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Effects of Mechanical Ventilation, Muscle Paralysis, and Posture on Ventilation–Perfusion Relationships in Anesthetized Man

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Ventilation–perfusion relationships of the fast ventilated and slowly ventilated compartments of the lung were estimated from analysis of nitrogen clearance curves and rate of increase of arterial oxygen tension during nitrogen clearance. Six subjects were studied first awake, breathing spontaneously, and then again during anesthesia, muscle paralysis, and mechanical ventilation in the supine position. Five other subjects were studied in the lateral position, first awake and then during anesthesia. Induction of general anesthesia, muscle paralysis, and mechanical ventilation did not significantly alter the mean $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratio in supine subjects; this suggests no increased difference between the ventilation–perfusion ratios in the fast ventilated and slowly ventilated compartments. This conclusion is supported by data that showed no significant increase in arterial–alveolar CO_2 tension difference, alveolar deadspace, or shunt. Unlike the ratios for awake subjects in the lateral position, the $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratios decreased consistently after induction of anesthesia. In the awake lateral subjects, mean $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ was 0.08 above unity, whereas in the anesthetized lateral subjects, the mean value was 0.25 below unity; this suggests a larger difference between the ventilation–perfusion ratios in the two compartments. Also, arterial–alveolar CO_2 tension difference and alveolar deadspace increased significantly after induction of general anesthesia in the lateral subjects. (Key words: Inspired gas distribution; Pulmonary capillary blood-flow distribution; Ventilation–perfusion ratios; Alveolar deadspace.)

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DURING ANESTHESIA, muscle paralysis, and mechanical ventilation, intrapulmonary gas distribution is different from, and probably more uniform than, that in awake, spontaneously breathing subjects.[1,2] When this alteration in intrapulmonary gas distribution is not accompanied by appropriate changes in the distribution of pulmonary capillary blood flow, altered ventilation–perfusion ratios which would lead to disturbances in pulmonary gas exchange could result.

The present study is a test of this possibility. We used a method described by Finley,[3] which consists of analysis of pulmonary nitrogen clearance curves and the rate of increase of arterial oxygen tension during nitrogen clearance. The method is based on the principle that, during nitrogen clearance, the rate of increase of alveolar oxygen tension depends on intrapulmonary distribution of inspired oxygen to the fast ventilated and slowly ventilated compartments of the lung, and the rate of increase of arterial oxygen tension depends on the distribution of pulmonary capillary blood flow to these compartments and on the magnitude of the intrapulmonary shunt.

In the supine position, induction of general anesthesia, muscle paralysis, and mechanical ventilation did not significantly alter the mean $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratio, suggesting no increased difference between the ventilation–perfusion ratios in the fast ventilated and slowly ventilated compartments. In the lateral position, induction of general anesthesia resulted in a significant reduction of $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$. An increased difference between the ventilation–perfusion ratios of the two compartments during general anesthesia is suggested by the fact

that the mean $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratio was 0.25 below unity, compared with 0.08 above unity for the awake lateral subjects.

Methods

Eleven healthy young adult subjects (physicians and nurse anesthetists)¶ participated in this study. Six were studied in the supine position, first awake, breathing spontaneously, and then while anesthetized, paralyzed, and mechanically ventilated. Five other subjects were studied in both lateral decubitus positions, first awake and again during anesthesia. Anesthesia was induced and maintained with intravenously administered thiopental (total dose 16–27 mg/kg), supplemented with intravenous injections of meperidine hydrochloride (total dose 1–2 mg/kg). Muscle paralysis was accomplished by continuous intravenous infusion of succinylcholine chloride (total dose 8–17 mg/kg). Depth of anesthesia and degree of muscular relaxation were judged by use of clinical signs only. The larynx and trachea were sprayed with 4 per cent lidocaine, and a cuffed endotracheal tube was inserted. Mechanical ventilation (Bird Mark 4 driven by a Mark 7) was adjusted to achieve a $Paco_2$ of approximately 40 torr. The lungs were hyperinflated three times to an end-inspiratory airway pressure of approximately 30 cm H_2O immediately before each period of nitrogen clearance in order to provide similar volume histories. Mean anesthesia time was 2 hours.

The method of pulmonary nitrogen clearance (nitrogen meter) and its analysis have been described.[1,4] Two arterial blood samples (4 ml each, drawn into 5-ml heparinized glass syringes) were obtained prior to each nitrogen clearance period ($F_{IO_2} = 0.22$, compressed analyzed gas). Numerous samples (16 to 45) were obtained in rapid sequence during the first 30 breaths during nitrogen clearance, and two final samples were obtained at the end of the 7-minute nitrogen clearance period. The syringes were stored in ice, and the blood was analyzed for *p*H, P_{O_2}, P_{CO_2}, S_{O_2}, and Hb using IL 313 electrodes and an IL Co-Oximeter. The electrodes were calibrated with humidified analyzed gases before each determination. Appropriate corrections in blood-gas tensions were made for the differences between the body temperature (esophageal thermistor) and that of the electrode water bath,** storage loss of oxygen,†† membrane factor,‡‡ and dilutional effect of heparin in syringe deadspace.§§

The sequential differences between peak oxygen tension toward the final part of N_2 clearance (time f) and oxygen tensions during any earlier part of the nitrogen clearance (time t), after hemoglobin was fully saturated, were calculated (ΔPa_{O_2}). (See Appendix for definition of symbols.) Similarly, sequential differences between final end-tidal nitrogen tensions at time f (corrected for N_2 contained in inspired gas) and nitrogen tensions during any earlier part of the nitrogen clearance (time t) were calculated ($\Delta P_{ET_{N_2}}$). Cumulative effective ventilation was calculated by adding the effective ventilation ($V_T - V_{D_{anat}}$) for sequential breaths during the N_2 clearance. ΔPa_{O_2} and $\Delta P_{ET_{N_2}}$ (corrected for lag of N_2 meter, 0.05 sec) values were plotted semilogarithmically as a function of the ratio of cumulative effective ventilation to functional residual capacity (FRC) ($\Sigma \dot{V}_{eff}/FRC$) (fig. 1). This ratio was used to normalize the data for changes

¶ Consent to participate was given after suitable time for consideration had been allowed and after the nature of the study, the manner in which it would be conducted, and possible risks were carefully outlined to each subject in a lengthy interview.

** P_{O_2} values less than 150 torr were corrected by using the Severinghaus slide rule[9]; for P_{O_2} values greater than 150 torr, the nomogram of Hedley-Whyte *et al.* was used.[10]

†† Correction factors for storage loss of oxygen during cooling were determined *in vitro*. This was accomplished by sequential measurements of P_{O_2} obtained from blood samples drawn into 5-ml syringes, which were immediately stored in ice. An exponential decrease in oxygen tension occurred primarily within the first 10 minutes. Storage loss of oxygen depended on the level of initial oxygen tension. Accordingly, measured oxygen tensions were multiplied by 1.04 when P_{O_2} was greater than 450 torr and by 1.03 when P_{O_2} was between 350 and 450 torr; no correction was made when P_{O_2} was less than 350 torr.

‡‡ Blood-gas membrane factor (n = 35) was 2.49 ± 0.13 per cent (mean ± SE).

§§ Average deadspace of 5-ml syringes was 0.11 ± 0.01 ml (n = 7); therefore, the following correction was made:

$$P_{O_2}\text{ (blood)} = \frac{P_{O_2}\text{ (meter reading)} \times 4.11 - 0.2095 \times (P_B - P_{H_2O}^{39}) \frac{\alpha H_2O^{37}}{\alpha H_2O^{39}} \times 0.11}{4}.$$

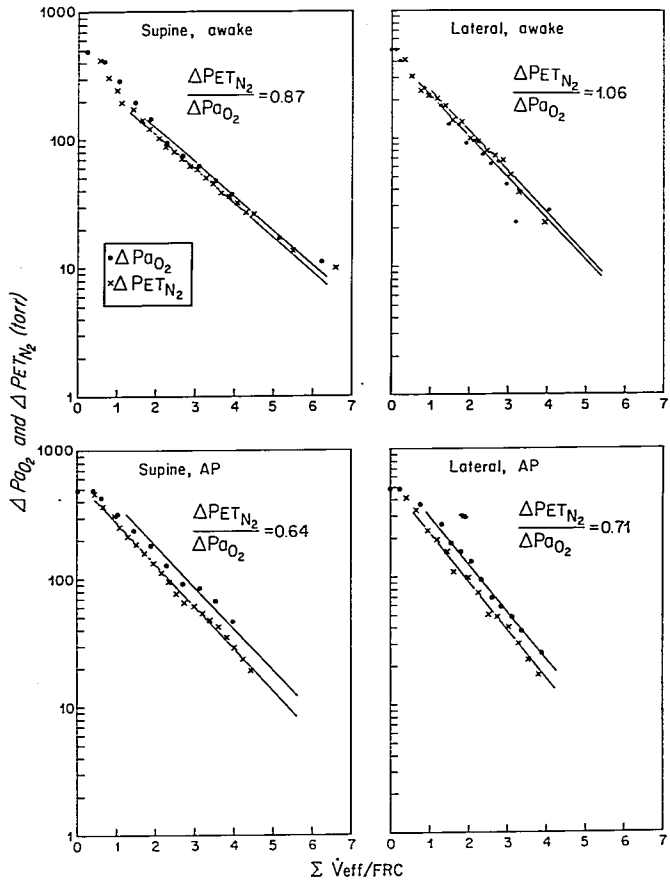

FIG. 1. ΔPa_{O_2} and ΔPET_{N_2} of one subject in the supine and another in the lateral decubitus position before and after anesthesia and mechanical ventilation, plotted semilogarithmically as a function of the ratio of cumulative effective ventilation ($\Sigma \dot{V}_{eff}$) to functional residual capacity (FRC). AP = anesthetized, paralyzed, and mechanically ventilated subject. Note that ΔPET_{N_2} and ΔPa_{O_2} curves are closer together in the awake than in the anesthetized, paralyzed, and mechanically ventilated subjects. This pertains in both supine and lateral positions.

TABLE 1. Physical Characteristics and Lung Volumes of the Subjects (Sitting, Awake, BTPS)

	Mean	Range
Physical characteristics		
Age, years	28	23-33
Height, cm	178	167-188
Weight, kg	77	60-97
Lung volumes, liters		
Total lung capacity	7.43	5.60-8.84
Vital capacity	5.48	4.13-6.56
Functional residual capacity	4.10	3.06-4.89
Residual volume	1.95	1.38-2.40
Expiratory reserve volume	2.16	1.60-2.74

in tidal volume and FRC. Plotting was done after correction for the time delay in increase of peripheral arterial oxygen tensions resulting from the circulation time between pulmonary capillaries and sample site. Circulation time was estimated by the time taken for an earpiece oximeter to show an increase in saturation at the beginning of the nitrogen clearance. This increase in saturation was easily recognized in all subjects. A best-fitting straight line was drawn through the ΔPa_{O_2} points, and another was drawn through the ΔPET_{N_2} points (fig. 1). These lines were parallel during the later part of the nitrogen clearance, indicating that the ratio $\Delta PET_{N_2}/\Delta Pa_{O_2}$ was constant; that is, the rate of decrease of alveolar nitrogen tension and the rate of increase of arterial oxygen tension were the same at this time.

Cardiac output ($\dot{Q}_T$) was measured by the direct Fick method.¶¶ The shunted fraction of cardiac output ($\dot{Q}_s$) was estimated by the standard shunt equation from blood sampled after 7 minutes of oxygen breathing. The nonshunted blood flow ($\dot{Q}_c$) was obtained by subtracting $\dot{Q}_s$ from $\dot{Q}_T$. Effective ventilation per minute ($\dot{V}_{eff}$) was obtained by multiplying respiratory frequency by ($V_T - V_{D_{anat}}$).

Physiologic deadspace was estimated from the Enghoff modification of the Bohr equation.***

Alveolar deadspace was calculated as the difference between physiologic deadspace and anatomic deadspace (analysis of nitrogen clear-

¶¶ Oxygen uptake ($F_{I_{O_2}} = 0.22$, compressed analyzed gas) was calculated from volume (gasometer) and composition (duplicate Haldane analyses) of expired gas collected during a 10-minute period, which was started approximately 20 minutes after completion of N_2 clearance. Arterial (radial) and mid-right atrial (located by ECG[11]) blood samples were drawn by continuous sampling throughout the fifth and sixth minutes of gas collection. Oxygen contents were calculated from Hb, S_{O_2}, and P_{O_2}.

*** The mean expired CO_2 tension (of three breaths sampled immediately before and three after the nitrogen clearance) was calculated from measurements of simultaneously obtained expiratory flow tracings (pneumotachograph, volume obtained by graphic integration) and CO_2 tracings, corrected for a 0.1-second lag of the infrared CO_2 analyzer. The infrared CO_2 analyzer was calibrated with dry analyzed gases (CO_2 in O_2).

TABLE 2. Data Relative to the Ventilation-Perfusion Ratio

Index*	Supine						Lateral					
	Awake†			AP†			Awake			AP		
	No.	Mean	SE	No.	Mean	SE	No.	Mean	SE	No.	Mean	SE
$\Delta PET_{N_2}/\Delta Pa_{O_2}$	6	0.81	0.04	6	0.72	0.05	5	1.08‡	0.12	5	0.75§	0.08
$\dot{V}_{eff}/\dot{Q}_c$	6	0.96	0.18	6	1.01	0.17	5	0.82	0.08	5	0.97	0.13
f_1	4	0.87	0.06	6	0.92	0.02	3	0.89	0.03	5	0.91	0.70

* ΔPET_{N_2} = difference between end-tidal nitrogen tensions at times f and t; ΔPa_{O_2} = difference between arterial oxygen tensions at times f and t; $\dot{V}_{eff}/\dot{Q}_c$ = overall ventilation-perfusion ratio; f_1 = fractional size of slowly ventilated compartment.

† Awake = conscious, breathing spontaneously; AP = anesthetized, paralyzed, and mechanically ventilated.

‡ Borderline-significant difference ($P < 0.1$ but $P > 0.05$) between supine awake and lateral awake.

§ Significant difference ($P < 0.05$) between spontaneous and mechanical ventilation in the lateral position (differences or rank-sum).

TABLE 3. Data Relative to Pulmonary Gas Exchange

Index*	Supine						Lateral					
	Awake†			AP†			Awake			AP		
	No.	Mean	SE	No.	Mean	SE	No.	Mean	SE	No.	Mean	SE
$Pa_{O_2}(FI_{O_2} = 0.22)$, torr	6	82	4	6	77	4	5	86	2	5	81	1
$Pa_{CO_2}(FI_{O_2} = 0.22)$, torr	6	36	1	6	40	2	5	37	1	5	37	2
$a\text{-}AD_{CO_2}(FI_{O_2} = 0.22)$, torr	6	0.0	0.7	6	1.0	0.6	5	−1.0‡	0.6	5	4.0	1.1
V_{Dalv}, ml§	6	−4	11	6	18	9	5	−10‡	7	5	61	16
$A\text{-}aD_{O_2}(FI_{O_2} = 0.22)$, torr	6	11	2	6	17	1	5	12	3	5	20	3
$\dot{Q}_s/\dot{Q}_T$ at $FI_{O_2} = 1.0$	6	0.06	0.004	6	0.07	0.01	5	0.07	0.002	5	0.08	0.01
$\dot{Q}_T(FI_{O_2} = 0.22)$, l/min	4	6.1	1.0	4	4.8	0.7	4	6.4	0.7	4	5.5	0.3
V_T, ml	6	574	39	6	562	59	5	620	65	5	647	46
Respiratory frequency, breaths/min	6	12	1	6	10	1	5	10	2	5	10	1

* Pa_{O_2} = arterial O_2 tension; Pa_{CO_2} = arterial CO_2 tension, mean of Pa_{CO_2} measured before and after completion of N_2 clearance; $a\text{-}AD_{CO_2}$ = arterial–alveolar CO_2 tension difference (alveolar P_{CO_2} was measured at midvolume of expiration); V_{Dalv} = alveolar deadspace; $A\text{-}aD_{O_2}$ = alveolar–arterial O_2 tension difference; $\dot{Q}_s/\dot{Q}_T$ = fraction of shunted blood; $\dot{Q}_T$ = cardiac output; V_T = tidal volume.

† Awake = conscious, breathing spontaneously; AP = anesthetized, paralyzed, and mechanically ventilated.

‡ Significant difference ($P < 0.05$) between spontaneous and mechanical ventilation (differences or rank-sum).

§ Anatomic deadspace was obtained by analysis of nitrogen clearance curves. Although this method is liable to error, we chose it in preference to the Fowler method because during passive expiration (in paralyzed man) expiratory flow increases rapidly during the beginning of an exhalation, and correction for lag time of the nitrogen meter becomes critical. The negative alveolar deadspace values are attributed primarily to errors in the determination of the anatomic deadspace.

ance curves).[4] $a\text{-}AD_{CO_2}$ was calculated as the difference between arterial P_{CO_2} and alveolar P_{CO_2} (infrared CO_2 analyzer, alveolar P_{CO_2} at midvolume of expiration).

Errors in the estimation of $\Delta PET_{N_2}/\Delta Pa_{O_2}$ ratios are introduced through random errors in the measurements of arterial oxygen and end-tidal nitrogen tensions and through errors in the estimation of circulation time from pulmonary capillary to peripheral sampling site. An additional error is introduced into the analysis by selecting the highest arterial oxygen tension during the nitrogen clearance as the final value. We also calculated ΔPa_{O_2} values, utilizing the mean value of the last two to 13 measurements, as the final oxygen tension approached a plateau value (time f); the data obtained led to the same conclusions.

Results

The physical characteristics and lung volumes of the 11 subjects (ten men and one woman) are summarized in table 1. All lung volumes and their subdivisions were within the normal range.

Figure 1 shows typical semilogarithmic plots of ΔPET_{N_2} and ΔPa_{O_2} as a function of the ratio of cumulative effective ventilation to functional residual capacity of one subject in the supine and another in the lateral decubitus position before and after anesthesia and mechanical ventilation. These plots show that the ΔPET_{N_2} and ΔPa_{O_2} lines are closer together for awake than for anesthetized, paralyzed, and mechanically ventilated subjects. This indicates a larger difference between the ventila-

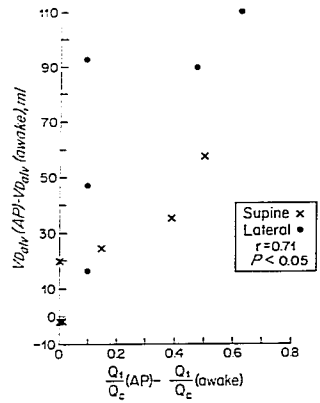

FIG. 2. Changes in alveolar deadspace plotted against changes in fractional perfusion of the slowly ventilated compartment. Values plotted on both axes represent the differences between anesthesia, paralysis, and mechanical ventilation and awake, spontaneous respiration. There is a high correlation (r = 0.71).

tion–perfusion ratios of the two compartments in the anesthetized, paralyzed subjects.

With the subjects in the supine position, the $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratio was less than unity in every subject under both conditions. The ratios decreased in five of six subjects, but the mean changes did not achieve statistical significance (table 2). No consistent changes in the mean values of the fractional sizes of the two compartments or those of the overall ventilation–perfusion ratios were observed.

With the subjects in the lateral position, the $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratios were larger than unity in three subjects. The ratios decreased in all five subjects after induction of general anesthesia, and the mean value of $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ decreased significantly from 1.08 to 0.75. Mean values for fractional sizes of the two compartments and for the overall ventilation–perfusion ratio did not change significantly.

No significant changes in Pa_{O_2}, $A\text{-}aD_{O_2}$, $\dot{Q}_s/\dot{Q}_T$, or $\dot{Q}_T$ were observed (table 3). $a\text{-}AD_{CO_2}$ and $V_{D_{alv}}$ increased significantly in the lateral position but not in the supine position, during anesthesia, paralysis, and mechanical ventilation. The changes in alveolar deadspace with mechanical ventilation correlated well (r = 0.71) with the changes in fractional perfusion of the slowly ventilated compartment ($\dot{Q}_1/\dot{Q}_c$) (fig. 2).

Discussion

The method used in this study is based on the principle that during nitrogen clearance the rate of decrease of alveolar nitrogen tension depends on the intrapulmonary distribution of inspired oxygen to the fast ventilated and slowly ventilated compartments of the lungs. In contrast, the rate of increase of arterial oxygen tension depends on the distribution of pulmonary capillary blood flow to these compartments and on the magnitude of the intrapulmonary shunt. The final value of arterial oxygen tension attained at the end of washout depends on the magnitude of the intrapulmonary shunt. Therefore, the ratio $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ provides information about the distribution of ventilation and perfusion.

It follows from equation 8 of the Appendix that, when this ratio equals unity during the later part of nitrogen clearance, the ventilation–perfusion ratios of both fast ventilated and slowly ventilated compartments must equal the overall ventilation–perfusion ratio. When the ratio is smaller than unity, however, the increase in peripheral arterial oxygen tension lags behind that of alveolar oxygen tension and, therefore, behind that of end-capillary oxygen tension in the slowly ventilated compartment. Such a situation can exist when one or both of the following circumstances occur: 1) there is a right-to-left shunt; 2) the ventilation–perfusion ratio of the slowly ventilated compartment is smaller than the overall ventilation–perfusion ratio.

The effect of a right-to-left shunt on $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ was eliminated in this study by taking the differences between final arterial oxygen tension (time f) and the arterial oxygen tensions occurring at any time during the clearance period (time t). (See formulas 2 and 3 of the Appendix.) Thus, a ratio smaller than unity indicates that the ventilation–perfusion ratio of the slowly ventilated compartment is smaller than the overall ventilation–perfusion ratio.

As is pointed out above, any $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ equal to unity indicates equal ventilation–perfusion ratios of the two compartments. Any deviation from unity (above or below) indicates a difference between the ventilation–perfusion ratios of the two compartments. Thus, when the fractional sizes of the two compartments remain unchanged, the magnitude of the difference between the ventilation–perfusion ratios is indicated by the difference between the value of $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ and unity. Because of the relative sizes of the two compartments, relatively small changes in the ventilation–perfusion ratio of the slowly ventilated compartment will be accompanied by relatively large changes in the ventilation–perfusion ratio of the fast ventilated compartment. We found that in five of six subjects in the supine position $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ values decreased, but the mean values were not significantly changed. In contrast, the $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$'s decreased consistently in the lateral position, and the mean value in the anesthetized state was 0.25 below unity, compared with 0.08 above unity for the awake subjects. This suggests that there was a larger difference between the ventilation–perfusion ratios of the two compartments in the lateral position during anesthesia.

We cannot separate the effect of general anesthesia on these measurements from that of mechanical ventilation, and the literature contains conflicting data. When they compared spontaneous ventilation and mechanical ventilation during general anesthesia, Severinghaus and Stupfel[5] found in dogs, and Nunn and Hill[6] in man, no change in the V_D/V_T ratio. These findings are in contrast to those of Bitter and Rahn,[7] who demonstrated increased alveolar deadspace during positive-pressure breathing in anesthetized dogs, and Folkow and Pappenheimer,[8] who found increased alveolar deadspace when they breathed, while awake, against a constant positive pressure of 20 cm H_2O.

An increase in the ventilation–perfusion ratio of one compartment indicates either that its perfusion has decreased or ventilation has increased or that both of these changes have occurred. A reduction in perfusion of a compartment could result from one or both of the following: 1) the fast ventilated and slowly ventilated compartments have shifted their anatomic locations; 2) the perfusion of the fast-ventilated compartment was decreased. We cannot state which of these situations occurred. That ventilation shifts preferentially to the nondependent lung in anesthetized and mechanically ventilated subjects[2] suggests that a larger portion of the fast ventilated compartment may reside in the nondependent lung. Reduction in perfusion of the nondependent lung could be caused by a progressive decrease in pulmonary blood flow per alveolus in nondependent regions belonging to zone 2 ($Pa > P_A > Pv$) or by pulmonary arterial hypotension secondary to a lower cardiac output.

In summary, we could not demonstrate a significant alteration of the mean $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ ratio in the supine position after induction of general anesthesia, muscle paralysis, and mechanical ventilation, and the shunt and the alveolar deadspace were not increased significantly. In contrast, in the lateral decubitus position, $\Delta P_{ET_{N_2}}/\Delta Pa_{O_2}$ decreased significantly. That the mean value in the lateral anesthetized state was 0.25 below unity compared with 0.08 above unity in the lateral awake state suggests an increased difference between the ventilation–perfusion ratios of the two compartments after induction of general anesthesia. This conclusion is supported by the significant increases in the alveolar deadspace and arterial–alveolar CO_2 tension difference.

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Appendix

The lung can be divided into a fast ventilated compartment and a slowly ventilated compartment. The amount of oxygen in peripheral arterial blood equals the sum of the O_2 in blood perfusing capillaries of the fast ventilated and slowly ventilated compartments plus that in the shunted blood. Thus:

$$\dot{Q}_T Ca = \dot{Q}_1 Cc_1 + \dot{Q}_2 Cc_2 + \dot{Q}_S C\bar{v} \qquad (1)$$

in which $\dot{Q}_T$ is cardiac output, $\dot{Q}_1$ and $\dot{Q}_2$ are blood flow rates of slowly and fast ventilated compartments, Q_S is shunted blood flow rate, Ca, Cc_1, and Cc_2 are oxygen contents of arterial blood and blood from capillaries of the slowly and fast ventilated compartments, respectively, and $C\bar{v}$ is the mixed venous oxygen content (in this and the subsequent formulas, the subscript O_2 has been omitted). Rearranging formula 1:

$$\dot{Q}_T Ca - \dot{Q}_S C\bar{v} = \dot{Q}_1 Cc_1 + \dot{Q}_2 Cc_2.$$

$$\dot{Q}_T = \dot{Q}_1 + \dot{Q}_2 + \dot{Q}_S \quad \text{and} \quad \dot{Q}_c = \dot{Q}_1 + \dot{Q}_2:$$

therefore, $\dot{Q}_T = \dot{Q}_S + \dot{Q}_c$; substituting

$$\dot{Q}_c Ca + \dot{Q}_S(Ca - C\bar{v}) = \dot{Q}_1 Cc_1 + \dot{Q}_2 Cc_2,$$

therefore:

$$Ca = \frac{\dot{Q}_1}{\dot{Q}_c} Cc_1 + \frac{\dot{Q}_2}{\dot{Q}_c} Cc_2 - \frac{\dot{Q}_S}{\dot{Q}_c}(Ca - C\bar{v}) \qquad (2)$$

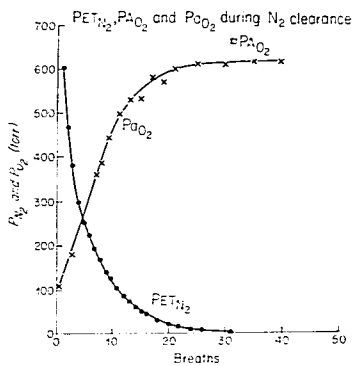

Fig. 3. Decrease in end-tidal nitrogen tension ($P_{ET_{N_2}}$) and simultaneous increase of arterial oxygen tension (Pa_{O_2}) during N_2 clearance, plotted as a function of number of breaths. PA_{O_2} indicates calculated alveolar oxygen tension.

During nitrogen clearance, as alveolar nitrogen tension decreases, alveolar and peripheral arterial oxygen tensions increase (fig. 3). Assume that throughout the later part of N_2 clearance: 1) arteriovenous oxygen content difference [$Ca - C\bar{v}$] remains constant and 2) the proportions of blood flow through the fast ventilated and slowly ventilated compartments and shunt remain constant. Consider the change in arterial oxygen content late in the course of nitrogen clearance between time f at the end of N_2 clearance and some earlier time t, then:

$$\Delta Ca = \frac{\dot{Q}_1}{\dot{Q}_c} \Delta Cc_1 + \frac{\dot{Q}_2}{\dot{Q}_c} \Delta Cc_2, \qquad (3)$$

in which $\Delta C = C_f - C_t$

It follows that ΔCa is independent of the magnitude of the shunt. Assuming hemoglobin is fully saturated at times t and f, then oxygen content is linearly related to oxygen tension, and equation (3) becomes:

$$\Delta Pa = \frac{\dot{Q}_1}{\dot{Q}_c} \Delta Pc_1 + \frac{\dot{Q}_2}{\dot{Q}_c} \Delta Pc_2 \qquad (4)$$

The amount of nitrogen contained in expired gas during nitrogen clearance at any time equals (subscript N_2 has been omitted):

$$\dot{V}_{et} F_{AT} = \dot{V}_1 F_{A_1} + \dot{V}_2 F_{A_2}$$

Since F and P are directly proportional, P can be substituted for F.

$$\dot{V}_{eff}P_{AT} = \dot{V}_1P_{A_1} + \dot{V}_2P_{A_2} \quad (5)$$

in which $\dot{V}_{eff}$ is the product of respiratory frequency times tidal volume minus anatomic deadspace, P_{AT} is alveolar nitrogen tension, $\dot{V}_1$ and $\dot{V}_2$ are effective ventilation of slowly and fast ventilated compartments, and P_{A_1} and P_{A_2} are nitrogen tensions of gas exhaled from slowly and fast ventilated compartments. Late in nitrogen clearance, between times t and f, equation (5) becomes:

$$\dot{V}_{eff}\Delta P_{AT} = \dot{V}_1\Delta P_{A_1} + \dot{V}_2\Delta P_{A_2}, \quad (6)$$

$$\text{in which } \Delta P = P_f - P_t$$

Assume that alveolar equals end-tidal nitrogen tension ($P_{AT} = P_{ET}$). If the fast ventilated compartment is completely cleared between times t and f ($P_{A_2} = 0$) and if there is no diffusion limitation for oxygen ($P_A = Pc$ and $Pc_2 = 0$) and if the water vapor and carbon dioxide tensions remain constant ($\Delta P_{A_{N_2}} = \Delta P_{A_{O_2}}$), then equation (4) reduces to:

$$\Delta Pa = \frac{\dot{Q}_1}{\dot{Q}c}\Delta Pc \quad \text{or} \quad Pc = \Delta Pa\,\frac{\dot{Q}c}{\dot{Q}_1},$$

and equation (6) reduces to:

$$\dot{V}_{eff}\Delta P_{ET} = \dot{V}_1\Delta Pc \quad (7)$$

Substituting for Pc in equation 7, we obtain,

$$\dot{V}_{eff}\Delta P_{ET} = \dot{V}_1 \times \Delta Pa\,\frac{\dot{Q}c}{\dot{Q}_1}$$

or

$$\frac{\dot{V}_1}{\dot{Q}_1} = \frac{\dot{V}_{eff}}{\dot{Q}c} \times \frac{\Delta P_{ET_{N_2}}}{\Delta Pa_{O_2}} \quad (8)$$

The validity of the assumptions was discussed by Finley,[3] who stressed that the fractional perfusion calculated by this method occurs under the condition of ventilation with 100 per cent oxygen. Division of the lung into only two compartments does not preclude a spread of the ventilation-perfusion ratio within each compartment; therefore, this method of analysis does not give an indication of the true degree of variation of the ventilation–perfusion ratios within the lungs.

CNS Function

HYPERBARIC OXYGEN AND ORGANIC BRAIN SYNDROME The effect of repeated exposures to a hyperbaric oxygen environment on intellectual deficits was studied in elderly patients diagnosed as having diffuse brain damage (chronic brain syndrome). The clinical estimates of severity ranged from mild to severe, with durations of impairment ranging from two to five years. The patients were treated with 100 per cent oxygen by mask at 2.5 atmospheres pressure for 90 minutes twice daily, for accumulated exposures of at least 41 hours. Only ten of 16 patients completed the course of therapy. Of these, only one showed a slight, but not significant, improvement in memory testing, and this patient was believed to be suffering chiefly from a depressive reaction rather than organic brain syndrome. The Tiens' Organic Integrity Test results, if valid and reliable, suggested that the treatment might actually have had a deleterious effect. The authors conclude that within a general hospital setting, hyperbaric oxygen treatment has no value for unselected patients with the chronic organic diffuse brain damage. (*Goldfarb, A. I., and others: Hyperbaric Oxygen Treatment of Organic Mental Syndrome in Aged Persons, J. Gerontol. 27: 212–217, 1972.*) ABSTRACTER'S NOTE: If the symptoms reflect anatomic loss of functioning cells, there is little theoretical reason to suspect that hyperbaric oxygen would benefit such a patient.