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Research Article

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The Pressure-Volume Relationship of the Normal Pulmonary Capillary Bed *

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In isolated lung preparations (1, 2) and in normal subjects (3, 4), acute pulmonary vascular congestion increases breath-holding diffusing capacity for carbon monoxide (DL_{CO}) by increasing the instantaneous volume of blood available for CO absorption (V_c). Conversely, in normal men, procedures that decrease pulmonary vascular pressure decrease DL_{CO} (4, 5); yet, the pulmonary capillary bed of the lung chronically subjected to increased intravascular pressure is less able to decrease its volume in response to procedures designed to decrease pulmonary vascular pressure (6). Although this may be the consequence of structural changes in the lung, this observation suggests that the curve relating DL_{CO} to pulmonary vascular pressure may reach a plateau, beyond which changes in pulmonary vascular pressure produce no further changes on DL_{CO}. Such a relationship does not imply a solution to the question whether increased intravascular pressure recruits a limited number of capillaries or dilates capillaries within a limited range. In either case, a plateau of the DL_{CO}-vascular pressure curve would be anticipated.

This study was undertaken to examine the behavior of the normal pulmonary capillary bed acutely subjected to increased intravascular pressure with two specific aims in mind: *1*) to describe, in normal man, the effects on DL_{CO} of graded increases in intravascular pressure and to determine whether a plateau does indeed exist; *2*) if such a limit exists, to determine the effect of exercise on DL_{CO} in individuals who have already experienced the maximal effect of acute passive congestion on DL_{CO}.

Methods

Twenty trained normal men, ages 21 to 36, were used in this study. Their physical characteristics are summarized in Table I. They came to the laboratory from their usual work and were studied after resting 15 to 30 minutes. There was no attempt to insure a truly basal state.

The basic variables measured were DL_{CO}, right atrial pressure, and oxygen consumption. These were measured in the following experimental situations: *1*) In nine resting subjects, DL_{CO} and right atrial pressure were measured with the subjects supine and tilted 60° and 30°

TABLE I

*Physical characteristics of the experimental subjects**

Subject	Age	Height	Weight	V_A†
		cm	*kg*	*L*
B.R.	25	185	83.0	6.42
J.H.	24	188	79.5	7.16
T.S.	24	180	83.0	5.93
M.L.	25	185	83.0	6.80
J.S.	29	178	72.7	5.80
B.H.	26	188	86.3	6.47
B.M.	29	178	68.0	5.43
T.B.	21	183	77.2	7.28
J.B.	27	173	79.5	5.10
B.K.	25	180	79.5	6.26
J.L.	36	180	81.7	4.43
S.G.	33	178	70.5	4.97
W.D.	34	188	90.8	7.16
C.S.	30	180	77.2	6.03
J.Mc	24	175	70.5	5.93
R.D.	32	190	81.7	8.13
D.K.	25	180	79.5	6.28
J.R.	35	180	79.5	6.42
B.L.	27	180	83.0	6.66
J.C.	25	183	86.3	7.53

* Normal male physicians, medical students, or paramedical technicians.

† Alveolar volume (V_A) is expressed in liters and derived from the breath-holding neon dilution during the diffusing capacity for carbon monoxide (DL_{CO}) determination, corrected to body temperature, pressure, saturated with water (BTPS).

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head-up and 15°, 30°, and 60° head-down. Subsequently, head-up positions are indicated as negative tilt and head-down positions as positive tilt. The angle of tilt is expressed as the acute angle of the table with horizontal. *2*) In six subjects, $D_{L_{CO}}$ and right atrial pressure were measured with the subjects at 0°, + 60°, and + 60° with a pressure suit inflated and at + 60° just after having had arterial thigh tourniquets inflated at − 15°. *3*) In 11 subjects, $D_{L_{CO}}$ and oxygen consumption were measured with the subjects at rest, sitting, and at + 60° and while doing arm exercise at a work rate of 50 w, sitting, and at + 60°.

With this experimental design, it is possible to relate the effects of graded changes in central vascular pressure to $D_{L_{CO}}$ and to study the effects of exercise on $D_{L_{CO}}$ in subjects whose pulmonary vascular bed was already well filled by pressure.

The subjects were tilted on a motor-driven tilt table and suspended head-down by a harness attached around the pelvis. During head-up tilt, they remained motionless with their feet supported by a foot board. $D_{L_{CO}}$ and right atrial pressure (RAP) were measured within the first 30 seconds of tilt. In five subjects $D_{L_{CO}}$ and RAP were also measured after 5 minutes in the + 60° position.

The pressure suit used in this study is the same one used previously in this laboratory (3, 5). It is a single-chamber, balloon type garment [1] that covers the feet, legs, and abdomen and can be inflated to a pressure of 100 mm Hg within 5 seconds by a standard Air Force G-valve. All determinations for comparisons with those made during suit inflation were carried out with the subject wearing the laced but uninflated suit. During suit inflation, $D_{L_{CO}}$ was measured 15 to 30 seconds after the suit pressure had reached 100 mm Hg.

The arterial thigh tourniquets used are 8-inch pneumatic cuffs that were placed as high as possible on the thighs and, with the subjects at − 15°, were inflated abruptly to 250 mm Hg by opening a large bore connector to a previously pressurized bottle. Right atrial pressures and $D_{L_{CO}}$ were measured after the subject was tilted to the + 60° position.

Exercise was performed with one arm working a bicycle ergometer at a work rate of 50 w. $D_{L_{CO}}$ was measured at the end of 2 minutes of such exercise performed sitting and at + 60°. Ventilation and mixed expired oxygen concentration were monitored continuously during exercise and rest, sitting, and at + 60°. The subjects breathed air from a recording Tissot spirometer through a Hans-Rudolph valve. A portion of the mixed expirate was pumped continuously from a mixing chamber through a paramagnetic oxygen analyzer. The 90% response time of this sampling system was 30 seconds. O_2 consumption was calculated from the ventilation and corresponding expired O_2 concentrations after lag-time correction. In all cases, O_2 consumption was calculated after a steady state of ventilation and mixed expired O_2 concentration had been achieved. The minute volume of ventilation was not corrected for changing respiratory quotient. The error introduced by this simplification does not exceed 1%.

Carbon monoxide diffusing capacity was measured in duplicate by the Krogh breath-holding technique as modified by Ogilvie, Forster, Blakemore, and Morton (7) and as previously reported in detail from this laboratory, using a gas chromatograph for analysis of alveolar samples (6). Pulmonary capillary blood volume (Vc) and the diffusing capacity of the pulmonary capillary membrane (D_M) were determined by the method of Roughton and Forster (8), using duplicate measurements of $D_{L_{CO}}$ at two different alveolar O_2 tensions under each condition and assuming 2.5 as the ratio of permeability of the red cell membrane to that of its interior. Vc was corrected to an O_2 capacity of 20 ml per 100 ml blood.

Functional residual capacity (FRC) and the volume inspired (V_I) for the $D_{L_{CO}}$ determinations were not controlled during tilt or pressure suit inflation. However, the total alveolar volume (V_A) in each situation was estimated from the neon dilution during the 10-second breath-holding period. $V_A = (N_{EI}/N_{EA}) \times V_I$. In a previous study of this method in this laboratory using 50 normal men, V_A averaged 99.7% of the sum of the inspiratory capacity determined with a spirometer and the functional residual capacity determined with a total body plethysmograph (9). Changes in FRC during tilt and pressure suit inflation were estimated with a bag-in-box spirometer system with which a steady base line was obtained during spontaneous breathing before, during, and after a change in position or suit inflation. The recorded difference approximates the difference in FRC in the two situations.

Right atrial pressure was recorded using a radiopaque catheter placed fluoroscopically just within the right atrium. Mean pressure was obtained by electrical integration. In the supine position, reference zero was taken at the axis of intersection of a plane through the second anterior interspace and the mid-thoracic plane. During tilting, the recorded pressure was corrected to the new horizontal plane through the same axis.

The data obtained were analyzed, using an analysis of variance technique. The probabilities expressed are based on a method of least significant differences (10).

Results

Right atrial pressure. Mean right atrial pressure increased progressively from 1.0 mm Hg to 20.1 mm Hg when nine subjects were tilted from − 60° to + 60° (Table II). The increase in mean atrial pressure produced by + 60° tilt was maintained over a 5-minute period (Table III). In six other subjects, mean atrial pressure recorded at + 60° was further increased from 20.0

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[1] This suit was made by the David Clark Co., Worcester, Mass. In some previous publications (3, 4), it has been referred to as a G-suit. This suit, however, is not a standard aviator's G-suit and cannot be used in that way; it provides much more G protection than the aviator's G-suit.

TABLE II

Right atrial pressure during body tilting

Subject	Right atrial pressure —60°*	–30°	0°	+15°	+30°	+60°
			mm Hg			
B.R.	–2.6	3.7	9.2	15.0	17.6	26.9
J.H.	1.2	2.0	7.0	14.8	15.2	20.2
T.S.	0	5.0	8.6	13.6	16.8	18.8
M.L.	1.3	5.4	6.4	12.3	17.3	18.1
J.S.	1.0	3.8	6.0	11.3	12.0	13.7
B.H.	–2.6	2.1	10.0	14.8	17.8	22.4
B.M.	1.4	4.3	7.8	12.8	14.6	18.7
T.B.	3.5	2.2	8.7	16.5	17.4	20.2
J.B.	5.7	7.3	8.8	14.9	18.8	21.6
Mean	1.0	4.0	8.1	14.0	16.4	20.1
SD	2.6	1.8	1.4	1.6	2.1	3.6
p		← 0.01 →	← 0.001 →	← 0.001 →	← 0.025 →	← 0.001 →

* Degree of tilt: – indicates head-up tilt; + indicates head-down tilt.

TABLE III

Duration of $\mathrm{DL_{CO}}$ and right atrial pressure (RAP) change at +60° (5 subjects)

	0°	+60° (30 sec)*	+60° (5 min)†
$\mathrm{DL_{CO}}$, *ml/min × mm Hg*	38.3 ± 10.0	45.4 ± 10.0	44.9 ± 10.9
p		← 0.005 →	← NS →
RAP, *mm Hg*	8.5 ± 1.2	21.4 ± 3.4	21.0 ± 3.4
p		← 0.001 →	← NS →

* $\mathrm{DL_{CO}}$ and RAP within 30 seconds of reaching +60° position.
† $\mathrm{DL_{CO}}$ and RAP after 5 minutes at +60°.

to 28.5 mm Hg by pressure suit inflation and decreased to 14.6 mm Hg by inflation of thigh tourniquets before head-down tilt (Table IV). Thus, a wide range of central vascular pressures was produced, in one group by changes in body position and in another group, in a constant position, by means designed to prevent blood from leaving the legs in the head-down position or designed to transfer blood out of the legs and lower abdomen. The recorded changes in right atrial pressure are probably not the consequence of changes in intrapleural pressure associated with changes in lung volume since the decrease in FRC observed during the greatest degree of head-down tilt averaged only 0.3 ± 0.2 L. No further decrease in FRC was observed during inflation of the pressure suit in the + 60° position. Using an open circuit helium technique, Blair and Hickam (11) found a similar decrease in FRC in the head-down position and Ross, Lord, and Ley (3) found that inflation of this pressure suit did not consistently affect FRC.

$\mathrm{DL_{CO}}$, V_c, and D_M during tilt. While mean right atrial pressure increased progressively from – 60° through + 60° positions, $\mathrm{DL_{CO}}$ (Table V) and V_c (Table VI) reached a maximum at +15°. Greater degrees of tilt produced no further in-

TABLE IV

Effects of tilt, pressure suit inflation, and arterial thigh tourniquets on $\mathrm{DL_{CO}}$ and right atrial pressure

Subject	$\mathrm{DL_{CO}}$ 0°*	+60°	+60° (Pressure suit)†	+60° (Tourniquets)‡	Right atrial mean pressure 0°	+60°	+60° (Pressure suit)	+60° (Tourniquets)
		ml/min × mm Hg					*mm Hg*	
B.M.	25.8	29.6	29.5	25.9	10.0	21.2	28.5	16.4
M.L.	40.3	48.9	48.9	43.1	8.8	23.2	33.7	16.7
B.K.	35.0	42.0	40.4	41.2	10.0	20.5	26.8	16.6
J.L.	31.7	34.6	33.6	33.4	9.0	21.0	31.0	15.0
T.S.	36.1	46.3	47.6	43.5	9.5	20.4	26.3	12.7
J.B.	41.7	46.3	46.9	47.3	8.0	13.8	24.4	9.9
Mean	35.1	41.3	41.2	39.1	9.2	20.0	28.5	14.6
SD	5.8	7.6	8.1	7.9	0.8	3.2	3.4	2.7
p		← 0.005 →	← NS →			← 0.001 →	← 0.001 →	
				← NS →				← 0.001 →

* Degree of tilt: – indicates head-up tilt; + indicates head-down tilt.
† G-suit inflated to 100 mm Hg.
‡ Pneumatic cuffs around the thighs were inflated to 250 mm Hg in –15° position just before tilting to the +60° position.

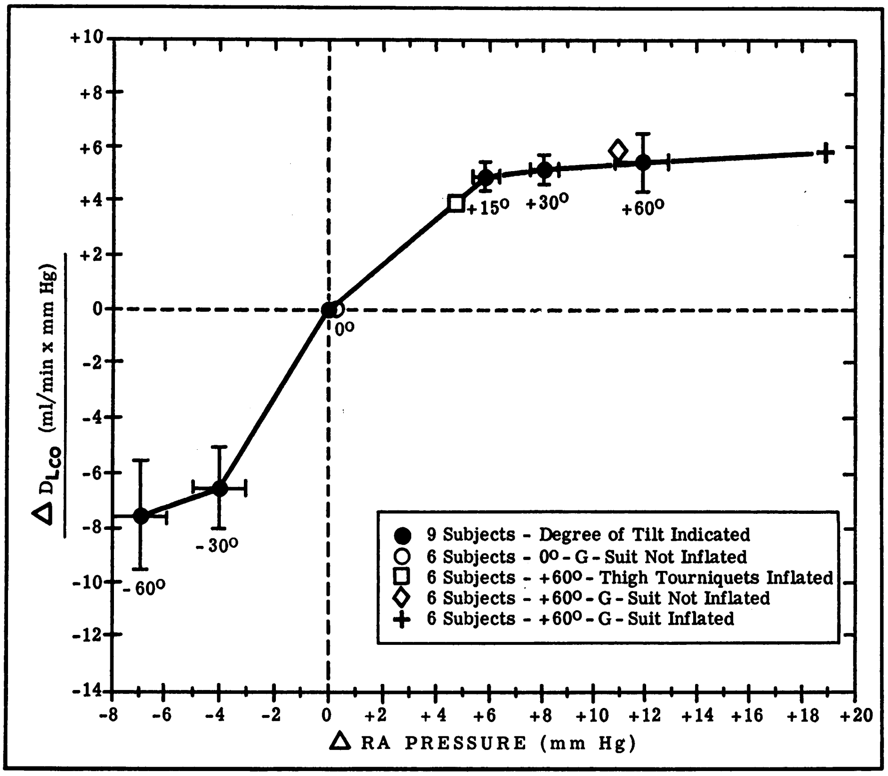

FIG. 1. RELATIONSHIP OF CHANGE IN DIFFUSING CAPACITY (ΔDLCO) TO CHANGE IN RIGHT ATRIAL PRESSURE (ΔRA) PRODUCED BY TILTING, PRESSURE SUIT INFLATION, AND ARTERIAL THIGH TOURNIQUETS. Brackets indicate ± standard error of the mean ΔRA and ΔDLCO for each position.

crease in either DLCO or Vc. The relationship of changes in mean right atrial pressure to changes in DLCO is shown graphically in Figure 1.

Tilting from 0° to − 30° decreased DM from 135 to 108 ml per minute × mm Hg (Table VII). Greater tilt in either direction did not affect DM.

TABLE V

Effects of body tilting on the diffusing capacity of the lung (DLCO)

Subject	−60°*	−30°	0°	+15°	+30°	+60°
			DLCO *ml/min* × *mm Hg*			
B.R.	30.2	33.0	48.9	53.5	51.8	54.5
J.H.	34.3	35.4	46.3	51.8	51.8	52.2
T.S.	33.5	30.8	35.8	41.4	44.5	44.5
M.L.	29.2	31.7	42.5	50.8	50.2	52.2
J.S.	20.1	21.5	27.1	31.0	31.1	30.9
B.H.	33.9	37.3	37.1	45.1	45.2	46.6
B.M.	18.3	18.5	23.2	27.3	27.4	29.0
T.B.	44.1	42.5	48.0	51.2	52.2	51.2
J.B.	38.2	38.6	41.7	44.3	45.6	45.8
Mean	31.3	32.1	38.9	44.0	44.4	45.2
SD	8.2	7.8	9.1	9.4	9.2	9.3
p		NS	0.05	0.005	NS	NS

* Degree of tilt: − indicates head-up tilt; + indicates head-down tilt.

TABLE VI

Effects of body tilting on pulmonary capillary blood volume (Vc)

Subject	−60°*	−30°	0°	+15°	+30°	+60°
			Vc *ml*			
B.R.	91	91	114	148	148	150
J.H.	64	67	90	100	103	108
T.S.	79	76	89	108	105	110
M.L.	80	91	91	133	143	133
J.S.	60	54	60	65	68	60
B.H.	80	83	88	105	100	105
B.M.	48	50	55	65	60	63
T.B.	67	75	89	104	99	111
J.B.	62	71	62	74	87	83
Mean	70	73	82	100	101	103
SD	13	14	19	29	30	30
p		NS	0.05	0.001	NS	NS

* Degree of tilt: − indicates head-up tilt; + indicates head-down tilt.

DM is a function of the surface area of the pulmonary capillary bed and Vc is a function of the pulmonary capillary blood volume. With the assumption that tilting does not alter the pulmonary capillary hematocrit or the diffusivity of the membrane component per unit area, the ratio, Vc/DM, is an expression of the volume/surface ratio of the effective pulmonary capillary bed. Despite rather wide changes in right atrial pressure during tilting and clear-cut changes in DL_{CO}, Vc/DM was not consistently affected by tilting (Table VIII). With the variability in estimation of Vc and DM observed in this study (Tables VI and VII), this ratio is only a crude index of the volume/surface relationship of the pulmonary capillary bed. With a method of least significant differences (10), it can be shown that, because of the large variance of the population, Vc/DM would have to increase from 0.7 to 1.0 before reaching the 5% level of significance.

DL_{CO} and O_2 consumption during exercise with and without pulmonary vascular congestion (Table IX). Oxygen consumption was not affected by head-down tilt at rest or during exercise. In seated subjects, arm exercise at a work rate of 50 w increased O_2 consumption from 334 to 1,230 ml per minute. During head-down tilt, a similar increase was observed during exercise at the same work rate, 323 to 1,101 ml per minute. In seated subjects, DL_{CO} increased from 32.8 to 42.2 ml per minute × mm Hg during exercise. The same exercise at + 60°, with an equivalent change in oxygen consumption, increased DL_{CO} from 43.6 to 46.8 ml per minute × mm Hg. DL_{CO} during exercise at + 60° was higher than that obtained during the same exercise performed while seated. Alveolar P_{O_2}, determined from chromatographic analysis of alveolar samples obtained at the end of the 10-second breath-holding period, averaged 124 ± 3 mm Hg in the subjects sitting at rest and 121 ± 4 mm Hg at + 60° (p = NS). During exercise, alveolar P_{O_2} was 106 ± 4 mm Hg, sitting, and 109 ± 7 mm Hg at + 60° (p = NS). Thus, the effects of position on DL_{CO} at rest and exercise are not dependent upon differences in alveolar P_{O_2}. With the available values for the reaction rate of CO with hemoglobin at different O_2 tensions (12) used and with the assumption that DM and Vc do not change, this decrease in alveolar P_{O_2} during exercise is insufficient to account for the observed increases in DL_{CO}.

TABLE VII

Effects of body tilting on the diffusing capacity of the pulmonary capillary membrane (DM)

Subject	−60°*	−30°	0°	+15°	+30°	+60°
			DM *ml/min × mm Hg*			
B.R.	67	72	118	111	95	95
J.H.	125	125	167	200	200	177
T.S.	91	80	91	111	105	106
M.L.	60	63	125	125	111	125
J.S.	58	95	167	133	100	83
B.H.	100	118	122	125	134	134
B.M.	50	40	59	44	100	83
T.B.		180	167	154	200	150
J.B.	200	200	200	200	133	200
Mean	94	108	135	134	133	135
SD	50	54	44	48	40	38
p	NS ←→	0.05 ←→	NS ←→	NS ←→	NS ←→	

* Degree of tilt: − indicates head-up tilt; + indicates head-down tilt.

Discussion

Studies based on a variety of techniques have suggested that the upper zones of the lungs of normal subjects are relatively under-perfused and underfilled in upright positions (13–18). Direct observation of pulmonary capillary behavior has shown that numerous individual capillaries at any one time may be empty of erythrocytes (19).

TABLE VIII

Effects of body tilting on the relationship of pulmonary capillary blood volume to membrane diffusing capacity (Vc/DM)

Subjects: 9	−60°*	−30°	0°	+15°	+30°	+60°
$\frac{Vc}{DM}$', $\frac{ml\ blood}{ml\ CO/min \times mm\ Hg}$	0.9 ± 0.4	0.8 ± 0.4	0.7 ± 0.2	0.9 ± 0.4	0.8 ± 0.4	0.8 ± 0.4
p	←NS→					

* Degree of tilt: − indicates head-up tilt; + indicates head-down tilt.

TABLE IX

Effects of exercise on DLCO during head-down tilt

Subject	DLCO S*	DLCO +60°	DLCO S + Ex	DLCO +60° + Ex	O_2 consumption S	O_2 consumption +60°	O_2 consumption S + Ex	O_2 consumption +60° + Ex
		ml/min × mm Hg				*ml/min*		
S.G.	28.2	35.8	36.0	38.4	257	307	1,150	1,170
W.D.	36.1	50.5	52.0	59.0	344	360	1,410	1,100
M.L.	34.8	51.4	49.6	53.7	313	305	1,550	1,285
C.A.	25.7	35.8	34.3	33.6	388	378	1,000	755
J.Mc	25.2	29.4	30.2	34.0	343	358	1,060	1,160
R.D.	43.7	53.3	44.6	50.7	380	260	1,110	1,345
D.K.	29.8	38.5	37.6	40.9	280	264	1,110	1,040
J.R.	27.1	39.1	43.1	47.0	278	263	1,150	1,030
B.L.	30.6	39.0	34.3	47.0	386	392	1,180	927
J.C.	39.5	47.7	51.6	48.3	313	283	1,240	1,160
B.R.	40.4	59.9	51.2	62.0	397	382	1,580	1,140
Mean	32.8	43.7	42.2	46.8	334	323	1,230	1,101
SD	6.4	9.4	8.1	9.4	50	52	196	163
p	←	0.001	→		← NS	→	← NS	→
	← 0.001	→				← 0.001	→	
		← NS	→					
			← 0.025	→				
		←	0.05	→				

* S, sitting; +60°, tilted 60° head-down; S + Ex, after 2 minutes exercise at 50 w, sitting; +60° + Ex, after 2 minutes exercise at 50 w, tilted 60° head-down.

Thus, it seems that the effective pulmonary capillary bed of resting normal individuals, particularly in upright positions, indeed has a definite capability for enlargement by means of recruiting such "empty" capillaries, particularly those of the upper zones where the normally low vascular pressure may be inadequate to maintain flow. Acute pulmonary vascular engorgement increases the volume of the pulmonary capillary bed either by recruiting such previously inactive capillaries or by dilating ones already in use (3, 4).

With the method of Roughton and Forster (8), it is possible to arrive at a quantitative expression of the diffusivity of the pulmonary capillary membrane (DM) as well as the pulmonary capillary blood volume (Vc) exposed to the alveolar carbon monoxide during the breath-holding period. Vc then is a function of the volume of the effective pulmonary capillary bed and DM is a function of its area. The limitations of these indirect measurements are well-known and have been discussed previously (20).

The present study was designed to define the limits of the relationship of changing central vascular pressure to changing size of the effective pulmonary capillary bed. Changes in right atrial pressure were used as an index of changes in transmural pulmonary capillary pressure. Evidence available from studies in normal men suggests that acutely induced increases in right atrial, pulmonary arterial, and pulmonary "wedge" pressures are equivalent (4, 21). Similar results have been produced during acute changes in central vascular pressures in dogs (22). Since right and left atrial pressures and pulmonary arterial pressures change by similar increments during acute changes in central vascular pressures, a change in right atrial pressure represents a reasonable index of a change in pulmonary capillary pressure. The intravascular pressure recorded does not truly represent transmural pressures, since intrapleural pressure is not determined. However, in the absence of a more substantial change in lung volume during tilting and pressure suit inflation, intrapleural pressure must be little affected, and changes in recorded pressure must closely reflect changes in transmural pressure.

The changes in right atrial pressure (Tables II to IV), $D_{L_{CO}}$ (Tables IV and V), and Vc (Table VI) and the relationship of changes in right atrial pressure to changes in $D_{L_{CO}}$ (Figure 1) confirm that increases in central vascular pressure increase $D_{L_{CO}}$ and Vc. However, $D_{L_{CO}}$ and Vc reach a maximum after relatively small changes in central vascular pressure. Larger increases in pressure, whether produced by gravity or pressure suit inflation, did not produce further increases in $D_{L_{CO}}$ or Vc. In the + 60° position, no change in $D_{L_{CO}}$ or Vc was observed during pressure changes over a 14 mm Hg range (Table IV), all of which were on the plateau of the $D_{L_{CO}}$ pressure curve. This study, therefore, shows a limit to the passive enlargement of the pulmonary capillary bed by pressure, and Figure 1 is an expression of the compliance of the pulmonary capillary bed over the range of pressure studied. If we assume that increased central vascular pressure does not affect the pulmonary capillary hematocrit, the rate of reaction of carbon monoxide with hemoglobin, or the diffusivity of the membrane per unit area, these results are compatible with two alternative explanations: *1*) that increased pulmonary capillary pressures recruit previously "empty" capillaries and that this recruitment is complete at relatively small increases in pressure, and/or *2*) that increased capillary pressure produces limited dilation of capillaries already "open." If the capillaries are cylindrical in shape, recruitment of "empty" capillaries should not affect the volume/surface ratio of the pulmonary capillary bed. Capillary dilation, however, should increase the volume/surface ratio, if dilation is accomplished without change in cross sectional configuration. If Vc is taken as a function of pulmonary capillary area, then Vc/D_M is some function of the volume/area relationship of the pulmonary capillary bed. Vc/D_M was not affected by the increased central vascular pressures produced in this study. Vc and especially D_M are greatly affected by variability in the measurement of $D_{L_{CO}}$ (20) and may be affected by changes in geometry. Such variability makes it impossible to detect small changes in the pulmonary capillary volume/surface relationship by this method. Consequently, limited capillary dilation cannot be excluded.

The decrease in RAP produced during head-up tilt was smaller than the increase during head-down tilt (Table I). This is undoubtedly the consequence of the numerous protections against pooling blood in the dependent abdomen and legs and suggests the relative inadequacy of such protections operating against gravitational stresses in a head-down position. Although the range of pressures was not large, Figure 1 suggests that $D_{L_{CO}}$ did not continue to decrease as RAP decreased below 4.0 mm Hg. The data do not permit a definitive explanation of this curve in the lower ranges. However, in a head-up position, it is probable that pressure sufficient to maintain cardiac filling is sufficient for filling and perfusion of most of the pulmonary capillary bed below heart level so that decreases in central vascular pressure in a head-up position cannot be great enough to decrease $D_{L_{CO}}$ further without producing serious impairment of cardiac filling.

The maintenance over a 5-minute period of the increase in RAP and $D_{L_{CO}}$ produced by head-down tilt is in contrast with the changes previously reported with pressure suit inflation, where central vascular pressure begins to decrease after 30 seconds and is near preinflation levels at 5 minutes (23). The stability of this effect in the head-down position makes it possible to evaluate the effect of continued pulmonary vascular congestion on the $D_{L_{CO}}$ changes due to exercise.

Despite extensive investigation, the mechanism whereby exercise increases breath-holding diffusing capacity remains obscure (24, 25). Prior studies have shown that the $D_{L_{CO}}$ increases during exercise are probably not dependent upon changes in ventilation (26), cardiac output (24), or blood pH (24). In subjects who have already achieved the maximal effect of pressure on the enlargement of the pulmonary vascular bed, mild exercise increases $D_{L_{CO}}$ even further (Table IX). The small decrease in alveolar P_{O_2} observed during exercise probably contributes slightly to the increase in $D_{L_{CO}}$ observed at + 60° during the mild exercise used in this study. However, previous studies, using more strenuous exercise, have consistently shown greater increases in $D_{L_{CO}}$ during exercise than can be achieved by congestion alone (27). Exercise, therefore, makes available some unexplained factor that increases the rate of CO transfer to an extent not possible by passive enlargement of the capillary bed. This factor may be an increased pulmonary capillary hematocrit, an increased rate of reaction of carbon monoxide with hemoglobin, or some means of enlarging the effective capillary bed more than can be obtained with pressure alone.

Summary

With body tilting, pressure suit inflation, and occlusive thigh tourniquets used to change central vascular pressures, the relationship of the diffusing capacity for carbon monoxide ($D_{L_{CO}}$) and pulmonary capillary blood volume (V_C) to pressure has been determined through a wide range of pressures. After a small increase in pressure, no further increase in $D_{L_{CO}}$ was observed despite large increases in central vascular pressure. There is, therefore, an upper limit to the passive enlargement of the normal pulmonary capillary bed. The curve relating $D_{L_{CO}}$ to pressure suggests that passive enlargement is the consequence of either recruitment of a limited number of capillaries or limited dilation of capillaries as pressure is increased.

Muscular exercise produces greater increases in $D_{L_{CO}}$ than can be produced by the maximal effect of passive congestion. This suggests that during muscular exercise $D_{L_{CO}}$ is increased by factors other than pressure alone.

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