure value (Figure 1). The venous volume which would have existed during hyperventilation if venous pressure had not changed was determined by applying the resting venous pressure value to the hyperventilation curve (Figure 1). Resting values for venous distensibility, volume and pressure represent the final set of resting measurements. Values reported during hyperventilation represent the first set of

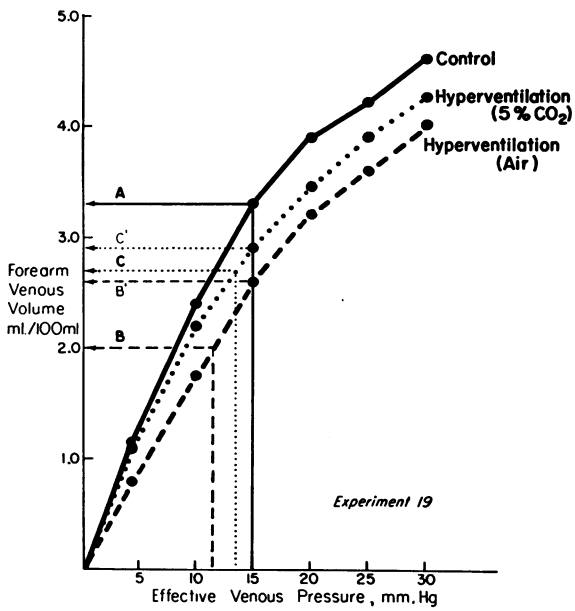

FIG. 1. VENOUS PRESSURE-VOLUME CURVES OBTAINED DURING A CONTROL PERIOD, DURING HYPERVENTILATION WHILE BREATHING AIR AND DURING HYPERVENTILATION WHILE BREATHING 5 PER CENT CO_2

A is the forearm venous volume during the control period. B is the forearm venous volume during hyperventilation while breathing air. B' is the forearm venous volume which would have existed during hyperventilation while breathing air if venous pressure had remained unchanged. C is the forearm venous volume during hyperventilation while breathing 5 per cent CO_2. C' is the forearm venous volume which would have existed during hyperventilation while breathing 5 per cent CO_2, if venous pressure had remained unchanged.

[4] Constructed by Sanborn Company, Waltham, Massachusetts.

TABLE I
Hyperventilation

Experiment No.	End-expiratory CO_2 tension			Ventilation		
	At rest	During hyperventilation		At rest	During hyperventilation	
	Breathing air		Breathing 5 or 7% CO_2*	Breathing air		Breathing 5 or 7% CO_2*
	mm. Hg	*mm. Hg*	*mm. Hg*	*L./min.*	*L./min.*	*L./min.*
10	37.8	27.4	62.2		24.4	38.4
11	42.3	25.6	58.7		28.4	48.1
12	46.0	22.4	65.2		43.5	65.9
13	46.9	25.4	57.0	7.8	28.8	47.5
14	34.3	22.3	53.0		27.0	38.4
15	34.9	21.7	39.9	5.1	45.2	38.0
16	42.1	22.6	45.8		25.0	37.1
17	45.8	26.8	52.6		23.5	21.5
18	48.3	29.3	52.2	5.8	16.3	19.9
19	48.2	25.2	55.2		22.6	30.5
20	43.1	25.8	49.8	6.5	21.2	26.0
Average	42.7	25.0	53.8	6.3	27.8	37.4
Standard Deviation	5.14	2.44	7.17	1.06	8.90	13.30

* Seven per cent CO_2 was used in Experiments 10 to 14; 5 per cent CO_2 was used in Experiments 15 to 20.

measurements obtained after hyperventilation was initiated.

Statistical analysis of the data was performed as described by Fisher (13).

RESULTS

Hyperventilation

End-expiratory CO_2 tension and respiratory minute-volume were not measured in the first 9 experiments. In the final 11 experiment (Table I) end-expiratory CO_2 tension averaged 42.7 mm. Hg during rest, 25.0 mm. Hg during hyperventilation while breathing air, and 53.8 mm. Hg during hyperventilation while breathing 5 or 7 per cent CO_2. The respiratory minute-volume averaged 27.8 L. per minute while overbreathing air and 37.4 L. per minute while overbreathing CO_2.

Venous pressure

Dependent forearm venous pressure fell in 17, increased in 2 and remained unchanged in 1 of 20 experiments during hyperventilation while breathing air (Table II). The average fall in pressure of 1.73 mm. Hg was significant ($p < 0.001$).

Venous pressure increased in 6, decreased in 3 and remained unchanged in 2 of the 11 experiments in which hyperventilation was repeated with 5 or 7 per cent CO_2 in the inspired gas. The average change in pressure was an *increase* of 0.77 mm. Hg. In the same 11 experiments venous pressure decreased in 10 and remained unchanged in 1 during hyperventilation while breathing air; the average change in pressure was a *decrease* of 2.24 mm. Hg. This venous pressure response observed while overbreathing air was significantly different from that observed while overbreathing CO_2 ($p < 0.001$).

Venous distensibility

Active venous constriction occurred in 19 of 20 experiments (Table II) during hyperventilation while breathing air. This reduction in venous distensibility was significant ($p < 0.001$) and averaged 0.87 ml. per 100 ml. of forearm tissue.

Active venous constriction occurred in each of the final 11 experiments during hyperventilation while breathing air and the decrease in venous distensibility averaged 0.60 ml. per 100 ml. Active venous constriction also occurred in each of these 11 experiments when hyperventilation was repeated while breathing 5 or 7 per cent CO_2 and the reduction in venous distensibility averaged 0.52 ml. per 100 ml. The venoconstrictor response observed while overbreathing air was not significantly different from that observed while overbreathing CO_2 ($p > 0.4$).

Venous volume

In 20 experiments the resting forearm venous volume averaged 2.88 ml. per 100 ml. of forearm

TABLE II

Forearm venous responses during hyperventilation

Experiment No.	Venous pressure			Venous distensibility			Venous volume				
	At rest	During hyperventilation		At rest	During hyperventilation		At rest	During hyperventilation			
		Breathing air	Breathing 5 or 7% CO_2		Breathing air	Breathing 5 or 7% CO_2		Breathing air		Breathing 5 or 7% CO_2	
	mm. Hg	*mm. Hg*	*mm. Hg*	*ml./100 ml.*	*ml./100 ml.*	*ml./100 ml.*	*ml./100 ml.*	*ml./100 ml.*	*ml./100 ml.**	*ml./100 ml.*	*ml./100 ml.†*
1	17.1	18.6		3.9	2.3		3.2	1.9	1.8		
2	9.5	9.1		5.4	3.9		3.1	1.9	2.1		
3	17.9	15.9		4.1	3.5		3.4	2.8	3.0		
4	16.0	13.0		4.3	3.8		3.3	2.7	3.0		
5	12.3	13.5		3.9	2.8		2.2	1.2	1.1		
6	15.7	10.4		4.9	4.9		3.4	2.9	3.2		
7	15.8	15.1		4.6	1.9		3.6	1.2	1.3		
8	17.2	17.0		4.1	2.5		3.2	1.7	1.7		
9	12.5	11.5		4.4	3.3		3.0	2.5	2.9		
10	13.7	11.0	15.5	3.1	2.2	2.4	2.1	1.2	1.3	1.6	1.5
11	14.0	11.3	17.5	3.8	3.6	3.3	2.6	2.3	2.6	2.3	2.0
12	8.8	5.0	8.5	3.5	2.6	3.0	1.5	0.4	0.8	1.2	1.3
13	10.0	6.3	12.0	4.9	4.7	4.3	3.1	2.2	3.1	2.8	2.5
14	12.5	11.3	15.0	4.1	3.9	3.3	2.7	2.2	2.3	2.0	2.2
15	9.0	9.0	9.0	3.5	2.4	2.5	1.9	1.0	1.0	1.2	1.2
16	8.5	7.5	9.0	3.5	2.6	3.1	1.4	0.9	1.0	1.1	1.0
17	12.5	11.0	12.5	5.7	5.3	5.5	3.8	3.5	3.6	3.5	3.5
18	15.0	13.0	15.5	3.0	2.8	2.9	2.3	1.7	1.9	2.2	2.2
19	15.0	11.5	13.5	4.6	4.0	4.3	3.3	2.0	2.6	2.7	2.9
20	14.0	11.5	13.5	6.4	5.4	5.8	4.4	3.5	3.7	3.8	3.9
Expers. 1–20 Average	13.35	11.63		4.29	3.42		2.88	1.99	2.20		
S. D.‡	2.965	3.405		0.865	1.128		0.956	0.889	0.926		
Expers. 10–20 Average	12.09	9.85	12.86	4.19	3.59	3.67	2.65	1.90	2.17	2.22	2.20
S. D.	2.545	2.541	3.033	1.097	1.167	1.153	0.942	1.003	1.045	0.921	0.946
Expers. 1–20 Aver. dif.§		−1.73			−0.87			−0.89	−0.68		
S. E.‖		0.391			0.148			0.110	0.130		
p¶		<0.001			<0.001			<0.001	<0.001		
Expers. 10–20 Aver. dif.§		−2.24	+0.77		−0.60	−0.52		−0.75	−0.47	−0.43	−0.45
S. E.		0.367	0.449		0.110	0.077		0.100	0.095	0.055	0.055
p		<0.001	>0.1		<0.001	<0.001		<0.001	<0.01	<0.001	<0.001
Expers. 10–20 Aver. dif.**			+3.01			+0.08				+0.32	−0.02††
S. E.			0.582			0.110				0.095	0.055
p			<0.001			>0.4				<0.01	>0.7

* Forearm venous volume which would have existed during air hyperventilation if venous pressure had not changed from the resting value.
† Forearm venous volume which would have existed during CO_2 hyperventilation if venous pressure had not changed from the resting value.
‡ Standard deviation.
§ Average difference between resting and hyperventilation values.
‖ Standard error.
¶ Probability.
** Average difference between air hyperventilation and CO_2 hyperventilation values.
†† Average difference between the venous volume change with air hyperventilation and with CO_2 hyperventilation if venous pressure had not changed from the resting value.

tissue. This volume decreased in each instance during hyperventilation while breathing air. The average decrease was 0.89 ml. per 100 ml. ($p < 0.001$) or 30.9 per cent of the average resting venous volume of the forearm. The reduction in volume which would have occurred if there had been only venous contriction and no change in venous pressure averaged 0.68 ml. per 100 ml. ($p < 0.001$) or 23.6 per cent of the average resting value. The reduction which would have occurred if there had been only a fall in venous pressure and no change in venous tone averaged 0.21 ml. per 100 ml. or 7.3 per cent of the resting value.

In the final 11 experiments the resting volume averaged 2.65 ml. per 100 ml. The average decrease was 0.75 ml. per 100 ml. while overbreathing air and 0.43 ml. per 100 ml. while overbreathing 5 or 7 per cent CO_2. The reduction in volume averaged 0.32 ml. per 100 ml. less while overbreathing 5 or 7 per cent CO_2 than while overbreathing air. This difference in response was significant ($p < 0.01$) and was attributed to the failure of venous pressure to fall while overbreathing CO_2 The venous volume decrease caused by venous constriction alone while overbreathing air averaged 0.47 ml. per 100 ml. and was not significantly different ($p > 0.7$) from the average decrease of 0.45 ml. per 100 ml. observed while overbreathing CO_2.

DISCUSSION

Burnum, Hickam, and McIntosh (14) found an appreciable increase in cardiac output during voluntary hyperventilation. This increase would require a pressure-volume readjustment within the venous system which would increase the availability of blood to the heart. It might be accomplished, at least in part, by peripheral venous constriction and shift of blood centrally. Recent studies (8, 10, 15) indicate that the veins are capable of active constriction to the extent that large amounts of blood may be moved from the limbs even in the face of an increased venous distending pressure. In the experiments reported here hyperventilation while breathing air was associated with shifts of blood from the limbs which averaged 30.9 per cent of the average resting venous volume of the forearm. Changes in volume attributable to active venous constriction alone averaged 23.6 per cent of the average resting forearm venous volume. Such shifts of blood from four extremities, if redistributed toward the heart, certainly would be consistent with an increased cardiac output.

Recent work strengthens the suggestion that peripheral venous constriction is an important component of the circulatory changes which occur during hyperventilation. Weissler, Leonard, and Warren (16) found the cardiac output to increase in recumbent subjects when tachycardia was induced by atropine. This response to atropine was significantly less when subjects were in the 60 degree upright position. The decreased response was attributed to pooling of blood in dependent parts of the body with resulting depletion of the central venous reservoir and a reduction in the amount of blood available to the heart. Gleason, Berry, Mauney, and McIntosh (17) observed that the increased cardiac output during hyperventilation was proportionate to the increase in heart rate in both the recumbent and the upright subject. These observations suggest that hyperventilation in the upright position is associated with a more adequate central venous reservoir. Peripheral venous constriction may serve to maintain or increase the availability of blood to the heart during overbreathing.

In our experiments venous constriction occurred to about the same extent during hyperventilation while breathing either air or 5 or 7 per cent CO_2. However, peripheral venous pressure did not fall while overbreathing CO_2 as it did while overbreathing air. This failure of venous pressure to fall accounts for the smaller shift of blood from the limbs when the inspired gas contained a high concentration of CO_2.

SUMMARY

Forearm venous distensibility, pressure and volume were measured before and during voluntary hyperventilation in 20 experiments. In 11 of these experiments the measurements were repeated during voluntary hyperventilation with 5 or 7 per cent CO_2 in the inspired gas. The following observations were made:

1. Forearm venous pressure decreased during hyperventilation while breathing air and averaged

a slight increase during hyperventilation while breathing CO_2.

2. Active forearm venous constriction occurred regularly during hyperventilation. The response observed while overbreathing air was not significantly different from that observed while overbreathing CO_2.

3. Blood shifted out of the forearm veins in each instance during hyperventilation while breathing air. This decrease in forearm venous volume averaged 30.9 per cent; the decrease attributable to venous constriction alone averaged 23.6 per cent; and the decrease caused by the fall in venous pressure alone averaged 7.3 per cent of the average resting value.

4. Blood also shifted from the forearm veins during hyperventilation while breathing CO_2. However, the volume change was significantly less than while overbreathing air because forearm venous pressure failed to fall.

5. It is suggested that peripheral venous constriction may serve to increase the availability of blood to the heart during hyperventilation.

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