The Effect of Gas Inflow on the Regulation of CO₂ Levels with Hyperventilation during Anesthesia

Kunio Suwa, M.D.,* and Hideo Yamamura, M.D.†

The authors describe a method by which a normal CO₂ level may be achieved during hyperventilation, simultaneously regulating fresh gas flow rate ($V_f$: l/min, ambient temperature) into an anesthesia circle system from which the carbon dioxide absorber has been removed. Using a tidal volume of 15 ml/kg and a respiratory rate of 16/min, $P_{ACO₂}$ may be approximated as

$$P_{ACO₂} \approx \frac{0.8 \dot{V}_{CO₂}}{V_f},$$

where $\dot{V}_{CO₂}$ is calculated according to the formulas of Kleiber. In 35 patients studied, the $P_{ACO₂}$ values observed agreed well with the calculated values when the latter were above 30 torr. With increases in $V_f$, observed values generally exceeded calculated values, indicating increasing fresh gas flow bypassing the patient. (Key words: $P_{ACO₂}$; Hyperventilation; Normocarbia; Radford's nomogram; Anesthesia circle system.)

Use of mechanical deadspace for the simultaneous achievement of large minute ventilation and normal $P_{ACO₂}$ in the management of patients undergoing prolonged artificial ventilation has been studied. This paper describes a method of achieving a normal CO₂ level with a large minute ventilation by eliminating the carbon dioxide absorber from the ordinary anesthesia circle system and at the same time regulating the flow rate of fresh gas.

---

* Associate in Anesthesia, Present address: Department of Anesthesia, School of Medicine, University of California, San Diego, La Jolla, California.
† Professor and Chairman in Anesthesia. Received from the Department of Anesthesia, Faculty of Medicine, University of Tokyo, 7-IHongo, Bunkyo-Ku, Tokyo, Japan. Accepted for publication June 30, 1970.

A part of this investigation was presented in the Symposium, Inspiration—Ventilation Requirement, at the fourth World Congress, London, September, 1968.

Clinical Study

**Method**

Thirty-five patients given anesthesia for surgical procedures were studied. They had no cardiac or pulmonary disease. Premedication consisted of atropine only. Anesthesia was induced with nitrous oxide and halothane, and intubation was achieved with the aid of $d$-tubocurarine (0.7 mg/kg). Anesthesia was maintained with a mixture of nitrous oxide and oxygen (about 2:1), with additional small amounts of $d$-tubocurarine. All patients lay supine, and none were tilted in any direction by more than five degrees; five were in the lithotomy position.

Ventilation was controlled with a constant-volume time-cycled ventilator (AIKA R-120 or R-100®), using a tidal volume of 15 ml/kg at a rate of 16/min. Fresh gas flow ($V_f$) was between 2.6 and 7.5 l/min (the maximum value of $V_f/V_E$ was 0.50), and the canister was removed from the circle system, or the CO₂ absorbent was removed from the container.

The anesthesia circle included two corrugated rubber tubes, the total volume of which was 980 cc, including the volume of the Y-connector. The residual part of the circle varied in volume from 210 to 3,400 cc. The circuit of the respirator included two corrugated plastic tubes, the volume of which was 590 cc, including the volume of the Y-connector. Overflow took place at the tail end of the reservoir bag of the respirator. Gas inflow was at the inspiratory side close to the inspiratory valve, and the ventilator connection was at the expiratory side of the expiratory valve. The two unidirectional valves were away from the patient, separated by corrugated rubber tubes.

Arterial blood samples were drawn through a catheter inserted into a radial artery.
Samples were obtained every hour during anesthesia, but only the value obtained an hour after the initiation of controlled ventilation was used for analysis. When the one-hour value was less than 30 mm Hg or more than 50 mm Hg, the value at two hours was used, because of the possibility of an unstable state. Analyses of arterial blood samples were performed at 37°C using a glass electrode for pH, a Severinghaus electrode for PCO2 and a modified Clark electrode for PO2.

The values for PaCO2, obtained (X) were compared with the values calculated (Y) using equations 8 and 9 (below) by calculating the correlation coefficients and the root mean square errors with the appropriate formulas. The significance levels of the correlations were checked by the table of Fisher and Yates.4 The regression lines were calculated by the method of least squares.

**Theory and Model Experiment**

**Theory**

By ignoring a small difference between inspired and expired minute volumes, the following equation can be written:

\[
\dot{V}_{CO2} = \alpha \left( P_{ECO2} - P_{ICO2} \right) \dot{V}_E, \tag{1}
\]

where \( \dot{V}_{CO2} \) is the amount of CO2 eliminated (ml/min, STPD), \( P_{ECO2} \) and \( P_{ICO2} \) are expired and inspired CO2 partial pressures (torr), \( \dot{V}_E \) is minute ventilation (l/min, BTPS) and \( \alpha \) is the factor converting the fraction into partial pressure.

The Bohr equation for anatomic deadspace stands as:

\[
\frac{V_D}{V_T} = \frac{P_{ICO2} - P_{ECO2}}{P_{ICO2} - P_{ECO2}}, \tag{2}
\]

where \( V_D \) is anatomic deadspace, \( V_T \) is tidal volume, and \( P_{ICO2} \) is alveolar partial pressure of CO2 (torr).

Substitution for \( P_{ECO2} \) in equation 2 by the expression obtained from equation 1 produces:

\[
P_{ICO2} = P_{ICO2} + \frac{a \dot{V}_{CO2}}{\dot{V}_E} \cdot \frac{V_T}{V_D - V_T}. \tag{3}
\]

Therefore, to calculate PaCO2, we must know six factors: \( P_{ICO2}, \alpha, \dot{V}_{CO2}, V_T, \) respiratory rate, and \( V_D \).

In the clinical setting, \( V_T \) and respiratory rate can be measured with appropriate accuracy and \( \alpha \) is known to be 0.563 mm Hg when \( V_T \) is expressed in BTPS and 0.8 mm Hg when \( V_T \) is expressed in ATPS with the temperature close to 21°C (75.2°F) and barometric pressure between 700 and 750 mm Hg.5 Methods of estimating \( \dot{V}_{CO2} \) from body weight, sex and other factors have been described.5,6

Data for \( P_{ICO2} \) in a circle system without an absorber are not available, although the analysis of the circle system done by Eger and Ethans is closely related. In essence, they analyzed the effects of inflow and valve placement in a circle absorber system on the conservation of fresh gas and the preferential elimination of alveolar gas, during both spontaneous and controlled ventilation.

With the ventilator used in this study the excess gas overflows; therefore, the overflow valve of the anesthesia circle was kept closed, so that the overflow point was at the bag, as in the study of Eger and Ethans. This is a common characteristic of ventilators used in the operating room in combination with circle systems.

The system, then, became identical to either system A or system C as analyzed by Eger and Ethans, depending upon the positions of inflow and inspiratory valves.

\( P_{ICO2} \) of system C (inflow point between the inspiratory valve and the bag) without an absorber can be written,

\[
\frac{P_{ICO2}}{P_{ECO2}} = \frac{\dot{V}_E - \dot{V}_T}{\dot{V}_E}, \tag{4}
\]

\((\dot{V}_T \leq \dot{V}_E)\)

where \( \dot{V}_T \) is fresh gas inflow. This means that, if fresh gas inflow is smaller than minute ventilation, all fresh gas is inspired by the patient, the difference between \( \dot{V}_E \) and \( \dot{V}_T \) being the mixed expired gas.7

The \( P_{ICO2} \) of system A (the inflow point between the inspiratory valve and the patient) requires further analysis. Let us imagine a system in which fresh gas inflow and gas from the expiratory side of the circuit are completely
mixed before arrival at the Y-connection to the patient, and in which there is also complete mixing between gas expired by the patient and gas entering the expiratory side of the circuit directly from the inspiratory side, before arriving at the ventilator connection.

If the unidirectional valves are competent, and no leaks are present, the flow in the circuit, approaching the inflow point for fresh gas, should equal $V_E$. The $P_{\text{CO}_2}$ ($P'_{\text{ECO}_2}$) is different from $P_{\text{ECO}_2}$ because it is already diluted by some fresh gas.

The relationship between $P_{\text{CO}_2}$ and $P'_{\text{ECO}_2}$ can be written as:

$$\left(V_E + \dot{V}_t\right)P_{\text{CO}_2} = \dot{V}_E X P'_{\text{ECO}_2}; \quad (5)$$

which means that the dilution of gas ($P'_{\text{ECO}_2}$) by fresh gas ($P_{\text{CO}_2} = \text{zero}$) results in the value for $P_{\text{CO}_2}$. The relationship between $P_{\text{ECO}_2}$ and $P'_{\text{ECO}_2}$ is:

$$\left(V_E + \dot{V}_t\right)P'_{\text{ECO}_2} = \dot{V}_E P_{\text{ECO}_2} + \dot{V}_t P_{\text{CO}_2}; \quad (6)$$

where the left-hand side is the amount of CO$_2$ passing through the expiratory limb of the circle, which is equal to the sum of the expired CO$_2$ (the first term of the right-hand side) and the CO$_2$ bypassing the patient (the second term). From these two, the following relationship is derived:

$$\frac{P_{\text{CO}_2}}{P_{\text{ECO}_2}} = \frac{1}{1 + \dot{V}_E \frac{\dot{V}_t}{V_E} + \left(\frac{\dot{V}_t}{V_E}\right)^2}. \quad (7)$$

As is shown later, measured $P_{\text{CO}_2}$ is smaller than that given by this equation. The $P_{\text{CO}_2}$ of this equation is not much different from that in equation 4, provided that $\dot{V}_t/V_E$ is small (when $\dot{V}_t/V_E$ is equal to 0.5, equation 4 yields the value of 0.5, while equation 7 yields 0.51). For the sake of simplicity, let us use equation 4 for $P_{\text{CO}_2}$. Equation 5 then becomes:

$$P_{\text{ACO}_2} = \frac{\alpha V_{\text{CO}_2}}{\dot{V}_E} + \frac{\alpha V_{\text{CO}_2}}{\dot{V}_E} \frac{V_D}{V_T - V_D}. \quad (8)$$

If we make the minute ventilation and the tidal volume large enough to ignore the second term of the right-hand side of equation 8, it may be written as:

$$P_{\text{ACO}_2} = \frac{\alpha V_{\text{CO}_2}}{\dot{V}_E}. \quad (9)$$

These two expressions will be tested by comparing the $P_{\text{ACO}_2}$ values obtained with the $P_{\text{ACO}_2}$ values calculated.

$V_{\text{CO}_2}$ was calculated using the formulas of Kleiber, with the correction factor for body habitus ignored, and with the appropriate changes of coefficient as previously described by Radford.

$$V_{\text{CO}_2}(\text{ml/min STPD}) = 8.2414 \times W^{0.7}[1 + 0.004(30-A)], \quad \text{male} \quad (10)$$

$$V_{\text{CO}_2}(\text{ml/min STPD}) = 7.61635 \times W^{0.7}[1 + 0.004(30-A)], \quad \text{female} \quad (11)$$
where W is body weight in kg and A is age in years. Furthermore, since the age correction influences \( V_{CO_2} \) relatively little (between the ages of 10 and 50 years, the error is ± 8%), simpler formulas were also tested and age corrections were ignored.

\[
V_{CO_2} = 8.2414 \times W^{0.74}, \text{ male} \tag{12}
\]
\[
V_{CO_2} = 7.61635 \times W^{0.74}, \text{ female} \tag{13}
\]

Anatomic deadspace was estimated from body weight

\[
V_d (ml) = 1.5 \times W (kg)
\]

Four values of \( P_{ACO_2} \) were calculated by applying equations 8 and 9, in conjunction with equations 10 through 13.

**MODEL EXPERIMENTS**

In order to determine the \( P_{ACO_2} \) in a circle system similar to system A of Eger and Ethans under conditions such as those used in our study, an experiment using a model lung (see figure 1) was performed. The "lung" has the structure of an anesthesia circuit, including an input of carbon dioxide and mimicking carbon dioxide elimination by the lung. The compliance of the "lung" was adjusted to 20 ml/cm H2O at a tidal volume of 750 ml. This "lung" was attached to another anesthesia circle without a carbon dioxide absorber and ventilated with a volume-limited time-cycled ventilator (AIKAI, R-120). The functional residual capacity of the "lung" was 1.8 l, while the volume of the anesthesia circuit was 2.1 l; anatomic deadspace was 6 ml.

A special pressure-reducing valve (ASAHI Ind. Co., Ltd., AFC 35) was used to provide a constant inflow rate of CO2. Dry CO2 was introduced into the "lung" at a rate of 173 ml/min (STPD). The "lung" was ventilated with a tidal volume of 750 ml at a rate of 16/l/min. Oxygen was used as the fresh gas flow, varying between 1 and 15 l/min as determined by a flowmeter which was calibrated repeatedly against a spirometer. Ventilation and gas flow were measured with a pneumotachograph and a Wright respirometer.

Mixed inspired and alveolar gases were sampled at the points shown in figure 1 and analyzed for CO2 by means of an infrared analyzer (HORIBA, MCD-1). Direct determination of \( PE_{CO_2} \) in such a system was not possible. Since the anatomic deadspace was so small in this "lung," however, the difference between \( P_{ACO_2} \) and \( PE_{CO_2} \) was ignored, and they were treated as if they were the same. \( P_{ACO_2}/PE_{CO_2} \) values were always found to be smaller than those calculated by equation 7, but generally exceeded the values obtained from equation 4 (fig. 2). Use of equation 4 as an approximation of \( P_{ACO_2} \), therefore, seems justified as long as \( V_d/V_e \) is small.

**FIG. 2.** Results of the model-lung experiment. The theoretical minimum and maximum are calculated by equations 4 and 7, respectively.

**FIG. 3.** Results of the clinical study. The ordinate values are calculated by applying equation 9, together with equations 10 and 11. Statistical analysis indicates that if a \( P_{ACO_2} \) of 40 torr is predicted, the observed value should be 41.11 ± 3.34 torr (mean ± mean root square error).
Results

The observed \( \text{Paco}_2 \) ranged between 16.1 and 55.3 torr. The agreement between the observed and calculated values is shown in the example given in figure 3. All correlations are significant \((P < 0.001)\); the values, together with the regression formulas, are given in table 1. When the combination of equations 9, 10, and 11 was used, the correlation coefficient was 0.8018, and the regression line \( Y = 1.274X - 11.980 \); the root mean square error was 5.95 torr. The regression line crosses the line of identity at a \( \text{Paco}_2 \) of 43.7 torr.

When the statistics were calculated for those 20 points for which the calculated \( \text{Paco}_2 \) values exceeded 30 torr, the correlation coefficient was 0.9819, and the regression line \( Y = 0.980X - 0.295 \). The mean root square error was 5.35 torr.

Discussion

The observed \( \text{Paco}_2 \) values tended to be somewhat higher than those calculated by equation 8 or equation 9. This was especially so when the fresh gas flow was high and \( \text{Paco}_2 \) was low. With the calculated values lower than 30 torr, 14 of 15 observed values were higher than those calculated, almost invalidating the applicability of equation 8 in this range. This suggests that the approximation of \( \text{Paco}_2 \) by equation 7 is not sufficiently good when fresh gas flow is high relative to minute ventilation. There was a considerable improvement of the correlation coefficient, and the regression line approached the line of identity, when the calculated \( \text{Paco}_2 \) exceeded 30 torr, indicating that this calculation is reliable as a rough approximation of \( \text{Paco}_2 \).

Although the gas inlet was located on the patient side of the inspiratory valve, it could have been on the opposite side without invalidating the analysis. In fact, it may be predicted from the study of Eger and Ethans that the latter arrangement might improve the applicability of equations 8 and 9.

The use of a more complicated formula (equation 8) in calculating \( \text{Paco}_2 \) resulted in a modest lowering of the correlation coefficients (0.7812 to 0.7775, 0.8018 to 0.7986). Because of its simplicity, equation 9 seems preferable, so long as tidal volume and ventilatory rate are kept sufficiently large. In this study, the second term on the right-hand side of equation 8 is in the order of 5 per cent of the first term. On the other hand, use of the age correction in estimating \( \text{CO}_2 \) production improved the correlation coefficient. Although the difference is small (0.7812 to 0.5018), this correction may be desirable.

Removal of the \( \text{CO}_2 \) absorber from the anesthesia circuit is not new. A report has been made by Benson, and the authors are aware of the analysis and the use of this method by H. H. Hart and W. E. Martin. This investigation, therefore, may be regarded as a refinement of techniques already known. It is probably unwise to rely solely on this method in predicting the normal \( \text{Paco}_2 \), because the individual variations observed were not small, and because \( \text{VCO}_2 \) can be anticipated to vary with time and circumstance. Furthermore, occurrence of an arterial-alveolar \( \text{Paco}_2 \) difference during anesthesia is well known. This method should provide a good first approximation, however, when used in conjunction with blood-gas analysis. The actual steps in applying this method for approximating \( \text{Paco}_2 \) of 40 torr are:

1) Calculate \( \text{VCO}_2 \) from Kleiber's formulas (equations 10 & 11).

---

* Personal communication.
2) \( V_T = 15 \text{ ml/kg} \) at a rate of 10/min. This need not be accurate but should be sufficiently large.
3) \( V_I (1/\text{min}) = 0.02 \text{ VCO}_2 (1/\text{min, STPD}) \).
4) Remove the canister from the circle. Excess gas overflow should be achieved in the ventilator, not from the overflow valve of the circle.
5) The two one-way valves should be apart from the patient.

Tables for estimating CO\(_2\) production vs. body weight, sex and age, generated by computer, are now available upon request.

The authors are indebted to Dr. Edmund L. Eger, II, for the valuable criticism given through the Editorial Offices of the Journal, and to Dr. Henrik H. Bendixen for advice and encouragement. Miss Mayo Saito and Mr. Tsuyoshi Katachi assisted in carrying out the study and Miss Mie Hata and Mrs. Marilynn Gauthier helped in the preparation of the manuscript.

References

Drugs

**Ketamine** Ketamine was used in 28 pediatric cardiac catheterizations. Ketamine has the following advantages: it is fast and pleasant; it has a short hypnotic action and provides complete analgesia; there is no depression of circulation or respiration; doses can be repeated safely, thus prolonging anesthesia as necessary; emergence is smooth with minimal postoperative nausea and vomiting; and no increased cardiac irritability was observed. Intravenous administration was far superior to intramuscular injection. Ketamine is the agent of choice for patients undergoing cardiac catheterization. (Szappanos, G. G., Bopp, P., and Fournet, P. C.: The Use and Advantage of Ketalar as an Anesthetic Agent in Pediatric Cardiac Catheterization and Angiocardiography, Der Anaesthesist 18: 365 (Nov.) 1969.)

**Succinylcholine** Intraocular pressures were measured during ocular operations in 80 children and ten adults. \( d \)-Tubocurarine (0.04 mg/kg), given three minutes before the succinylcholine, prevented the increase in intraocular pressure usually seen after succinylcholine alone. (Dickmann, P., Goecke, M., and Wiemers, K.: The Modification of Intraocular Pressure Increases Following Succinylcholine by Non-depolarising Muscle Relaxants, Der Anaesthesist 18: 370 (Nov.) 1969.)