Effects of Pulmonary Vascular Congestion on Postural Changes in the Perfusion and Filling of the Pulmonary Vascular Bed *

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Measured by a variety of techniques, the overall ventilation-perfusion relationship of the normal human lung is different in supine and upright positions, and in the upright position, the upper regions of the lung are relatively poorly perfused (1-4). Similarly, pulmonary diffusing capacity (D_L) is reduced when normal subjects change from supine to upright positions (5, 6); in the upright position, carbon monoxide absorption is greater in the lower portions of the lung than in the upper portions (7). These differences are probably related to a gravity dependent gradient of perfusion and capillary filling caused by the inability of the normally low pulmonary arterial pressure to provide uniformly adequate perfusion against the hydrostatic gradient that must be present in the pulmonary vascular bed of normal adult humans in an upright position (2, 8).

The present investigation was undertaken to determine *a*) whether the normal postural changes in physiologic dead space and diffusing capacity are present in patients in whom the pulmonary vascular pressure should be great enough to insure perfusion of the entire lung in the upright position and *b*) whether an acute increase in pulmonary vascular pressures affects the arterial-alveolar CO_2 gradient and alveolar dead space of normal men in an upright position.

Methods

Thirty-four adult patients having clinical cardiac catheterizations and 20 trained normal subjects were

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used in this study. The patients' surface areas, pulmonary vascular pressures, and diagnoses are listed in Table I. Those patients with mean pulmonary arterial pressure greater than 20 mm Hg are grouped separately and are considered to have pulmonary hypertension. With few exceptions, all patients with pulmonary hypertension had mitral valvular disease. The normal subjects were healthy men whose ages were between 22 and 36 and whose mean surface area was $1.89 \pm 0.4 \text{ m}^2$. Their pulmonary vascular pressures were assumed to be normal.

Tilting was performed on a motor-driven tilt table. Measurements were made in random sequence; subjects were flat or tilted 60° with their heads up. The change in lung volume that occurred during tilting was measured with a bag-in-box spirometer system, in which a steady base line is obtained during spontaneous breathing before and after a change in position, the recorded difference representing the difference in lung volume in the two positions. Measurements of physiologic dead space were begun 15 to 30 seconds after the subjects reached the 60° position. During a different tilt, diffusing capacity was measured 1 minute after reaching the 60° position.

The effect of acute pulmonary vascular engorgement on alveolar dead space and arterial-alveolar P_{CO_2} gradient was studied in several normal, trained subjects before and after inflation of a full pressure half suit over the lower half of the body. The suit used was a single-chamber, balloon-type garment¹ that covers the feet, legs, and abdomen and can be inflated to the desired pressure (100 mm Hg) within 5 seconds by a standard Air Force G valve. The suit was laced on the subject carefully to provide even distribution of pressure. All determinations for comparison with those made during suit inflation were carried out with the subject wearing the laced but uninflated suit. In this portion of the study, the subject was seated on a bicycle saddle with his legs dangling. All determinations reported here as being made during suit inflation were carried out after

¹ This suit was made by the David Clark Company, Worcester, Mass. In previous reports (9, 10) 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.

the suit had been inflated to a pressure of 100 mm Hg for 30 seconds, a pressure which, in previous studies, produced a mean rise in central venous pressure of 23 mm Hg in seated subjects (9). Direct measurements of intrapleural pressure reported elsewhere suggest that this rise is not the consequence of increased intrathoracic pressure (10).

When the pressure suit was used, the subject breathed into a double bag, bag-in-box spirometer system. The first bag was discarded; the second was used for a 2-minute collection of expired air that was measured by evacuation into a spirometer. The subject was trained to observe the pen writing on the spirometer paper, to control tidal volume and breathing frequency, and to avoid changes in lung volume during inflation of his pressure suit.

Pulmonary arterial and transseptal left atrial pres-

TABLE I
Physical and hemodynamic characteristics

Patient	S.A.*	Diagnosis	Pulmonary arterial mean pressure	Left atrial mean pressure
	m ²		mm Hg	mm Hg
Group A†				
W. J.	1.96	Normal	18	12
J. A.	2.06	Normal	16	
E. T.	1.53	Myxedema	14	7
P. B.	1.55	PS	13	7
N. W.	1.47	MS, MI	18	16
J. C.	1.46	PS, AI	17	6
C. S.	1.58	MS, AI	19	15
H. A.	1.52	MS	17	12
G. J.	1.63	MS	18	16
F. C.	1.77	AS	14	10
Group B				
G. S.	1.76	MS	27	15
M. M.	1.54	MS	44	20
T. E.	1.90	MS, MI	61	26
J. N.	1.52	MS	35	31
T. S.	1.68	MS, MI	34	22
D. E.	1.37	MI	40	22
A. C.	1.74	MS, MI	46	18
B. J.	1.58	MS	27	21
F. P.	1.81	AS	23	12
G. G.	1.68	MS, MI	33	22
M. W.	1.60	MS, MI	22	15
T. V.	1.97	MS	36	22
R. S.	1.75	MS	45	16
J. No.	1.82	MS	38	16
M. R.	1.85	MS	32	22
V. C.	1.56	MS	73	25
P. A.	1.57	MS	30	22
M. K.	1.55	MS	77	27
E. P.	1.48	MS, MI	35	25
B. D.	1.64	MS, MI	27	23
H. G.	1.53	MS	50	30
M. Mo.	1.57	MS	67	30
B. T.	1.76	MS	41	23
M. B.	1.45	MS	75	42

* S.A. = surface area, PS = pulmonic stenosis, MS = mitral stenosis, MI = mitral insufficiency, AI = aortic insufficiency, and AS = aortic stenosis.

† Group A, pulmonary arterial mean pressure < 20 mm Hg. Group B, pulmonary arterial mean pressure > 20 mm Hg.

ures were measured by standard catheterization methods. With subjects supine, pressures were measured, recorded on a photographic recorder, electronically integrated, and referred to the midthoracic level.

The data presented in the tables were analyzed using a paired comparison *t* test in those instances in which each subject served as his own control. Otherwise the *t* test was done on the means of the groups compared (11).

Physiologic dead space (V_D). Arterial blood was withdrawn from an indwelling needle over a 2-minute period during which expired gas was collected using a Krogh valve and a Douglas bag. Gas volumes were measured in a spirometer and corrected to body temperature and pressure, saturated (BTPS). Tidal volume was calculated from the expired minute volume (BTPS) and the observed breathing frequency. The P_{CO_2} of arterial blood and expired gas was determined with a glass electrode system.² In this laboratory, by this method, duplicate determinations of blood P_{CO_2} from separate collecting syringes agree with a mean difference of 0 ± 1 mm Hg. The P_{CO_2} of blood tonometered³ with gas of known P_{CO_2} for 20 minutes was only 0.2 ± 0.2 mm Hg different from the P_{CO_2} of the gas as determined in a micro-Scholander gas analyzer. Arterial P_{CO_2} was assumed to represent "ideal" alveolar P_{CO_2} (12), and physiologic dead space was calculated by the Bohr Equation (13):

$$V_D = \frac{P_{ACO_2} - P_{ECO_2}}{P_{ACO_2}} (V_T) - V_{D(\text{apparatus})}$$

$$V_{D(\text{apparatus})} = 40 \text{ ml.}$$

The ratio V_D/V_T expresses the ratio of calculated physiologic dead space to the average tidal volume during the period of measurement.

When the effects of acute central engorgement were studied, end tidal P_{CO_2} was measured, by a Beckman infrared CO_2 meter with breathe-through cell attachment, and averaged more than 10 breaths during the 2-minute collection period. The Beckman meter was calibrated with the same known gases used in calibration of the P_{CO_2} meter.

The slope of the expired CO_2 curve was observed before and after pressure suit inflation as an index of the sequence of pulmonary emptying.

Alveolar dead space was calculated according to this formula:

$$V_{D(\text{alveolar})} = \frac{P_{ACO_2} - P_{ACO_2}}{P_{ACO_2}} (V_T).$$

Pulmonary diffusing capacity (D_L) and capillary blood volume (V_c) determinations. D_L was determined in 10 normal subjects and 10 patients with mitral stenosis and pulmonary hypertension by the Krogh breath-holding technique modified by Forster and co-workers (14, 15). The technique previously reported for our laboratory

² Instrumentation Laboratories, Boston, Mass.

³ L. Eschweiler and Co., Kiel, Germany.

(9) was further modified as described by Lawson and Johnson (16) and Smith and Hamilton (17) for the use of the gas chromatograph. For calculation of V_e by the method of Roughton and Forster (18), D_L was determined at two different alveolar O_2 tensions in each subject under each condition by using different concentrations of O_2 in the inspired gas mixture. Determinations were made in duplicate with each subject lying flat and tilted to 60° . After a maximal expiration, the subject made a full inspiration of a gas mixture containing 0.4% CO, 1.0% neon, and 21% O_2 in nitrogen from the bag-in-box connected to a spirometer so that the inspired volume and breath-holding time could be measured on the spirometer tracing. After a breath-holding period of approximately 10 seconds, an alveolar sample was collected.

The CO, Ne, N_2 , and O_2 contents of the inspired gas mixture and expired alveolar samples were determined in a gas chromatograph.⁴ Five-ml gas samples were introduced into the gas sample inlet through a drier and CO_2 absorber (Ascarite). CO_2 absorption in this manner results in a small (about 1 ml per mm Hg per minute) underestimate of D_L . Since P_{ACO_2} varied within a rather narrow range in this study, the comparison of D_L in individual subjects, supine and tilted, was not affected by the small error. The standard inspired gas mixture was analyzed with each group of alveolar samples. Helium was used as the carrier gas. A sharp Ne peak appeared rapidly after injection of the gas sample. The flows of O_2 , Ne, and CO were differentially slowed by passage through a molecular sieve column so that they arrived at the thermal conductivity detector at different times with a separate peak being written for each. Heights of the Ne and CO peaks were linear for concentration, and, within the ranges of concentrations occurring in D_L determinations, both Ne and CO peak heights are reproducible to well within 5% of the total height. Peak heights of the oxygen chromatogram were not linear with concentration, but the area of the chromatogram determined by Disc Chart Integrator⁵ was linear with concentration and reproducible to within 5% of the total area with serial determinations. By this method, duplicate determinations of D_L on the same and different days are reproducible within 1.8 ± 0.9 ml per minute per mm Hg.

Chromatogram peak heights of inspired Ne and CO (Ne_I , CO_I) and alveolar Ne and CO (Ne_A , CO_A) were used in calculations of D_L . The alveolar volume (V_A) was calculated from the Ne dilution and inspired volume (V_I).

$$V_A = \frac{Ne_I}{Ne_A} \times V_{IATPS}$$

$$V_{ASTPD} = V_{IATPS} \times \text{temperature correction factor.}^6$$

⁴ Model GC-2500, Micro-Tek Instrument Co., Baton Rouge, La.

⁵ Model 201-B, Honeywell, Minneapolis, Minn.

⁶ ATPS = ambient temperature, pressure, saturated. STPD = standard temperature, pressure, dry.

D_L was calculated as follows:

$$\frac{\frac{Ne_A}{Ne_I} \times CO_I - f_{CO}}{CO_A - f_{CO}} = \frac{CO_O}{CO_A}$$

$$D_L \text{ (ml/min/mm Hg)} = \frac{(V_{ASTPD})(60)}{(t)(P_B - 47)} \times \ln \frac{CO_O}{CO_A}$$

where f_{CO} is a correction for CO tension in equilibrium with COHb determined as previously described (14), CO_O is the initial alveolar CO at the beginning of breath holding, and t is breath-holding time in seconds.

V_e was calculated by the technique outlined in detail by Roughton and Forster (18). The mean capillary O_2 tension was estimated by the technique suggested by McNeill, Rankin, and Forster (19). θ for the appropriate O_2 tension was obtained from the data of Roughton, Forster, and Cander (20). Blood O_2 capacity was determined spectrophotometrically (21, 22) in each subject, and calculations of V_e were corrected to an O_2 capacity of 20 ml per 100 ml blood.

Results

Physiologic dead space (Table II). In 5 normal subjects and 10 patients with mean pulmonary arterial pressures of less than 20 mm Hg, the mean physiologic dead space (V_D) increased from 142 ± 40 to 201 ± 55 ml ($p = 0.001$), and V_D/V_T increased from 0.30 ± 0.05 to 0.37 ± 0.06 ($p = 0.001$) during tilt. In the group with pulmonary hypertension, V_D was less affected by tilting, 192 ± 81 to 208 ± 84 ml ($p = 0.05$).

The increase in V_D in the group with normal pressures was greater than the increase in V_D in the group with pulmonary hypertension ($p = 0.025$). V_D/V_T was not consistently affected by tilting in the group with pulmonary hypertension, 0.39 ± 0.05 to 0.41 ± 0.04 ($p = 0.2$). The supine V_D in those with normal pressure, 142 ± 40 ml, was different from the supine V_D in those with high pulmonary vascular pressure, 192 ± 81 ml ($p = 0.05$). Tilting did not affect breathing frequency in either group, but V_T increased from 476 ± 163 to 552 ± 167 ml ($p = 0.001$) in the normal pressure group. There was no change in V_T during tilting in those with pulmonary hypertension. Lung volume increased to the same extent in both groups (Table III).

Diffusing capacity (D_L) and pulmonary capillary blood volume V_c (Table IV). In 10 normal subjects (surface area, 1.89 ± 0.40 m²), mean pulmonary diffusing capacity (D_L) decreased with tilting from 39.2 ± 7.7 to 31.5 ± 6.7 ml per

TABLE II
Effects of tilting subjects 60°, head up

Subject	f*		V_T		P_{aCO_2}		P_{ECo_2}		V_D		V_D/V_T	
	F	T	F	T	F	T	F	T	F	T	F	T
	breaths/min		ml		mm Hg		mm Hg		ml		ml	
Group A†												
W. J.	11.5	11.5	551	582	46.3	46.0	29.4	24.7	161	229	.29	.39
J. H.	21.5	15.0	412	622	44.1	39.8	27.6	22.7	114	228	.28	.37
E. T.	14.0	13.0	284	334	48.2	50.7	24.4	19.9	100	163	.35	.49
P. B.	12.5	14.0	338	347	41.6	38.4	26.5	21.2	83	115	.25	.33
N. W.	16.5	11.5	455	666	42.8	43.3	22.8	22.4	176	275	.39	.41
J. C.	18.5	15.5	366	465	40.8	37.0	22.0	20.0	129	174	.35	.39
C. S.	25.0	22.5	404	464	38.4	32.8	20.0	17.3	137	171	.37	.38
H. H.	11.5	12.0	395	527	48.4	48.7	27.0	25.0	139	222	.35	.42
G. J.	13.0	13.0	497	586	45.2	43.2	24.2	22.4	192	241	.38	.41
F. C.	16.0	17.0	374	417	41.2	37.2	26.2	23.1	96	117	.26	.28
N-1	14.5	15.5	365	437	45.0	45.4	26.4	23.3	126	186	.31	.40
N-2	10.5	9.5	876	975	44.8	41.2	32.5	27.8	201	276	.23	.28
N-3	9.5	9.0	757	752	42.8	40.4	31.3	26.7	164	215	.22	.28
N-4	21.5	19.5	447	473	41.5	39.9	27.9	25.1	106	136	.24	.29
N-5	18.5	17.5	618	637	39.4	37.8	23.7	19.2	206	273	.30	.43
Mean	15.6	14.4	476	552	43.4	41.4	26.4	22.7	142	201	.30	.37
SD	4.6	3.7	163	167	3.0	4.8	3.4	3.0	40	55	.05	.06
p	0.1		0.001		0.01		0.001		0.001		0.001	
Group B												
G. S.	12.0	13.5	243	200	48.6	51.6	10.1	18.0	122	91	.50	.45
M. M.	22.0	23.5	370	390	43.8	44.1	22.0	20.3	137	171	.37	.44
T. E.	31.0	28.5	332	341	45.6	44.9	24.0	22.6	114	129	.34	.38
J. N.	14.5	15.0	1,280	1,260	36.8	35.7	23.2	22.0	433	444	.34	.35
T. S.	14.5	18.0	688	555	40.7	40.0	22.1	21.3	257	219	.37	.39
D. E.	12.0	13.0	565	584	48.2	47.5	22.7	23.9	259	251	.46	.42
A. C.	16.0	16.0	346	423	48.6	44.6	25.8	22.9	121	152	.35	.36
B. J.	22.5	22.5	292	319	42.0	40.6	18.2	18.0	126	138	.43	.44
F. P.	20.5	25.0	415	378	41.1	41.2	22.4	20.1	148	154	.36	.41
G. G.	15.5	17.7	525	589	43.8	43.0	22.8	19.1	211	287	.40	.49
M. W.	14.5	13.5	456	560	42.6	39.3	26.0	24.8	138	167	.30	.30
H. V.	10.5	13.0	650	745	42.4	42.8	25.0	24.3	241	282	.37	.38
R. S.	13.0	11.0	512	560	48.8	49.3	23.4	23.8	227	250	.44	.45
J. No.	25.5	27.5	486	476	38.7	37.6	20.7	18.0	186	208	.40	.44
M. R.	18.0	18.5	426	480	45.2	42.6	22.2	21.1	178	199	.42	.42
V. C.	21.0	18.0	418	452	39.3	37.6	18.8	18.8	178	186	.43	.41
Mean	17.7	18.4	420	441	43.5	42.6	21.8	21.3	192	208	.39	.41
SD	5.6	5.5	165	176	3.8	4.3	3.8	2.4	81	84	.05	.04
p	0.2		0.4		0.1		0.4		.05		0.2	

* f = frequency, V_T = tidal volume (BTPS = body temperature and pressure, saturated), P_{aCO_2} = arterial PCO_2 , P_{ECo_2} = expired gas PCO_2 , V_D = physiologic dead space (BTPS), F = flat, T = 60° head-up tilt, and N = normal subjects.

† Group A, patients without pulmonary hypertension (mean pulmonary arterial pressure < 20 mm Hg) and normal subjects. Group B, patients with pulmonary hypertension (mean pulmonary arterial pressure > 20 mm Hg.)

minute per mm Hg ($p = 0.001$). There was no decrease in D_L during tilt in 10 patients with mitral stenosis (surface area, 1.62 ± 0.4 m²) 20.7 ± 6.0 to 20.6 ± 7.1 ($p = NS$). D_L (supine) was smaller in the group with mitral stenosis than D_L (supine) in the normal group ($p = 0.001$). Tilting decreased pulmonary capillary blood volume (V_c) from 95 ± 17 to 75 ± 19 ml ($p = 0.001$) in the normal group but did not affect V_c in the group with mitral stenosis 97 ± 24 to $100 \pm$

TABLE III
The effect of 60° head-up tilt on functional residual capacity (FRC)

	No.	Change in FRC
		ml
Group A*	6	+420 ± 61
Group B	5	+400 ± 154

* Group A, pulmonary arterial mean pressure < 20 mm Hg. Group B, pulmonary arterial mean pressure > 20 mm Hg.

TABLE IV
Effect of 60° head-up tilt on DL and V_c

Subject	DL*		V _c		D _M		V _A		Capacity	V _c /V _A
	F	T	F	T	F	T	F	T		
	ml/mmHg/min		ml		ml/mmHg/min		L			
Group A†										
N-6	26.6	21.2	74	46	81	133	4.54	4.41	15.9	16.3
N-7	46.4	38.5	133	118	107	85	5.55	5.58	20.0	23.9
N-8	33.2	27.6	122	76	59	59	4.24	4.57	19.3	28.9
N-9	33.0	28.3	100	71	65	68	5.52	5.49	20.0	18.1
N-10	43.9	36.0	94	78	100	100	5.34	5.27	21.1	17.6
N-11	35.0	23.9	89	74	100	50	5.38	5.50	19.1	16.5
N-12	51.9	41.8	104	87	67	63	6.80	6.50	19.1	15.3
N-2	45.7	39.1	96	82	125	135	5.25	5.65	21.2	18.3
N-13	39.6	30.9	82	58	140	140	4.26	4.69	19.4	19.3
N-14	36.6	27.8	95	62	87	87	4.95	5.12	19.9	19.2
Mean	39.2	31.5	99	75	93	92	5.18	5.28	19.4	19.3
SD	7.7	6.7	17	19	26	34	.76	.62	1.5	3.0
p	0.001		0.001		NS		0.4			
Group B										
J. No.	29.0	29.7	115	95	44	53	3.85	4.38	18.3	29.8
M. R.	32.7	36.2	114	114	64	73	3.65	3.75	19.5	31.2
P. A.	23.1	21.2	94	75	37	37	3.25	3.52	18.5	28.9
M. K.	12.8	13.1	71	115	16	15	1.91	1.90	19.1	37.2
E. D.	18.1	18.1	70	67	31	33	2.56	2.68	16.6	27.3
B. D.	19.3	19.6	116	98	26	30	2.47	3.25	15.7	46.9
H. G.	16.6	15.5	55	83	28	27	1.98	2.16	20.0	27.8
M. Mo.	20.7	20.2	122	122	28	28	2.98	3.09	15.5	40.7
B. T.	16.7	15.6	94	113	25	22	3.00	3.27	17.6	31.3
M. B.	17.9	16.6	121	115	22	24	2.73	2.89	16.6	44.3
Mean	20.7	20.6	97	100	32	34	2.84	3.09	17.7	34.5
SD	6.0	7.1	24	19	14	17	.20	.73	1.6	7.2
p	NS		NS		NS		0.01			

* DL = breath-holding diffusing capacity for carbon monoxide, V_c = pulmonary capillary blood volume (corrected to an oxygen capacity of 20 vol per 100 ml), D_M = pulmonary capillary membrane diffusing capacity for carbon monoxide, V_A = breath-holding alveolar volume (BTPS), Capacity = blood oxygen capacity, and V_c/V_A = pulmonary capillary blood volume/alveolar volume.

† Group A, normal men. Group B, patients with mitral valvular disease and mean pulmonary arterial pressure > 20 mm Hg.

19 ml ($p = \text{NS}$). There was no difference in V_c in the two groups. D_M was not affected by tilting in either group, but mean D_M in the group with mitral stenosis, 32 ml per minute per mm Hg, was clearly less than that in the normal pressure group, 93 ml per minute per mm Hg ($p = 0.001$). V_A was equivocally increased by tilting in both groups. V_A was less in the abnormal group, 2.84 ± 0.20 L, than in the normal group, 5.18 ± 0.76 L ($p = 0.001$). V_c/V_A, the relationship of pulmonary capillary blood volume to alveolar volume, was greater in the group with mitral stenosis, 34.5 ± 7.2 ml per L, than in the normal group, 19.3 ± 3.0 ml per L ($p = 0.001$).

Alveolar dead space and a-A CO₂ gradient dur-

ing pressure suit inflation (Table V). Pressure suit inflation decreased a-A CO₂ gradient from 3.9 ± 1.5 mm Hg to 2.6 ± 1.8 mm Hg ($p = 0.005$) and decreased alveolar dead space from 64 ± 33 to 38 ± 26 ml ($p = 0.025$). Tidal volume and FRC were satisfactorily controlled and did not change during pressure suit inflation. The usual response to pressure suit inflation is a decrease in lung volume. These subjects avoided this change.

Since the slope of the expired CO₂ curve was not affected by pressure suit inflation, we suggest that the effort to maintain the lung volume constant did not appreciably affect the sequence of alveolar emptying.

TABLE V

*The effect in normal men of acute central vascular engorgement produced by pressure suit inflation on a-A CO_2 gradient, $V_{D(alveolar)}$, and V_T **

	a-A		$V_{D(alveolar)}$		V_T	
	S↓	S↑	S↓	S↑	S↓	S↑
	mm Hg		ml		ml	
N-1	6.2	5.7	62	54	500	618
N-15	4.8	4.3	49	54	529	589
N-9	3.8	2.4	50	38	554	689
N-16	1.1	0.6	21	9	797	666
N-17	4.1	1.9	60	24	653	562
N-18	3.0	1.8	66	33	968	896
N-19	3.1	0.3	63	5	850	759
N-20	4.9	3.5	137	85	1,224	1,185
Mean	3.9	2.6	64	38	759	745
SD	1.5	1.8	33	26	251	207
p	0.005		0.025		NS	

* a-A = arterial-alveolar CO_2 gradient, $V_{D(alveolar)}$ = alveolar dead space, V_T = tidal volume, S↓ = before pressure suit inflation, and S↑ = after pressure suit inflation.

Discussion

Orth, in 1887, was apparently the first to appreciate that normal pulmonary arterial pressure is not adequate to overcome the effect of gravity in the lung of the upright normal human (23). The consequence is a gradient of ventilation-perfusion relationships that has been described in detail by West (8).

Evidence has been presented by those using either O^{15} or Xe^{133} that the relative perfusion of the upper zone of the lung is increased in patients with mitral stenosis (4, 24). Isotope techniques have shown a reversal of the normal gradient of perfusion in patients with severe mitral stenosis (24), in whom selective increase in resistance to flow through the lower regions must occur.

A postural effect on regional ventilation-perfusion relationships has been proposed by Riley and co-workers (25) and by Bjurstedt, Hesser, Liljestrand, and Matell (26) to explain their observations that physiologic dead space is greater in normal men upright than supine. They have suggested that, with relative underperfusion, a part of the alveolar ventilation distributed to the upper regions of the lung appears as dead space. The present study confirms these observations during tilting in normal men but demonstrates failure of the physiologic dead space to increase to the same extent in a group of patients with pulmonary hy-

pertension associated with congestion (Table II). The difference in response of the two groups to tilting is not simply a difference in FRC response to tilting (Table III). The normal group increased tidal volume slightly during tilting; those with pulmonary hypertension did not. The increase in tidal volume is relatively so small, however, that it could not account for the increase in V_D in the normal group unless it appeared totally in the V_D compartment. Furthermore, the ratio V_D/V_T increased in the normal group, whereas it did not in the hypertensive group. It would seem, therefore, that the difference in V_D response to tilting in these two groups is related to pulmonary hypertension and is quite compatible with the suggestion made by Riley and co-workers (25) and by Bjurstedt and co-workers (26).

The decrease in D_L and V_c observed during tilting in normal subjects (Table IV) has been described previously (5, 6). Using CO^{15} , Dollery, Dyson, and Sinclair have shown that there is a regional gradient of carbon monoxide absorption in upright normal men (7). Since D_{LCO} is relatively independent of blood flow (27-30), this gradient of CO uptake suggests a gradient of effectively ventilated pulmonary capillary volume in upright normal men. These observations suggest that pressure in the normal pulmonary vascular system is insufficient to perfuse the upper portions of the lung or to maintain the capillary volume in the upper regions. The normal decrease in D_L and V_c during tilting does not occur in patients with pulmonary hypertension due to mitral stenosis (Table IV). These data again demonstrate the dependence of D_L and V_c upon pulmonary vascular pressure but do not separate the roles of pulmonary arterial and pulmonary venous pressure.

The role of systemic venous tone in regulating pulmonary capillary volume and pressure and the possibility that the difference between the normal group and the group with pulmonary congestion reflects increased systemic venous tone known to occur in heart failure (31) is an unresolved problem. The observations of Lewis, McElroy, Hayford-Welsing, and Samberg (6) that the postural decrease in D_L and V_c in upright normal men can be prevented with norepinephrine suggest that venous tone may affect the maintenance

of pulmonary capillary blood volume in upright positions.

Since acute pulmonary vascular engorgement produced by pressure suit inflation increases the volume of blood in the lungs (32) and increases pulmonary vascular pressures and D_L (9), its effect on arterial-alveolar (a-A) CO_2 gradient and alveolar dead space was studied. If a portion of that gradient and dead space was the consequence of relative underperfusion of the upper zone of the lung and if inflation of the pressure suit improved the perfusion of those areas, this procedure would be expected to decrease the a-A CO_2 gradient and alveolar dead space of upright normal men. Severinghaus and Stupfel (33) have examined the problem of a-A CO_2 gradients and alveolar dead space in detail, and in general they relate a-A CO_2 gradient and alveolar dead space to changes in distribution of lung perfusion. Bjurstedt and co-workers (26) and Matell (34) found that the arterial-end-tidal CO_2 gradient of normal upright men averaged 2 to 3 mm Hg. In the present study, the a-A CO_2 gradient was 3.9 ± 1.5 mm Hg, and alveolar dead space was 64 ± 33 ml in a group of normal men upright on a bicycle saddle with their legs dangling (Table V). With tidal volume, breathing frequency, and FRC controlled, pressure suit inflation reduced both a-A CO_2 gradient and alveolar dead space. These changes suggest that acute pulmonary congestion improved the evenness of perfusion in relation to ventilation. As was pointed out by Severinghaus and Stupfel (33), increased unevenness of ventilation may also decrease the a-A CO_2 gradient if the better ventilated areas empty earlier in expiration. The decrease in a-A CO_2 gradient observed during pressure suit inflation may in part represent unevenness of ventilation, with better ventilated areas emptying first; however, the similarity of expired CO_2 slopes before and after pressure suit inflation suggests that this is not a major factor. These results are most compatible with the concept that the uppermost areas of the pulmonary vasculature are poorly perfused and poorly filled in normal men and that acute pulmonary congestion, with elevation of pulmonary vascular pressures, distributes the pulmonary perfusion and pulmonary capillary blood volume more evenly.

Despite the better filling of the congested lung,

several studies have shown decreases in diffusing capacity in patients with mitral stenosis (35-39). In this group of patients with chronic pulmonary vascular congestion, pulmonary capillary blood volume was normal (Table IV). If the pulmonary capillary blood volume (V_c) is related to the alveolar volume (V_A), simultaneously measured by neon dilution, the ratio V_c/V_A (Table IV) expresses this relationship and emphasizes that, for a given alveolar volume, pulmonary capillary blood volume is consistently and considerably increased in patients with pulmonary congestion. The reduction in V_A is probably related to the decreased vital capacity known to occur in situations of chronic pulmonary congestion (36, 37).

Several factors participate in this reduction in D_L observed in these patients with chronic pulmonary vascular congestion:

1) This group of patients had a lower oxygen capacity than the normal group. D_L is dependent upon hemoglobin content of the blood, although the relationship is not linear. Since the mean O_2 capacity of the normal group was 19.4 ± 1.5 ml O_2 per 100 ml blood and the mean O_2 capacity of the congested group was 17.7 ± 1.6 ml O_2 per 100 ml blood, a small part of the lower D_L may be related to the observed decrease in O_2 capacity.

2) The patients in the abnormal group were somewhat smaller in size (1.62 ± 0.40 m²) than the normal subjects (1.89 ± 0.40 m²). D_L is known to be correlated with surface area (40).

3) The diffusing property of the pulmonary capillary membrane (D_M) is low. This reflects the thickening of the alveolar walls described by Parker and Weiss (41).

The observed association of increased physiologic dead space (V_D), decreased alveolar volume (V_A), and increased relative pulmonary capillary blood volume (V_c/V_A) is unique and perhaps meaningful in terms of the disturbed pulmonary architecture reported by Parker and Weiss in 1936 (41). These physiologic changes suggest that the lung in mitral stenosis has a mixture of functional abnormalities: pulmonary capillary congestion relative to a restricted over-all alveolar volume, but also areas of ventilated but poorly perfused alveoli. Certainly this must reflect the pulmonary capillary engorgement Parker and Weiss found in the upper zones of the lung and

the interstitial fibrosis and lack of capillary engorgement found in the lower zones. With these histologic changes in mind, it is not at all surprising that the regional pulmonary circulation does not tend to rearrange itself during changes in posture in patients with chronic pulmonary vascular congestion.

Summary

Postural changes in ventilation-perfusion relationships and in pulmonary capillary filling were studied by observing the effect of 60° head-up tilt on physiologic dead space (V_D), pulmonary diffusing capacity (D_L), and pulmonary capillary blood volume (V_c) in normal subjects and in patients with and without pulmonary hypertension secondary to mitral stenosis. Tilting decreased D_L and V_c in normal subjects but not in patients with chronically congested lungs and pulmonary hypertension. Tilting also increased V_D and V_D/V_T in normal subjects and patients with normal pulmonary vascular pressure more than in patients with chronic pulmonary congestion and hypertension. The difference in the response of the two groups to tilting may depend upon differences in systemic venomotor activity in addition to the differences in supine pulmonary vascular pressures and regional pulmonary vascular resistances.

Acute central vascular engorgement produced by pressure suit inflation decreased the a-A CO_2 gradient and alveolar dead space of upright normal men. This suggests that the upright normal lung is inadequately perfused and that the pressure suit, which increases pulmonary vascular pressure and blood volume, improves the perfusion of the previously underperfused regions.

In a group of patients with chronic pulmonary congestion, V_D was greater and D_L was less than in a group of normal subjects. A portion of the decrease in D_L is the consequence of lower hemoglobin concentration and smaller body size, and a portion is the result of decreased diffusivity of the pulmonary capillary membrane. The pulmonary capillary blood volume (corrected to an O_2 capacity of 20.0 ml per 100 ml) was not abnormal in the patients with pulmonary congestion, but the ratio, V_c/V_A , was consistently increased over the normal group and represents a useful expression of the filling of the pulmonary capillaries.

References

1. Martin, C. J., F. Cline, Jr., and H. Marshall. Lobar alveolar gas concentrations: effect of body position. *J. clin. Invest.* 1953, **32**, 617.
2. Mattson, S. B., and E. Carlens. Lobar ventilation and oxygen uptake in man. Influence of body position. *J. thorac. Surg.* 1955, **30**, 676.
3. West, J. B., and C. T. Dollery. Distribution of blood flow and ventilation-perfusion ratio in the lung, measured with radioactive CO_2 . *J. appl. Physiol.* 1960, **15**, 405.
4. Ball, W. C., Jr., P. B. Stewart, L. G. S. Newsham, and D. V. Bates. Regional pulmonary function studied with xenon¹³³. *J. clin. Invest.* 1962, **41**, 519.
5. Bates, D. V., and J. F. Pearce. The pulmonary diffusing capacity; a comparison of methods of measurement and a study of the effect of body position. *J. Physiol. (Lond.)* 1956, **132**, 232.
6. Lewis, B. M., W. T. McElroy, E. J. Hayford-Welsing, and L. C. Samberg. The effects of body position, ganglionic blockade and norepinephrine on the pulmonary capillary bed. *J. clin. Invest.* 1960, **39**, 1345.
7. Dollery, C. T., N. A. Dyson, and J. D. Sinclair. Regional variations in uptake of radioactive CO in the normal lung. *J. appl. Physiol.* 1960, **15**, 411.
8. West, J. B. Regional differences in gas exchange in the lung of erect man. *J. appl. Physiol.* 1962, **17**, 893.
9. Ross, J. C., T. H. Lord, and G. D. Ley. Effect of pressure suit inflation on the pulmonary diffusing capacity. *J. appl. Physiol.* 1960, **15**, 843.
10. Daly, W. J., and R. H. Behnke. The behavior of the venous reservoir as affected by atropine. *Trans. Ass. Amer. Physns* 1962, **75**, 277.
11. Snedecor, G. W., and W. G. Cochran. *Statistical Methods Applied to Experiments in Agriculture and Biology*, 5th ed. Ames, Iowa, The Iowa State College Press, 1956.
12. Riley, R. L., J. L. Lilienthal, Jr., D. D. Proemmel, and R. E. Franke. On the determination of the physiologically effective pressures of oxygen and carbon dioxide in alveolar air. *Amer. J. Physiol.* 1946, **147**, 191.
13. Bohr, C. Über die Lungenathmung. *Skand. Arch. Physiol.* 1891, **2**, 236.
14. Forster, R. E., W. S. Fowler, D. V. Bates, and B. Van Lingen. The absorption of carbon monoxide by the lungs during breathholding. *J. clin. Invest.* 1954, **33**, 1135.
15. Ogilvie, C. M., R. E. Forster, W. S. Blakemore, and J. W. Morton. A standardized breathholding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. *J. clin. Invest.* 1957, **36**, 1.
16. Lawson, W. H., Jr., and R. L. Johnson, Jr. Gas chromatography in measuring pulmonary blood

- flow and diffusing capacity. *J. appl. Physiol.* 1962, 17, 143.
17. Smith, J. R., and L. H. Hamilton. $D_{L_{CO}}$ measurements with gas chromatography. *J. appl. Physiol.* 1962, 17, 856.
 18. Roughton, F. J. W., and R. E. Forster. Relative importance of diffusion and chemical reaction rates in determining rate of exchange of gases in the human lung, with special reference to true diffusing capacity of pulmonary membrane and volume of blood in the lung capillaries. *J. appl. Physiol.* 1957, 11, 290.
 19. McNeill, R. S., J. Rankin, and R. E. Forster. The diffusing capacity of the pulmonary membrane and the pulmonary capillary blood volume in cardiopulmonary disease. *Clin. Sci.* 1958, 17, 465.
 20. Roughton, F. J. W., R. E. Forster, and L. Cander. Rate at which carbon monoxide replaces oxygen from combination with human hemoglobin in solution and in the red cell. *J. appl. Physiol.* 1957, 11, 269.
 21. Drabkin, D. L., and J. H. Austin. Spectrophotometric studies. II. Preparation from washed blood cells; nitric oxide hemoglobin and sulphemoglobin. *J. biol. Chem.* 1935, 112, 51.
 22. Hickam, J. B., and R. Frayser. Spectrophotometric determination of blood oxygen. *J. biol. Chem.* 1949, 180, 457.
 23. Orth, J. Ätiologisches und Anatomisches über Lungenschwindsucht. Berlin, Hirschwald, 1887.
 24. Dollery, C. T., and J. B. West. Regional uptake of radioactive oxygen, carbon monoxide, and carbon dioxide in the lungs of patients with mitral stenosis. *Circulat. Res.* 1960, 8, 765.
 25. Riley, R. L., S. Permutt, S. Said, M. Godfrey, T. O. Cheng, J. B. L. Howell, and R. H. Shepard. Effect of posture on pulmonary dead space in man. *J. appl. Physiol.* 1959, 14, 339.
 26. Bjurstedt, H., C. M. Hesser, G. Liljestrand, and G. Matell. Effects of posture on alveolar-arterial CO_2 and O_2 differences and on alveolar dead space in man. *Acta physiol. scand.* 1962, 54, 65.
 27. Hatch, I. F. Carbon monoxide uptake in relation to pulmonary performance. *Arch. industr. Hyg.* 1952, 6, 1.
 28. Ross, J. C., R. Frayser, and J. B. Hickam. A study of the mechanism by which exercise increases the pulmonary diffusing capacity for carbon monoxide. *J. clin. Invest.* 1959, 38, 916.
 29. Turino, G. M., M. Brandfonbrener, and A. P. Fishman. The effect of changes in ventilation and pulmonary blood flow on the diffusing capacity of the lung. *J. clin. Invest.* 1959, 38, 1186.
 30. Daly, W. J., J. C. Ross, and R. H. Behnke. The effect of changes in the pulmonary vascular bed produced by atropine, pulmonary engorgement, and positive-pressure breathing on diffusing and mechanical properties of the lung. *J. clin. Invest.* 1963, 42, 1083.
 31. Wood, J. E., J. Litter, and R. W. Wilkins. Peripheral venoconstriction in human congestive heart failure. *Circulation* 1956, 13, 524.
 32. Bondurant, S., J. B. Hickam, and J. K. Isley. Pulmonary and circulatory effects of acute pulmonary vascular engorgement in normal subjects. *J. clin. Invest.* 1957, 36, 59.
 33. Severinghaus, J. W., and M. Stupfel. Alveolar dead space as an index of distribution of blood flow in pulmonary capillaries. *J. appl. Physiol.* 1957, 10, 335.
 34. Matell, G. Time-courses of changes in ventilation and arterial gas tensions in man induced by moderate exercise. *Acta physiol. scand. (supl.)* 1963, 58, 206.
 35. Carroll, D., J. Cohn, and R. L. Riley. Pulmonary function in mitral valvular disease: distribution and diffusion characteristics in resting patients. *J. clin. Invest.* 1953, 32, 510.
 36. Dogliotti, G. C., P. F. Angelino, A. Brusca, R. Gargagni, F. Gavosto, G. Magri, and E. Minetto. Pulmonary function in mitral valve disease. Hemodynamic and ventilatory studies. *Amer. J. Cardiol.* 1959, 3, 28.
 37. Friedman, B. L., J. de J. Macias, and P. M. Yu. Pulmonary function studies in patients with mitral stenosis. *Amer. Rev. resp. Dis.* 1959, 79, 265.
 38. Williams, M. H., Jr. Pulmonary function studies in mitral stenosis before and after commissurotomy. *J. clin. Invest.* 1953, 32, 1094.
 39. Auchincloss, J. H., Jr., R. Gilbert, and R. H. Eich. The pulmonary diffusing capacity in congenital and rheumatic heart disease. *Circulation* 1959, 19, 232.
 40. Burrows, B., J. E. Kasik, A. H. Niden, and W. R. Barclay. Clinical usefulness of the single-breath pulmonary diffusing capacity test. *Amer. Rev. resp. Dis.* 1961, 84, 789.
 41. Parker, F., Jr., and S. Weiss. The nature and significance of the structural changes in the lungs in mitral stenosis. *Amer. J. Path.* 1936, 12, 573.