CYCLIC VARIATIONS IN BLOOD OXYGENATION WITH THE RESPIRATORY CYCLE

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EXTRACTION of oxygen from alveolar gas and addition of carbon dioxide to alveolar gas is a continuous process occurring during all phases of the respiratory cycle. Gas exchange with the ambient atmosphere is cyclic, occurring only during one phase of the respiratory cycle. Therefore, the composition of alveolar gas cannot remain constant but exhibits cyclic variations with the phases of the respiratory cycle. The interval of time during which pulmonary capillary blood is in equilibrium with alveolar gas is much shorter than the duration of a respiratory cycle.[1] Cyclic variations in alveolar gas composition will, therefore, cause cyclic variations in the oxygen and carbon dioxide tensions of arterial blood.

DuBois and associates[2,3] analyzed cyclic variations in alveolar oxygen and carbon dioxide tensions. They concluded that during inspiration alveolar oxygen tension increased because addition of oxygen to alveolar gas occurred more rapidly than extraction of oxygen from alveolar gas. Alveolar carbon dioxide tension decreased because dilution of alveolar gas was more rapid than the addition of carbon dioxide to alveolar gas from the blood. During exhalation alveolar oxygen tension fell because oxygen was removed from a diminishing alveolar volume by the blood without the addition of fresh oxygen to alveolar gas. Alveolar carbon dioxide tension increased because carbon dioxide was added to a diminishing alveolar volume with no removal of carbon dioxide from alveolar gas (fig. 1).

Frumin and co-workers[4] reported that during artificial ventilation of anesthetized humans, arterial oxygen saturation increased 8 per cent and arterial oxygen tension increased 10 mm. of mercury when the pressure in the airway during exhalation was changed from −5 cm. to +5 cm. of water. A theoretical analysis based on the results of this study suggested that cyclic variations in alveolar oxygen tension were less when the functional residual capacity was kept large by the imposition of +5 cm. of water resistance to exhalation than when the functional residual capacity was made small by the application of −5 cm. of water pressure during exhalation. The calculated decrease in magnitude of cyclic variations in alveolar oxygen tension could, however, only account for one third of the observed increase in arterial oxygen saturation.

Physical laws relating volumes and pressures of gasses indicated that for any given rate of extraction of oxygen from alveolar gas, cyclic variations in alveolar oxygen tension become larger as the functional residual capacity decreases and as the respiratory rate decreases. It is possible that at very small functional residual capacities alveolar oxygen tension might fall to very low levels during exhalation, particularly at slow respiratory rates. This would decrease mean alveolar oxygen tension with resultant arterial hypoxemia. The studies of both DuBois and Frumin suggest that in spontaneously breathing conscious subjects or in artificially ventilated anesthetized subjects with closed thoraces cyclic variations in alveolar oxygen tension are not of sufficient magnitude to cause arterial hypoxemia. When the thorax is opened the chest wall no longer limits the degree to which the lung may collapse during exhalation. With the resulting small functional residual capacities, cyclic variations in alveolar oxygen tension large enough to cause some degree of arterial hypoxemia might occur. It was of interest, therefore, to obtain information concerning the magnitude of cyclic variations in the oxygenation of arterial blood with the thorax open.

This report describes the measurement of cyclic variations in arterial oxygen saturation with the respiratory cycle in dogs with open

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thoraces and a study of some factors which modify the magnitude of the cyclic variations.

Methods

Left thoracotomy was done on dogs during pentobarbital anesthesia and succinylcholine immobilization. The animals were artificially ventilated with room air through a nonrebreathing circuit composed of a Bennett BA-2C ventilator, a tightly fitting cuffed endotracheal tube and a Frumin nonrebreathing valve. The dogs remained in the lateral position throughout the study. No intrathoracic manipulations were done until the respiratory portion of the study had been completed.

End-expiratory carbon dioxide tension was measured with a Beckman Model LB-1 infrared carbon dioxide analyzer which was calibrated with commercially obtained air-carbon dioxide mixtures whose exact composition was determined by Scholander analysis. Gas was sampled at a rate of 150 cc./minute through a small (internal diameter 0.82 mm.) catheter whose tip was close to the distal end of the endotracheal tube. Respiratory rate was 6 or 7 breaths/ minute and the inflating pressure delivered by the ventilator was adjusted to provide an end-expiratory carbon dioxide tension of between 20 and 30 mm. of mercury. Airway pressure during exhalation was varied by either permitting free exhalation through the nonrebreathing valve or by connecting the expiratory port of the valve to a large bore tube whose tip was 4 cm. under water and, therefore, imposed a 4 cm. of water resistance to exhalation. In certain other experiments the respiratory rate was increased from 6–7/ minute to 18–30/minute or 35 per cent oxygen-65 per cent nitrogen or 100 per cent oxygen was used as the inflating gas. Pressure in the airway was measured with a small catheter whose tip was in the endotracheal tube with a Statham PM5TC pressure transducer and an Ensco SGA-3 pressure amplifier which were calibrated with a water manometer. Expiratory flow rate was measured by flowing exhaled gases either directly from the nonrebreathing valve or from the bottle containing the under-water tube through a pneumotachograph head connected with a Statham PM97TC pressure transducer and an Ensco SGA-3 pressure amplifier. Minute volume and tidal volume were obtained by electronic integration of expiratory flow rate using an Ensco P1-1 integrator which had been calibrated by putting known volumes of air through the pneumotacograph with a calibrated 2,000 cc. syringe and measuring the deflection from the baseline for each volume.

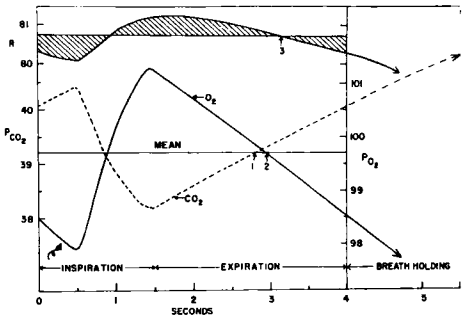
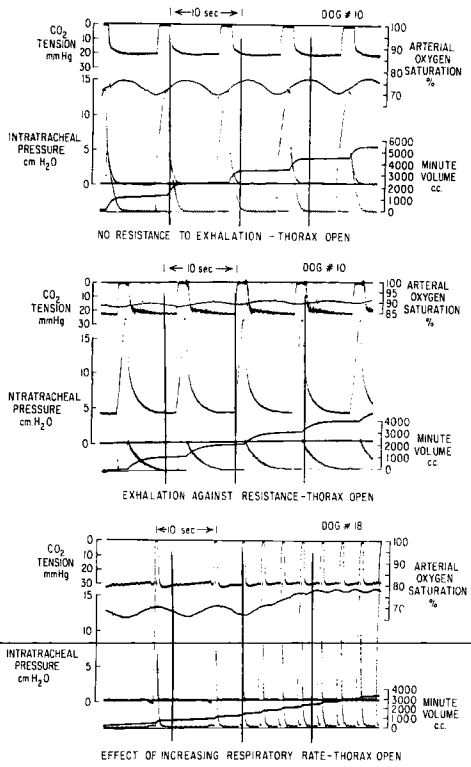


FIG. 1. Cyclic changes in the alveolar gases during a normal respiratory cycle. From Rahn, H., and Fenn, W. A.: A Graphical Analysis of The Respiratory Gas Exchange, Washington, D. C., American Physiological Soc., 1955. Reproduced through courtesy of authors and publishers. (Adapted from DuBois, Britt, and Fenn.[2])

Arterial oxygen saturation was measured with a Waters XC–50B cuvette and one channel of an Ensco Model OSA-2B Dual Channel Oximeter Amplifier. Femoral arterial blood was drawn from a small (internal diameter 0.82 mm., length 10 cm.) catheter through the cuvette at a constant rate by a motor-driven syringe. Calibration of the oximeter was rechecked frequently. Pulmonary artery to femoral artery circulation time was measured with the same catheter-cuvette-amplifier system. The system was rebalanced while the dog was ventilated with 100 per cent oxygen. Evans blue dye 0.5 cc. was injected into the pulmonary artery and the time required for the dye to appear in femoral arterial blood was measured. Blood withdrawn from the femoral artery was reinfused via the femoral vein after each determination of saturation or circulation time. The outputs of the carbon dioxide analyzer, the oximeter amplifier, pressure amplifiers and the integrator were recorded simultaneously using a Minneapolis-Honeywell Visicorder.

Duplicate arterial blood samples were withdrawn as close in time as possible to oximetric



FIGS. 2, 3, and 4. Representative recordings of the various parameters studied. From above downward: carbon dioxide tension in inspired and expired gas, arterial oxygen saturation, intratracheal pressure, integrated pneumotachogram, and expiratory pneumotachogram.

saturation determinations made when the animal exhaled freely to atmosphere and again when exhalation occurred against resistance. These were analyzed spectrophotometrically for oxygen saturation using the wave lengths 660 and 805 millimicrons.[5] Experiments in which mean oxygen saturation determined by oximeter and the oxygen saturation determined by the spectrophotometric technique differed by more than 2 per cent were considered unsatisfactory and discarded. Arterial oxygen tension was derived from arterial oxygen saturation and end-expiratory carbon dioxide tension using dissociation curves for dog blood.[6] Because of the difficulty of transforming saturations into tensions in the flat upper region of the dissociation curve the record of any dog with an arterial oxygen saturation greater than 95 per cent was considered unsuitable for analysis. At the elevation of our laboratory (4,900 feet) the average barometric pressure is 640 mm. of mercury and the partial pressure of inspired oxygen ($P_{I_{O_2}}$) was taken as $20.9 \times (640–47)$ or 124 mm. of mercury. The respiratory quotient was assumed to be unity and the partial pressure of alveolar oxygen ($P_{A_{O_2}}$) was calculated from the simplified form of the alveolar gas equation $P_{A_{O_2}} = P_{I_{O_2}} - P_{A_{CO_2}}$.[7]

RESULTS

Eight dogs which provided records suitable for analysis are the subject of this report. When the animals exhaled freely to atmosphere the lungs achieved a state of marked collapse during each exhalation. Minute volumes approximated minute volumes reported in the unanesthetized, spontaneously breathing dog,[8] but because of the slow rate, tidal volumes were greater than normal. End-expiratory carbon dioxide tensions were between 20 and 30 mm. of mercury. Peak airway pressure was attained rapidly and declined rapidly so that the expiratory pause occupied one half to four fifths of the respiratory cycle. The record of arterial oxygen saturation exhibited cyclic variations resembling a sine wave whose frequency was identical to that of the respiratory rate. The average maximum arterial oxygen saturation achieved during the cycle was 82 per cent and the corresponding average maximum arterial oxygen tension was 48 mm. of mercury. The average minimum saturation was 72 per cent and the corresponding minimum tension achieved during the cycle was 38 mm. of mercury. Thus, the variation between average maximum and minimum values during the cycle was 10 per cent saturation and 10 mm. of mercury tension. The mean arterial oxygen saturation and tension, taken as the arithmetic mean of maximum and minimum values, was 77 per cent and 42 mm. of mercury. The mean alveolar-arterial oxygen difference was 59 mm. of mercury (fig. 2, table 1).

When exhalation occurred against resistance the lungs remained partially inflated during exhalation. Peak pressure was increased so that the inflating pressure was close to that applied when the animals exhaled freely to atmosphere. Minute volumes were generally

slightly less and end-expiratory carbon dioxide tensions were 1 to 8 mm. of mercury higher when exhalation occurred against resistance than during the period of free exhalation. Peak pressure was attained rapidly and declined rapidly to 4 cm. of water and remained at this value during the expiratory pause. The expiratory pause occupied one half to four fifths of the respiratory cycle. Sine wave-like fluctuations with a frequency identical to the respiratory rate again occurred in the record of arterial oxygen saturation. The average maximum arterial oxygen saturation occurring during the cycle was 91 per cent and the corresponding tension was 66 mm. of mercury. The average minimum saturation was 88 per cent and the corresponding minimum tension occurring during the cycle was 59 mm. of mercury. The variation between average maximum and minimum values during the cycle was 3 per cent saturation and 7 mm. of mercury tension. The mean arterial oxygen saturation and tension, again taken as the arithmetic mean of maximum and minimum values was 90 per cent and 62 mm. of mercury. The mean alveolar-arterial oxygen difference was 34 mm. of mercury (fig. 3, table 1). The decrease in alveolar-arterial oxygen difference from 59 to 34 mm. of mercury with the imposition of resistance to exhalation is significant ($P < 0.01$). The decrease in the magnitude of cyclic variations in arterial oxygen saturation and tension from 10 per cent and 10 mm. of mercury during free exhalation to 3 per cent and 7 mm. of mercury during exhalation against resistance is also significant, ($0.02 < P < 0.01$).

When the respiratory rate was increased from 6–7/minute to 18–30/minute during free exhalation to atmosphere tidal volumes and end-expiratory carbon dioxide tensions decreased and minute volumes increased. Mean

TABLE 1

SUMMARY OF EXPERIMENTAL FINDINGS

Dog	Insp. & Exp. Press.	Resp. Rate	T.V. (cc.)	M.V. (cc.)	$P_{A_{CO_2}}$ (mm. Hg)	Mean S_{O_2} and P_{aO_2}		Maximum S_{O_2} and P_{aO_2}		Minimum S_{O_2} and P_{aO_2}		Fluctuations in S_{O_2} and P_{aO_2}	
						(%)	(mm. Hg)	(%)	(mm. Hg)	(%)	(mm. Hg)	(%)	(mm. Hg)
6	15.5–0	7	750	5,250	20	90	58	91	62	88	54	3	8
	18–3.5	7	500	3,500	24	93	72	93	72	92	68	1	4
9	14–0	6	1,250	7,500	24	78	43	82	48	73	39	9	9
	17–4	7	875	6,125	28	86	55	87	57	85	53	2	4
12	16–0	7	500	3,500	20	75	39	80	43	71	35	9	8
	19–3.5	7	330	2,310	28	92	70	93	74	91	66	2	8
	15–0	24	330	7,920	15			89	52	88	51	1	2
14	16–0	7	390	2,730	27	68	36	79	45	59	31	20	14
	19–3.5	6	440	2,640	28	90	62	92	70	88	59	4	11
	16–0	18	330	5,940	26			79	46	75	41	4	5
	16–0	30	330	9,900	20			92	66	92	66	0	0
17	16.5–0	6	775	4,650	28	81	48	88	59	75	43	13	16
	19–4	6	500	3,000	33	90	64	92	72	89	63	3	9
19	16–0	7	310	2,170	24	82	48	86	53	79	43	7	10
	18–2	6	250	1,500	28	88	59	89	60	87	57	2	3
	16–0	18	250	4,500	21			88	55	88	55	0	0
22	15–0	6	560	3,360	20	74	37	81	44	69	33	12	11
	16–3	6	440	2,640	23	88	56	90	59	86	52	4	7
	15–0	21	500	10,500	19			91	60	91	60	0	0
24	16–0	10	470	4,700	18	66	31	69	33	62	29	7	4
	19–3	10	500	5,000	22	89	57	90	59	87	53	3	6
	16–0	18			21			68	34	64	31	4	3

Insp. and Exp. Press.—Intratracheal pressure during inspiration and exhalation; Resp. Rate—Respiratory rate; T.V.—Tidal volume; M.V.—Minute volume; $P_{A_{CO_2}}$—Alveolar carbon dioxide tension (in this study taken as identical with the end-expiratory carbon dioxide tension); S_{O_2}—Arterial oxygen saturation; P_{aO_2}—Arterial oxygen tension.

arterial oxygen saturations increased but because no blood samples were obtained for spectrophotometric analysis during this phase of the study no attempt was made to calculate alveolar-arterial oxygen differences with increased rates of respiration. Under these conditions cyclic variations in arterial oxygen saturation were greatly decreased or eliminated (fig. 4, table 1). With 35 per cent oxygen-65 per cent nitrogen as the inflating gas, cyclic variations in arterial saturation were 1–9 per cent less than with air. Oxygen (100 per cent) abolished cyclic variations in saturation in all cases. Pulmonary artery-femoral artery circulation time varied from five to nine seconds. When the pulmonary-femoral time lag in each dog was corrected using that animal's particular circulation time, it was found that blood which was maximally saturated during the cycle was in the lung during inspiration and blood that was minimally saturated during the cycle was in the lung toward the end of the expiratory pause.

Discussion

Despite many known difficulties inherent in the application and interpretation of oximetry, it is the only technique presently available with a response time sufficiently rapid to study cyclic variations in arterial oxygenation within a single respiratory cycle.[9] One important consideration was the relationship of the form and magnitude of the cyclic variations as recorded by the instrument to the form and magnitude of the cyclic variations in arterial oxygen saturation actually occurring in the blood. Fox and associates studied the dynamic response characteristics of systems for continuous recording of concentration changes in a flowing liquid using various catheter-cuvette systems and a mechanical injecting device to produce square waves of blood with and without dye. They concluded that the dynamic response of the systems improved when the internal diameter of the catheter was small, when the catheter was short, and when the rate of flow through the system was rapid.[10] Therefore, in our experiments a short, small bore catheter was used and the rate at which blood was drawn through the cuvette was 40 cc./minute. This was found to be the rate at which the cyclic variations in oxygen saturation became maximum with this particular catheter-cuvette system. Because of the variable, unpredictable amount of dampening found by Fox with various catheter-cuvette systems it was apparent that no conclusions could be made concerning the actual wave forms of the cyclic variations in saturation in our experiments. It was also apparent that the magnitude of the cyclic variations in saturation recorded by the catheter-cuvette system in our experiments represented minimal values, *i.e.*, the actual magnitude of change between maximum and minimum saturations in any cycle could have been larger but probably not smaller.

The use of end-expiratory carbon dioxide tensions in the transformation of oxygen saturations into oxygen tensions introduces a certain amount of error into the experimental results. Alveolar dead space increases at small functional residual capacities.[11] With the low resting expiratory volumes in our experiments it is probable that much of the tidal volume was ventilating nonperfused areas of the lung, so that the mean arterial carbon dioxide tension was probably several millimeters of mercury greater than the end-expiratory carbon dioxide tension. However, since the saturation isopleths on the blood dissociation diagram diverge as carbon dioxide tension increases, the calculated magnitude of cyclic variations in arterial oxygen tension is again probably smaller than that which actually occurred in the blood. It was assumed that the mean oxygen saturation was the arithmetic mean between maximum and minimum saturations achieved during the cycle. This also may have introduced a certain amount of error into the interpretation of the experimental results. It is, however, probably the best approximation of mean arterial oxygen saturation in the absence of information concerning the actual wave form of the cyclic variations.

Any alveolar-arterial oxygen difference can be the result of two mechanisms: (1) a "membrane component" caused by incomplete equilibrium between alveolar gas and pulmonary capillary blood, and (2) a "physiologic shunt" caused by the contamination of maximally oxygenated pulmonary capillary blood with blood which has been shunted directly from the venous side of the circulation or has passed

through areas of the lung which are relatively hypoventilated.[12] The alveolar-arterial oxygen differences measured in our experiments are somewhat larger than, but in general agreement with those reported by Williams. By studying the alveolar-arterial oxygen difference at three levels of oxygenation he concluded that in the open-chest dog the membrane component is negligible and the entire alveolar-arterial oxygen difference is caused by the physiologic shunt.[13]

Both the degree of the physiologic shunt and the magnitude of cyclic variations in alveolar oxygen tension with the respiratory cycle should determine the mean arterial oxygen tension and hence the mean arterial oxygen saturation. The relationship between these two variables in determining the mean oxygen tension may be clarified by considering a lung with an infinitely large functional residual capacity. In this lung the removal of oxygen during exhalation would not appreciably lower the oxygen tension in the alveoli and cyclic variations in alveolar oxygen tension would be absent. In this instance the arterial oxygen tension at any given alveolar oxygen tension would be determined only by the proportion of the total cardiac output involved in the physiologic shunt. As the functional residual capacity becomes small, cyclic variations in alveolar oxygen tension with the respiratory cycle occur. The magnitude of these cyclic variations determines the degree to which arterial oxygen tension falls below the maximum possible arterial oxygen tension. The physiologic shunt may be regarded as a shunt in space which determines the maximum arterial oxygen tension that can be achieved during the respiratory cycle. Cyclic variations in alveolar oxygen tension with the respiratory cycle may be regarded as a shunt in time which determines the degree to which mean arterial oxygen tension differs from the maximum tension attainable for the particular amount of physiologic shunt occurring at the moment. As the magnitude of cyclic variations in alveolar oxygen tension increase, the difference between maximum attainable arterial oxygen and mean arterial oxygen tension increases and the mean arterial oxygen tension decreases. Cyclic variations in alveolar oxygen tension do not in themselves cause an alveolar-arterial oxygen difference. If the value for alveolar oxygen tension used in calculating the alveolar-arterial oxygen difference is taken at a time in the respiratory cycle when it is significantly different from the mean alveolar oxygen tension for the cycle, an apparent increase or decrease in the alveolar-arterial oxygen difference may occur. It is possible that a portion of the large alveolar-arterial oxygen differences in our experiments was caused by taking the value for $P_{A_{O_2}}$ used in calculating alveolar-arterial oxygen differences at the end of exhalation when the mean $P_{A_{O_2}}$ actually occurred later in the cycle at some time during the expiratory pause. The largest part of the significant decrease in alveolar-arterial oxygen difference produced by imposition of resistance to exhalation was probably caused by the more even relative distribution of pulmonary blood flow and inspired gas which occurs as the functional residual capacity increases.[11]

Using representative values from the literature for the various parameters of ventilation in the dog and making certain assumptions it was possible to approximate the magnitude of cyclic variations in alveolar oxygen tension and to approximate the effect of varying the functional residual capacity and the respiratory rate.

Assume for 20-kg. dog with an open thorax:

(1) Oxygen consumption and carbon dioxide production = 190 cc./minute.[14]
(2) $P_{A_{CO_2}} = 30$ mm. of mercury; Barometric pressure = 640 mm. of mercury; $P_{I_{O_2}} = 119$ mm. of mercury.
(3) Alveolar ventilation $= \dot{V}_{CO_2} \times .863 / P_{A_{CO_2}} = 5{,}466$ cc./minute.
(4) Anatomical dead space = 45 cc.
(5) Functional residual capacity exhaling against 4 cm. of water resistance = functional residual capacity in closed thorax = 700 cc.[15]
(6) When resistance to exhalation is removed functional residual capacity decreases by a factor of four times compliance of the lung. Therefore, functional residual capacity during free exhalation is 330 cc.[14]
(7) Pulmonary filling and emptying are instantaneous.

These assumptions permit the calculation of alveolar volume and composition at four different points in the respiratory cycle: (1) at the beginning of inspiration, (2) at the end of instantaneous filling, (3) at the end of instantaneous emptying, and (4) at the end of the expiratory pause. Since the end-expiratory carbon dioxide tension was measured experimentally and the volume of the lung at this point is the functional residual capacity, the alveolar oxygen tension can be calculated using the alveolar air equation and the volume of the alveolar oxygen at the end of exhalation can also be derived. Then, using the assumed values enumerated above the other values in table 2 may be calculated.

If ventilation is stopped in a dog which has been respired on room air arterial oxygen saturation falls because the extraction of oxygen from the alveolus by pulmonary capillary blood continues. Each expiratory pause may be considered as a short period of apnea. Using the laws relating the volumes and pressures of gases the fall in oxygen tension in millimeters of mercury in the alveoli during a period of apnea can be calculated using the following equation:

$$\text{Decrease in alveolar oxygen tension (mm. of mercury)} = \frac{\text{Volume of alveolar } O_2 \text{ at onset of apnea} - \text{Volume of alveolar } O_2 \text{ at end of apnea}}{\text{Lung volume during apnea}} \times P_B$$

where P_B = barometric pressure. Thus, the fall in alveolar oxygen tension during an apnea is directly related to the volume of oxygen taken from the alveoli during the apnea and inversely related to the lung volume during apnea. The inverse relationship between decrease in alveolar oxygen tension and lung volume during apnea was verified experimentally.[16] The magnitude of cyclic variations in alveolar oxygen tension with the respiratory cycle is determined by the amount by which alveolar oxygen tension falls below the maximum tension achieved during the cycle. The relationship expressed in the above equation indicates that cyclic variations in alveolar oxygen tension increase as the lung volume during exhalation and the expiratory pause decreases. In our experiments cyclic variations in arterial oxygen saturation were significantly smaller when the functional residual capacity of the lung was kept large by the imposition of resistance to exhalation than when it was permitted to come to its normal resting expiratory position. The above equation also indicates that when oxygen consumption per respiratory cycle decreases, cyclic variations in alveolar oxygen tension also decreases. When the respiratory rate increases the quantity of oxygen extracted from the alveoli per breath decreases. In our experiments cyclic variations in arterial oxygen saturation were smaller at rapid respiratory rates than at slow respiratory rates. It is possible that some of the observed results may have been due to a greater degree of dampening of the cyclic variations in the catheter-cuvette system at higher frequencies. Reference to the above equation indicates that the magnitude of cyclic variations in alveolar oxygen tension is independent of alveolar composition. In our experiments inhalation of gases with high oxygen tensions diminished or abolished cyclic variations in arterial oxygen saturation. It is probable, therefore, that although cyclic variations in alveolar oxygen tension still occur under these conditions alveolar oxygen tension remained at a level above the minimum level necessary for complete oxygenation of the arterial blood throughout all or most of the respiratory cycle. In addition, in the flat, upper portion of the oxygen dissociation curve of hemoglobin, large changes in oxygen tension cause little variation in oxygen saturation.

Another mechanism which may have contributed to cyclic variations in arterial oxygen saturation is cyclic variation in the degree of physiologic shunt with the phases of the respiratory cycle. Distribution of pulmonary blood flow[11] and pulmonary hemodynamics[17] vary significantly with lung volume. It is possible that the amount of blood shunted from the venous to the arterial circulation either directly or through relatively hypoventilated portions of the lung, might vary as the volume of the lung changes within a single respiratory cycle. This mechanism would cause a cyclic variation in the alveolar-arterial gradient. Results of

TABLE 2

EFFECT OF CHANGES OF FUNCTIONAL RESIDUAL CAPACITIES AND RESPIRATORY RATE ON THEORETICAL VARIATIONS IN ALVEOLAR VOLUME AND COMPOSITION WITH RESPIRATION

	Alveolar Volume (cc.)	P_{ACO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	cc.'s of Alveolar Oxygen
Beginning of Inspiration	700	59	60	65
End of Instantaneous Filling	1657	25	94	240
End of Instantaneous Emptying	700	30	89	97
End of Expiratory Pause	700	59	60	65

FRC = 700 cc. Rate = 6/minute Mean P_{AO_2} = 77 mm. Hg

	Alveolar Volume (cc.)	P_{ACO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	cc.'s of Alveolar Oxygen
Beginning of Inspiration	330	92	27	14
End of Instantaneous Filling	1287	25	94	189
End of Instantaneous Emptying	330	30	89	46
End of Expiratory Pause	330	92	27	14

FRC = 330 cc. Rate = 6/minute Mean P_{AO_2} = 61 mm. Hg

	Alveolar Volume (cc.)	P_{ACO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	cc.'s of Alveolar Oxygen
Beginning of Inspiration	700	45	74	81
End of Instantaneous Filling	1201	25	94	176
End of Instantaneous Emptying	700	30	89	97
End of Expiratory Pause	700	45	74	81

FRC = 700 cc. Rate = 12/minute Mean P_{AO_2} = 84 mm. Hg

our experiments do not permit conclusions as to the magnitude of the contribution of cyclic variation in physiologic shunt to the observed cyclic variations in arterial oxygen saturation. It is thought that such a contribution must be small, however, because the magnitude of cyclic variations in alveolar oxygen tension with the respiratory cycle calculated theoretically was more than adequate to account for the entire cyclic variation in arterial oxygen saturation.

One important consideration when working under conditions where marked cyclic variations in blood gas tensions might be expected to occur is in obtaining a representative blood sample for analysis. Marked variations in oxygen saturation between duplicate blood samples sometimes occurred early in the study. It was subsequently realized that these samples had been withdrawn from the artery as rapidly as possible. When the blood samples were withdrawn over a period of several respiratory cycles, duplicate samples agreed within the limits of reproducibility of the method used.

It should be emphasized that the experimental conditions were chosen to accentuate cyclic variations in arterial oxygen saturation. It is possible that under certain circumstances large cyclic variations in arterial oxygen saturation might cause a significant degree of hypoxemia in man. In anesthesia this would be most likely to occur during an intrathoracic procedure when the oxygen tension in the anesthetic mixture approximates that of air and when the ventilatory rate is slow. It is contemplated that the present study will be repeated in man under operating room condi-

tions. It is of interest to note that the types of pressure curves for artificial ventilation that interfere least with circulation [18] would probably be associated with the largest cyclic variations in arterial oxygen saturation. Although the present tendency in the design of anesthesia apparatus is toward the complete elimination of resistance to breathing, the imposition of a small resistance to exhalation under some conditions encountered during the conduct of anesthesia might significantly improve oxygenation of the blood.

Summary

Cyclic variations in arterial oxygen saturation of 10 per cent between maximum and minimum values with a frequency identical to the respiratory rate occurred in dogs with open thoraces being artificially ventilated with air at rates of 6 to 7 breaths per minute when they were allowed to exhale freely to atmosphere. With the imposition of 4 cm. of water resistance to exhalation, cyclic variations in arterial oxygen saturation decreased to 3 per cent between maximum and minimum values. With more rapid ventilatory rates or with a greater than atmospheric concentration of oxygen in the inflating gas, cyclic variations in arterial oxygen saturation also diminished or disappeared. It is thought that the most likely explanation for these cyclic variations in arterial oxygen saturation is cyclic variations in alveolar oxygen tension as a consequence of the variations of the volume and composition of alveolar gas with the phases of the respiratory cycle.

As the magnitude of cyclic variation in arterial oxygen saturation increases mean oxygen saturation of the arterial blood decreases below the maximum saturation attainable during the respiratory cycle. This mechanism might cause hypoxemia under certain conditions during the conduct of anesthesia in man.

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REFERENCES

1. Roughton, F. J. W.: Average time spent by the blood in human lung capillary and its relation to rates of CO_2 uptake and elimination in man, Amer. J. Physiol. **143**: 621, 1945.
2. DuBois, A. B., Britt, A. G., and Fenn, W. O.: Alveolar carbon dioxide during respiratory cycle, J. Appl. Physiol. **4**: 535, 1951.
3. DuBois, A. B.: Alveolar CO_2 and O_2 during breath holding, expiration and inspiration, J. Appl. Physiol. **5**: 1, 1952.
4. Frumin, M. J., Bergman, N. A., Holaday, D. A., Rackow, H. L., and Salanitre, E. S.: Alveolar arterial O_2 differences during artificial respiration in man, J. Appl. Physiol. **14**: 694, 1959.
5. Nahas, G. G.: Simplified lucite cuvette for spectrophotometric measurement of hemoglobin and oxyhemoglobin, J. Appl. Physiol. **13**: 147, 1958.
6. Rahn, H., and Fenn, W. A.: A Graphical Analysis of The Respiratory Gas Exchange. Washington, D. C., American Physiological Society 1955, Chart VII.
7. Comroe, J. R., Forster, R. E., DuBois, A. B., Briscoe, W. A., and Carlson, E.: The Lung. Chicago, Year Book Publishers, 1955, p. 184.
8. Altman, P. L., Gibson, J. F. Jr., and Wang, C. C., editors: Handbook of Respiration. Philadelphia, W. B. Saunders, 1958, Table 41, p. 41.
9. Nilsson, N. J.: Oximetry, Physiol. Rev. **40**: 1, 1960.
10. Fox, I. J., Sutterer, W. F., and Wood, E. H.: Dynamic response characteristics of systems for continuous reading of concentration changes in flowing liquid, J. Appl. Physiol. **11**: 390, 1957.
11. Severinghaus, J. W., and Stupfel, M.: Alveolar dead space as index of distribution of blood flow in pulmonary capillaries, J. Appl. Physiol. **10**: 335, 1957.
12. Comroe, J. R., Forster, R. E., DuBois, A. B., Briscoe, W. A., and Carlson, E.: The Lung. Chicago Year Book Publishers, 1955, p. 92.
13. Williams, M. H.: Alveolar-arterial oxygen tension differences in open chest dogs, Amer. J. Physiol. **184**: 109, 1956.
14. Altman, P. L., Gibson, J. F., Jr., and Wang, C. C., editors: Handbook of Respiration. Philadelphia, W. B. Saunders, 1958, Table 149, p. 285 and Section 95, part IX, p. 137.
15. Kilburn, K. H., McDonald, J., and Piccinni, F. P.: Effects of ventilatory pattern and body position on lung volume in dogs, J. Appl. Physiol. **15**: 801, 1960.
16. Bergman, N. A.: Effect of variations in lung volume and alveolar gas composition on rate of fall of oxygen saturation during apnea, Anesthesiology **22**: 128, 1961.
17. Edwards, W. S.: Effects of lung inflation and epinephrine on pulmonary vascular resistance, Amer. J. Physiol. **167**: 756, 1951.
18. Motely, H. L., Cournand, A., Werko, L., Dorsdale, D. T., Himmelstein, A., and Richards, D. W.: Intermittent positive pressure breathing, J. A. M. A. **137**: 370, 1948.