Hemodynamic Effects of Intermittent Positive Pressure Respiration

Beverly C. Morgan, M.D., Wayne E. Martin, M.D.,† Thomas F. Hornbein, M.D.,‡ Edward W. Crawford, M.D.,§ Warren G. Guntheroth, M.D.¶*

The hemodynamic effects of intermittent positive pressure ventilation were studied in lightly anesthetized dogs following recovery from implantation of pulsed ultrasonic flow transducers on the aorta and vena cava. A partial rebreathing system was utilized to maintain constant Pa_{CO_2}. Data were obtained during spontaneous respiration and using a respirator, with peak airway pressures of 10, 20 and 30 cm. of water, inspiratory to expiratory ratios of 1:2, 1:1 and 2:1. Maximum values for stroke volume and cardiac output occurred during spontaneous breathing. Cardiac output and aortic stroke volume decreased with increasing airway pressure and increasing inspiratory to expiratory ratios. Venous return was inhibited by increasing pressure, and changes in vena caval flow were reflected in changes in aortic flow within the time of two heart beats. The circulatory effects of positive pressure breathing are related to the mean intrathoracic pressure and the effect on venous return.

FOLLOWING demonstration in animals [1, 2] of the impairment of circulation by positive pressure breathing, similar effects on cardiac output in man have been demonstrated by application of the Fick principle,[3, 4] ballistocardiography [5] and indicator dilution methods. Cournand and his co-workers [3] observed an inverse relationship between increasing mask pressure and cardiac output during intermittent positive pressure breathing. The decrease in cardiac output was closely related to mask pressure and could be improved by an expiratory phase of adequate duration. In acute experiments in animals, Brecher [7] demonstrated by means of a bristle flowmeter, that positive pressure breathing decreased venous return. In these studies, arterial carbon dioxide tension (Pa_{CO_2}) undoubtedly varied as the character of ventilation was changed; variation in Pa_{CO_2} may have contributed to the change in cardiac output associated with positive pressure breathing.

The present study was designed to evaluate the effects of varying degrees of intermittent positive pressure breathing (IPPB) on aortic and vena caval blood flow in intact animals. At constant Pa_{CO_2} we attempted to define a ventilation pattern that would produce minimal interference with circulation.[8]

Materials and Methods

Pulsed ultrasonic flow transducers were implanted [9, 10] on the superior vena cava and on the descending thoracic aorta in 6 mongrel dogs weighing 18 to 26 kg.; in one animal, a transducer was placed on the left pulmonary artery. The pulsed ultrasonic flowmeter is based upon the principle that sound waves passing through moving fluid travel with greater net velocity downstream than upstream. Bursts of ultrasonic waves (3 megacycles) travel along the path between two barium titanate crystals mounted diagonally

* Assistant Professor, Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington.

† Senior Resident, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington.

‡ Assistant Professor, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington. Supported by PHS Research Career Program Award HE-9617-01.

§ Assistant Professor, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington.

¶ Associate Professor, Department of Pediatrics, Head, Division of Pediatric Cardiology, University of Washington School of Medicine, Seattle, Washington.

Accepted for publication March 18, 1966. This work was supported by the Washington State Heart Association and U. S. Public Health Service Grant HE-03998-08.

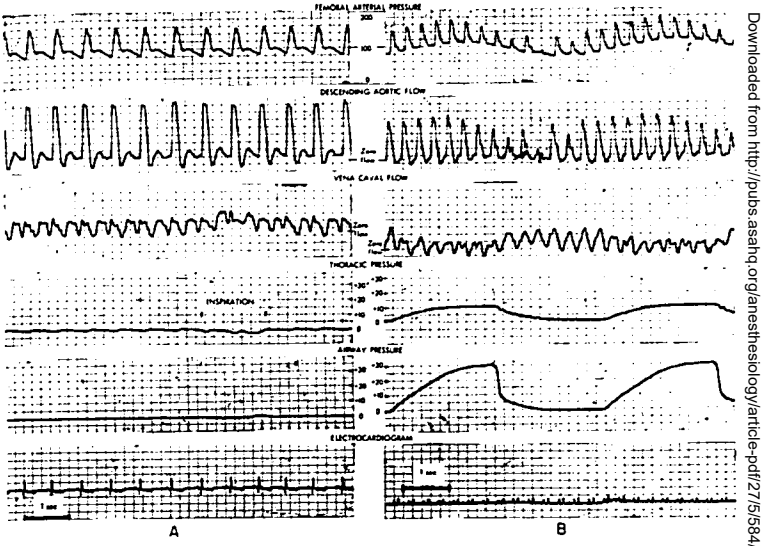

FIG. 1. Effects of spontaneous respiration (A) and positive pressure ventilation (B). Note relatively slight changes in intrathoracic pressure with normal respiration; in B, note wide swing in arterial blood pressure.

across a bivalve plastic cylinder, alternating in direction 400 times per second. When there is no motion in the fluid between the crystals, the transit time of sound is equal in both directions; with movement of the fluid, the velocity of flow is linearly related to the difference between the transit times upstream and downstream.

Five to 39 days postoperatively, when the animals had recovered, they were lightly anesthetized with morphine 1–1.5 mg./kg. intramuscularly and pentobarbital 10–12 mg./kg. intravenously; no attempt was made to evaluate the effects of IPPB upon a background of other anesthetics. Following tracheal intubation with a cuffed tube (10–12 mm. diameter), the animals breathed 100 per cent oxygen from a nonrebreathing system for 15 minutes to assure denitrogenation. Blood flows were recorded from the previously implanted transducers, and pleural pressure was recorded from a flat silastic balloon which had been placed in the pleural space at the time of surgery. Airway pressure was monitored via an 18 gauge needle inserted in the endotracheal tube. Arterial pressure was measured via a catheter in the femoral artery; this catheter also permitted anaerobic sampling of blood for determinations of P_{O_2}, P_{CO_2} and *p*H using a modified Clark, a Severinghaus and a Radiometer electrode, respectively.

By adjustment of the flow of oxygen into a container from which the animal rebreathed, inspired CO_2 concentrations could be altered to maintain arterial P_{CO_2} at control values in spite of varying minute volume of ventilation. Constancy of Pa_{CO_2}, as ascertained by intermitten blood gas analyses, was facilitated by continuous monitoring of airway P_{CO_2} using a Beckman LS-I infrared carbon dioxide analyzer. A Bird Mark 9X respirator was used in conjunction with a recording Ventimeter to

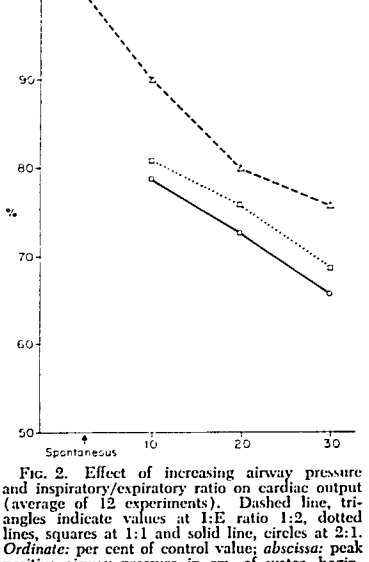

FIG. 2. Effect of increasing airway pressure and inspiratory/expiratory ratio on cardiac output (average of 12 experiments). Dashed line, triangles indicate values at 1:E ratio 1:2, dotted lines, squares at 1:1 and solid line, circles at 2:1. *Ordinate:* per cent of control value; *abscissa:* peak positive airway pressure in cm. of water, beginning with spontaneous respiration.

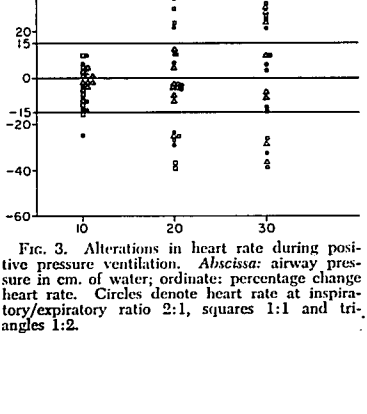

FIG. 3. Alterations in heart rate during positive pressure ventilation. *Abscissa:* airway pressure in cm. of water; ordinate: percentage change heart rate. Circles denote heart rate at inspiratory/expiratory ratio 2:1, squares 1:1 and triangles 1:2.

generate and record the breathing patterns used.

Twelve studies were performed, and observations were made during spontaneous respiration as well as during intermittent positive pressure breathing with peak inspiratory pressures of 10, 20 and 30 cm. of water. At peak inspiratory pressures, inspiratory to expiratory time ratios of 1:2, 1:1 and 2:1 were employed for 10-minute periods. The sequence was randomized and spontaneous breathing periods were utilized every 30 minutes to allow recovery and stabilization.

Zero level for vena caval flow was determined by intravenous administration of acetylcholine in dose sufficient to produce transient cardiac arrest (3–5 mg.). Stroke volume was determined by planimetric integration. Cardiac output was calculated as the product of stroke volume and heart rate; each determination was made over several respiratory cycles.

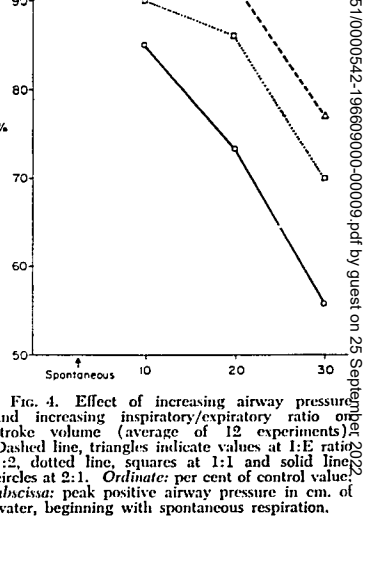

FIG. 4. Effect of increasing airway pressure and increasing inspiratory/expiratory ratio on stroke volume (average of 12 experiments). Dashed line, triangles indicate values at 1:E ratio 1:2, dotted line, squares at 1:1 and solid line, circles at 2:1. *Ordinate:* per cent of control value; *abscissa:* peak positive airway pressure in cm. of water, beginning with spontaneous respiration.

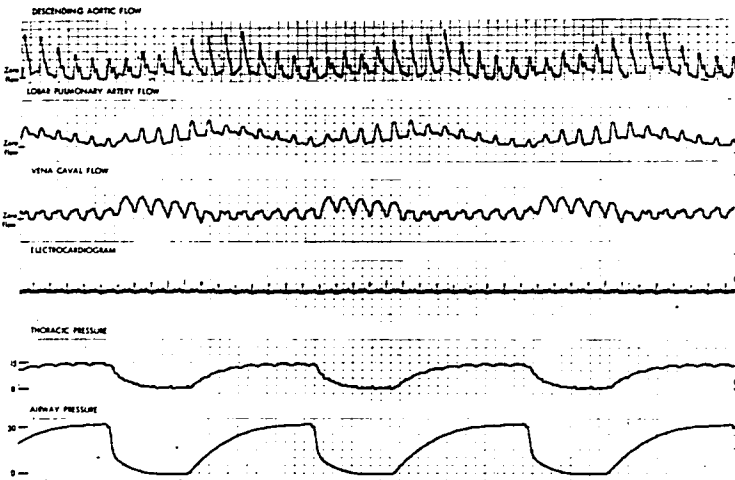

FIG. 5. Effects of positive pressure ventilation on vena caval, left pulmonary arterial and aortic flow.

Flow in the descending aorta was considered to be an adequate representation of cardiac output since only relative changes were of interest. Data obtained were expressed as per cent of control (spontaneous respiration).

Results

The blood flow patterns observed during spontaneous respiration were similar to those previously described.[11] Maximum values for stroke volume, cardiac output, and venous return occurred during spontaneous respiration. The effect of increasing airway pressure on aortic and vena caval flow is illustrated in figure 1. At lower airway pressures, vena caval flow was mildly affected. At peak airway pressures of 30 cm. of water, vena caval flow approached zero level, followed by a surge of forward flow as airway pressure fell toward zero. During intermittent positive pressure ventilation, therefore, the surge in vena caval blood flow which normally occurs with spontaneous inspiration occurred during expiration at a time when intrathoracic pressure was approaching zero (fig. 1).

Cardiac output decreased progressively with increase in airway pressure and with prolongation of inspiratory to expiratory ratios; at peak airway pressure of 30 cm. of water, inspiratory to expiratory ratio 2:1, cardiac output (average of 12 experiments) was 35 per cent below control (fig. 2). The decrease in aortic stroke volume was more pronounced than that observed in cardiac output because of the frequent occurrence of compensatory tachycardia (fig. 3); at peak airway pressure of 30 cm. of water, inspiratory to expiratory ratio 2:1, aortic stroke volume (average of 12 experiments) was 44 per cent below control (fig. 4).

Left pulmonary arterial flow was recorded in one animal (fig. 5) to compare the timing of alterations in the pulmonary and systemic circulation. An increase in vena caval flow was observed within one heart after the positive pressure was released. Pulmonic flow began to increase within one beat of increased caval flow, and aortic flow was augmented within two beats of caval; peak aortic and pulmonic flow were delayed several beats,

TABLE 1. Relation of Airway Pressure to Intrathoracic Pressure (measurements in cm. H_2O)

Animal	Postoperative Day	Intrathoracic Pressure at Airway Pressure of 10	20	30
S 9	7	3	8	13
S 11	5	4	6	10
	9	4	7	9
	12	4	6	9
S 12	15	5	10	15
	17	6	12	16
	39	5	10	15
S 13	15	5	10	15
	17	3	6	10
	30	6	11	16
S 15	6	6	10	16
S 16	6	4	7	10
	9	4	7	10
	14	6	12	20

however. The right ventricular stroke volume, as judged from the flow pulse in the left pulmonary artery, was maximum at the end of expiration and peak left ventricular stroke volume was reached as a volume of blood was displaced through the lung to the left heart, two beats later. The greatest delay between increased flow in the cava and increased flow in the aorta was the interval of only two heart beats.

Systolic and diastolic femoral arterial pressure at peak airway pressure of 10 cm. of water did not vary more than 10 mm of mercury from control values. However, at 30 cm. of water peak airway pressure, definite pulsus paradoxus occurred with a decrease in systolic, diastolic and pulse pressures (fig. 1B).

Heart rate showed minimal variation from control at peak airway pressure of 10 cm. of water (fig. 3). At peak airway pressure of 20 cm. of water, several animals showed deviation from control values greater than 15 per cent, with a decrease in heart rate occurring almost as commonly as an increase, while peak pressures of 30 cm. of water were often associated with tachycardia.

Intrathoracic pressure varied during positive pressure breathing from 30 to 66 per cent of airway pressure. The percentage of airway pressure transmitted to the pleural space remained relatively constant in any one animal over the range of pressures and ventilatory patterns (table 1).

Utilizing the controlled partial rebreathing system, end-expiratory CO_2 was maintained constant at control levels (4.2 to 6 per cent); maximum variation during any experiment was 0.2 per cent. Arterial P_{CO_2} during spontaneous respiration varied from 39–50 mm. of mercury, while maximum variation during an experiment was limited to ± 3 mm. of mercury. Pa_{O_2} was 425–550 mm. of mercury. Control arterial *p*H was 7.32 to 7.37, with a maximal variation of $\pm$ 0.02.

Discussion

The impairment of circulation by positive pressure breathing has been demonstrated by numerous techniques in man and animals. The mechanisms responsible for these changes have been subject to speculation. Increased pulmonary vascular resistance has been implicated in the fall in cardiac output,[12, 13, 14] while others have suggested that decreased right heart filling was responsible.[1, 4] In previous studies of the effect of positive pressure breathing on cardiac output, Pa_{CO_2} has not been maintained constant. Otis and his co-workers[15] showed a fall in Pa_{CO_2} produced by hyperventilation, associated with a fall in cardiac output. The present study was performed under conditions of constant Pa_{CO_2} to evaluate the mechanical effects on the circulation independent of changes in P_{CO_2} which may be associated with IPPV. Whether the hypocapnia associated with IPPV results in further impairment of cardiac output remains to be investigated.

In experiments on animals with an open chest, Hubay, Brecher, and Clements[14] concluded that increased pulmonary vascular resistance was primarily responsible for the reduction in cardiac output. However, Werko found that changes in pulmonary vascular resistance were small and apparently unrelated to changes in cardiac output in normal man subjected to IPPB. Even with considerably increased resistance to flow, such as

surgical constriction of the main pulmonary artery, there was no fall in cardiac output, provided that venous return was not restricted.[16]

Opening the chest has been shown to decrease cardiac output in a manner similar to positive pressure ventilation when the chest is closed.[17] In both instances there is an increase in the average extracardiac pressure (by the loss of normally negative intrathoracic pressure when the chest is opened), causing an immediate rise in venous pressure and a decrease in venous return.[18] In addition, the "cardiac output curve" is adversely affected since the effective filling pressure of the ventricles is reduced.[17] Compensation for the decrease in cardiac output may be produced by an increase in sympathetic tone, and perhaps by increased muscular activity,[17] tending to increase the driving pressure ("mean circulatory pressure") returning blood to the heart.

In our investigation, increased intrathoracic pressure produced an immediate decrease in vena caval flow, followed by a decrease in pulmonary arterial and then aortic flow. Vena caval flow decreased progressively with increasing intrapleural pressure; as pleural pressure fell during the expiratory phase, flow from the cavae increased, and the sequence described above was reversed.

Our data confirm the importance of the time relation of the inspiratory to expiratory phase of the respiratory cycle demonstrated by Cournand *et al.*[3] The effect of positive pressure breathing on cardiac output is related to the mean intrathoracic pressure over a complete respiratory cycle. Prolonged inflation (such as 2:1 ratio, inspiration to expiration) with modest positive pressure (20 cm. of water) reduced cardiac output more than higher pressure for a shorter period (1:2 ratio at 30 cm. of water).

The animals, although anesthetized, were all in excellent health at the time of study, and significant alteration in circulatory function occurred. These observations may significantly underestimate the potential effects of IPPB, since the fall in cardiac output which occurs has been shown to be accentuated when the capacity for reconstituting the gradient from peripheral veins to the heart (increasing the "mean circulatory pressure"[17]) is impaired, such as in hemorrhagic shock, sympathetic blockade (high spinal anesthesia), or anesthetic depression.[19]

Summary

Hemodynamic effects of varying degrees of intermittent positive pressure ventilation were studied in lightly anesthetized dogs following recovery from implantation of pulsed ultrasonic flow transducers on aorta and vena cava. Data were obtained during spontaneous respiration, and with the use of a Bird Mark 9X respirator at constant ventilatory rate, and peak airway pressures of 10, 20 and 30 cm. of water. At each pressure, inspiratory to expiratory ratios of 1:2, 1:1 and 2:1 were applied. A partial rebreathing system was utilized to maintain end-expiratory P_{CO_2} constant.

Maximum values for stoke volume and cardiac output occurred during spontaneous breathing. As airway pressure was increased, aortic stroke volume and cardiac output progressively decreased. At each airway pressure, decrease in stroke volume and cardiac output was accentuated by increasing the inspiratory to expiratory ratio. At peak airway pressure of 30 cm. of water, inspiratory to expiratory ratio of 2:1, the stroke volume was reduced 44 per cent, while cardiac output was 33 per cent below control. Venous return was inhibited by increasing pressure, approaching zero level with peak airway pressure of 30 cm. of water; the forward surge of vena caval flow occurred during expiration. Changes in venous flow were reflected in changes in aortic flow within the time of two heart beats.

The circulatory effects of positive pressure breathing are related to the mean intrathoracic pressure and the effect on venous return.

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PHARMACOGENETICS Hereditary factors may modify the response of man and animal to drugs. The prolongation of response to succinylcholine in the presence of genetic variants of pseudocholinesterase has been extensively analyzed. About 50 per cent of the patients who reacted in the operating room with prolonged effects from succinylcholine were homozygotes for atypical pseudocholinesterase. Fifteen per cent of the cases were due to one or other of the genetic variants of this enzyme, while in the remaining cases one has to look for other causes. During the past years, considerable progress has been made in understanding the defects of porphyria and thereby the possibility of a disastrous action to barbiturates. There are a number of hereditary predispositions to an abnormal drug effect in which the biochemistry of the damaging mechanism is not understood. Besides individual differences in the response to drugs, there may also be racial differences. Most important is perhaps the simple reminder from genetic studies that an abnormal drug response which is rare in a population may recur within families and particularly within groups of siblings. (*Kalow, W.: Pharmacogenetic Problems in Anesthesia, Der Anaesthesist 15: 13 (Jan.) 1966.*)