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A Preliminary Report on Experimental Studies of Continuous Positive-pressure Ventilation (CPPV) and High-frequency Positive-pressure Ventilation (HFPPV)

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ABSTRACT

In a previous study on dogs the ventilatory pattern of a conventional respirator (SV-900) was compared with that produced by a prototype system for volume-controlled high-frequency positive-pressure ventilation (HFPPV). At comparable arterial carbon dioxide tensions the intratracheal peak and mean pressures and the total peripheral vascular resistance (TPR) were higher but cardiac output (CO), stroke volume (SV) and oxygen flux (OF) lower during ventilation with SV-900 at a ventilatory frequency of 20/min than during HFPPV at a ventilatory frequency of 60/min.

In the present study on 10 dogs, using ventilatory frequencies (f) of 20, 40, 50 and 60, the experimental conditions were light pentobarbital anaesthesia and normoventilation. With a prototype system (system H), functionally with no compression volume, the tidal volume of the ventilator system ($V_{T_{TOT}}$) was equal to the effective tidal volume (V_{T_E}) and by increasing f to 60/min, V_{T_E} could be reduced to only 65% of that at f=20/min and the peak and mean airway pressures were consequently reduced.

The alveolar gas distribution was studied by mass-spectrometric analyses of pulmonary nitrogen clearance curves in terms of nitrogen clearance ratio (NCR). With ventilator system H, functionally with no compression volume, the alveolar gas distribution was significantly improved in comparison with the conditions with the conventional respirator system (SV-900). It seems, therefore, that ventilation with a ventilator which has a negligible compression volume and therefore can be set at a high ventilatory frequency, may cause less interference with cardio-circulatory function, and with the improved intrapulmonary gas distribution which it implies, offers advantages in the critically ill patient.

INTRODUCTION

During spontaneous breathing the pressure gradient over the lungs and great veins promotes the venous return and diastolic filling of the heart. In intermittent positive-pressure ventilation (IPPV) and continuous positive-pressure ventilation (CPPV), however, the intra- and transpulmonary pressure relationships become altered in comparison with those normally occurring in spontaneous breathing. As a consequence the respiratory rate becomes important as a factor determining the mean intrathoracic pressure (12, 13, 16). It is a well known fact that the circulatory effects of mechanical ventilation are often closely related to direct and indirect effects of the increased mean

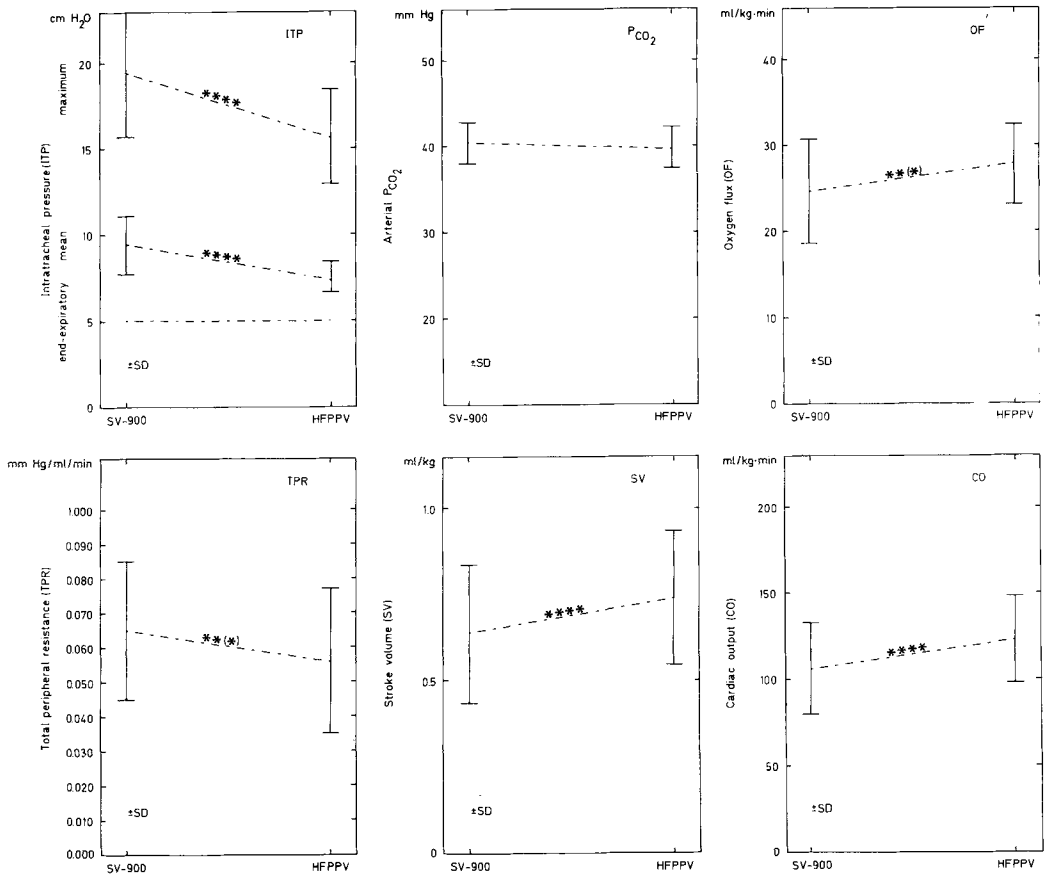

Fig. 1. Mean values (±SD) of measured and calculated parameters in 5 dogs during fairly deep pentobarbital anaesthesia and ventilation with SV-900 at a ventilatory frequency (f) of 20/min and a prototype system (system G) for HFPPV (13) at f of 60/min, with both ventilators at a PEEP of 5 cm H_2O, and with an arterial PCO_2 of about 40 mm Hg. The intratracheal pressures were significantly lower at comparable arterial carbon dioxide tensions. The differences noted in the other parameters in the figure, i.e. stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR) and oxygen flux (OF), are due to the different ventilatory patterns. Levels of significance are indicated as described under "Methods". Modified and reproduced by permisson (7).

intrathoracic pressure, and due to the reflex control mechanisms of the peripheral circulation (1), IPPV/CPPV is usually accompanied by peripheral vasoconstriction (4, 11, 18). The ventilatory and circulatory effects of IPPV have therefore been the subject of extensive experimental and clinical investigations.

It is well documented that those IPPV/CPPV patterns which promote uniform gas distribution in the lungs may have negative circulatory effects, as they may in various ways affect the cardiac output, functional residual capacity and distribution of ventilation and perfusion in the lungs, thereby altering

the physiological dead space and venous admixture. In simplified terms, it may be stated (see Fig. 3) that the ventilatory pattern in IPPV is the result of the combined conditions created by the ventilator and the pulmonary systems (14, 15, 16).

In a previous study in dogs (7) comparisons were made between the ventilatory patterns of a conventional volume-controlled respirator, Siemens-Elema Servo Ventilator (SV-900) and a prototype of a ventilator system, system G (13), for volume-controlled high-frequency positive-pressure ventilation, HFPPV (9, 12). At comparable arterial carbon dioxide tensions the intratracheal peak and mean pressures and total peripheral vascular resistance were higher, but the cardiac output, stroke volume and oxygen flux lower during ventilation with SV-900 (ventilatory frequency 20/min) than during HFPPV (ventilatory frequency 60/min). This is illustrated in Fig. 1.

In the present study on 10 dogs further comparisons were made between the ventilatory patterns of SV-900 and the prototype of a ventilator system for volume-controlled ventilation, system H (13). Ventilatory frequencies (f) of 20, 40, 50 and 60 per min were used, and the experimental conditions were otherwise identical, i.e. light pentobarbital anaesthesia and normoventilation. A preliminary report (17) has been presented.

METHODS AND PROCEDURES

The animal experiments of this investigation were performed in October 1977.

Animals and anaesthesia: The experiments were performed on endotracheally intubated young mongrel dogs of both sexes and anaesthesia was induced with 5% thiopental sodium (Penthothal sodium^{R}, Abbott SA, Belgium; 25 mg x kg^{-1} body weight) i.v. and maintained by continuous i.v. administration of pentobarbital (Nembutal^{R}, Abbott SA). Before administration of muscular relaxants, the cerebral activity was determined by means of a cerebral function monitor (6), CFM (Devices mod. 4640, Devices Ltd., U.K.). In order to ascertain that it corresponded to a level of very light anaesthesia .With the CFM recording as guidance (6), this level of anaesthesia was then kept constant throughout the experimental procedures by means of continuous infusion of pentobarbital at a mean rate of 2.5 mg x kg^{-1} x h^{-1}. Pancuronium bromide (Pavulon^{R}, N.V. Organon, Netherlands) was given for muscle relaxation by means of continuous infusion (0.08 mg x kg^{-1} x h^{-1}). After induction of anaesthesia an infusion of 5.5% glucose solution (Pharmacia AB, Sweden) was started. The body temperature was maintained at 37-38° C (thermostatic control) and sodium bicarbonate (0.6 M) solution was continuously infused i.v. in order to avoid anaesthesia-induced metabolic acidosis (5). If necessary, the acid-base balance was corrected before every experimental sequence in order to minimise acid-base effects on cardiac output and venous admixture (3, 10, 19).

Measurements: The arterial systemic blood pressure (ASP), central venous pressure (CVP) and intratracheal pressure (ITP) were measured as described (7). The thermistor catheter (Devices mod. CV 3753 F3) was used for measurements of pulmonary arterial pressure (PAP) and cardiac output (CO; Cardiac Output Computer 3750, Devices Instr. Ltd., U.K.). Cardiac output was measured by the thermodilution technique and 10 ml of 5.5% glucose solution at room temperature was injected in 2 s by means of a thermodilution injector (OMP 3700, OMP Laboratories, Inc., USA) fitted with a thermodilution syringe set

(OMP 3830). The injection was initiated in the early phase of expiration. The error of the thermodilution method was studied separately in one of the dogs and in 30 determinations the coefficient of variation was 4%. The value of CO in each experimental situation was the mean value obtained by three successive determinations at intervals of 2-3 min. The catheters for pressure measurements were connected to transducers (EM 751A, Elcomatic Ltd., U.K.), which in turn were connected to amplifiers (BAP 001, Simonsen & Weel A/S, Denmark), and recordings were made by means of a rectilinear pen recorder (Mx 412, Devices Ltd.). The heart rate (HR) was determined from the ASP recordings. Fractions of inspired and expired gases were measured by mass spectrometry (Centronic MGA-200, 20th Century Electronics Ltd., U.K.). The relative humidity of the insufflated gas mixture was measured with a humidity indicator (HMI 11, Vaisala Oy, Finland). The haemoglobin concentration (Hb), oxygen saturation (S_{O_2}), P_{O_2}, P_{CO_2}, pH, base excess and HCO_3^- were determined by means of an automatic acid-base analyser (ABL 1, Radiometer A/S, Denmark). Blood lactate was measured with an automatic apparatus (Roche Lactate Analyzer 640, Roche Bioelectronics, Switzerland).

The total static lung-chest compliance was determined twice under complete neuromuscular block both at the beginning and at the end of the whole experiment (7). Ventilatory volumes were determined by means of a Tissot spirometer (total volume 120 l). After collection of expiratory gas in a Douglas bag during ventilation with pure oxygen, mass-spectrometric analyses of nitrogen wash-out permitted calculation of the functional residual capacity (FRC). By means of continuous determinations of the expired nitrogen concentration during ventilation with pure oxygen, the nitrogen clearance ratio (NCR) was obtained.

Ventilators and experimental procedures: A conventional volume-controlled respirator (SV-900) and a prototype of a ventilator system (13) for volume-controlled HFPPV (system H) were used. Ventilatory frequencies (f) of 20, 40, 50 and 60 per min were applied and positive end expiratory pressure (PEEP) was set at 5 cm H_2O (7, 14). All comparisons were made at normoventilation, i.e. arterial P_{CO_2} 40 mm Hg (Fig. 2). The oxygen fraction of the inspired gas ($F_{I_{O_2}}$) was 0.21 (with the exception of nitrogen wash-out periods) and the relative humidity 98-100% (36° C). With SV-900 the working pressure was set at 85 cm H_2O and inspiration at 25% of the ventilatory cycle without an end-inspiratory pause, i.e. constant-flow-generated, time-cycled ventilation (7, Table 2); the internal volume (IVA) of the patient circuit (PC) was 1,650 ml and the internal static compliance (ISC) of the patient circuit 2.6 ml x $(cm\ H_2O)^{-1}$. With system H there was a decelerating-flow inspiration with a relative insufflation time (t%) of 22% (7, Table 2; 12, Table 1), i.e. pressure/flow-generated, time-cycled volume-controlled ventilation (14, Table 1); the IVA of PC was 50 ml and the ISC 0.06 ml x $(cm\ H_2O)^{-1}$.

Ventilation was given with SV-900 and system H in all dogs (starting in every other dog with either ventilator system and a ventilatory frequency of either 20 or 60 per min). Each experimental sequence at these ventilatory frequencies was performed twice in all dogs but the second time the order of ventilators was reversed in the same manner as in a previous investigation (7, Table 1). With ventilatory frequencies of 40 and 50 per min (not studied until duplicate studies at ventilatory frequencies of 20 and 60 were completed for both ventilator systems), only some selected parameters were subjected to investigation. In each experimental sequence the minute ventilation was adjusted until the arterial P_{CO_2} was close to 40 mm Hg during ventilation with 21% O_2 (see Fig. 2) and the measurements were performed after not less than 20 min of ventilation, as has been previously discussed (7).

Calculations: Calculations were made according to a previous study (7) and gas volumes are given at body temperature, barometric (ambient) pressure and saturated with water wapour at 37° C (BTPS).

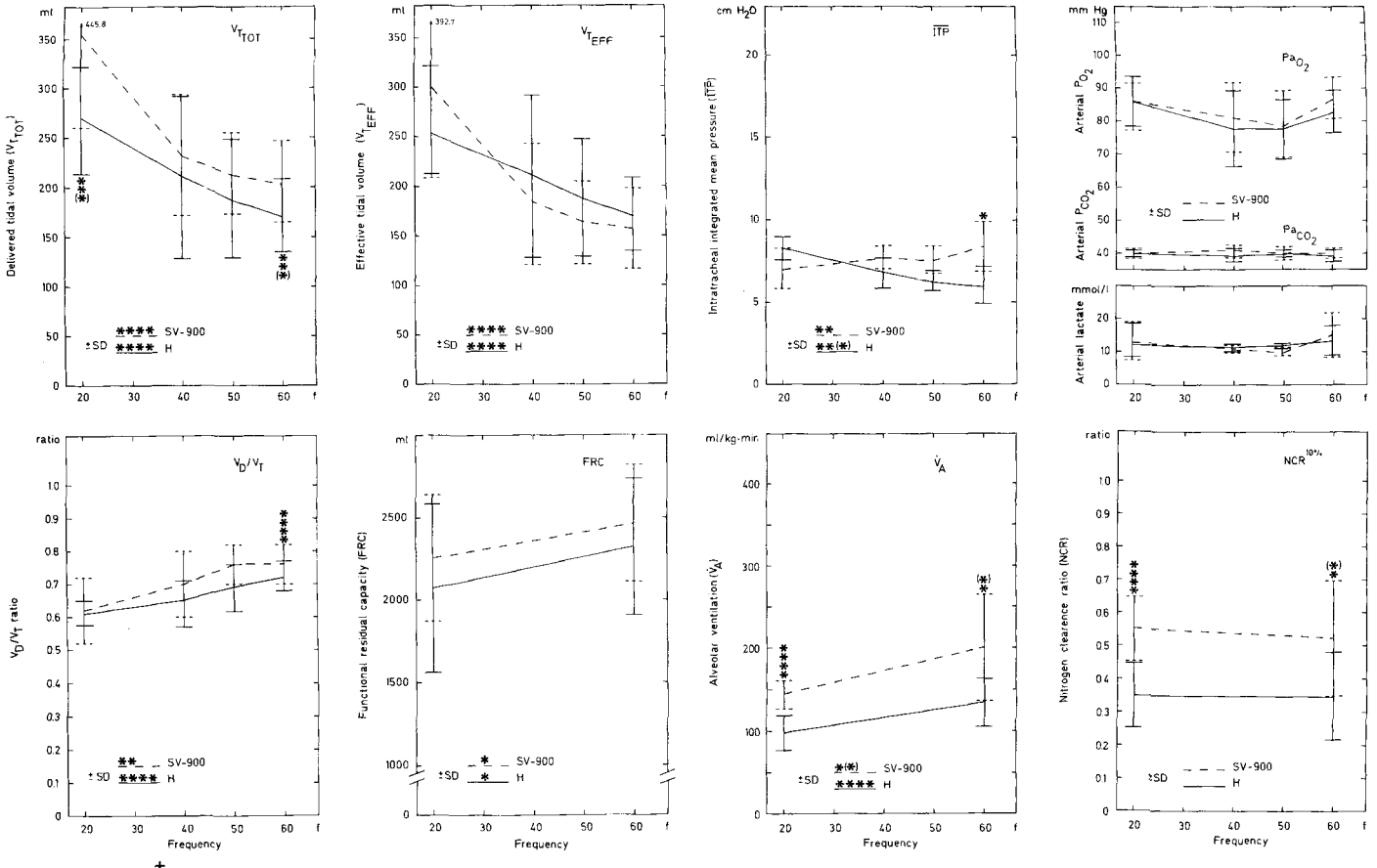

Fig.2.Mean values ($\pm$SD) of measured and calculated parameters in 10 dogs during very light pentobarbital anaesthesia and ventilation with SV-900 and system H (13) to an arterial P_{CO_2} of 40 mm Hg.Ventilatory frequencies (f) of 20,40,50 and 60 per min were used and PEEP was set at 5 cm H_2O.With system H (functionally with no compression volume) the tidal volume of the ventilation system ($V_{T_{TOT}}$) was equal to the effective tidal volume ($V_{T_{EFF}}$),(Text continued on next page).

(Fig.2,continued)

and by increasing f to 60, $V_{T_{EFF}}$ could be reduced to only 65% of that at f of 20 and the mean airway pressure was consequently reduced. During inspiration of pure oxygen,mass-spectrometric analyses of the pulmonary nitrogen clearance ratio (NCR) showed highly significantly better conditions with system H than with SV-900 at ventilatory frequencies of 20 and 60 per min. The significance of differences between mean values are indicated as described under "Methods".

The nitrogen clearance ratio (NCR) with inspiration of pure oxygen and initiated at functional residual capacity (FRC) was calculated as follows:

$$NCR^{10\%} = \frac{\text{Alveolar-ventilation volume (ml) reducing end-expiratory } N_2 \text{ to } 10\%}{\text{Functional residual capacity}}$$

All differences mentioned in the text were tested for statistical significance by means of Student's t-test for paired data, using the following probability levels (P): x = $P \leq 0.05$; x(x) = $P \leq 0.025$; xx = $P \leq 0.01$; xx(x) = $P \leq 0.0025$; xxx = $P \leq 0.001$, and xxxx = $P \leq 0.0005$.

RESULTS

As illustated in Fig. 2, with an incresing ventilatory frequency (f) from 20 to 60 per min both ventilator systems resulted in significant increases in V_D/V_T and FRC. With system H (functionally with no compression volume) the tidal volume of the ventilator system ($V_{T_{TOT}}$) was equal to the effective tidal volume ($V_{T_{EFF}}$) and by increasing f to 60 (despite increased V_D/V_T) $V_{T_{EFF}}$ could be reduced to only 65% of that at a ventilatory frequency of 20. The mean airway pressure was consequently reduced.

The alveolar gas distribution was studied by mass-spectrometric analyses of pulmonary nitrogen clearance curves. With system H the nitrogen clearance ratio (NCR) was considerably improved from that obtained with SV-900, especially at a ventilatory frequency of 20 ($P < 0.0005$), but also at 60 per min ($P < 0.025$).

DISCUSSION

In a previous study (7) the ventilatory pattern of a conventional respirator (SV-900) constituted the norm for comparison with that produced by an experimental system, system G (12), for volume-controlled HFPPV. With the exception of the different ventilatory patterns the experimental conditions were kept identical (fairly deep pentobarbital anaesthesia and normoventilation, i.e. arterial P_{CO_2} 40 mm Hg, pH 7.4 and constant $F_{I_{O_2}}$ of the inspired air). At comparable arterial carbon dioxide tension the intratracheal peak and mean pressures were also higher with SV-900 than during HFPPV (Fig. 1). The total peripheral resistance (TPR) was lower with HFPPV, although the cardiac output (CO) and stroke volume (SV) were greater. Calculations of the tension-time index (TTI) revealed no differences between the two ventilator systems. The

lower TPR in association with a higher cardiac output during ventilation with HFPPV indicated that during fairly deep anaesthesia the ventilatory pattern in volume-controlled HFPPV interfered less with the cardiovascular function, which could only have been due to dissimilarities between the ventilatory patterns of the compared systems.

In the present study on 10 dogs it was found that parameters that may be corrected by regulatory and compensatory mechanisms operative during very light intravenous pentobarbital anaesthesia (6) did not show any significant differences either between different types of ventilators or between ventilatory frequencies, when the arterial P_{CO_2} was identical (40 mm Hg). In other words, and in contrast to the previous findings (Fig. 1), all parameters directly or indirectly associated with the circulatory conditions were compensated for the effects of the different ventilatory patterns used ("active" parameters). On the other hand, parameters that may be regarded as being "passive", i.e. mainly associated with the physical conditions arising from the different ventilatory patterns (Fig. 2), showed functionally important differences both with different types of ventilators and with different ventilatory frequencies. Such "passive" parameters closely related to the properties of the ventilator systems and to the ventilatory frequencies used are the delivered tidal volume ($V_{T_{TOT}}$), the effective tidal volume ($V_{T_{EFF}}$), the intratracheal mean airway pressure (ITP_{mean}), the functional residual capacity (FRC) and the nitrogen clearance ratio (NCR).

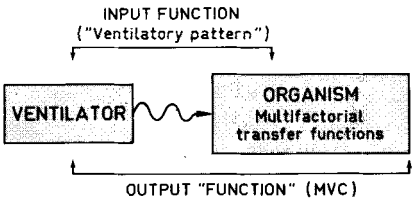

Fig. 3. Schematic diagram of the combined conditions created by the ventilator and the pulmonary systems - the "ventilatory pattern". The effect of the ventilatory pattern on the individual, i.e. its "systemic effects", is reflected by the output "function" called MVC. Reproduced by permisson (7, 14).

As stated previously (7, 14, 15, 16, 17), and as indicated in Fig. 3, the "passive" parameters belong to the "ventilatory pattern", i.e. the input function. The "active" parameters (see Fig. 1) associated with circulation and oxygen transport, however, are under autonomic and homeostatic control during light pentobarbital anaesthesia (6). This means that the "active" parameters are closely related to the multifactorial transfer functions of the organism and they are components of the output "function", which may be called the "Multifactorial Ventilatory Capacity" (MVC).

In critically ill patients, it is reasonable to suggest that some of the homeostatic control mechanisms are no longer able to cope with the situation, i.e. that vital regulatory and compensatory mechanisms are no longer operative. Thus, patients in circulatory shock or patients with pulmonary dysfunction will "react" to differences in the "ventilatory pattern" due to insufficient homeostasis. This is our clinical experience in infants with the respiratory distress syndrome, IRDS (8) and in the adult respiratory distress syndrome, ARDS (2). A ventilator which has a negligible compression volume and which is set at a rather high frequency (f=60-100/min) may offer definite advantages in such patients (2, 7, 13, 14, 15, 16).

Although our experimental and clinical investigations indicate that it is easier to adapt a patient to a ventilator which has a negligible compression volume and is set at a high frequency, more extensive clinical studies with a prototype system, system H (13), for volume-controlled ventilation must be available before the merits of high frequencies can be compared with those of the traditional techniques and ventilatory frequencies of volume-controlled ventilation (15, 16).

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REFERENCES

1. Abboud, F.M., Heistad, D.D., Mark, A.L. & Schmid, P.G.: Reflex control of the peripheral circulation. In Progress in Cardiovascular Diseases, Vol XVIII, No 5: 371, 1976.
2. Bjerager, K., Sjöstrand, U. & Wattwil, M.: Long-term treatment of two patients with respiratory insufficiency with IPPV/PEEP and HFPPV/PEEP. Acta Anaesth Scand, Suppl 64: 55, 1977.
3. Carson, S.A.A., Chorley, G.E., Hamilton, F.N., Lee, D.C. & Morris, L.E.: Variation in cardiac output with acid-base changes in the anesthetized dog. J Appl Physiol 20: 948, 1965.
4. Conway, C.M.: Haemodynamic effects of pulmonary ventilation. Brit J Anaesth 47: 761, 1975.
5. Danielson, B., Grängsjö, G., Karlmark, B., Ulfendahl, H.R. & Wolgast, M.: Acid-base status in dogs during long term anaesthesia. Uppsala J Med Sci 80: 77, 1975.
6. Dubois, M., Savege, T.M., O´Carroll, T.M. & Frank, M.: General anaesthsia and changes on the cerebral function monitor. Anaesthesia 33: 157, 1978.

7. Eriksson, I., Jonzon, A., Sedin, G. & Sjöstrand, U.: The influence of the ventilatory pattern on ventilation, circulation and oxygen transport during continuous positive-pressure ventilation - An experimental study. Acta Anaesth Scand, Suppl 64: 149, 1977.

8. Heijman, K., Lindqvist, B., Nilsson, L.-G., Sjöstrand, U. & Wranne, L.: Neonatal respiratory care by means of CPAP and HFPPV. In preparation.

9. Jonzon, A., Öberg, Å., Sedin, G. & Sjöstrand, U.: High-frequency positive-pressure ventilation by endotracheal insufflation. Acta Anaesth Scand, Suppl 43: 5, 1971.

10. Prys-Roberts, C., Kelman, G.R., Greenbaum, R. & Robinson, R.H.: Circulatory influences of artificial ventilation during nitrous oxide anaesthesia in man. II: Results: The relative influence of mean intrathoracic pressure and arterial carbon dioxide tension. Brit J Anaesth 39: 533, 1967.

11. Qvist, J., Pontoppidan, H., Wilson, R.S., Lowenstein, E. & Laver, M.B.: Hemodynamic responses to mechanical ventilation with PEEP: The effect of hypervolemia. Anesthesiology 42: 45, 1975.

12. Sjöstrand, U.: Review of the physiological rationale for and development of high-frequency positive-pressure ventilation - HFPPV. Acta Anaesth Scand, Suppl 64: 7, 1977.

13. Sjöstrand, U.: Pneumatic systems facilitating treatment of respiratory insuffiency with alternative use of IPPV/PEEP, HFPPV/PEEP, CPPB or CPAP. Acta Anaesth Scand, Suppl 64: 123, 1977.

14. Sjöstrand, U.: Summary of experimental and clinical features of high-frequency positive-pressure ventilation - HFPPV. Acta Anaesth Scand, Suppl 64: 165, 1977.

15. Sjöstrand, U.: Experimental and clinical studies of the hemodynamic consequences of intermittent positive-pressure ventilation (IPPV) and high-frequency positive-pressure ventilation (HFPPV). V Europ Congr Anaesth 515. Excerpta Medica Int Congr Ser No 452, 1978.

16. Sjöstrand, U.: High-frequency positive-pressure ventilation (HFPPV) - A review. Crit Care Med 7/8: 1979/80 (In press).

17. Sjöstrand, U., Borg, U., Eriksson, I., Lyttkens, L. & Wattwil, M.: Minor circulatory interference and improved alveolar gas distribution during continuous positive-pressure ventilation by means of high ventilatory frequency and a ventilator system of negligible compression volume. V Europ Congr Anaesth 516. Excerpta Med Int Congr Ser No 452, 1978.

18. Werkö, L.: The influence of positive pressure breathing on the circulation in man. Acta Med Scand, Suppl 193: 1947.

19. Yamamura, H., Kaito, K., Ikeda, K., Nakajima, M. & Okada, K.: The relationship between physiological shunt and cardiac output in dogs under general anesthesia. Anesthesiology 30: 406, 1969.

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