

Pulmonary and Cardiovascular Effects of Apneic Oxygenation in Man

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Apneic oxygenation was studied in 13 patients undergoing Jako-laryngoscopy with a pharyngeal catheter for oxygen administration and 18 patients having minor surgical procedures with a cuffed endotracheal tube in place for oxygen administration. Arterial P_{O_2} , P_{CO_2} and pH, functional residual capacity (FRC), alveolar P_{O_2} , oxygen uptake, arterial blood pressure, and the electrocardiogram were observed. There was essentially no difference in oxygenation achieved with the two methods of oxygen administration. The majority of patients (22) tolerated apneic oxygenation for 15 minutes or longer. Nine patients could not tolerate apneic oxygenation for more than 5 minutes. These patients had relatively smaller masses, for a predicted FRC/weight ratio of predicted and actual FRC's and larger body 36.7 ± 9 ml/kg, whereas the other patients had a predicted FRC/weight ratio of 53.3 ± 7.7 ml/kg. Because of the smaller FRC and larger body mass, accumulation of alveolar nitrogen resulted in higher P_{AN_2} 's and lower P_{AO_2} 's in patients with low FRC/weight ratios. (Key words: Apneic oxygenation; Functional residual capacity; Alveolar nitrogen; Jako-laryngoscopy; Oxygen uptake.)

DRAPER, Whitehead, and Spencer¹ first studied apneic oxygenation in 1947. Holmdahl² published his experimental results in dogs, along with a review of the literature, in 1956.

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Since that time apneic oxygenation has been used in clinical procedures such as direct laryngoscopy, tonsillectomy, and bronchoscopy.

Frumin, Epstein, and Cohen,³ in a study of apneic oxygenation in man in 1959, were able to maintain 100 per cent arterial oxygen saturation for as long as 30 to 40 minutes in their patients. Their patients tolerated P_{aCO_2} 's as high as 130 torr and arterial pH values around 7.0. However, true apneic conditions were not maintained for the entire period because the investigators used the onset of spontaneous ventilation as the indication for more muscle relaxant, thus allowing their patients to breathe during the "apneic period."

Heller and associates,⁴ in 1963, were the first to measure P_{aO_2} in apneic patients. They studied six patients. When the endotracheal tube was left open to room air during apnea, hypoxia occurred within 5 minutes. When the endotracheal tube was connected to a reservoir of 100 per cent oxygen, P_{aO_2} was still about 400 torr after 5 minutes, but about 100 torr less than it had been at the start of apnea. Heller and associates stated that accumulating alveolar carbon dioxide and nitrogen can account for only a slight decline in P_{aO_2} and that some other factor was also operative in determining the total decrease in P_{aO_2} observed. They postulated changes in pulmonary ventilation-perfusion ratios as the additional factor.

Because of the speculations of Heller *et al.*,⁴ and because of reports of unsatisfactory results of apneic oxygenation,^{5,6} including death of a patient,⁶ we have reappraised the technique to determine: 1) the effectiveness of apneic oxygenation in maintaining P_{aO_2} after 5 minutes. 2) the effectiveness of different methods of administration of oxygen to apneic patients. 3) changes in arterial P_{CO_2} and pH; 4) the role of tissue nitrogen stores during the apneic period; 5) functional residual capacity

changes during oxygenation; 6) oxygen uptake during apnea; 7) the possible association between apneic oxygenation and adverse changes in cardiovascular homeostasis, as reflected by blood pressure and the electrocardiogram.

Methods

Thirteen patients, mean age 46.8 years, undergoing Jako-laryngoscopy (laryngoscopy with a suspension laryngoscope for use with binocular microscopic vision), were subjected to apneic oxygenation via pharyngeal catheter. Eighteen patients, mean age of 38.1 years, undergoing minor surgical procedures, received apneic oxygenation via endotracheal tube preoperatively. The patients were informed of the procedures to be performed and consent was obtained.

Preoperatively, every patient was examined by chest x-ray, ECG, complete blood count, urinalysis, determination of arterial blood gases, and pulmonary function studies. Each patient received 8-12 mg morphine, 5 mg diazepam, and 0.4 mg atropine intramuscularly approximately an hour before operation. In the patients subjected to Jako-laryngoscopy, after a 10-minute period of pulmonary denitrogenation with 100 per cent oxygen delivered by mask via a Sierra nonbreathing valve, anesthesia was induced with thiopental, 5 mg/kg, and maintained by slow intravenous infusion of 0.2 per cent thiopental. After pretreatment with 3 mg *d*-tubocurarine, apnea was initiated with succinylcholine, 1 mg/kg, and maintained by slow intravenous infusion of 0.2 per cent succinylcholine. Oxygen, 6 l/min, was delivered through a nasopharyngeal cannula. Topical application of 4 per cent lidocaine was used to facilitate insertion of the Jako-laryngoscope.

In patients scheduled for minor surgical procedures, anesthesia was induced with thiopental, 5 mg/kg, by slow intravenous infusion of 0.2 per cent thiopental. After pretreatment with 3 mg *d*-tubocurarine, paralysis was achieved with succinylcholine, 1 mg/kg, and maintained with slow intravenous infusion of 0.2 per cent succinylcholine. Following topical application of 4 per cent lidocaine, an endotracheal tube was placed and the cuff in-

flated. After a 10-minute period of pulmonary denitrogenation by hyperventilation with 100 per cent oxygen via a Sierra nonbreathing valve, the apneic period was begun with the endotracheal tube connected to an oxygen-filled Collins spirometer.

During denitrogenation, end-tidal nitrogen was continuously monitored by an in-line Vertek 3400 nitrogen analyzer. End-tidal nitrogen was recorded less than 0.01 per cent in all patients at the start of apnea. A percutaneous catheter was placed in the radial artery and blood samples were taken every minute during the apneic period and analyzed immediately for P_{aO_2} , P_{aCO_2} , and pH on an Instrumentation Laboratory Model 113-127 analyzer. Arterial pressure and the ECG were monitored continuously. Oxygen saturation was monitored by means of a Waters XP 350 oximeter on the earlobe.

The Jako-laryngoscopy patients were made apneic for periods of 10 to 23 minutes, depending on the duration of the surgical procedure, or until they showed evidence of arterial oxygen desaturation. Following apneic intervals the trachea was intubated and the patients were hyperventilated again with 100 per cent oxygen via a Sierra nonbreathing valve for 5 minutes, then allowed to remain apneic for 5-7 minutes with the endotracheal tube open to room air.

The patients scheduled for minor surgical procedures remained apneic for 5 minutes (five patients), 10 minutes (seven patients), or 15 minutes (six patients). Functional residual capacity in the supine position was determined using the closed-system helium-dilution method described by Comroe *et al.*,⁷ with patients awake and asleep, and immediately after apnea. Oxygen uptake was measured in awake, asleep, and postapneic patients over 5-minute periods, using a closed circuit with a Collins spirometer filled with 100 per cent oxygen and an in-line carbon dioxide absorber. By maintaining spontaneous constant-tidal-volume ventilation when the patient was awake and controlled constant-tidal-volume ventilation during the asleep pre- and post-apneic periods, any change in FRC during oxygen uptake was minimized.

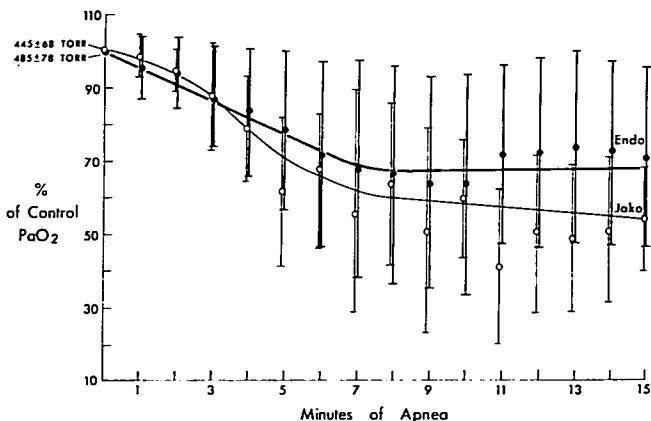


FIG. 1. P_{aO_2} expressed as percentage of control, over a 15-minute period of apneic oxygenation in 18 patients with cuffed endotracheal tubes in place ("Endo") and 13 patients undergoing Jako-laryngoscopy with pharyngeal catheters in place for oxygen administration ("Jako"). The standard deviations show no significant difference between the groups. Mean zero-time arterial P_{O_2} 's are given.

The amount of nitrogen accumulated in the lungs during apnea was calculated by measuring the percentage of nitrogen in the post-apneic FRC system and the absolute size of the postapneic FRC. The volume of carbon dioxide accumulated in the lungs during apnea

was calculated from the P_{aCO_2} at the end of apnea (assuming equilibration with the alveolar gas) and the measured postapneic FRC. During apnea, loss of oxygen from the spirometer bell does not equal oxygen consumption (\dot{V}_{O_2}). The accumulation of carbon dioxide

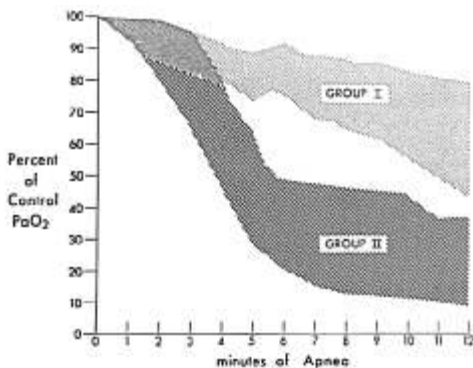


FIG. 2. P_{aO_2} expressed as percentage of control over a 12-minute period of apneic oxygenation for all patients oxygenated by the two methods studied. By the fourth minute two distinct groups had appeared: those who maintained P_{aO_2} well (Group I); and those who did not (Group II). Shaded areas represent total scatter for all patients in the group.

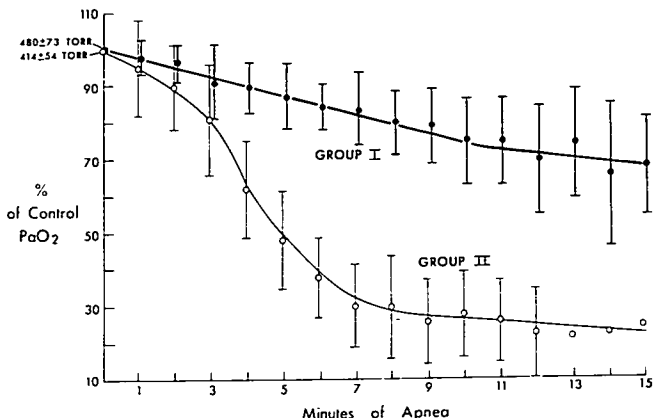


FIG. 3. Mean percentages of control PaO_2 for Group I and Group II patients. PaO_2 's for Group II had declined to 50 per cent of control after 5 minutes of apneic oxygenation, whereas Group I patients still had PaO_2 's that were 90 per cent of control. A significant difference between the two groups occurred at 4 minutes. Mean zero-time PaO_2 's are shown.

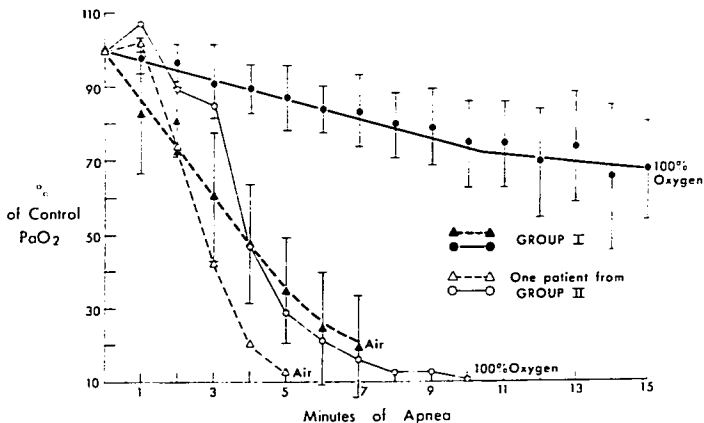


FIG. 4. Comparison of patients in Group I with one Group II patient during apnea with 100 per cent oxygen (solid lines) and with air (broken lines). The differences between Group I and Group II are apparent when 100 per cent oxygen is used but become less evident when only air is used during the apneic period. (Other Group II patients were not subjected to air apnea.)

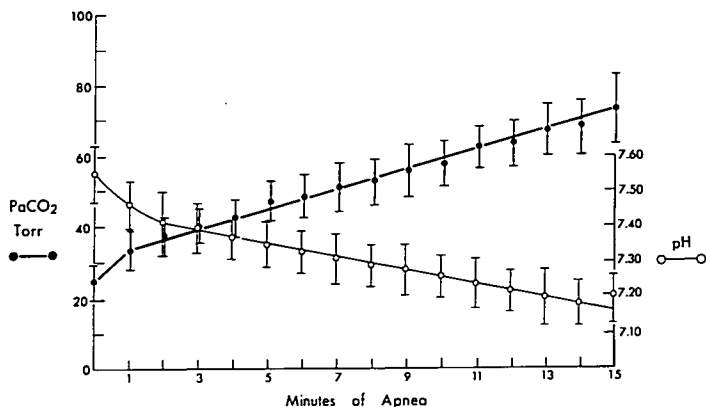


FIG. 5. P_{aCO_2} and pH during 15 minutes of apneic oxygenation. This illustration includes all patients in Groups I and II because values in the two groups were the same.

and nitrogen in the lungs, as well as a reduction in FRC, would reduce oxygen taken in from the spirometer, giving an erroneously low value for \dot{V}_{O_2} . Total corrected \dot{V}_{O_2} , therefore, is obtained by adding the volume taken from the spirometer, the volume of carbon di-

oxide and nitrogen accumulated in the lungs, and any measured decline in FRC during apnea. Patients who experienced arterial desaturation were excluded from these data. Apnea was verified by absence of ventilatory movement on the Collins tracing.

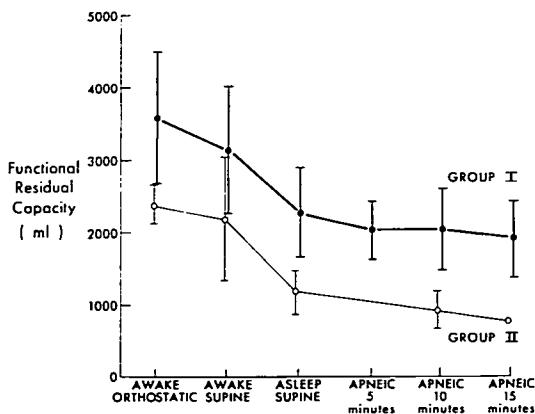


FIG. 6. Functional residual capacities before and after various periods of apnea. Group II patients had consistently lower FRC's than Group I patients. FRC's changed in a similar fashion in the two groups.

Results

Pa₀₂

Changes in Pa₀₂ are expressed as percentages of control in figure 1. In the Jako-laryngoscopy patients, after 15 minutes of apnea, Pa₀₂ had declined 47.1 ± 14 per cent from an initial value of 485 ± 78 torr at the beginning of apnea. The other patients had a 30.1 ± 24 per cent decline from an initial Pa₀₂ of 445 ± 68 torr. There was no significant difference between the Pa₀₂'s before or during apnea with the two methods of oxygen delivery, so we pooled these results. When this is done and the decreases in Pa₀₂ for all patients are graphed (fig. 2), it becomes evident that the patients fall into two distinct groups: 22 patients in whom Pa₀₂'s were well maintained (Group I), and nine patients in whom they were not (Group II). By 4 minutes, the Pa₀₂ of Group I (428 ± 32 torr, mean \pm SE) was significantly different from that of Group II (254 ± 53 torr) (fig. 3).

When the endotracheal tube was left open to room air during a second period of apnea in patients of Group I (fig. 4), the Pa₀₂ declined much more rapidly than when oxygen was used. When one Group II patient underwent an apneic period with room air, his Pa₀₂ declined very rapidly, reaching hypoxic levels by 5 minutes with a Pa₀₂ of 51 torr.

Pa_{CO2} AND pH

From an initial value of 24.5 ± 5.1 torr, Pa_{CO2} increased to 73.2 ± 9.9 torr after 15 minutes of apnea. The decline in pH was respiratory in nature, with no significant change in base excess. From an initial value of 7.55 ± 0.08 , pH declined to 7.20 ± 0.07 after 15 minutes of apnea (fig. 5). Pa_{CO2} and pH values in Group I and Group II were not significantly different.

NITROGEN

Group I patients accumulated 169.5 ± 43.5 ml of nitrogen in the lungs during the 15-minute apneic interval. Group II patients accumulated 277.5 ± 45.0 ml of nitrogen during the same interval.

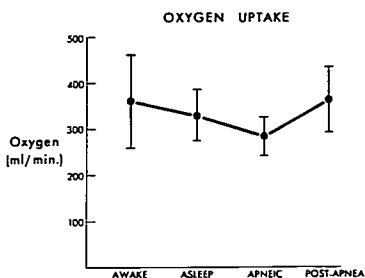


FIG. 7. Oxygen uptake was not changed significantly except during apnea, when it declined to 285 ± 44 ml/min.

FUNCTIONAL RESIDUAL CAPACITY

Functional residual capacity (FRC) decreased equally in Groups I and II (fig. 6). The largest decrease of FRC (mean 953 ml) occurred at the time of induction of anesthesia (difference between the awake supine and the asleep measurements). The slight downward trend of the FRC during apnea was not statistically significant. More important, however, all FRC values of Group I patients were significantly larger than those of Group II patients. Awake, orthostatic FRC's were $3,572 \pm 882$ ml in Group I and $2,390 \pm 261$ ml in Group II. These values were significantly different from those predicted by Needham's formula,⁷ $3,925 \pm 380$ ml for Group I and $3,030 \pm 212$ ml for Group II. The difference is significant at the 1 per cent level.

OXYGEN UPTAKE

Under similar experimental conditions (awake, asleep, apneic, and postapneic) no significant difference between oxygen uptakes in the two groups could be shown. However, both groups had decreases in oxygen uptake during apnea which were significantly ($P < .01$) different from both pre- and postapneic values (fig. 7).

CARDIOVASCULAR CHANGES

No patient whose trachea was intubated with an endotracheal tube experienced cardiac

arrhythmia. However, seven of the 13 patients in the Jako-laryngoscopy group had premature ventricular contractions. The arrhythmias occurred after various periods of apnea and could not be correlated with Pa_{O_2} , Pa_{CO_2} , pH, or blood pressure. This implies a reflex etiology of the arrhythmias, most likely the result of surgical manipulation of the larynx. Heavier premedication or more thorough local anesthesia of the larynx should minimize or eliminate this problem.

Discussion

Bendixen *et al.*^{8,9} and Panday and Nunn¹⁰ found that normal patients undergoing general anesthesia with controlled or spontaneous ventilation had A-a oxygen gradients of 200 to 300 torr while breathing 100 per cent oxygen. They postulated the development of atelectasis with increased intrapulmonary shunting as the cause of the widening A-a gradient. Studies by Don *et al.*,¹¹ Laws,¹² and Hickey *et al.*¹³ show that FRC falls dramatically upon the induction of general anesthesia in the supine position. This corroborates the postulation of Bendixen *et al.*^{8,9} and Panday and Nunn¹⁰ that atelectasis develops. Don *et al.*¹¹ state that this atelectasis is not progressive during general anesthesia, as witnessed by the relatively constant FRC measurements later in the course of anesthesia. Heller *et al.*⁴ suggest that development of progressive atelectasis with shunting may be the cause of ever-widening A-a gradients during apneic oxygenation. Our data corroborate the findings of Bendixen *et al.*^{8,9} Panday and Nunn,¹⁰ and Heller *et al.*⁴ in that the A-a gradients, after induction and at the start of apnea, were about 200 torr. Our FRC data show a marked decline from awake supine to asleep supine values, with little further decrease during apnea. This suggests the development of considerable shunt with induction but, contrary to the speculation of Heller *et al.*,⁴ very little increase in shunting resulting from atelectasis during apnea.

We have shown that during apnea a 6-liter oxygen flow through a pharyngeal catheter is as efficient in maintaining Pa_{O_2} as an endotracheal tube delivering 100 per cent oxygen to the airway. This is considerably more effi-

cient than delivering room air to the airway. Our results in apneic patients ventilated with air were essentially the same as those obtained by Heller *et al.*⁴ in 1963, when they showed a decline in Pa_{O_2} of 300 torr in 5 minutes; we found a decline in Pa_{O_2} of 295 torr in 5 minutes.

During apneic oxygenation, 22 of our 31 patients (Group I) had Pa_{O_2} changes similar to those seen by Heller *et al.*⁴ when they evaluated six patients undergoing apneic oxygenation with endotracheal tubes in place for 5 minutes. Their patients had an average Pa_{O_2} of 419 torr after 5 minutes of apneic oxygenation, whereas our Group I patients had Pa_{O_2} 's of 415 torr after 5 minutes and 322 torr after 15 minutes of apnea.

Nine of our 31 patients (Group II), however, had Pa_{O_2} changes not reported or predicted by any previous investigator. These patients had rapid declines of Pa_{O_2} , reaching 196 torr after 5 minutes and 91 torr after 15 minutes of apnea.

To explain the reason for this difference between the two groups of patients, one must consider changes in lung volume (FRC) and changes in alveolar gas composition. Although the mean heights of patients in the two groups were identical (172 cm), Group II patients were heavier, with a mean weight of 82.5 ± 13 kg compared with 71.3 ± 5.7 kg in Group I. As Don¹¹ and Hickey¹³ predicted, the heavier Group patients had a mean final FRC of 839 ± 248 ml, whereas Group I patients had a mean final FRC of $1,907 \pm 517$ ml (fig. 7). The importance of this difference becomes apparent when one considers the composition of alveolar gas at the end of apnea.

We found that the increase in Pa_{CO_2} , and therefore P_{ACO_2} , was approximately 50 torr in each group. A 50-torr increase in P_{ACO_2} would cause 50-torr decreases in Pa_{O_2} in both groups, but would not account for the differences between the groups.

Alveolar nitrogen concentrations were not the same in the two groups. Though alveolar nitrogen was eliminated by hyperventilation with 100 per cent oxygen prior to apnea, tissue nitrogen, and therefore mixed venous nitrogen tension, was still high in both groups. On the basis of body weight, one could pre-

diet that Group II patients would have a greater amount of total body nitrogen as well as increased cardiac output¹⁴ and, therefore, a higher rate of nitrogen return to the lung. Our findings verify this: Group I patients had 169 ± 43.5 ml and Group II patients, 277.5 ± 45.0 ml of nitrogen return. Nitrogen returning to the lung will replace alveolar oxygen and thereby lower $P_{A_{O_2}}$. Because Group II patients had smaller FRC's than Group I patients, together with increased nitrogen return, they experienced more rapid decreases in alveolar and, therefore, arterial P_{O_2} than did Group I patients. In summary, these changes in $P_{A_{O_2}}$ during apneic oxygenation can be accounted for by the concomitant increases of $P_{A_{CO_2}}$ and, more importantly, $P_{A_{N_2}}$ in the two groups (fig. 8).

Although there was a slight diminution in oxygen uptake after administration of thiopental and succinylcholine, it was not significant (fig. 7). Two opposing influences are involved. It has been shown that oxygen consumption decreases 10 to 15 per cent with the induction of general anesthesia¹⁵⁻¹⁷; however, succinylcholine increases oxygen consumption, although this effect can be reduced markedly by pretreatment with a nondepolarizing muscle relaxant.¹⁸ We believe these two opposing effects were responsible for our results.

We did find a highly significant decline ($P < .01$) in oxygen uptake from the asleep value to the apneic value. Hypercapnia depresses oxygen utilization.¹⁹⁻²¹ Holmdahl² reported a decrease in oxygen uptake in anesthetized, paralyzed dogs during apnea with increasing hypercarbia. Our study has shown the same decrease in man.

Once ventilation was resumed at the end of apnea, and P_{CO_2} returned to eucapnic levels, oxygen uptake returned to the preapneic level.

The predicted orthostatic FRC-to-weight ratio is a useful index for predicting preoperatively whether a given patient will fall into Group I or Group II. Our Group I patients had predicted FRC/weight ratios of 53.7 ± 7.7 ml/kg, whereas Group II patients had predicted FRC/weight ratios of 36.7 ± 9.0 ml/kg. There was significant correlation between high FRC/weight ratios and good performance

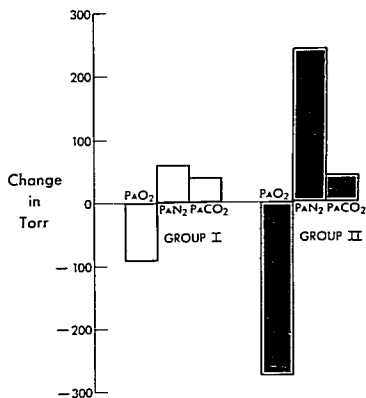


FIG. 8. Changes of alveolar gas after 15-minutes of apneic oxygenation in Group I and Group II. The decrease in $P_{A_{O_2}}$ was nearly totally accounted for by the increases in $P_{A_{N_2}}$ and $P_{A_{CO_2}}$. The $P_{A_{CO_2}}$'s were essentially the same in the two groups, but $P_{A_{N_2}}$ in Group II patients was significantly greater, thereby accounting for the different declines of $P_{A_{O_2}}$.

during apneic oxygenation (Group I patients). Although significant (correlation coefficient .56, SE 0.18) this correlation was relatively low, indicating that this ratio is not always dependable. We found that by applying rather stringent criteria one can exclude all Group II patients from being subjected to the technique at the expense of excluding some Group I patients also. We recommend that only patients with predicted FRC/weight ratios of 50 ml/kg or more have apneic oxygenation for longer than 5 minutes.

In conclusion, we feel that apneic oxygenation is useful for certain types of surgery, and with proper patient selection, so long as 15 minutes of operating time may be expected with it. Thorough preoperative patient evaluation and determination of the predicted FRC/weight ratio provide a useful guide for selecting patients. Adequate nitrogen washout and hyperventilation with 100 per cent oxygen must precede the apnea, and a pharyngeal catheter must be used for oxygen administration. In addition to the standard intraoperative

monitoring, a means of monitoring oxygenation is essential. We have found an ear oximeter to be useful, using the onset of desaturation as the signal for termination. This is particularly important in patients with low predicted FRC/weight ratios.

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