PULMONARY GAS EXCHANGE DURING DELIBERATE HYPOTENSION

BY

JAMES E. ECKENHOFF, G. E. HALE ENDERBY, ALEX LARSON, ANTHONY EDRIDGE AND DONALD E. JUDEVINE

From the Department of Anesthesia, Schools of Medicine, University of Pennsylvania, Philadelphia, U.S.A., and the Department of Anaesthetics, The Queen Victoria Hospital, East Grinstead, Sussex, England.

SUMMARY

Respiratory physiological deadspace may increase from 35 per cent of the tidal volume in the normal anaesthetized, normotensive and supine patient to as much as 80 per cent in the hypotensive patient in the head-up tilt. Increased mean airway pressure, hypotension, sudden head-up tilt or maintenance of tilt, all tend to increase the respiratory deadspace. Arterial and end-tidal P\(_{\text{CO}_2}\) differences parallel the deadspace changes. The average P\(_{\text{CO}_2}\) difference in the supine normotensive patient was 9 mm Hg, but during maintained head-up body tilt during hypotension, this difference increased to as much as 25 mm Hg. These data emphasize the need for careful control of respiration, with higher than normal tidal volumes and oxygen concentrations during deliberate hypotension. They are equally applicable to other hypotensive states including shock.

During the course of experiments surveying the influence of deliberate hypotension upon the human circulation, the observation was often made that arterial P\(_{\text{CO}_2}\) seemed higher than expected considering the apparent adequacy of pulmonary ventilation. At the termination of hypotension and operation in a 15° to 28° head-up position in three of twenty-eight patients observed, the electrocardiogram revealed a sudden onset of ventricular extrasystoles, lasting from 7 to 12 minutes. Arterial blood samples withdrawn from the three patients after the appearance of the arrhythmia, and during a period when the arterial carbon dioxide level should have been decreasing if it had been high, revealed P\(_{\text{CO}_2}\) values as high as 96, 74 and 115 mm Hg. In one patient, a 69-year old male, minute volumes of respiration had been measured at 5.0 and 5.48 l./min; in the second, a 24-year female, minute volumes of 6.95 and 9.50 l./min had been observed with a total gas flow from the anaesthetic machine of 8 l./min; in the third, a 25-year male, the total gas flows were 6.5 l./min from the anaesthetic machine. An exhausted soda lime canister was ruled out as the explanation.

These observations caused us to seek an explanation for the appearance of the hypercapnia.

METHODS

Measurements were made in twenty-five patients scheduled for elective plastic surgical procedures. Fifteen were male; the age range was 16 to 69 years, with a median age of 32 years, and all were in good health. All had had levorphan 1–2 mg, and atropine or hyoscine 0.4 mg intramuscularly for premedication. Anaesthesia was induced with thiopentone, up to 250 mg intravenously, tracheal intubation was facilitated with suxamethonium 50–75 mg intravenously, and anaesthesia was maintained with nitrous oxide and oxygen (3:2 or 2:2 ratio) and halothane 0.5 to 1.5 per cent through a Fluotec vaporizer. Muscular paralysis was maintained with decamethonium 4–6 mg. In most instances respiration was controlled throughout. Ganglionic blockade was produced with either pentolinium (Ansolysen 4–12 mg and/or trimetaphan (Arfonad), up to 40 mg. In twelve patients the administration of the ganglionic blocking agent was preceded by an injection of guanethidine (Ismelin) 10 mg intravenously.

This work was supported (in part) by Grants H-6428 and RG-9070 from the United States Public Health Service, National Institutes of Health; by a Fellowship from the Commonwealth Fund, New York; and by the Department of Anaesthetics of the Queen Victoria Hospital, East Grinstead, Sussex, England.

750
Judging from the failure of appearance of tachycardia, it is doubtful if a complete ganglionic blockade existed in any patient. Observations were made before, during or after ganglionic blockade and the surgical procedure. In addition to these procedures for producing hypotension, a head-up body tilt (maximum 32°) and increased mean airway pressure were employed as needed to obtain the desired level of blood pressure (Enderby, 1958).

Two groups of experiments were conducted:

**Group 1** (14 patients). A standard Boyle machine with its circle filter system (Mark 2) was employed for the administration of the anaesthetic. A unidirectional valve. A large Waters canister packed Y-piece at the connection of the corrugated tubing to the endotracheal tube. A Wright anemometer was included between endotracheal tube and unidirectional valve. A large Waters canister packed with coarse inert material was included at the distal end of the 3-foot length of corrugated tubing just proximal to the expiratory entrance into the circle filter head. This was intended as a mixing chamber for expired gas to allow for sampling to obtain mean expired carbon dioxide tension. The samples were withdrawn through a T-piece located between mixing chamber and circle head.

Periodically before, during or after deliberate hypotension, and at varying mean airway pressures, respiratory rate and minute volumes were determined during a 3 to 5-minute steady state, immediately followed by the simultaneous withdrawal of arterial blood and mixed expired air samples. Fifteen ml blood samples were drawn into heparinized 20-ml Luer Lok syringes, capped and immediately immersed in iced water until analysis. Air samples were likewise drawn into 20-ml dry syringes, capped and the syringes stored upright resting on the plunger. Analyses of P_{O_2}, P_{CO_2} and pH (on blood samples) were made by means of an electrode system incorporating a Clarke oxygen electrode, a Severinghaus P_{CO_2} electrode and a microcapillary pH electrode (EIL model SIH33). The accuracy observed was 1.1 mm Hg (SD ± 1.4) for P_{O_2}, 1.57 mm Hg (SD ± 1.06) for P_{CO_2}, and 0.003 units (SD ± 0.003) for pH. Physiological deadspace was determined by the formula:

\[ V_{dp} = V_T \frac{(P_{CO_2} - P_{TECO_2})}{P_{CO_2}} \]

All deadspace calculations include endotracheal tube, connectors, Wright anemometer and valve system where used. The total instrument deadspace excluding the anemometer was 80 ml. Nunn and Ezi-Ashi (1962) have estimated the deadspace of the Wright anemometer at less than 30 ml.

**Group 2** (11 patients). In a second group of experiments, a similar technique was employed except that mixed expired air samples were not collected but instead simultaneous arterial and end-tidal gas samples were obtained. The latter was withdrawn by means of a plastic tube inserted through the endotracheal tube: with its tip at the distal end of the tracheal tube. At the end of a normal expiratory phase of controlled ventilation, with the patient apnoeic, a 20-ml gas sample was withdrawn quickly while compression was exerted manually on the chest wall.

**Sources of error in the experimental method.**

At the time these experiments were conducted, there was a minimum of scientific equipment available to validate the accuracy of the instruments used. The devices were all theoretically acceptable, but subsequent reconstruction of the system and testing has revealed three sources of error:

**The Wright anemometer.** Subjecting our instrument to calibration with pulsatile gas flows and a Tissot spirometer has revealed inaccuracies in the measurement of the flows used in these experiments of as much as 20 per cent, dependent upon respiratory tidal volume and rate. This defect has been noted before (Nunn and Ezi-Ashi, 1962).

**The mixing chamber.** Serial samples from the expired air mixing chamber had indicated sufficiently close agreement to suggest proper mixing. However, when a continuous stream of air was drawn from the distal end of the chamber, through an infra-red carbon dioxide analyzer, the tracings indicated that complete mixing might not occur. The maximal error noted was 10 per cent, depending upon the phase of respiration in which the sample might have been taken, the respiratory rate and the tidal volume.

**Distensibility of corrugated tubing.** Careful observation of the valve system near the endotracheal tube revealed that at elevated airway pressures, gas could flow from the inspiratory to the expiratory side of the system without having par-
anticipated in pulmonary ventilation. This occurred because with inspiration, pressure was built up in the slightly distensible corrugated tubing. As airway pressure decreased during expiration, gas moved through the valves from the inspiratory to the expiratory tubing as pressures on the two sides of the valves were equalized. This error would create somewhat lower than actual expired carbon dioxide values.

Because of these errors, we have not refined the data by correcting the gas volumes for temperature and atmospheric pressure. However, in spite of the errors, affecting chiefly the physiological deadspace calculation, the data are thought useful. The exact experimental conditions of this report are not easily reproducible, although an effort is being made to repeat the work. We believe the problems for further research uncovered, the warnings inherent to those who would use deliberate hypotension, and the suggestions apparent for the treatment of other hypotensive states justify the report.

RESULTS

Arterial Carbon Dioxide Tension and Minute Volume of Respiration.

Simultaneous measurements were made 92 times in the 25 patients. The relationship between these two variables is presented graphically in figure 1. Despite a minute volume of respiration of 6 to 15 l/min, in 29 of the 92 observations, the \( P_{\text{a}CO_2} \) was above 40 mm Hg.

The calculated alveolar ventilation in the 14 patients in whom mixed expired \( P_{CO_2} \) was measured was correlated with \( P_{aCO_2} \) (fig. 2). The usual hyperbolic relationship was found to exist between alveolar ventilation and \( P_{aCO_2} \).

Arterial blood was withdrawn 100 times in these 25 patients. The level of \( PO_2 \) was above 100 mm Hg in all except five instances (\( P_{aO_2}: 93, 89, 85, 76, 64 \) mm Hg).
PULMONARY GAS EXCHANGE DURING DELIBERATE HYPOTENSION

83, 77 mm Hg) despite the PCO₂ levels previously listed. In three of these instances mean airway pressure throughout the respiratory cycle had been maintained at 35, 23 and 24 cm H₂O. In all three, the P aCO₂ was 37 mm Hg or below. The observation of a P aO₂ of 85 mm Hg was made 10 minutes after a patient had been returned to the level position, when the P aCO₂ was also elevated—58 mm Hg.

**Respiratory Deadspace.**

The respiratory deadspace was measured in 14 patients (table I).

*Initial ("control") measurements.*

Data were obtained from eight observations in 5 normotensive patients (Nos. 33, 34, 35, 36, 37) without a one-way valve system at the endotracheal tube. The average V D/VT ratio (ratio between physiological deadspace and tidal volume of respiration) (Nunn and Hill, 1960) was 0.34 with the range between 0.18 and 0.48. Inclusion of the one-way valve in the breathing system increased this figure to an average of 0.53. The latter observations were made 6 times in five normotensive patients (Nos. 39, 42, 43, 44, 46) and the range was 0.31 to 0.62.

**The effect of positive airway pressure.**

The influence on respiratory deadspace of changing mean airway pressure with the patient supine was studied in eight normotensive patients. The response was variable and appeared dependent upon the effect the increased airway pressure had on blood pressure. If blood pressure remained unchanged or increased (five patients, Nos. 33, 34, 36, 37, 42) in response to elevated airway pressure, the deadspace did not change appreciably. If, on the other hand, blood pressure declined (three patients, Nos. 35, 39, 43) deadspace increased (average increase from 0.34 to 0.48).
<table>
<thead>
<tr>
<th>Expt. No.</th>
<th>Age</th>
<th>Sex</th>
<th>Start anaesthesia</th>
<th>Time of sample</th>
<th>Body position*</th>
<th>Arterial blood pressure (mm Hg)</th>
<th>Pulse rate (bpm)</th>
<th>Resp. rate</th>
<th>Airway pressure (cm H2O)</th>
<th>Resp. minute volume (L/min)</th>
<th>Tidal vol (ml)</th>
<th>P ACO2 (mm Hg)</th>
<th>Paco2 (mm Hg)</th>
<th>P ACO2 (mm Hg)</th>
<th>Pao2 (mm Hg)</th>
<th>PAO2 (mm Hg)</th>
<th>Alveolar ventilation (L/min)</th>
<th>V T/ F V</th>
<th>V P V</th>
<th>Arterial pH</th>
</tr>
</thead>
</table>
Changing from horizontal position to head-up tilt.

Observations were made in five normotensive patients (Nos. 33, 34, 35, 44, 46) who were placed in an average of 26° head-up tilt. Measurements were made between 6 and 14 minutes after tilting. Deadspace increased in four and remained unchanged in one. The average change in the \( V_d/V_t \) ratio was from 0.47 (0.33 to 0.62) in the horizontal position to 0.58 (0.40 to 0.73) in the head-up tilt. In four of these patients, blood pressure at the heart level did not vary with position change.

Maintaining the patient in the head-up tilt with increased airway pressure.

Data were secured in seven patients on the influence of maintained body tilt averaging 26° and increased mean airway pressure for from 18 to 77 minutes. Deadspace increased from the first to the last observation in five of the seven patients (Nos. 25, 29, 30, 44, 46), remained unchanged in the sixth (No. 35), and decreased in the seventh (No. 34). The increase in the \( V_d/V_t \) ratio was from an average of 0.55 (0.25 to 0.73) to 0.67 (0.49 to 0.80).

Return from head-up tilt to horizontal position.

Two patients, one of whom had been tilted head-up (32°) for 62 minutes (No. 29) and the other (25°) for 77 minutes (No. 30), were studied before and 10 and 19 minutes respectively after being returned to the horizontal position. Between the first and second observations, controlled respiration had ceased and the patients were breathing spontaneously. In the first patient, the \( V_d/V_t \) ratio rose from 0.53 to 0.79 and the \( P_{aco2} \) rose from 27 to 81 mm Hg. In the other the ratio decreased from 0.76 to 0.71.

Arterial-End tidal \( P_{aco2} \) and \( P_{o2} \) differences.

Arterial-end tidal \( P_{aco2} \) and \( P_{o2} \) data were collected from eleven patients (table 1).

Initial ("control") measurements.

Data were obtained from eight patients without ganglionic blockade (Nos. 67, 68, 69, 70, 71, 72, 73, 74) in the supine position before head-up tilt. The arterial-end tidal \( P_{aco2} \) (A-a\(P_{aco2}\)) difference ranged from 2.7 to 13.5 mm Hg (average 9 mm Hg) and the A-a\(P_{o2}\) difference ranged from 32 to 142 mm Hg (average 70 mm Hg). The period of measurement was between 50 and 110 minutes (average 75 minutes) after induction of anaesthesia.

Increasing airway pressure in the horizontal position.

Arterial-end tidal carbon dioxide and oxygen tensions were examined in one patient (No. 73) whose mean airway pressure had been increased from 7 to 33 cm H\(_2\)O and in another (No. 71) from 6 to 12 cm H\(_2\)O. In neither did the A-a\(P_{aco2}\) difference change appreciably, and in both the A-a\(P_{o2}\) difference increased.

Changing from horizontal to head-up position.

Observations were made six times in five patients (Nos. 66, 67, 70, 72, 74). In four, the A-a\(P_{aco2}\) and A-a\(P_{o2}\) difference increased and in the same four, the mean blood pressure declined by at least 22 mm Hg. In the other two patients, the A-a\(P_{aco2}\) difference diminished while A-a\(P_{o2}\) difference doubled in one and remained essentially the same in the other. Blood pressure decreased in the first of these two patients and remained unchanged in the second.

Increase in airway pressure in the head-up position.

Three sets of data were collected in two patients (Nos. 70, 72); in one before and after ganglionic blockade. In all three instances, increased airway pressure resulted in a widening of the A-a\(P_{aco2}\) difference and in two of the A-a\(P_{aco2}\) difference as well. In one the oxygen difference became less; this was also the only patient in whom mean arterial pressure was elevated during the second observation.

Effect of maintained head-up tilt.

Observations were made in seven hypotensive patients (Nos. 67, 68, 69, 70, 71, 73, 74) at the termination of operation. The average A-a\(P_{aco2}\) difference was 14 mm Hg with a range from 9.4 to 29.4 mm Hg. The average A-a\(P_{o2}\) difference was 95 mm Hg with a variation from 48 to 129 mm Hg. The average head-up tilt for this group was 26°; average blood pressure 41 mm Hg, and average duration of tilt 41 minutes.

Sudden release of airway pressure in the head-up position.

Observations were made in one hypotensive patient (No. 65). The airway pressure decreased
Return from head-up to horizontal position.

Data were collected from 5 hypotensive patients (Nos. 67, 68, 69, 71, 73). In two the A-aPco₂ difference decreased, in two it remained unchanged, and in one it increased. In four patients the A-aPo₂ difference diminished (average decrease 115 to 67 mm Hg), and in two the A-aPo₂ difference decreased. Mean blood pressure was elevated in all patients.

DISCUSSION

The data presented in figure 1 confirm in part the observations made in the introduction to this paper. There it was noted that 3 of 28 patients unrelated to this group but subjected to deliberate hypotension developed ventricular extrasystoles at the conclusion of anaesthesia, and were found later to have marked hypercapnia in spite of minute volumes of respiration above 5 l./min. In 91 observations in the 25 patients reported herein, the PaCO₂ exceeded 40 mm Hg in nearly one-third of the analyses, in spite of respiratory minute volumes of 7 or more l./min. Yet data from 52 samples withdrawn from 14 patients emphasized the fact that when alveolar ventilation was 4 or more l./min, PaCO₂ was always below 40 mm Hg (fig. 2). If the minute volume of respiration exceeded 6 l. and alveolar ventilation was below 4 l./min, it is apparent that a large proportion of the inspired air was not ventilating normally perfused alveoli.

During inhalational anaesthesia respiratory deadspace is made up of anaesthetic apparatus deadspace, conducting airway deadspace, non-perfused or under-perfused alveoli and under-ventilated alveoli. This space is not static but varies under many circumstances. Elevation in carbon dioxide tension, increased tidal volume of respiration, adrenaline and atropine have been shown to increase deadspace (Severinghaus and Stupfel, 1957). While apparatus deadspace is often included in data from anaesthetized man, this should be a reasonably constant fraction throughout an anaesthetic. Nunn and Hill (1960) have shown the ratio between physiological deadspace and tidal volume of respiration (Vd/Vt) to be fairly constant at 0.35 in supine man anaesthetized with thiopentone and nitrous oxide and immobilized with d-tubocurarine. However, there is evidence that this ratio can vary widely. Courand and associates (1943) have shown ratios as high as 0.55 to 0.64 during haemorrhage and in shock in man. An elevated Vd/Vt ratio (0.55) has been observed in dogs anaesthetized with pentobarbitone and in haemorrhagic shock (Gerst, Rattenborg and Holaday, 1959) and Freeman and Nunn (1963) have reported this ratio to be as high as 0.78 in dogs in haemorrhagic shock and anaesthetized with halothane.

The data reported herein indicate that effective alveolar ventilation may be reduced during nitrous oxide-halothane anaesthesia with deliberate hypotension and head-up body tilt. As much as three-fourths of tidal exchange may become useless in so far as affecting gas exchange with blood is concerned. While changes in anatomical deadspace may participate in this diminution, it appears that a more plausible explanation rests in changes in alveolar ventilation in relation to alveolar perfusion. Our initial observations on physiological deadspace with supine patients provided data similar to those reported by Nunn and Hill (1960), namely that approximately one-third of tidal exchange ventilated deadspace. The incorporation of a one-way valve system increased the value. The effect of an increased airway pressure was variable. If blood pressure remained unchanged or increased in response to the airway pressure, deadspace was unaltered or decreased. This implies that alveolar perfusion remained adequate in the face of improved ventilation of alveoli. If blood pressure declined, deadspace increased. The suggestion here is that the increased airway pressure reduced venous return, cardiac output and alveolar perfusion. Head-up tilt increased physiological deadspace and maintenance of the tilt caused an additional increase. The mechanism of the latter response must relate to a reduced cardiac output and gravitational pooling of blood, thereby altering ventilation-perfusion ratios. The observations obtained from patients immediately after return to the horizontal position suggest that the restoration of normal physiological deadspace awaits
establishment of normal pulmonary circulation. It points to the need for continuing adequate respiration at the termination of deliberate hypotension.

The data comparing arterial and end-tidal Pco₂ levels complement and agree with the deadspace measurements. They further suggest that the prime changes under these conditions occur in the alveoli. It is of interest that haemoglobin desaturation of oxygen was not observed more often. This unquestionably relates to the fact that the oxygen tension of the inspired gases was sufficiently high to compensate for the reduced ventilation/perfusion ratios. If a lower oxygen concentration had been inhaled, hypoxia would have been more frequent. We have noted arterial Po₂ values as low as 68 mm Hg in patients breathing 20 per cent oxygen and 80 per cent nitrous oxide during deliberate hypotension (Eckenhoff et al., in press).

The relationship between increased respiratory deadspace associated with hypotension caused by haemorrhage has been noted before in man (Cournand et al., 1943) and in animals (Gerst, Rattenborg and Holaday, 1959; Freeman and Nunn, 1963). This report indicates that a similar relationship may exist in hypotension regardless of cause. In the hypotension of haemorrhage, physiological deadspace increases because of pulmonary vascular constriction and reduced blood volume, thereby diminishing the amount of blood exposed to alveolar air. In the hypotension reported herein, deadspace increases because of vascular dilatation and pooling of blood away from the pulmonary bed without a reduction of blood volume. This reduces cardiac output (our preliminary data would suggest a reduction of 75 per cent at times) and presumably the dilatation of pulmonary vessels and gravitational effects cause some alveoli to be over-perfused without adequate ventilation and others to have little other than ventilation.

While this study has been conducted in patients subjected to deliberate hypotension and tilted in a head-up position, one suspects that similar effects might occur in supine patients who pool blood away from the thoracic cavity. Halothane produces vascular relaxation and predisposes to hypotension. Prolonged maintenance of the supine position by an anaesthetized patient might lead to pooling of blood in the dependent portion of the body and increase the physiological deadspace. The effect of various anaesthetic agents on this parameter in the normotensive supine patient is currently under study.

There are many clinical implications of these data. Those related to the minute attention to respiration required during deliberate hypotension are especially noteworthy. Respiratory exchange must be maintained above the usually adequate levels and the oxygen content of inspired air must be more than 20 per cent, probably more appropriately 35 to 40 per cent. If the head-up tilt has been employed, respiration must be carefully assisted after the return to a horizontal position, to a normal exchange volume and to a normal blood pressure. In all likelihood, similar applications exist to the patient in shock. He should have greater than room air oxygen concentration to assure adequate oxygenation of blood and some respiratory assistance to assure carbon dioxide removal because of the increased respiratory deadspace.

REFERENCES


