

The Hemodynamic Effects of Changes in Blood Volume during Intermittent Positive-pressure Ventilation

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The hemodynamic effects of changes in blood volume during intermittent positive-pressure ventilation (IPPV) were studied in lightly anesthetized dogs following recovery from implantation of pulsed ultrasonic flow transducers on vena cava and aorta. Alveolar ventilation was maintained in excess of normal, and arterial carbon dioxide tension (P_{aCO_2}) was varied by alteration of concentration of inspired CO_2 . Blood volume was altered by the bleeding of 20 per cent of estimated blood volume, following this, by reinfusion of the shed blood plus an equal amount of dextran. During each of these periods low (peak airway pressure 10 cm H_2O , inspiratory-to-expiratory ratio 1:2) and high (peak airway pressure 30 cm H_2O , inspiratory-to-expiratory ratio 2:1) levels of ventilation were employed. The three variables, blood volume, P_{aCO_2} , and intrathoracic pressure, exerted separate effects on stroke volume (S.V.) and cardiac output (C.O.): C.O. and S.V. increased with increasing blood volume and with rising P_{aCO_2} , but decreased with increasing intrathoracic pressure. These findings suggest that the deleterious effects of high levels of intrathoracic pressure on cardiac output may be compensated by expanding blood volume.

THE INCREASE in extracardiac pressure produced by intermittent positive-pressure ventilation (IPPV) has been shown to decrease the distending pressure of the right ventricle and impede systemic venous return, resulting in lowered cardiac output.¹ Infusion of blood has been shown to cause an increase in the

mean circulatory pressure, resulting in a moderate rise in cardiac output.² However, there have been no systematic attempts to compensate for the circulatory effects of intermittent positive-pressure ventilation by expansion of blood volume. The purpose of the present study was to investigate the effects of alterations in blood volume on venous return and cardiac output of animals subjected to IPPV with known levels of P_{aCO_2} .

Materials and Methods

Pulsed ultrasonic flow transducers^{3,4} were implanted under aseptic conditions on the superior and/or inferior vena cava and on the descending thoracic aorta in mongrel dogs of both sexes. Following a minimum of seven days' recovery, the animals were lightly anesthetized with morphine, 1.5 to 2 mg/kg intramuscularly, and pentobarbital (Nembutal®), 10 to 12 mg/kg intravenously. A supplementary dose of 30 to 60 mg of pentobarbital was administered as required to maintain a stable anesthetic level throughout the four-to-five-hour experiment; however, no additional doses of anesthetic were given between determinations when results were compared. Tracheal intubation was accomplished and 100 per cent oxygen administered via a nonrebreathing system for 15 minutes for denitrogenation. End-tidal CO_2 concentration was monitored continuously from an 18-gauge needle in the endotracheal tube, using a Beckman LS-1 infrared carbon dioxide analyzer, sampling at a rate of 500 ml/min. A Bird 9X respirator with a recording ventimeter was used to generate the patterns of IPPV.

Aortic and vena caval blood flows were recorded from the implanted transducers. Intrathoracic pressure was measured by means of a

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TABLE 1. Changes in Cardiac Output and Stroke Volume

Blood Volume	Ventilation	Paco ₂	Mean Stroke Volume (Percent Control) 9 Experiments			Mean Cardiac Output (Percent Control) 9 Experiments			Arterial Blood Pressure**
			Mean	SD	SE	Mean	SD	SE	
Hypovolemic	Low	20	29	10.0	3.32	46	12.1	4.04	144/84
		40	36	10.7	3.57	51	13.7	4.59	140/80
		60	42	11.9	3.97	60	18.7	6.63	138/72
	High	20	17	4.2	1.42	32	10.1	3.36	***
		40	23	7.3	2.45	41	11.7	3.90	
		60	31	10.2	3.41	51	15.9	5.31	
Normovolemic	Low	20	86	12.0	4.02	92	10.2	3.42	155/90
		40	100*			100*			152/80
		60	109	11.7	3.90	124	16.6	5.53	150/76
	High	20	56	16.2	5.40	77	11.8	3.95	***
		40	66	14.3	4.78	81	9.1	3.06	
		60	83	14.9	4.97	103	14.7	4.90	
Hypervolemic	Low	20	109	20.8	6.96	114	48.2	16.0	172/110
		40	121	29.9	9.98	133	48.7	16.2	166/97
		60	144	31.4	10.49	171	51.4	17.1	160/86
	High	20	96	13.6	4.53	106	39.2	13.0	***
		40	110	26.4	8.81	118	44.3	14.7	
		60	132	32.4	10.81	154	43.7	14.5	

SD = standard deviation; SE = standard error.

* Assumed control.

** In torr; mean value for nine experiments.

*** Values for high-level ventilation not given because of wide pressure swings during the respiratory cycle.

20 × 25 mm flat silastic balloon (containing sufficient saline solution to allow coupling), which had been placed in the pleural space at the time of surgery. Airway pressure was monitored via an 18-gauge needle in the endotracheal tube, while arterial and venous pressures were measured by cannulation of femoral vessels, the venous catheter being placed in the abdominal vena cava. Arterial blood samples were obtained for determination of Pa_O₂, Pa_{CO}₂ and pH, using modified Clark, Severinghaus and Radiometer electrodes, respectively, and correction of gas tensions and pH for temperature was performed using the blood gas calculator of Severinghaus.⁵ Two-ml samples were collected at ten-minute intervals to confirm Pa_{CO}₂ as calculated from end-tidal CO₂ and to assure adequate oxygenation and absence of metabolic acidosis; less than 40 ml of blood were removed from the animals for sampling, and this volume was replaced with saline solution.

Nine separate studies were performed on five dogs in the supine position. Observations were made during two levels of ventilation, low (peak inspiratory pressure 10 cm H₂O, inspiratory-to-expiratory ratio 1:2) and high (peak inspiratory pressure 30 cm H₂O, inspiratory-to-expiratory ratio 2:1).

Each respiratory pattern was employed for ten-minute periods at Pa_{CO}₂ values of 20, 40 and 60 torr, with randomization of the sequence of levels of ventilation and Pa_{CO}₂ values at each blood volume. Pa_{CO}₂ was changed by altering the CO₂ concentration of inspired gas. Each respiratory pattern at each Pa_{CO}₂ value was applied with the animal in the normovolemic state. Following this, each animal was bled 20 per cent of his blood volume (18 to 20 ml/kg)⁶ and the experiment repeated, following a stabilization period of 30 minutes. For the final portion of the study, the blood which had been removed aseptically was infused, and in addition, an equal amount

of dextran was administered to make the animal hypervolemic. A stabilization period of 30 minutes was allowed before data were recorded. Flow in the descending aorta was considered to be representative of cardiac output, since only relative changes were of interest. Zero flow was obtained by acetylcholine cardiac arrest. Stroke volume was obtained by electronic integration of aortic flow and by planimetry, and averaged over several respiratory cycles. Cardiac output was obtained by multiplying the stroke volume times the heart rate. Changes in stroke volume and cardiac output were plotted as percentages of those values obtained at normal blood volume, P_{aCO_2} 40 torr, low level of ventilation (peak pressure 10 cm H_2O , inspiratory-to-expiratory ratio 1:2). Comparison of data between groups was made using Student's *t* test.

Results

Three separate effects on stroke volume (S.V.) and cardiac output (C.O.) were observed

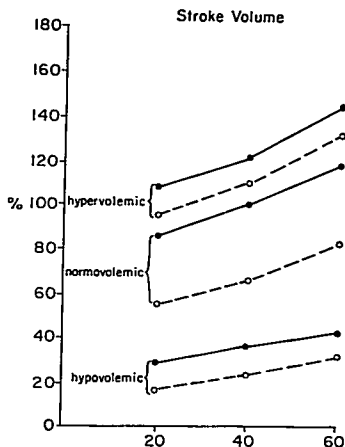


FIG. 1. Effects of level of ventilation, P_{aCO_2} and blood volume on stroke volume. Ordinate: Per cent change in stroke volume (average of nine experiments). Abscissa: P_{aCO_2} in torr. Solid line: low level of ventilation (peak pressure 10 cm H_2O , inspiratory-expiratory ratio 1:2); dashed line: high level of ventilation (peak pressure 30 cm H_2O , inspiratory-expiratory ratio 2:1).

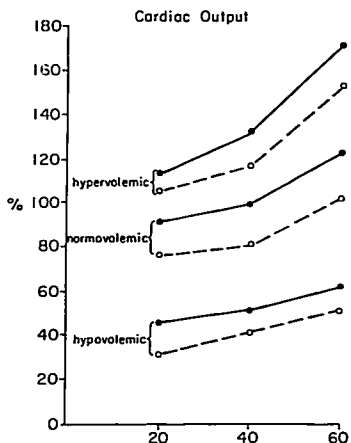


FIG. 2. Effects of level of ventilation, P_{aCO_2} and blood volume on cardiac output. Ordinate: Per cent change in cardiac output (average of nine experiments). Abscissa: P_{aCO_2} in torr. Solid line: low level of ventilation; dashed line: high level of ventilation.

served (table 1, figs. 1 and 2), the effects of increasing mean intrathoracic pressure (fig. 3), changes in P_{aCO_2} (fig. 4), and alteration in blood volume (fig. 5). Maximum values for S.V. and C.O. were recorded in the hypervolemic state, while minimum values were observed with the animal hypovolemic. At each blood volume, high levels of ventilation (peak pressure 30 cm H_2O , inspiratory-to-expiratory ratio 2:1) decreased the S.V. and C.O., compared with values obtained at low levels of ventilation (peak pressure 10 cm H_2O , inspiratory-to-expiratory ratio 1:2). At each blood volume and at each level of ventilation, changes in P_{aCO_2} also altered S.V. and C.O. with reference to control levels, with both variables increasing directly with increasing P_{aCO_2} (figs. 1 and 2).

In the hypovolemic animals, low levels of ventilation were associated with reduction in C.O. to 46 per cent (P_{aCO_2} 20 torr), 51 per cent (P_{aCO_2} 40 torr), and 60 per cent of controls (P_{aCO_2} 60 torr); at high levels of ventilation the values for cardiac output at 20, 40 and 60 torr P_{aCO_2} were, respectively, 32 per

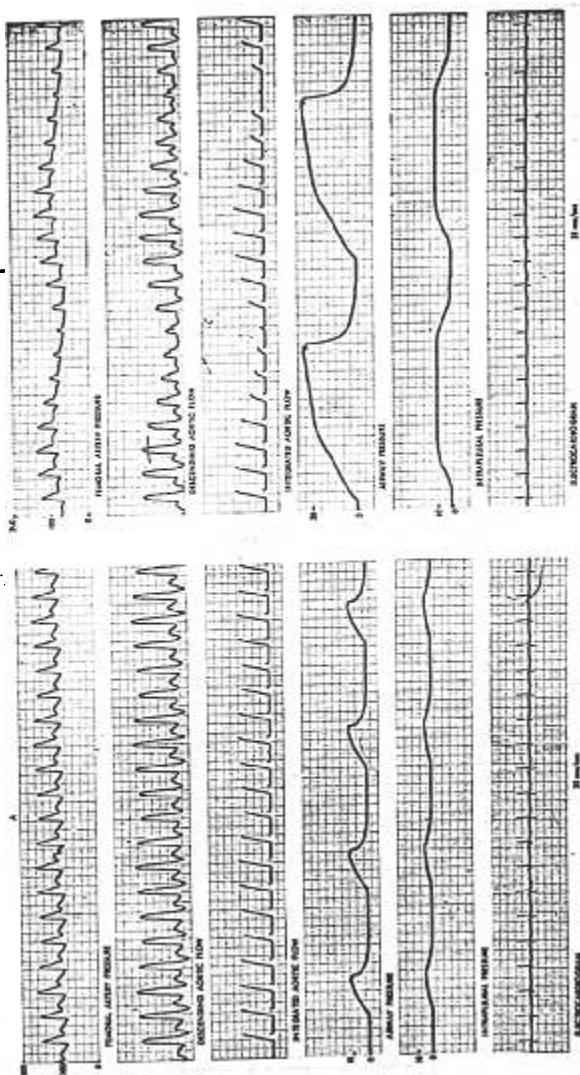


FIG. 3. Typical example of the effect of increasing intrathoracic pressure on aortic flow and arterial pressure. A (left) shows effect of low-level ventilation (peak airway pressure 10 cm H_2O , H_2O , inspiratory-expiratory ratio 2:1); B (right) shows effect of high-level ventilation (peak airway pressure 30 cm H_2O , H_2O , inspiratory-expiratory ratio 2:1). Femoral arterial pressure in mm H_2O ; airway, intrathoracic pressure in cm H_2O .

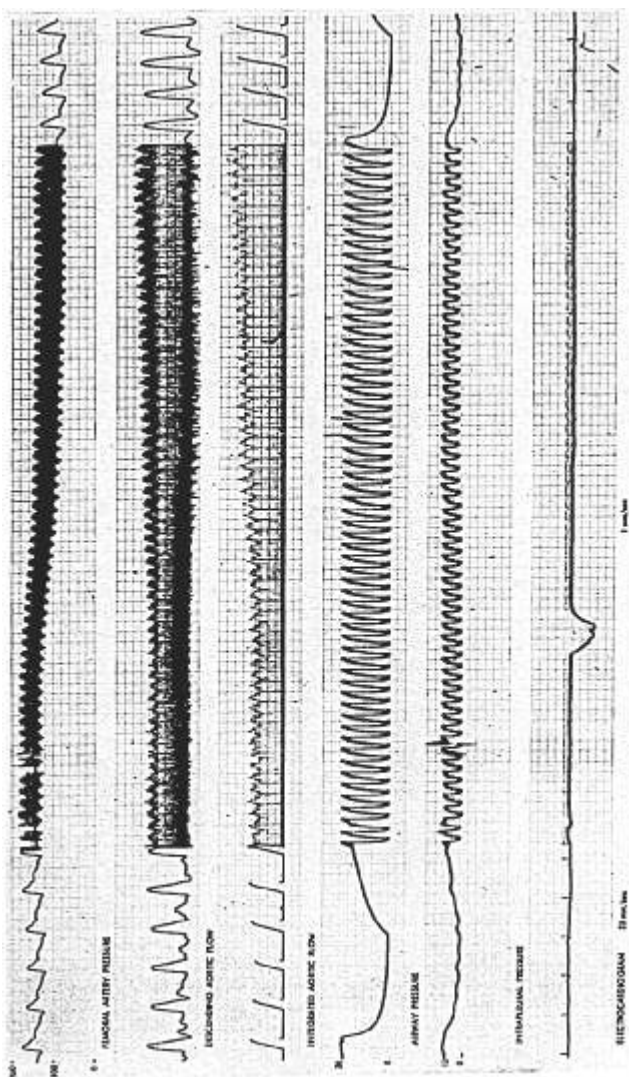


Fig. 4. Hemodynamic effect of increasing P_{aCO_2} by rapidly increasing CO_2 concentration in inspired gas. Femoral arterial pressure and femoral arterial flow, integrated arterial flow, and femoral venous pressure are recorded. P_{aCO_2} is 40 torr at beginning of record, 50 torr at end of record.

cent, 41 per cent and 51 per cent of controls (table 1, fig. 2). In the normovolemic animal, at low levels of ventilation, a P_{aCO_2} of 20 torr was associated with a cardiac output of 92 per cent, compared with the 100 per cent value obtained under conditions defined as control (low level of ventilation, P_{aCO_2} 40 torr); at P_{aCO_2} 60 torr the cardiac output was 124 per cent of control. During high levels of ventilation with normovolemia, the per cent cardiac output obtained at P_{aCO_2} values of 20, 40 and 60 torr, respectively, were 77 per cent, 81 per cent and 103 per cent. In the hypervolemic animal, cardiac output, at low levels of ventilation, was 114 per cent at P_{aCO_2} 20 torr, 133 per cent at P_{aCO_2} 40 torr, and 171 per cent at P_{aCO_2} 60 torr; the values at high levels of ventilation for 20, 40 and 60 torr, respectively, were 106 per cent, 118 per cent and 154 per cent. Comparable values were obtained for stroke volume (table 1, fig. 1).

Superior and/or inferior vena caval blood flow changes paralleled the changes in cardiac output. Venal caval blood flow was decreased by increasing mean intrathoracic pressure, decreasing blood volume, and decreasing P_{aCO_2} .

Changes in S.V. and C.O. at each P_{aCO_2} and to each condition of blood volume were compared at low vs. high levels of ventilation (table 2). The most significant differences were those secondary to changes in blood volume.

Changes in heart rate were more variable. Hypovolemia uniformly produced tachycardia of some degree; hypervolemia had a more variable effect on heart rate, a decrease in heart rate occurring in some animals in the hypervolemic state, while in others, heart rate increased. High levels of ventilation increased heart rates in all animals, as compared with low levels in both normovolemic and hypovolemic states. The hypervolemic state was more variable in this regard, the heart rate frequently being unchanged at high as compared with low levels of ventilation. It was of interest that the cardioacceleration of sinus arrhythmia occurred during expiration as intrathoracic pressure fell toward normal.

Arterial blood pressures were decreased by hemorrhage in all animals. Frequently, however, C.O. decreased by 50 per cent or more

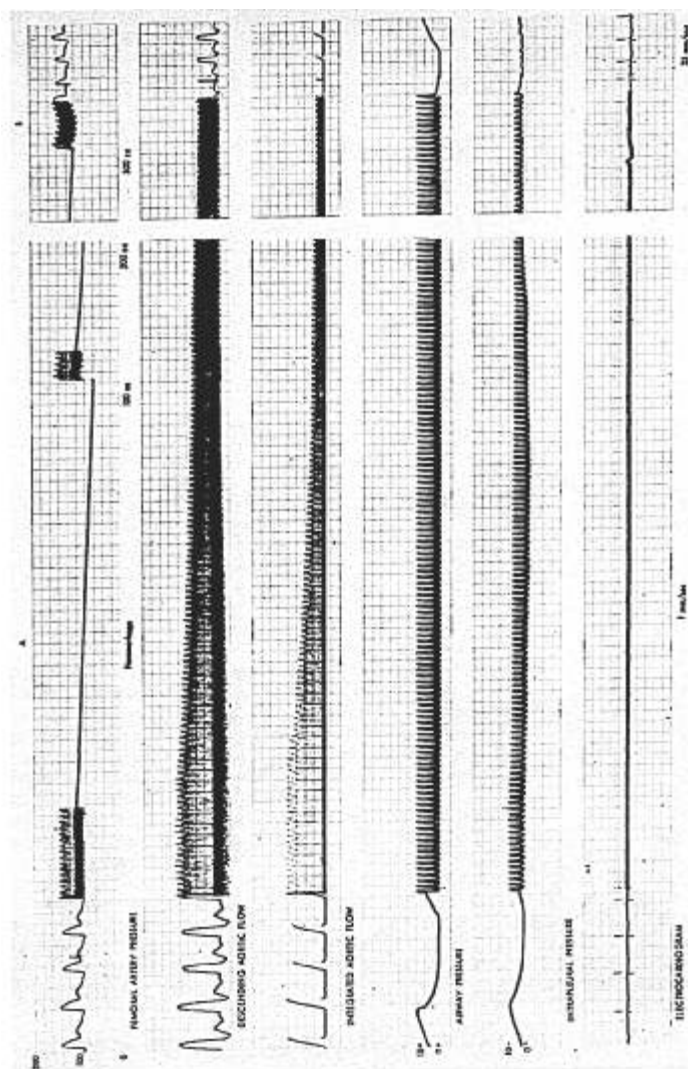
before any appreciable change in blood pressure was observed. Hypervolemia caused the arterial blood pressures to return to values which usually slightly exceeded those recorded during the normovolemic state. The average increase with hypervolemia in nine experiments in which systolic and diastolic arterial blood pressures were determined was approximately 15 torr.

Mean venous pressure (abdominal vena cava, average of nine experiments) at a low level of ventilation was 2.8 cm H_2O during hypovolemia, 3.6 cm H_2O in normovolemic animals, and 5.0 cm H_2O during hypervolemia.

Discussion

Hemodynamic consequences of induced changes in blood volume in dogs have been reviewed recently by Conway,⁷ who demonstrated an initial increase in C.O. and blood pressure, with increased blood volume; C.O. returned to normal levels after one to one and a half hours, with persistence of elevation of blood pressure. This experiment also demonstrated initial decreases in cardiac output and peripheral resistance after bleeding, with return to former levels after three hours, but did not, however, evaluate the effects of IPPV on the variables studied. In our experiments hypervolemia produced significant increases in cardiac output at any levels of ventilation and P_{CO_2} .

The mechanisms by which infusion of whole blood affects stroke volume and cardiac output have been detailed by Guyton *et al.*,² who showed that the infusion caused an increase in the mean circulatory pressure. The interaction between mean circulatory pressure, right atrial pressure, and venous return and cardiac output curves is somewhat complex, but a careful consideration of these relationships¹ permits at least qualitative predictions of the effects of varying degrees of IPPV and blood volume changes. Specifically, Guyton² demonstrated that the increase in intrathoracic pressure produced by IPPV decreased the distending pressure of the right ventricle (intracardiac pressure minus intrathoracic pressure) and elevated right atrial pressure, causing a decrease in venous return and decreased cardiac output. Ordinarily, compensatory



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Fig. 5. Changes in femoral arterial pressure, aortic flow, renal artery pressure, renal blood flow, aortic pressure, aortic flow, and renal vein pressure during the administration of 300 ml of 0.9% NaCl solution. The graphs show the response of these variables to the volume change. The left column shows the response to the first 150 ml, and the right column shows the response to the remaining 150 ml. The graphs are arranged in two columns and seven rows. The left column contains: 1. Femoral Artery Pressure (0-100 mmHg), 2. Descending Aortic Flow (0-300 ml/min), 3. Renal Artery Pressure (0-100 mmHg), 4. Renal Blood Flow (0-300 ml/min), 5. Aortic Pressure (0-100 mmHg), 6. Aortic Flow (0-300 ml/min), 7. Renal Vein Pressure (0-100 mmHg). The right column contains: 8. Femoral Artery Pressure (0-100 mmHg), 9. Descending Aortic Flow (0-300 ml/min), 10. Renal Artery Pressure (0-100 mmHg), 11. Renal Blood Flow (0-300 ml/min), 12. Aortic Pressure (0-100 mmHg), 13. Aortic Flow (0-300 ml/min), 14. Renal Vein Pressure (0-100 mmHg). Each graph shows a baseline period followed by a period of rapid change, likely corresponding to a volume intervention.

TABLE 2. Significance of Differences in Cardiac Output and Stroke Volume (*P* Value)

	Paco ₂ 20 torr		Paco ₂ 40 torr		Paco ₂ 60 torr	
	C.O.	S.V.	C.O.	S.V.	C.O.	S.V.
Effect of ventilation: high vs. low,						
Hypovolemic	<0.05	<0.01	<0.05	<0.05	>0.1	>0.1
Normovolemic	<0.05	<0.01	<0.05	<0.01	<0.05	<0.01
Hypervolemic	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1
	20-40 torr		40-60 torr		20-60 torr	
	C.O.	S.V.	C.O.	S.V.	C.O.	S.V.
Effect of Paco ₂ :						
Hypovolemic Low V	>0.1	>0.1	>0.1	>0.1	<0.05	<0.05
High V	>0.1	>0.1	>0.1	>0.1	<0.05	<0.01
Normovolemic Low V	—	—	—	—	<0.01	<0.01
High V	>0.1	>0.1	<0.01	<0.05	<0.01	<0.01
Hypervolemic Low V	>0.1	>0.1	>0.1	>0.1	<0.05	<0.05
High V	>0.1	>0.1	>0.1	>0.1	<0.05	<0.05
	Hypo-normovolemic		Normo-hypervolemic		Hypo-hypervolemic	
	C.O.	S.V.	C.O.	S.V.	C.O.	S.V.
Effect of blood volume						
Paco ₂ 20 torr Low V	<0.001	<0.001	<0.05	<0.05	<0.001	<0.001
High V	<0.001	<0.001	<0.05	<0.001	<0.001	<0.001
40 torr Low V	—	—	—	—	<0.001	<0.001
High V	<0.001	<0.001	<0.05	<0.001	<0.001	<0.001
60 torr Low V	<0.001	<0.001	<0.05	<0.02	<0.001	<0.001
High V	<0.001	<0.001	<0.01	<0.01	<0.001	<0.001

C.O. = cardiac output; S.V. = stroke volume.

mechanisms occur rapidly, tending to return the cardiac output toward normal. These mechanisms include a shift of a portion of blood from the lungs and heart into the systemic circulation as well as vasoconstriction via autonomic reflexes.¹

The effect of IPPV, from Guyton's curves, would be exaggerated by hypovolemia, although this combination was not actually reported by his laboratory. Carr and Essex⁸ showed a close relationship between blood volume, venous pressure and survival during positive-pressure ventilation. They measured arterial and venous pressure in dogs subjected to positive-pressure ventilation and demonstrated that hemorrhage decreased the animal's tolerance to increased intrathoracic pressure, which was improved by partial retransfusion. Our study confirms these findings and extends

the earlier study by demonstrating that graded increases in blood volume increase cardiac output and stroke volume during comparable levels of IPPV.

It is worth noting that the dog is better equipped to withstand IPPV or hemorrhage than man. The dog's spleen is highly contractile and is capable of autotransfusion of as much as 19 per cent of the total blood volume⁹; it delivers blood of high hematocrit in response to a wide variety of stressful stimuli.¹⁰ The human spleen has relatively little reservoir function, which presumably would exaggerate the effects on cardiac output of IPPV and hemorrhage, as compared with our results in dogs. In addition, our animals were lightly anesthetized with reflexes intact,¹¹ whereas deep surgical anesthesia in man may inhibit or abolish compensatory reflex mechanisms.¹²

Thus, the anesthetized, hypovolemic human patient may be particularly sensitive to the deleterious cardiovascular effects of IPPV.

Previously, we demonstrated progressive decreases in S.V. and C.O. with increasing mean intrathoracic pressure during varying levels of IPPV at constant P_{aCO_2} .¹³ We subsequently showed a separate effect of increasing S.V. and C.O. with increasing P_{aCO_2} at comparable levels of IPPV,¹⁴ and comparable changes in cardiac output with alterations in P_{aCO_2} in anesthetized man have been shown recently.¹⁵ The present thus adds a third factor influencing S.V. and C.O. during IPPV, the blood volume.

From a clinical point of view, it is clear that hypovolemic patients represent a group with increased risk when surgical anesthesia with IPPV is required. In addition to the obvious measures of blood or plasma volume expanders, simple postural maneuvers are helpful. Berneus *et al.*¹⁶ demonstrated that the head-down or Trendelenburg position restored cardiac output in patients during IPPV by restoring the central blood volume. We have shown that simple elevation of the legs, with the trunk level, accomplished a comparable restoration without the disadvantages of the Trendelenburg position.¹⁷ Vasoconstrictor therapy also has been demonstrated as an effective method of increasing the central blood volume and cardiac output,¹⁸ although this method is less physiologic except in situations in which reflexes have been abnormally abolished or inhibited.

In summary, IPPV, particularly with high pressures and prolonged inflation cycle, is a hazard to normal cardiac function, and its effects, which will be exaggerated by respiratory alkalosis, may be disastrous to a patient with hypovolemia.

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