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## Diffusing Capacity and Pulmonary Capillary Blood Flow at Hyperbaric Pressures \*

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The pulmonary diffusing capacity ( $DL_{CO}$ ) has been observed to fall when the alveolar oxygen tension rises from 80 to 600 mm Hg (1, 2). By using the single breath technique in a hyperbaric pressure chamber, we have been able to extend the range of oxygen tensions studied up to 3,200 mm Hg.

Also we have measured in these experiments the effect of exposure of the pulmonary capillary bed to a partial pressure of oxygen of approximately 2,600 mm Hg for a period of 10 minutes.

In addition, prompted by the suggestions of J. S. Haldane (3), who postulated that inert molecules such as nitrogen may impede the mean free path of carbon monoxide molecules to the alveolar membrane and decrease the rate of uptake of carbon monoxide, we have studied the effect of large partial pressures of nitrogen on  $DL_{CO}$ .

### Methods

In a hyperbaric chamber operating up to 4.8 atmospheres absolute pressure, a modification of the Krogh single breath technique (1) was used to measure the diffusing capacity for carbon monoxide ( $DL_{CO}$ ). Simultaneously pulmonary capillary blood flow ( $\dot{Q}_c$ ) was measured by adding acetylene to the inspired mixture (4, 5). Neon instead of helium was used as the inert tracer gas (6). At sea level, the volume of the pulmonary parenchymal

tissue in milliliters ( $V_T$ ) was measured by plotting the acetylene disappearance with different times of breath holding in each subject (4).

The concentrations of neon, carbon monoxide, and acetylene were approximately constant in the inspired mixture, being 0.5%, 0.4%, and 0.5%, respectively, with a balance of oxygen and nitrogen. Four separate inspired mixtures were employed in which the oxygen concentrations were 6%, 21%, 60%, and 98%. By breathing different concentrations of oxygen for a few breaths followed by a breath of one of the inspired mixtures described, the alveolar oxygen tension of the subject during the breath holding period could be varied at will.

Neon, carbon monoxide, acetylene, and carbon dioxide concentrations were measured on a gas chromatograph (6)<sup>1</sup> that has an error of  $\pm 1\%$ . The oxygen concentration of the gases was measured on a mass spectrometer<sup>2</sup> that has an accuracy of within 1%. The residual volume in each subject was measured by the closed circuit helium technique (7). The pressure in the chamber in pounds per square inch was indicated on a calibrated Bourdon tube recording gauge outside the chamber that had a resolution of within  $\frac{1}{2}$  pound per square inch (50 mm Hg).

The plasma CO tension was estimated by having the subject rebreathe oxygen and hold his breath for 2 minutes and then measuring the carbon monoxide concentration in the expired sample (2, 8). This procedure was repeated at intervals throughout the experiment and the equilibrated capillary CO tension for each estimation of  $DL_{CO}$  calculated by interpolation to the prevailing oxygen tension. The apparatus used was similar to that previously described (5), mylar bags<sup>3</sup> and copper and tygon tubing only being incorporated, as acetylene is absorbed by rubber.

The partial pressure of nitrogen ( $P_{N_2}$ ) in the alveoli during the breath-holding period was estimated thus:  $P_{N_2} = P_B - (P_{H_2O} + P_{O_2} + P_{CO_2})$ , where  $P_B$  is the total barometric pressure,  $P_{H_2O}$  is the water vapor pressure

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<sup>1</sup> We found that the values of the neon/CO ratio drifted by 2% throughout the day of each experiment. We have therefore incorporated a correction factor to compensate for the drift on the basis of hourly sampling of the standard mixture. The neon/ $C_2H_2$  ratio remained constant throughout the day.

<sup>2</sup> Model 21-620 A, Consolidated Engineering Co., Pasadena, Calif.

<sup>3</sup> Supplied by Vac-Pac, Baltimore, Md.

TABLE I  
Physical characteristics of experimental subjects

Subject	Sex	Age	Height	Weight	Surface area
		years	inches	pounds	m <sup>2</sup>
REF	M	44	74	170	2.02
RWH	M	34	70	155	1.86
GGP	M	28	73	175	2.02
GWK	M	21	78	165	2.06
JRN	F	29	67	145	1.76

at body temperature, and  $P_{O_2}$  and  $P_{CO_2}$  are partial pressures of oxygen and carbon dioxide, respectively, in alveolar gas.

The mean intracapillary oxygen tension at which the breath-holding maneuver was performed was calculated from the expired alveolar oxygen tension by assuming a diffusing capacity for oxygen of 20 ml O<sub>2</sub> per (mm Hg × minutes) (9).

The alveolar oxygen tension present during the 5 to 10 minutes before the breath-holding procedure was calculated from the alveolar air equation (10). For convenience, this oxygen tension will be called hereafter the "preparatory level" to distinguish it from the mean in-

tracapillary oxygen tension at which the breath-holding maneuver was performed.

The subjects studied included four males and one female who were symptomless and whose chests radiologically showed no active pulmonary disease or other abnormality. Their physical characteristics are shown in Table I. All were experienced in respiratory maneuvers.

The following experimental procedure was performed in each subject. At sea level, two control measurements, one at approximately 600 mm Hg and another at approximately 120 mm Hg mean intracapillary oxygen tension, were performed in the chamber with the doors open. The chamber was then sealed and the air compressed to 3.5 atmospheres absolute pressure. At least four breath-holding maneuvers were performed at this pressure at mean intracapillary oxygen tensions from 200 to 2,400 mm Hg. Between each maneuver a gas mixture containing 6% oxygen in a balance of nitrogen was inspired for 5 to 8 minutes through a tight fitting mask so that at 3.5 atmospheres the preparatory level oxygen tension was approximately equal to that of breathing air at sea level (110 mm Hg).

After these measurements at 3.5 atmospheres the subjects were divided into groups A and B and the procedure continued as follows. In each of two subjects (RWH and GGP) in group A three further breath-hold-

TABLE II  
Diffusing capacity ( $DL_{CO}$ ) and pulmonary capillary blood flow ( $\dot{Q}_c$ ) in two subjects in group A

Subject	Condition*	"Preparatory level" alveolar oxygen tension	Mean intracapillary oxygen tension	$P_{N_2}$ in alveol†	$DL_{CO}$	$\dot{Q}_c$	
		mm Hg	mm Hg	mm Hg	ml CO/ (min × mm Hg)	L/min	
RWH	Sea level	106	578	97	19.1	9.6	
		106	122	554	36.8	8.7	
	3.5 atmospheres	116	2,153	439	8.5	9.0	
		116	1,885	706	9.2	6.7	
		116	1,203	1,389	12.9	8.0	
		116	227	2,362	35.3	7.7	
		2,579	2,365	223	7.5	7.8	
		2,579	1,625	995	9.0	8.4	
		2,579	747	1,849	20.4	7.7	
	Sea level	106	585	88	17.8	9.2	
		106	125	555	33.6	7.7	
	GGP	Sea level	106	576	89	20.1	10.0
			106	114	558	41.6	8.0
		3.5 atmospheres	117	1,981	597	7.8	8.4
117			1,963	614	8.7	6.6	
117			1,142	1,436	11.8	5.7	
117			154	2,412	39.7	7.0	
2,593			2,320	254	7.2	4.3	
2,593			1,611	969	8.6	5.1	
2,593			931	1,651	13.2	5.8	
Sea level		106	593	74	17.4	7.5	
		106	117	559	34.8	5.9	

\* Measurements listed in order performed.

†  $P_{N_2}$  = partial pressure of nitrogen.

TABLE III  
*Diffusing capacity and pulmonary capillary blood flow in three subjects in group B*

Subject	Condition*	"Preparatory level" alveolar oxygen tension	Mean intracapillary oxygen tension	Nitrogen tension in alveoli	DL <sub>CO</sub>	Q <sub>c</sub>	
		mm Hg	mm Hg	mm Hg	ml CO/ (min × mm Hg)	L/min	
REF	Sea level	106	598	76	15.3	6.5	
		106	116	560	28.4	5.0	
	4.8 atmospheres	180	3,095	483	5.4	4.3	
		180	3,115	465	5.8	4.4	
	3.5 atmospheres	117	2,257	332	6.9	4.4	
		117	1,807	788	8.0	3.3	
		117	1,705	889	7.4	4.2	
		117	1,103	1,491	9.5	3.6	
		117	243	2,335	20.8	5.3	
	Sea level	106	590	84	12.8	5.4	
		106	117	559	26.7	6.6	
	JRN	Sea level	106	607	78	9.7	7.3
			106	139	548	18.5	5.5
		3.5 atmospheres	117	2,175	419	3.5	5.3
117			1,865	730	3.9	4.8	
117			1,555	1,054	4.5	4.5	
117			1,215	1,383	6.1	4.6	
117			284	2,311	14.1	4.2	
4.8 atmospheres		180	3,195	396	2.0	4.4	
		180	3,065	526	1.8	4.8	
Sea level		106	654	31	9.0	6.0	
		106	120	558	16.7	4.4	
GWK		Sea level	106	572	76	19.8	7.8
			106	108	566	41.3	9.9
		3.5 atmospheres	117	2,205	392	6.8	5.5
	117		1,850	746	8.1	6.6	
	117		1,545	1,051	9.1	5.3	
	117		1,230	1,378	9.8	3.9	
	117		182	2,414	18.1	4.8	
	4.8 atmospheres	180	2,965	620	5.1	5.3	
		180	2,915	671	4.8	5.5	
	Sea level	106	593	88	16.0	5.9	
		106	113	567	28.5	5.9	

\* Measurements listed in the order performed.

ing maneuvers were performed at 3.5 atmospheres, varying the mean intracapillary oxygen tension at the time of breath holding from 600 to 2,400 mm Hg. However, approximately 100% oxygen was administered through a mouthpiece for a preliminary 10 minutes before each run, maintaining a preparatory level oxygen tension of approximately 2,600 mm Hg for this time, and not 110 mm Hg as in the experiments above.

With three subjects (REF, JRN, and GWK) in group B, the pressure was increased to 4.8 atmospheres, where duplicate measurements were made at a mean intracapil-

lary oxygen tension of 3,000 mm Hg. Between measurements a mixture of 6% oxygen in nitrogen was inspired through a mask for 5 to 8 minutes.

Graduated decompression took between 3 and 4 hours during which time the subject was reclining and intermittently sleeping in an easy chair. The final controls were performed on return to sea level.

Estimations of plasma CO tension as described above were made between every second breath-holding maneuver. At each barometric pressure the highest oxygen tension runs were performed first.

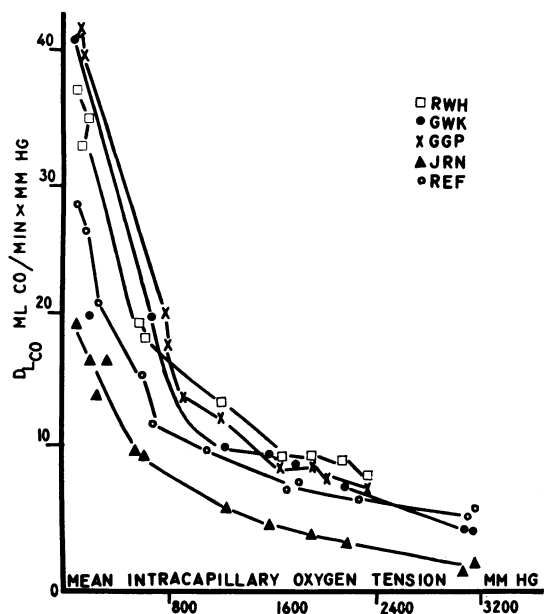


FIG. 1. EFFECT OF MEAN INTRACAPILLARY OXYGEN TENSION ON PULMONARY DIFFUSING CAPACITY ( $D_{LCO}$ ) IN FIVE SUBJECTS. The lines show the trend in each subject.

Results

The results are shown in Tables II and III. The pulmonary diffusing capacity ( $D_{LCO}$ ) in milliliters CO per (minute  $\times$  millimeters Hg) decreased in all subjects with rising mean intracapillary oxygen tension (Figure 1). In the three subjects in group B (JRN, REF, and GWK) where duplicate measurements were made at 4.8 atmospheres and the mean intracapillary oxygen tension was between 2,900 mm Hg and 3,200 mm Hg, the

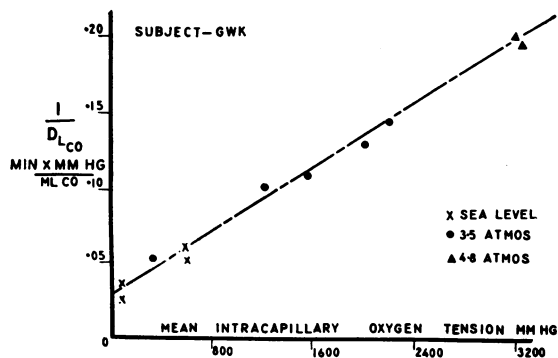


FIG. 2. THE RELATIONSHIP BETWEEN  $D_{LCO}$  AND MEAN INTRACAPILLARY OXYGEN TENSION AT SEA LEVEL AND AT 3.5 AND 4.8 ATMOSPHERES PRESSURE IN SUBJECT GWK. The straight line is the regression based on all the points.  $r = .992$ .

diffusing capacity was reduced on the average to 15% of the value measured at normal alveolar oxygen tension (approximately 110 mm Hg).

$1/D_{LCO}$  increased approximately in a linear relation with the mean intracapillary oxygen tension (see Figure 2). The average correlation coefficient between  $1/D_{LCO}$  and mean intracapillary oxygen tension in the five subjects was 0.986.

Figure 3 shows  $1/D_{LCO}$  measured after a preceding preparatory level of 116 mm alveolar oxygen tension and again after a preparatory level of approximately 2,580 mm oxygen tension in one subject (RWH). The mean intracapillary oxygen tension at which  $D_{LCO}$  was measured is shown on the abscissa. The straight, dashed line is the re-

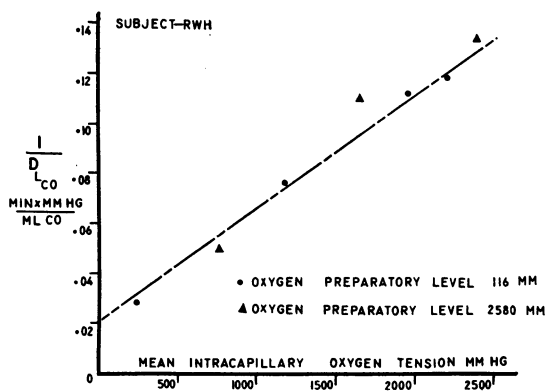


FIG. 3. THE EFFECT OF DIFFERENT PREPARATORY LEVELS OF OXYGEN ON  $D_{LCO}$ . The straight line is the regression based on the lower preparatory level points. The higher preparatory level points lie within 2 SE of this line.

gression line based on the measurements made after a preparatory level at the lower oxygen tension. The higher preparatory level points lie within 2 SE of this line. In the other subject who performed these maneuvers (GGP), there was also no consistent difference observed between the values of  $D_{LCO}$  measured after different preparatory levels of  $O_2$  tension.

The partial pressure of nitrogen ( $P_{N_2}$ ) present at the time of breath holding varied from 30 mm to 2,400 mm Hg. Figure 4 shows the values of  $1/D_{LCO}$  plotted against the mean intracapillary oxygen tension with the  $P_{N_2}$  values indicated as numbers. The presence of large partial pressures of nitrogen did not affect the value of  $1/D_{LCO}$  in a consistent fashion in any of the subjects studied.

The control values of  $D_{LCO}$  after the whole procedure consistently fell in all five subjects in com-

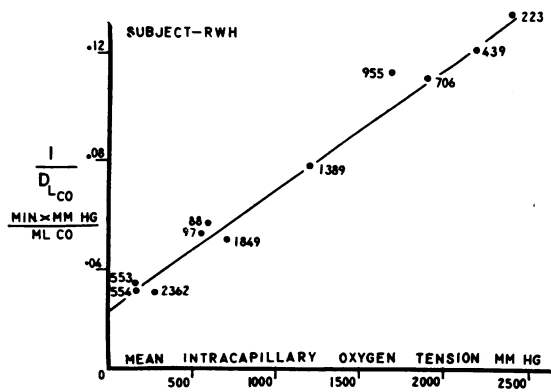


FIG. 4. EFFECT OF INDEPENDENT VARIATION OF THE PARTIAL PRESSURE OF NITROGEN (PN<sub>2</sub>) ON DL<sub>CO</sub>. The figures beside the points are values of PN<sub>2</sub> present at the time of breath holding in millimeters Hg. The straight line is a regression line relating DL<sub>CO</sub> and the intracapillary oxygen tension.

parison with those measured before. The average fall from the initial value was 14.4% with normal alveolar oxygen tensions (120 mm Hg) and 13.0% with oxygen tensions of approximately 570 mm Hg.

The pulmonary capillary blood flow (Q<sub>c</sub>) fell from the mean value of 7.9 L per minute at sea level to 5.8 L per minute at 3.5 atmospheres, which represents a 27% drop from the initial value. In two subjects (RWH and REF) Q<sub>c</sub> returned after the whole procedure to the original sea level value. The final average control value of Q<sub>c</sub> in the other three subjects (GWK, JRN, and GGP) was 66%, 82%, and 75%, respectively, of their initial sea level control.

Of the two subjects in group A, the average Q<sub>c</sub> of subject GGP dropped from 7.0 L per minute to 5.1 L per minute after approximately 100% oxygen had been inspired for 10 minutes at 3.5 atmospheres, but Q<sub>c</sub> increased slightly in RWH (Figure 5). There was no obvious difference in Q<sub>c</sub> measured at 3.5 atmospheres and 4.8 atmospheres in the three subjects in group B. No correlation was seen between Q<sub>c</sub> and the mean intracapillary oxygen tension during breath holding.

**Discussion**

These experiments showed that the diffusing capacity for carbon monoxide decreases progressively with rising oxygen tension from 100 to 3,200 mm Hg. The mechanism for this decrease

is thought to be as follows. The rate of removal of carbon monoxide from the alveolar gas is limited, in part, by the rate of formation of carboxyhemoglobin in the red cell which, in turn, is proportional to the concentration of unsaturated hemoglobin molecules present. As a consequence of the rising P<sub>O<sub>2</sub></sub> in the red cell, fewer unsaturated hemoglobin molecules are available for the formation of carboxyhemoglobin. These data show that even in the presence of a mean intracapillary oxygen tension of approximately 3,000 mm Hg, there is a measurable diffusing capacity for carbon monoxide, which can only mean there is still unsaturated hemoglobin present. This is not so surprising when it is considered that although there may be only a minute amount of unsaturated hemoglobin present at any instant, it is the net result of extremely rapid association with and dissociation from oxygen.

In the above experiments oxygen may have altered the actual properties of the pulmonary mem-

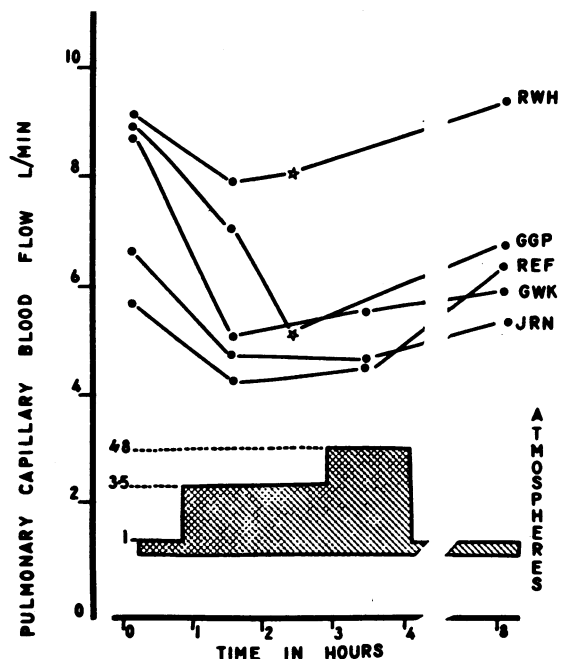


FIG. 5. EFFECT OF DIFFERENT BAROMETRIC PRESSURE ON THE AVERAGE VALUES OF CAPILLARY BLOOD FLOW IN FIVE SUBJECTS. The dots are measurements made after a preparatory level of approximately 110 mm O<sub>2</sub> tension, and the stars after a preparatory level of 2,580 mm O<sub>2</sub> tension. The abscissa is only an approximate time schedule and applies in all subjects with the exception of REF, where measurements at 4.8 atmospheres were performed before those at 3.5 atmospheres.

TABLE IV  
*Calculated values of Vc and DM above and below mean intracapillary oxygen tensions of 600 mm Hg\**

Subject	Vc		DM	
	Alveolar Po <sub>2</sub> <600 mm Hg†	Alveolar Po <sub>2</sub> >600 mm Hg‡	Alveolar Po <sub>2</sub> <600 mm Hg†	Alveolar Po <sub>2</sub> >600 mm Hg‡
	ml		ml CO/(min × mm Hg)	
RWH	112	119	57	91
GWK	103	98	67	77
REF	80	208	53	12
GGP	106	125	72	77
JRN	56	40	33	435

\* Vc = blood volume in the pulmonary capillaries; DM = diffusing capacity of the membrane.

† Using measured  $\theta$  relationship to oxygen tension.

‡ Using assumed  $\theta$  relationship to oxygen tension.  $\theta$  has been measured only at O<sub>2</sub> tensions less than 600 mm Hg, and values for higher oxygen tensions had to be obtained by extrapolation from the known data.

brane and vascular bed thereby affecting the diffusing capacity, DL<sub>CO</sub>. But, as previously pointed out (11), this seems unlikely since changes in the membrane and vascular bed would have to occur within the several seconds required for the measurement of DL<sub>CO</sub> by the single breath technique. In the preparatory level experiments we tested for possible changes in the pulmonary diffusing surface by having subjects breathe oxygen for 10 minutes at an alveolar oxygen tension of approximately 2,600 mm Hg. We attempted to separate possible effects on the pulmonary diffusing surface from changes in DL<sub>CO</sub> resulting from altered reaction kinetics within the red cell, which are influenced by the oxygen tension at the particular moment, by quickly (within 5 to 8 seconds) changing the alveolar oxygen tension and then measuring DL<sub>CO</sub>. We found that DL<sub>CO</sub> was affected only by the oxygen tension in the alveoli at the time of breath holding and not by the preparatory level and have concluded, therefore, that the diffusing surface and gas exchange vessels are not affected by breathing oxygen for 10 minutes with an alveolar partial pressure of approximately 2,600 mm Hg. Other investigators have reported pulmonary edema in animals (12) and a lowering of DL<sub>CO</sub> in human subjects (13) who breathed oxygen for longer periods at sea level, changes that infer injury to the pulmonary membrane and vascular bed. Possibly in our experiments a longer exposure to oxygen would have produced a decrease in diffusing capacity, but we voluntarily restricted our experiments to 10 minutes of oxy-

gen breathing at 3.5 atmospheres in order to reduce the likelihood of oxygen toxicity and seizures.

The concept of large numbers of nitrogen molecules impeding the diffusion of carbon monoxide molecules in the gas phase and thereby producing gradients within the alveolar air has been discussed previously (11). On theoretical grounds the nitrogen pressures in our experiments were not high enough to have impaired diffusion significantly. However, if this were an important facet and had affected the rate of gas diffusion within the alveolar air, a decrease in DL<sub>CO</sub> would have been found at increased atmospheric pressure when there were more nitrogen molecules present. In our experiments a variation of nitrogen partial pressures from 30 to 2,400 mm apparently did not affect DL<sub>CO</sub>, results which support the theory that diffusion within the alveolar gas itself is not a significant limitation to the passage of gas into the blood.

In these experiments a nearly linear relationship has been shown to exist between 1/DL<sub>CO</sub> and the mean intracapillary oxygen tension at the time of breath holding in all subjects. We have applied the equation (14),

$$1/DL_{CO} = (1/DM) + (1/\theta Vc), \quad [1]$$

to calculate the value of DM, the diffusing capacity of the membrane in milliliters CO per (minute × millimeters Hg), and Vc, the volume of the blood in milliliters in the pulmonary capillaries in all subjects using the measured values for  $\theta$  (14), the rate at which the red cells in 1.0 ml of pulmonary capillary blood will absorb CO in milliliters per minute per millimeter Hg plasma CO tension. If the ratio of permeability of the red cell membrane to that of the red cell interior is assumed to be 2.5,  $\theta$  is related to the intracorpuseular oxygen tension as follows (5):

$$1/\theta = 0.73 + 4.4 Po_2, \quad [2]$$

where Po<sub>2</sub> is the intracorpuseular oxygen tension in atmospheres.

Equation 2 has been used to calculate the value of 1/ $\theta$  from the measured mean intracapillary oxygen tension in all our experiments, and with this value, DM and Vc have been calculated from Equation 1. As Equation 2 is based on measurements of oxygen tensions only up to 600 mm Hg, the calculated values of DM and Vc from

oxygen tensions above 600 mm Hg have been kept separate from those measured at sea level (i.e., at oxygen tensions below 600 mm Hg). The results of these calculated values are shown in Table IV. When  $V_c$  calculated from values of  $\theta$  obtained by extrapolation to higher oxygen tensions are compared with  $V_c$  calculated from experimental values of  $\theta$  at oxygen tensions below 600 mm Hg, four of five subjects show similar results. Three of the five subjects also have comparable  $DM$  values. If the error of the method incurred at very high oxygen tensions, as explained in detail below, is taken into account, these results probably mean that  $1/\theta$  bears the same relationship to the mean intracapillary oxygen tension up to 3,000 mm Hg as defined up to 600 mm Hg tension by Equation 2.

In the measurement of  $DL_{CO}$  at high oxygen partial pressures, the ratio of the initial alveolar CO concentration to the final alveolar CO concentration ( $F_{ACO_0}/F_{ACO_t}$ ) approaches unity, and in this event any error is greatly magnified. The equilibrated plasma CO tension becomes critical as well. For example, if a subject has a  $DL_{CO}$  of 30 ml of CO per (minute  $\times$  millimeters Hg), an alveolar volume of 5,000 ml standard temperature and pressure, dry, and a breath-holding time of 10 seconds, a 5% error in the measured expired alveolar concentration of carbon monoxide will introduce a 7% error in the calculated  $DL_{CO}$ . However, if the  $DL_{CO}$  is 5 ml of CO per (minute  $\times$  millimeters Hg) with the same alveolar volume and breath-holding time, a 5% error in the measurement of the expired alveolar concentration will be magnified to a 32% error in the calculated  $DL_{CO}$ . This magnification of errors at high oxygen tension may explain, in part, the wide variation in some of the measurements of  $DM$  and  $V_c$  at oxygen tensions over 600 mm Hg (see Table IV).

The average control  $DL_{CO}$  decreased 14% in all subjects after the day's experiment in the chamber when compared to initial control values. To elucidate the matter further, two subjects, GGP and GWK, who had previously shown an average fall in  $DL_{CO}$  of 15% and 25%, respectively, were tested again. The subjects were seated in the chamber in easy chairs, but were not exposed to hyperbaric pressures or given any supplemental oxygen. Five measurements of  $DL_{CO}$  and  $\dot{Q}_c$  were made in each subject at 5-minute intervals in the morning and another five in the afternoon ap-

proximately 4 to 5 hours later. The results are shown in Table V, and we see that  $DL_{CO}$  dropped in much the same way as in the original experiments; the significance levels are shown. Since these subjects breathed only room air at sea level, this fall in  $DL_{CO}$  cannot be due to oxygen inhalation or to increased barometric pressure per se, but rather seems related to the subjects' prolonged inactivity, (15) and to changes in  $\dot{Q}_c$  (5). This is an interesting finding that will require further investigation.

We are aware of reports that during oxygen breathing at 2.0 to 3.5 atmospheres, normal men showed an unexplained alveolar-arterial oxygen tension difference indirectly measured to be as high as 100 mm Hg at 2.0 atmospheres (16), 400 mm Hg at 3.0 atmospheres (17), and 550 mm Hg at 3.5 atmospheres (18). On the other hand, no large alveolar-arterial oxygen tension difference was found by Rennie and Pappenheimer (19) in dogs breathing oxygen at 2 atmospheres ambient pressure. In recent applications of the oxygen electrode to the measurement of arterial  $P_{O_2}$  in hyperoxygenated subjects, large alveolar-arterial gradients were again reported (20). This possible increase in the alveolar-arterial oxygen gradient does not necessarily relate to the depression of  $DL_{CO}$  by oxygen observed in the present study. Even though the uptake of oxygen in the lungs normally appears to be partially limited by the rate at which oxygen can react with intracellular, unsaturated hemoglobin (21), this does not in any way imply that complete equilibration between alveolar and capillary oxygen tension would not be expected theoretically at the end of the capillary no matter how great the absolute alveolar oxygen tension. For example, the mixed venous blood entering the pulmonary capillary bed would have a relatively low  $P_{O_2}$  and therefore a normal  $DL_{O_2}$ , leading to nearly complete saturation of all the hemoglobin before the blood  $P_{O_2}$  could rise over 150 mm Hg. Once the hemoglobin is fully saturated, further increase in oxygen content in the blood is only in the form of physically dissolved gas, and the only limitation to further transfer is the diffusing capacity of the pulmonary membrane (22). In these circumstances, the reaction rate for oxygen with hemoglobin is of no further concern. For reasons previously given the pulmonary membrane does not appear to be affected by short



TABLE V  
*DL<sub>CO</sub> and Q̇<sub>c</sub> before and after a 4- to 5-hour period sitting at sea level*

Subject	DL <sub>CO</sub>		Q̇ <sub>c</sub>		Mean intracapillary oxygen tension	
	Before	After	Before	After	Before	After
	<i>ml CO/(min × mm Hg)</i>		<i>L/min</i>		<i>mm Hg</i>	
GGP	39.9 ± 6.7	35.7 ± 3.0	7.0 ± 0.6	6.4 ± 0.7	118	121
	p < 0.05		NS at 0.5 level			
GWK	34.1 ± 3.0	31.7 ± 2.6	4.5 ± 0.4	5.2 ± 1.0	112	117
	p < 0.1		NS at 0.1 level			

periods of high  $P_{O_2}$ , and, at an alveolar  $P_{O_2}$  of 2,000 mm Hg, equilibration of physically dissolved oxygen can be calculated to be 99% complete in less than 0.03 second, assuming a pulmonary capillary blood volume of 100 ml and a diffusing capacity for oxygen of the pulmonary membrane of 40 ml per minute per mm Hg (23, 24).

The fact that the plot of  $1/DL_{CO}$  against  $P_{O_2}$  (Figure 4) remains linear at the extremely high alveolar oxygen tensions implies that the mean capillary  $P_{O_2}$  continues to rise linearly as alveolar  $P_{O_2}$  rises.

Thus, since neither diffusion limitation, gross shunting of blood across the lungs, nor other mechanisms to interfere with the movement of oxygen have been identified as a consequence of short periods of oxygen breathing at high pressures, the authors are not now prepared to explain the apparent gross interference with oxygen uptake.

### Summary

The pulmonary diffusing capacity ( $DL_{CO}$ ) and capillary blood flow ( $Q_c$ ) were calculated from the disappearance of low concentrations of carbon monoxide and acetylene from the alveolar gas during breath holding. Such measurements were performed in five normal subjects in a hyperbaric pressure chamber at sea level and at 3.5 and 4.8 atmospheres absolute.

$DL_{CO}$  was found to decrease progressively with rising oxygen tension.  $1/DL_{CO}$  increased linearly with rising mean intracapillary oxygen tension from 110 to 3,200 mm Hg (average  $r = 0.986$ ).  $DL_{CO}$  was not changed significantly by independent variation of nitrogen partial pressure from 30 to 2,400 mm Hg at constant alveolar oxygen tension. The pulmonary diffusing surface did not measur-

ably alter with exposure to an alveolar oxygen tension of 2,400 mm Hg for 10 minutes before the measurement of  $DL_{CO}$ .

Control values at sea level of  $DL_{CO}$  and  $Q_c$  were done before and after the above studies. An average 14% decrease in  $DL_{CO}$  was found accompanied by a drop in  $Q_c$ . These changes were thought to result from the subjects' prolonged inactivity in the chamber during decompression rather than to be due to oxygen inhalation or to increased barometric pressure per se.

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