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Comparison of Blood and Alveolar Gas Composition during Rebreathing in the Dog Lung

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Introduction

In a recent exercise study, Jones et al. (1967)[10] found unexpectedly that if a subject rebreathed from a bag until steady state conditions for CO_2 were achieved, that the P_{CO_2} in the bag was persistently higher than that in the blood perfusing the lung. This observation has been subsequently confirmed and investigated by De Burgh et al. (1968),[4] Gurtner et al. (1969)[7] and Laszlo et al (1968)[11] in dogs, and by Jones etal. (1969)[9] and Clark (1968)[3] in man.

In the present study this problem has been reexamined, using the dog preparation of Cain and Otis(1960)[1] where one lung rebreathes continuously, while the other maintains the animal. In their study, Jones et al. (1967)[10] compared the rebreathed gas with systemic arterial blood"downstream" of the lung while Cain and Otis[1] and Gurtner et al.[7] made the comparison with mixed venous blood, that is "upstream". The Cain and Otis[1] preparation has been modified in an attempt to sample blood leaving, as well as that entering the lung.

Materials and Methods

Dog Preparation

Mongrel dogs of either sex, weighing between 9 and 23kg, were anesthetized with sodium pentobarbital (20-30mg/kg body weight) and the trachea was divided with a double brass cannula, one side of which was tied into the left main bronchus after opening the chest. The chest was closed, the pneumothorax reduced, and the animal allowed to breath spontaneously.A catheter was introducted into the pulmonary artery through the jugular vein, the position being checked by monitoring the blood pressure continuously, using a Statham P23AA transducer recording on a Grass 5D polygraph, and being confirmed at autopsy at the end of the experiment. This preparation is basically the same as that described by Cain and Otis[1] but it has been modified in two ways, first cannulating one of the veins from the left lower (diaphragmatic) lobe, and secondly in some experiments tying the brass cannula into the segmental bronchus to isolate the left lower lobe.

A one liter anesthetic bag was connected to the tube from the left lung, and after allowing rebreathing to occur for at least 15 minutes, simultaneous samples of gas from the bag and blood from the two catheters were taken. This sampling procedure was repeated at intervals of 10 to 15 minutes. Gas was collected in a 10cc glass syringe, and blood in 1cc disposable syringes. All analyses were performed on an Instrumentation Laboratory Inc. Ultra-micro pH and blood gas analysing system, model 113-S1; for gas, P_{CO_2} and P_{O_2} were measured, and for blood, P_{CO_2}, P_{O_2} and pH. These analyses were made immediately after collection, and the instrumental calibration for each type of measurement was checked between each set of samples. The gas readings were corrected for the temperature difference between the animal and the instrument, and the blood readings were corrected for three factors, the temperature difference, a systematic difference in instrumental readings of gases when free or carried in solution, and a sampling error resulting mostly from the use of heparin solution in the syringe to prevent clotting. In this study the analytical technique is very critical because of the small differences measured. This, therefore, has been discussed in the appendix.

Rectal temperature was recorded each time samples were collected, using a mercury thermometer. The

rectal and pulmonary temperatures should be very similar with the animal lying flat; Horvath et al. (1950)[8] found the blood in the pulmonary conus to be on average 0.25°C cooler than that in the rectal area, while Edwards (1964)[5] using an indirect method to estimate pulmonary capillary temperature, found no systematic difference between it and rectal temperature in dogs. Rectal temperature was compared with that in the rebreathing lung in 4 dogs, by inserting a 1mm caliber cathether thermistor probe as deeply as possible into the lung, but the author never found a detectable temperature difference between this, and a rectal thermistor probe.

The author did three types of experiment. (a) In the first, in which 3 dogs were used, the entire left lung was allowed to rebreath. A group of 6 sets of samples were taken, the animal was allowed to rest for an hour or two, then the process was repeated. (b) This process was refined in another study, where the author only allowed the left lower lobe to rebreath, that is the lung region from which the pulmonary venous blood was sampled. The same experimental plan was followed as before, using 4 pogs. (c)Preliminary analysis of these data, suggested a difference in the readings made before and after the rest period. It is reasoned that this could be due to a gradual reduction in the level of anesthesia, so the author repeated the procedure used in the second study, with 3 dogs, into which 120mg sodium pentobarbital was infused before the second group of readings.

Symbols Used

These follow standard usage in general but the following special points regarding subscripts should be noted.

$\bar{v}$ pulmonary arterial(i. e. mixed systemic venous)

a′ pulmonary venous(from rebreathing lung or lobe)

A alveolar(as samples from rebreathing bag)

a systemic arterial blood(femoral)

$\Delta P_{CO_2} = P_{ACO_2} - P\bar{v}_{CO_2}$

$\Delta P_{O_2} = P_{AO_2} - P\bar{v}_{O_2}$

Appendix

Consideration of Sampling and Measuring Techniques

In the collection and subsequent analysis of gas and blood samples there are a number of factars which can influence the measurements. These are discussed below.

Gas

1) Rebreathing bag

This was a one liter rubber anesthetic bag fitted with a stop cock. It was tested for leakage or diffusion, by connecting it through the brass cannula used to divide the trachea, to a respiratory pump giving a ventilation of 8 liters/minute. A 4% CO_2 mixture put in the bag, suffered a fall in P_{CO_2} of less than 1mm Hg over a 15 minute period.

2) Sampling

Gas was taken from the rebreathing bag in a 10cc glass syringe lubricated with lithium chloride paste or mineral oil. Before each sample was taken the syringe was checked for leaks, and gas was flushed in and out by working the plunger to and for 10 or 15 times to clear the dead space. The sample was then analyzed immediately. Any contamination with air would cause the apparent O_2 gradient to become more positive and the CO_2 gradient more negative.

3) Temperature

Any difference in temperature between the gas in the lung and in the measuring chamber will cause an error. The effect is one of the relative dilution of the gas by water vapour at the two temperatures, since the gas is saturated in both situations. The readings therefore were multiplied by the factor

$(P_B - P_{H_2O,D})/(P_B - P_{H_2O,B})$

Where P_B=barometric pressure, P_{H_2O}=saturated water vapour pressure and D and B relate to the dog and electrode water bath temperatures respectively. The dog's temperature was taken as that of the rectum.

4) Calibration

Calibrations of the CO_2 and O_2 electrodes were made using reference gases from cylinders previously analyzed with a Scholander apparatus. Slope standardization of the CO_2 assembly was performed daily with 5% CO_2 in O_2 and 10% CO_2 in N_2, and following subsequent calibration of the instrument to direct P_{CO_2} read out, the calibration was checked after each group of gas and blood samples using the 10% gas. The O_2 assembly was calibrated using the 10% CO_2

in N_2 as a zero, and room air as a high point on the 0—160mm Hg scale. Both points were checked after each group of gas and blood samples. Calibration checks for both CO_2 and O_2 were required to agree within 1mm Hg, of the levels previously recorded for the reference gases, or the preceding measurements were discarded.

Blood

1) Sampling

Syringes(disposable plastic, 1cc capacity)were prepared by flushing them and filling their dead space with heparin solution. Immediately before taking a blood sample the appropriate catheter was flushed by withdrawal of several ccs of blood. The sample was then taken into the syringe which was then capped until analysis, this being usually performed within 3 minutes.

Three possible sources of error were considered

a) dilution of blood with heparin solution remaining in the dead space of the syringe, this solution being in equilibrium with room air.

b) diffusion of gas through the walls of the syringe.

c) metabolism in the blood

Factors a, b, and c, were investigated together, using an empirical approach where the normal sampling technique was compared with a special method which minimized the effects of factors a and b.

Two dogs were anesthetized, catheters were placed in the pulmonary and femoral arteries, and a dose of heparin of 3000 units per Kg body weight was administered. Blood was sampled (following the usual withdrawal of 4ccs of blood to flush the catheter) by first taking a 3cc sample into a glass syringe, after working the plunger in and out several times to flush the syringe dead space, then 2 samples were taken from the dog using plastic syringes in the usual fashion. 3 sets of P_{CO_2} and P_{O_2} readings were made on the blood in the glass syringe, alternating with readings made with the plastic syringe samples. The data was plotted out on separate graphs for the two gases, against time (Fig.1, A), this period being the interval between sampling and insertion into the electrode assembly. The two values from the plastic syringe data(labelled "small syringe" on the figure) were connected with a dashed line, and a straight solid line was fitted by eye to the data from the glass("large") syringe. The vertical displacement of the two lines at any time, (labelled "error" on the diagram) represents the effects of dead space dilution and diffusion through the walls of the plastic syringe, since for the "large" syringe samples, the method of sampling and the construction of the barrel and plunger should minimize these two factors. The effects of metabolism in the blood will cause a slow change in values in the "large" syringe, but over a period of 10—15 minutes this effect was not pronounced. The author chose to measure the "error" at 3 minutes, which is the usual delay between sampling and beginning the blood gas measurements. The "error" seems mostly to reflect the dead space effect, since the two lines were nearly parallel and the "small" syringe gave elevated P_{O_2} and depressed P_{CO_2} readings relative to the "large" one, as would be expected with contamination by liquid equilibrated with air.

The author made 15 groups of measurements on the two dogs, with sampling alternating between the two catheters, in order to vary P_{O_2} as much as possible. P_{CO_2} was varied by giving one dog air, and the other a CO_2 air mixture to breath. The author obtained the 3 minute "error" values from graphs drawn for each gas and for each of the 15 groups of measurements, then plotted these values against the respective gas tensions (Fig. 1, B) and fitted linear y on x regression lines(solid lines on figure). The estimated values of the 3 minute "error" for O_2 were -1.47 and -0.80 mm Hg, and for CO_2 1.20 and 1.12 at gas tensions of O and 100mm Hg, respectively. This correction will reduce the observed value of CO_2 gradient but increase the O_2 gradient. No correction factors were calculated for pH as these measurements are not so critical to the study.

2) Temperature

Measurements of P_{CO_2}, P_{O_2} and pH made at the temperature of the electrode assembly were adjusted to the dog's rectal temperature using a slide rule (Radiometer blood gas calculator type BGC 1, Severinghaus, 1966)[13]. The thermometer used for measuring rectal temperature was checked against that used in the water bath of the electrode assembly. The

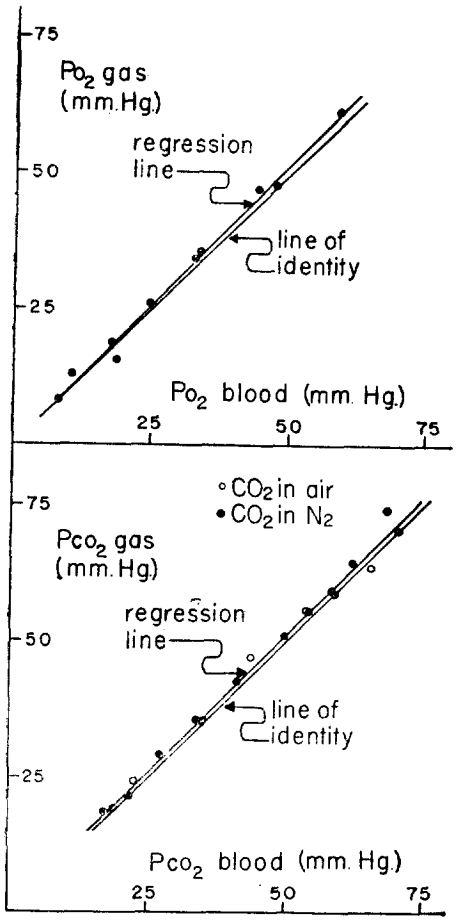

Fig. 1. Method of estimating sampling error. CO_2 (top) O_2 (bottom). Sample of the individual graphs drawn for each experiment (A), comparing readings made with "large", glass syringe (solid line) and "small", plastic syringe (dotted line) against time from taking samples. "Error" is the vertical distance between the lines at 3 minutes, "large" values minus "small" ones. Relationship of "error" to blood tensions levels (B), dotted line represents zero error, solid line, the regression slope.

temperature correction method for P_{CO_2} assumes a pH of 7.4, reduction of pH to 7.0 leads to 12% overcorrection, and this effect was allowed for in the calculation. Measurements of the temperature within the electrode chamber, using a thermistor probe, showed that the gas and blood samples reached the water bath temperature within the period of measurement.

The measurements for both CO_2 and O_2 rarely exceeded 30 or 40 mm Hg and in this range the temperature corrections are fairly small, about 1.5 or 2mm per °C as opposed to about 6mm per °C for O_2 readings in the normal systemic arterial range around 100mm Hg.

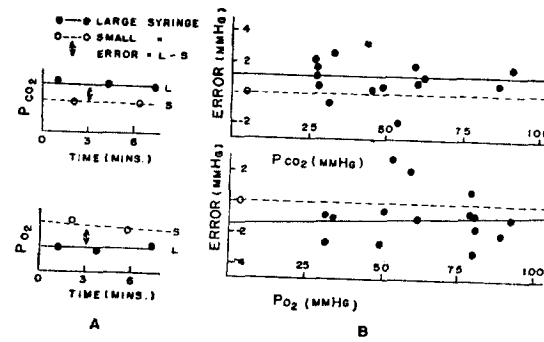

Fig. 2. In vitro comparison of gas and blood readinsg from tonometered samples for O_2 (top) and CO_2 (bottom), line of identify assumes the readings to be indentical. Regression line fitted to data (points represent individual readings).

3) Calibration

The electrode assembly was, as already stated, calibrated for CO_2 and O_2 using gases. Clark (1956)[2] in his original description of the O_2 electrode, observed that since this electrode continuously consumed O_2, the reading of O_2 in the liquid phase was dependant on the rate of diffusion of dissolved gas through the liquid. The P_{O_2} reading therefore tends to be lower in liquid equilibrated with O_2 mixtures, than in the gas mixture itself. The instruction manual of the present equipment suggests multiplying blood values of P_{O_2} by 1.02 to correct for this effect.

The author examined the magnitude of the effect for O_2, and also for CO_2 by comparing tonometered blood samples with the gas used. For O_2, 10 measurements were made over the range 8 to 60 mm Hg, using a gas mixing pump (Instrumentation Associates, Inc., Model 27/3F) to produce mixtures of O_2 in N_2; the order in which tests were made was randomized (Fisher and Yates, 1957)[6]. For CO_2 a similar procedure was used over the range 18—70mm, but 10 tests were done with CO_2 mixed with air, and 10 mixed with N_2 in order to examine any possible interreaction between CO_2 and measurements. The

data is presented in Fig. 2.

For both gases, the gas readings read consistently higher than blood, though the reason for this in the case of CO_2 was obscure. There was no apparent difference in the CO_2 readings between tests made in air or N_2, suggesting that interreaction was not an important factor (earlier tests in this laboratory had also always failed to reveal any interreaction between CO_2 and O_2 using either electrode). The equations linking gas and blood readings were respectively:

P_{CO_2} (gas) $=0.73+1.008\times P_{CO_2}$ (blood)

P_{O_2} (gas) $=0.010+1.044\times P_{O_2}$ (blood)

The author used these factors in correcting the blood data, combining them with the sampling correction just described.

Two other possible sources of error were investigated, instrumental hysteresis and contamination of one sample by another. Instrumental hysteresis (the artificial raising or lowering of P_{CO_2} and P_{O_2} readings because of the use of a reference gas immediately before, having, respectively a very high or low partial pressure of the gas) was checked repeatedly, by analyzing two gases of known composition immediately after one another, and there was never any detectable effect of this kind. The use of room air to check the O_2 calibration before gas sample measurement, might be expected to elevate P_{AO_2} and depress P_{ACO_2} so making the O_2 gradient more positive and the CO_2 gradient more negative, but reversal of the order of gas and blood analyses did not alter the measured gradients detectably. Contamination between samples could occur possibly if one blood sample was improperly flushed before making another reading. However, it was found to be immaterial whether one sample was flushed out with saline, or merely displaced by the next one, since the size of the measuring chamber was small compared with the sample size.

Slope standardization of the pH electrode was performed daily using standard buffers of 6.84 and 7.384 pH and the assembly was calibrated before each measurement using the second buffer. Repeat calibrations were required to agree within 0.01 units. Several blood samples were taken until the readings agreed within 0.01 units, the experience has been that the first reading always deviates by several hundredths of a unit from later ones. Additional checks were occasionally made using Radiometer S 1500 ampules with pHs at 38°C of 6.84 and 7.381 and these readings were found to be within 0.02 pH units of the expected values.

Results

The author has summarized the CO_2 and O_2 data for the three experiments in tables 1, 2 and 3, respectively. In the first column the author has given the mixed venous gas tension ($P\bar{v}$), since in the second study the author has shown $P\bar{v}_{CO_2}$ to be strongly correlated with both CO_2 and O_2 alveolar-blood gradients. The three possible gradients are given in the remaining columns, the blood tension gradient $Pa'-P\bar{v}$ (that is between blood leaving and entering the lung) the alveolar gas-pulmonary venous blood gradient, P_A-Pa' (the downstream gradient) and the alveolar gas-mixed venous blood gradient $P_A-P\bar{v}$ (the upstream gradient). Each value and S.D. in these tables is based on 6 readings except for the starred values in the O_2 tables where the first reading has been omitted; the achievement of steady state conditions for O_2 is more protracted than for CO_2, (second paper), and examination of the P_{AO_2} readings in these cases, suggested that sampling had begun prematurely in these particular experiments.

Examination of the data,suggested a common pattern in the second and third, dogs 4-10, and this to be expected since all were prepared the same way, with only the left lower lobe rebreating, the sole difference being the extra anesthetic given to dogs 8-10, which was found to have no effect on the results. Accordingly, in this discussion, the author has pooled these data, comparing them with those obtained on dogs 1-3 where the whole left lung rebreathed.

The author has made two statistical examinations of this data to see firstly if the various gradients differ significantly from zero, and secondly if the first and second sets of data differ significantly from each other, that is to see if there is a time effect. The author is concerned here with the consistency of the effect between dogs and not with the within dog variation which was indicated by the S.Ds. in the

Table 1. Comparison of Mixed Venous Gas Tensions and the Various Gradients Between Alveolar Gas, Pulmonary Arterial ($\bar{v}$) and Pulmonary Venous (a′) Blood Samples for 3 Dogs. Whole Left Lung Rebreathing.

(CO_2 data)	$P\bar{v}$		$Pa'-P\bar{v}$		P_A-Pa'		$P_A-P\bar{v}$	
	First	Second	First	Second	First	Second	First	Second
Dog 1	41.8	30.2	2.0	1.3	3.5	−0.1	5.5	1.2
S. D.	4.8	1.1	2.8	1.2	3.6	2.9	2.2	2.2
Dog 2	33.0	31.5	1.1	2.1	1.9	1.1	3.0	3.1
S. D.	2.5	0.7	1.4	1.6	2.4	3.3	2.9	2.4
Dog 3	44.4	33.2	2.6	2.4	3.5	−0.9	6.0	1.5
SD. .	4.9	1.6	1.7	0.9	2.1	2.1	2.2	1.6
Mean	39.7	31.6	1.9	1.9	3.0	0	4.8	1.9
(O_2 data)								
Dog 1	27.5	20.1	−5.3	0.1	9.6	3.9	4.2	4.0
S. D.	4.8	1.0	6.2	1.1	3.7	3.8	3.5	4.8
Dog 2	25.1*	17.8	4.8*	0.1	1.4*	4.2	6.2*	4.3
S. D.	3.0	2.8	4.1	2.3	3.7	3.0	2.7	3.2
Dog 3	32.8	21.0*	1.3	0.3*	3.8	9.6*	5.0	9.9*
S. D.	0.9	0.9	1.4	3.2	1.9	5.7	2.2	6.4
Mean	28.7	19.6	0.3	0.2	5.1	5.7	5.1	5.8

Time interval between first and second sets of readings.
Dog 1 : 144 mins, Dog 2 : 159 mins, Dog 3 : 170 mins.
*First reading in set omitted.

Table 2. Comparison of Mixed Venous Gas Tensions, and Gradients, for 4 Dogs, Lower Left Lobe Only Rebreathing.

(CO_2 data)	$P\bar{v}$		$Pa'-P\bar{v}$		P_A-Pa'		$P_A-P\bar{v}$	
	First	Second	First	Second	Second	First	First	Second
Dog 4	34.8	28.4	3.2	3.4	0.4	−2.0	3.7	1.3
S. D.	5.5	1.1	1.5	0.9	2.5	1.2	2.5	1.4
Dog 5	52.7	51.9	0.9	1.4	5.4	5.2	6.3	6.6
S. D.	3.1	2.0	2.2	1.1	3.0	2.2	0.8	1.8
Dog 6	25.9	24.7	4.1	5.3	0.1	−3.5	4.1	1.8
S. D.	1.4	1.4	1.0	2.8	1.3	2.5	1.4	1.8
Dog 7	48.3	42.2	3.5	6.1	−0.1	0.1	3.4	6.2
S. D.	1.3	1.5	1.5	2.0	0.7	1.1	1.5	2.5
Mean	40.4	36.8	2.9	4.0	1.5	0	4.4	4.0
(O_2 data)								
Dog 4	24.2	21.9	7.1	5.6	−3.2	7.9	3.9	13.5
S. D.	4.4	2.1	4.4	6.2	4.4	11.8	2.0	13.1
Dog 5	38.6*	27.2*	4.1*	−1.7*	−1.8*	4.2*	2.3*	2.5*
S. D.	0.6	1.4	5.4	5.2	4.9	4.4	1.0	1.7
Dog 6	22.5	25.3	−1.8	−4.5	4.3	12.0	2.5	7.5
S. D.	1.6	2.3	2.9	3.0	4.2	6.0	2.0	5.8
Dog 7	21.2	21.1	0.8	1.2	6.1	2.6	6.9	3.9
S. D.	1.2	0.6	2.6	1.9	3.7	3.0	2.2	2.0
Mean	26.1	23.7	2.5	0.2	1.5	6.8	4.0	7.0

Time interval between first and second sets of readings.
Dog 4 : 162 mins, Dog 5 : 193 mins, Dog 6 : 199 mins, Dog 7 : 190 mins.
* First reading in set omitted.

Table 3. Comparison of Mixed Venous Gas Tensions, and Gradients for 3 Dogs, Lower Left Lobe Only Rebreathing, 120mg Na Pentobarbital Injected Before Second Set of Readings.

(CO_2 data)	$P\bar{v}$		$Pa'-P\bar{v}$		P_A-Pa'		$P_A-P\bar{v}$	
	First	Second	First	Second	First	Second	First	Second
Dog 8	38.2	48.8	1.0	4.2	2.4	2.8	3.3	7.0
S. D.	1.9	2.9	0.8	3.0	1.3	2.4	1.6	2.1
Dog 9	34.4	33.8	0.1	2.4	2.9	−0.4	3.0	2.0
S. D.	5.0	1.9	1.1	1.9	1.8	1.3	1.9	1.1
Dog 10	30.6	36.7	4.0	4.4	0.7	−0.1	4.7	4.3
S. D.	2.0	0.4	1.4	1.7	1.4	4.4	1.8	3.0
Mean	34.4	39.8	1.7	3.7	2.0	0.8	3.7	4.4
(O_2 data)								
Dog 8	23.1	19.9	3.8	3.5	0.6	−0.1	4.4	3.4
S. D.	2.0	1.4	2.8	3.2	3.9	3.2	2.4	0.5
Dog 9	18.2	21.3	3.1	−0.2	1.0	4.3	4.1	4.1
S. D.	3.1	1.0	3.4	4.4	5.2	4.1	2.9	1.8
Dog 10	28.6*	20.8*	4.0*	−2.8*	3.6*	8.7*	7.6*	5.9*
S. D.	1.9	3.4	4.6	4.9	2.5	2.5	2.9	3.1
Mean	23.0	20.7	3.6	0.3	1.6	4.0	5.2	4.4

Time interval between first and second set of readings.
Dog 8 : 74 mins, Dog 9 : 122 mins, Dog 10 : 155 mins.
* First reading in set omitted.

tables. The mean values were used for each group of 5 or 6 individual readings as the raw data for this calculation, dividing the dogs into 2 groups 1, 2 and 3, and 4 to 10 (Table 4). The criterion for significance was the Students' t test, treating any estimates with a probability above 0.05 as insignificant.

Table 4. Overall Significance of Gradients and of the Time Effect(First and Second of Readings Compared)

(CO_2)	$Pa'-P\bar{v}$			P_A-Pa'			$P_A-P\bar{v}$		
	1st+2nd	1st	2nd	1st+2nd	1st	2nd	1st+2nd	1st	2nd
Dogs 1-3 (Table 1)	1.92	1.90	1.93	1.50	2.97	0.03	3.38	4.83	1.93
Significance	0.05	NS		0.01	NS		0.01	0.05	
Dogs 4-10 (Tables 2 &3)	3.14	2.40	3.89	0.99	1.69	0.30	4.12	4.07	4.17
Significance	0.01	0.05		NS	NS		0.01	NS	
(O_2)									
Dogs 1-3 (Table 1)	0.22	0.27	0.17	5.42	4.93	5.90	5.60	5.13	6.07
Significance	NS	NS		NS	NS		0.05	NS	
Dogs 4-10 (Tables 2 & 3)	1.59	3.01	0.16	3.59	1.51	5.66	5.18	4.53	5.83
Significance	NS	NS		0.05	NS		0.01	NS	

All values mean on respectively 3 dogs and 7 dogs.
1st are the first set of 6 readings obtained.
2nd are the last set of 6 readings obtained.
Significance for 1st+2nd probability that this value differed from zero.
Significance 1st and 2nd probability that these two means were different data populations.

One check on the validity of the CO_2 data, was to calculate HCO_3^- and base excess (Radiemeter BGC1 blood gas calculator) for both groups of readings from the two catheters, using the pH readings made concurrently, and assuming for the base excess estimates, a hemoglobin concentration of 15 grams/100 ccs blood (any errors in this assumptions are unimportant since the estimates are required solely for comparative purposes). The author has tabulated these estimates for the 10 dogs in table 5.

In studies 1 and 2 (dogs 1-7, tables 1 and 2) $P\bar{v}_{CO_2}$ always fell between the first and second sets of readings, indication of a reduction in the level of anesthesia, for in 2 of the 3 dogs given extra pentobarbital, $P\bar{v}_{CO_2}$ was higher in socond set of readings. $P\bar{v}_{O_2}$ declined in 8 out of the 10 dogs, suggesting a slight deterioration in gas exchange. Examination of the various CO_2 gradients in tables 1, 2 and 3 shows that only 7 of the 60 mean values presented were negative and that none of these negative values exceeded their respective S. Ds. An overall view of the variability of individual readings can be gathered from the fact that of the 60 means, 21 were less than their S.D, and 19 were more than double their S.D.

The analysis of the combined mean values for dogs 1-3 and 4-10 (Table 4) shows that all these combined means were positive and all were significantly different form zero except the downstream A-a′ gradient in dogs 4-10. The downstream gradient was always less than the upstream gradient, which suggested that the blood took up CO_2 in its passage through the rebreathing lung.

The only significant time effects were a fall in the upstream, A-$\bar{v}$, gradient in dogs 1-3, and a rise in the blood, á-$\bar{v}$, gradient in dogs 4-10, but in general there was a tendency for the upstream gradient to change only slightly (mean values for all dogs 4.30 and 3.50mm) while the downstream gradient decreased and the blood gradient increased with time.

Table 5. Plasma Bicarbonate and Base Excess for Pulmonary Artery ($\bar{v}$) and Pulmonary Vein (a′) Blood Samples on All Dogs Studied.

	HCO_3^- (mm. Eq/L)				Base excess (mm.Eq/L)			
	First	Second	First	Second	First	Second	First	Second
Dog 1	21.0	19.1	22.0	19.9	−4.2	−3.7	−3.2	−2.8
2	20.8	19.2	21.6	20.0	−2.4	−4.0	−1.7	−3.4
3	17.7	16.5	18.4	17.7	−9.5	−8.3	−9.3	−7.6
Mean	19.8	18.3	20.7	19.2	−5.4	−5.3	−4.7	−4.6
Dog 4	19.8	19.4	20.9	17.8	−4.2	−2.9	−3.5	−6.0
5	24.9	24.9	23.8	25.0	−1.8	−1.7	−3.1	−1.8
6	19.1	15.2	20.3	18.8	−2.3	−7.5	−2.0	−3.9
7	25.6	20.3	25.5	21.0	+0.2	−5.2	−0.9	−5.8
Mean	22.3(5)	19.9(5)	22.6	20.6(5)	−2.0	−4.3	−2.4	−4.4
Dog 8	18.4	17.7	17.5	17.6	−6.9	−10.7	−8.7	−11.6
9	22.0	20.1	21.9	21.5	−1.2	−3.7	−1.3	−2.6
10	21.0	19.9	21.6	19.7	−1.3	−4.7	−2.0	−5.7
Mean	20.5	19.2	20.3	19.6	−3.1	−6.4	−4.0	−6.6
Mean on 10 dogs	21.0	19.2	21.3(5)	19.9	−3.4	−5.2	−3.6	−5.1

HCO_3^- and base excesss calculated at 38°C. Base excess measurements asume hemoglobin concentration of 15 grams/100cc blood.

Of the 60 mean values for the various O_2 gradiesnts (Tables 1, 2 and 3) all but 9 were positive and of these negative mean values, only one exceeded its S.D. The readings were more variable than for CO_2, of the60 mean values, 26 were less than their respective S.Ds, and only 11 were more than double

their S.Ds.

The analysis of the combined mean values (Table 4) shows all these values were positive but in neither groups was the blood gradient significantly different from zero, nor was the downstream gradient in dogs 1-3. The data resembles that of the CO_2 results, in that the upstream gradient exceeds the downstream gradient, which suggests that the blood takes up O_2 as it passes through the lung but this effect is not significant. None of the time effects were significant, although there was a tendency for the blood gradient to fall in dogs 4-10 while the downstream gradient increased.

The analysis of the plasma HCO_3^- estimates (Table 5) shows these usually decreased with time; this was seen in the mixed venous estimates from every dog, and in the pulmonary vein estimates in 8 of the dogs. This difference probably represents the loss of base buffering power, since the average decline of HCO_3^- and base excess readings was about the same, (the base excess readings were initially negative, and this negativity increased with time). There was no systematic difference however between estimates of HCO_3^- or base excess made on simultaneous samples taken from the two sampling sites.

Discussion

Before the author can justifiably compare alveolar gas during rebreathing with the blood perfusing the lungs, needs to satisfy two criteria, an adequate time to allow steady state conditins to be achieved in the lungs, and representative sampling of blood entering and leaving the lungs. Jones et al. (1967)[10] partially fulfilled the second criterion, in that with both lungs rebreathing they could obtain representative samples of blood leaving the lung by sampling systemic arterial blood, but they did not take simultaneous mixed venous samples, nor were they able to prolong their rebreathing periods beyound a few seconds to fully satisfy the first criterion. The present method should fulfil the first criterion because of the greatly extended rebreathing period and also partly satisfies the second, in that the mixed venous samples, represent the common blood supply to the lungs. The author however has problems in obtaining representative samples of blood leaving the lungs.

The left lung is divided into three lobes, the diaphragmatic, apical and cardiac, the latter two being frequently fused (Miller, Ckristensen and Evans, 1964)[12]. Each lobe gives rise to a segmental vein which empties separately into the left atrium but the author observed that in the case of the diaphragmatic lobe, this vein is very short, being formed by the joining together of three smaller veins which emerge from the lung tissue. The author chose to study the lower lobe for two reasons, first it was a discrete structure, and secondly could cannulate one of the small veins and obtain blood samles without totally interrupting blood flow from that lobe.

There are two criticisms of this technique, that it gave unrepresentative samples, and that by occluding the vein the author caused backing up and stagnation of blood in the lobe. The author tried to eliminate the first objection in the later experiments by confining rebreathing to the lower lobe, and also found that samples taken from each of the small veins showed no appreciable differences in gas tensions between each other, suggesting that it was sufficient just to take blood from one vein. also varied the rate of sampling (withdrawing the syringe plunger at different speeds) for if there was marked inhomogeneity in the lobar vascular bed,this procedure might well cause changes in the recorded gas tensions, but no such differences were found.

The author examined the second objection by making a retrograde ink infusion through one vein into the lobe. This showed considerable anastomoses of vessels within the lobe, and it seems unlikely that much blood would be sequestered there by the cannulation. The author should in any case has removed most; if not all of this stagnant blood in the tissues adjacent to the vein, when the catheter was flushed with blood prior to each measurement.

The results show consistent positive upstream A-$\bar{v}$ gradients for both gases, for CO_2 the finding is in agreement with at least 6 other studies listed at the beginning of this paper but the O_2 gradient is less expected, as it seems previously only to have been reported by De Burgh Daly et al (1968)[4]. These workens were able to use high P_{AO_2} values, as they

were working with siolated lungs and they found gradients in normal conditions of up to 63mm, much larger than in this work; but if the author considers the effective changes in O_2 saturation that the respective alveolar and blood P_{O_2} values represent, the author finds in both the De Burgh Daly[4] study and this work a difference of about 10%, which suggests uhat it is the change of O_2 saturation, rather than the P_{O_2} differences which is important.

The initial A-a′ downstream gradients were rather smaller, though normally positive. This suggests that CO_2 and possibly O_2 have been taken up by the blood in its passage through the lung,but the author cannot give quantitative estimates of this process because of uncertainties with the pulmonary vein sampling. CO_2 uptake is to be expected because of its production as a result of lung tissue metabolism, but the source of O_2 is obscre for, as discussed in the theoretical paper the only apparent source is the systemic bronchial circulation and this appears quite inadequate for the task. In any case the O_2 a′-$\bar{v}$ gradient was not significanty different from zero on this number of animals, so this observation must be still considered tentative.

The time effect is puzzling. The upstream A-$\bar{v}$ CO_2 and O_2 gradients seem unaffected by time (an observation confirmed in the second paper while the slight fall between the first and second sets of readings suggest any deterioration with time was slight but the author found a consistent decrease in the A-a′ CO_2 and the a′-$\bar{v}$ O_2 gradients with time. The author wondered originally if this resulted from a diminution in the level of anesthesia, since the changes were particularly clear in a dog which was only lightly anesthetized in dogs 8-10, and this factor seems to be unrelated to the time change.

These data suggest that P_{CO_2} rises and P_{O_2} falls in the blood; changes that could occur in ischemia in metabolically active tissue. This time effect could well represent a deterioration of the preparation causing some reduction of blood flow through the lobe, and this would mean that the initial readings are the more reliable, since they are obtained in more physiological conditions. However it is important to remember that there was no systematic difference between base excess estimates made on blood from the pulmonary artery and vein as might be expected to occur if the blood had stagnated and acquired lactic acid from anaerobic metabolism, and this question needs further study.

The author considered several ways of extending this study, such as using an isolated lung preparation, like that of Laszlo et al (1968)[11] or the insertion of an oxygenator between the great veins or right heart and the pulmonary artery, to carry the burden of gas exchange, and to free both lungs for rebreathing sothat systemic arterial blood sampling could be employed. These preparations however, are complex, and the author has chosen instead to return to the original Cain and Otis[1] preparation, sampling alveolar gas and mixed venous blood alone, but varying the conditions more extensively than in this study. This work is presented in the next paper of this series (second poper).

Summary

The author used a dog preparation, in which either the left lung or the lower left lobe rebreathed continuously from a bag, to compare CO_2 and O_2 tensions in the rebreathed gas with those in blood entering or leaving the lung. In the 10 dogs studied, alveolar pressures for both gases were greater than in the blood; the"upstream" gradient (alveolar pulmonary arterial blood) exceeded the "downstream" gradient (alveolar-pulmonary venous blood) for both gases, but the difference was only significant for CO_2. The author attributed this effect to the production of CO_2 in lung tissue metabolism and its uptake by the blood. The difference in CO_2 tension between blood leaving and entering lung increased while the downstream gradient fell, an effect which was independant of the level of anesthesia. There was no evidence of a fall in base excess in blood passing through the lung, as would occur from the production of metabolic acids during anaerobic metabolism at the low levels found in the rebreathing lung in this preparation.

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References

1. Cain,, S.M. andA.B. Otis: Effect of carbonic anhydrase inhibition on mixed venous CO_2 tension in anesthetizeddogs. J. Appl. Physiol., 1960. 15:390.
2. Clark, L.C., Jr: Monitoring and control of blood and tissue O_2 tensions. Trans. Am. Soc. Artificial Internal Organs, 1956. 2:41.
3. Clark, T.J. H: The ventilatory response to CO_2 in chronic airways obstruction measured by a rebreathing method. Clin. Sci., 1968. 34:559.
4. De Burgh Daly, I., C.C. Michel, D.J. Ramsay and B.A. Waaler: Conditions governing the pulmonary vascular response to ventilation hypoxia and hypoxaemia in the dog. J. Physiol. (London) 1968. 196:351.
5. Edwards, A.W.T: Alveolar capillary temperature compared with aortic and bronchial wedge temperatures. J. Appl. Physiol., 1964. 19:760.
6. Fisher, R.A. and F. Yates: Statistical tables for biological agricultural and medical research. 5th Ed. Edinburgh: Oliver and Boyd, p.1957. 132.
7. Gurtner, G.E., S.H. Song and L. E. Farhi: Alveolar to mixed venous P_{CO_2} difference under conditions of no gas exchange. Respir. Physiol. In press, 1969.
8. Horvath, S.M., A. Rubin and E. L. Foltz: Thermal gradients in the vascular system. Am. J. Physiol., 1950. 161:316.
9. Jones, N.L., E.J.M. Campbell, R.H.T. Edwards and W. G. Wilkoff: Alveolar-to-blood P_{CO_2} difference during rebreathing in exercise. J. Appl. Physiol., In press, 1969.
10. Jones, N.L., E.J.M. Campbell, G.J.R. McHardy, B.E. Higgs and M. Clode: The estimation of carbon dioxide pressure of mixed venous blood during exercise. Clin. Sci., 1967. 32:311.
11. Laszlo, G., P. Caldini and H.N. Bane: CO_2 equilibrium in the isolated lung. Proc. International Union Physiol. Sci. 24 Congress, 1968. 7:254.
12. Miller, M.E., G.C. Christensen and H.E. Evans: Anatomy of the dog. Saunders, Philadelphia, 1964. p.734.
13. Sevringhaus, J.W. Blood gas calculator. J. Appl. Physiol., 1966. 21:1108.

反覆呼吸을 하는 犬肺에서의 血液 Gas와 肺胞 Gas의 比較에 關하여

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犬의 全左肺 또는 左肺下葉을 고무 囊으로 反覆呼吸(rebreathing)을 連續시키며 肺動脈(混合靜脈血液) 및 肺靜脈의 血中炭酸gas와 酸素를 反覆呼吸한 肺胞의 炭酸gas 및 酸素와 比較하였다. 이들 두 氣體에 있어서 肺胞 gas의 張力이 血液 gas의 張力보다 항상 컸으며, 또 肺胞와 肺動脈間의 傾斜度가 肺胞와 肺靜脈間의 傾斜度보다 컸으나 炭酸 gas에 있어서만 有意性이 있었다. 이 결과는 肺組織의 代謝過程에 依하여 炭酸 gas가 生成되어 血流로 運搬되어지기 때문이라 생각된다. 肺胞와 肺靜脈間의 傾斜度가 減少될때 肺動脈과 肺靜脈의 炭酸 gas 張力의 差異는 增加하였고 麻醉深度와는 無關하였다. 本實驗에서 反覆呼吸을 하는 肺內의 嫌氣性代謝(anaerobic metabolism)로 代謝性酸의 生成에 依하여 肺를 通過한 血液中 base exces 減少를 豫測할수 있었으나 그러한 證據는 없었다.