Modification of pulmonary gas mixing by postural changes

HAZEL A. JONES, E. E. DAVIES, AND J. M. B. HUGHES
Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 OHS, United Kingdom

JONES, HAZEL A., E. E. DAVIES, AND J. M. B. HUGHES. *Modification of pulmonary gas mixing by postural changes.* J. Appl. Physiol. 61(1): 75–80, 1986.—Mixing for two gases of markedly different gaseous diffusivity, helium (He) (mol wt = 4) and sulfur hexafluoride (SF_6) (mol wt = 146) has been studied by a rebreathing method in different postures. In nine normal subjects duplicate measurements were made in the erect (seated), supine, and lateral decubitus posture, at a constant tidal volume (700 ml) and frequency (1 Hz) starting from functional residual capacity (FRC). Additional measurements were made on four of the subjects, rebreathing seated erect at a volume similar to the relaxed FRC supine and supine at a volume similar to the relaxed FRC seated. In the supine posture the mean breath number to reach 99% equilibrium (n_{99}), was not significantly different for the two gases, 8.9 for He and 9.8 for SF_6. There was a difference ($P < 0.01$) when erect; n_{99} (He) = 8.2 and n_{99} (SF_6) = 10.9. The greatest He-SF_6 difference ($P < 0.001$) was in the lateral decubitus position n_{99} (He) = 10.1 and n_{99} (SF_6) = 15.9. The mean relaxed FRC as percent of seated was 71% supine and 75% in lateral decubitus posture. Rebreathing seated at a lower volume did not abolish the He-SF_6 mixing difference nor did rebreathing at a higher volume when supine induce a He-SF_6 mixing difference. Thus the effect of posture on gas mixing cannot be due solely to lung volume and must represent a convective and diffusive dependent change in the distribution of ventilation per unit lung volume.

posture; gas diffusion; mass spectrometry

FOR INTRAPULMONARY GAS MIXING, the relative importance of interregional vs. intraregional unevenness and parallel (convective) vs. stratified (diffusive) inhomogeneities is still unresolved. Several methods of investigation have been employed, the most widely used being the continuous analysis of a single expiration following an inspiration of a bolus or complete breath of insoluble marker gas (in the case of a full inspiration of O_2 the N_2 is the marker gas). Another technique involves measurement of the elimination (washout) of insoluble marker gas following an initial period of equilibration. Alternatively, the approach to equilibration (washin) of foreign marker gas can be measured in closed circuit before the washout phase starts. The washin and washout contain essentially the same information, but a disadvantage of the closed-circuit technique thus far has been the need to maintain a constant system volume in the presence of pulmonary gas exchange.

The contribution of molecular diffusion to the overall mixing process can be assessed if two gases of widely differing molecular weights, for example, helium (He) (mol wt = 4) and sulfur hexafluoride (SF_6) (mol wt = 146), are used, though the interdependence of the convective and diffusive processes is now well established (6, 25).

All these measurements measure the mixing efficiency of the lung as a whole. Inhomogeneity of function between or within discrete parts of the system can be measured with individual lung (19), lobar (21), or intralobular (8) sampling and by external scintillation detection following inhalation of radioactive gases (1, 16, 22).

Changes of posture provoke major changes in washout of gases from the lung (20), between lungs (19), in the interregional distribution of ventilation and lung expansion (16), and in the single-breath alveolar plateau (2), particularly in the lateral decubitus posture (11). Nevertheless, there has been no systematic examination of the He-SF_6 differences in different postures. We found that gas mixing was least efficient in the lateral decubitus posture, where there was the greatest delay of SF_6 relative to He but, unexpectedly, the He-SF_6 difference disappeared in the supine posture. This is contrary to current concepts that ascribe a significant portion of the nonuniformity of ventilation in the normal lung to the asymmetrical anatomy of the acinus (7, 26) but lends support to those who believe such asymmetry plays a minor role (3).

We have used a rebreathing washin technique described by us (15) that overcomes the problem of shrinkage due to gas exchange to study the rate of mixing for He and SF_6 in different postures.

METHODS

The mixing of the two insoluble gases He and SF_6 was studied in nine normal subjects (Table 1). Prior to each measurement, a small-volume (750 ml) anesthetic bag was filled with 650 ml of dry gas composed of 10% He-10% SF_6-30% O_2-50% argon (Ar). The subject paused at end expiration and was connected to the rebreathing bag. He then emptied and filled the bag at 1 Hz for 20 breaths, guided by a metronome. This rebreathing maneuver was carried out with the subject in the upright, supine, and lateral decubitus postures, repeat measurements being carried out in each case. In four of the subjects, additional measurements were made with the subject rebreathing from a volume above functional residual capacity (FRC) supine and below FRC seated.

During the rebreathing maneuver, the concentrations of all gases present were measured continuously at the mouth by a mass spectrometer (Centronic 200 MGA). Volume was measured using a spirometer and flow by a pneumotachograph positioned in the tube connecting the spirometer to a box enclosing the rebreathing bag. The signals from these monitoring systems were fed through an analog-to-digital converter into a computer (Digico μ16); after accounting for the delay due to passage of gas down the mass spectrometer sampling line, the computer calculated and printed out the time of each breath followed by the volume- and flow-weighted mean composition of the inspired gas. The composition that the insoluble gases would have had if there had been no net loss of volume from the system due to the uptake of soluble gas was calculated from the Ar/N_2 ratio (15). The FRC was calculated for each measurement by insoluble gas dilution using the Ar/N_2 corrected values for He and SF_6.

For each measurement, the difference between the mean inspired (bag) and the final equilibrium concentration for every breath was calculated using the corrected values for both He and SF_6. These values were normalized to the initial bag-equilibrium concentration difference (100%) and plotted on a logarithmic scale against breath number. From this plot the rate of mixing (λ, breaths^{-1}) was calculated as the exponential of the final mixing phase. The number of breaths required to reach 99% equilibration (n_{99}) was the same point on the abscissa at which the slope of the final mixing phase intersected 1% on the ordinate.

Analysis of variance was used to test for significant differences in mixing efficiency between the two gases in all postures.

RESULTS

In Fig. 1, the mixing for He and SF_6 is shown breath by breath in the three postures studied. Representative data from all nine subjects are displayed. The solid lines are the lines of best fit through the final phase for He and SF_6. Significant differences in mixing for the two gases are present in the seated ($P < 0.01$) and lateral decubitus ($P < 0.001$) postures, but not in the supine position. Table 2 shows the results for all the measurements made in all subjects rebreathing from FRC, in the form of n_{99}, the number of breaths required to reach 99% equilibration for both gases. There is a difference between n_{99} for He and SF_6 in seven of the subjects seated and eight subjects in the lateral decubitus position. This difference disappears in the supine posture in all but one subject (*DW*). FRC was lower in the supine and lateral decubitus position than seated.

Table 3 displays the data as the rate constant (λ) for the final approach to equilibrium for He and SF_6 as a

TABLE 1. *Anthropometric data for nine normal subjects*

Subj	Sex	Age, yr	Ht, m	Wt, kg	VC, liters	FEV_1, liters	Smoking History
HJ	F	33	1.63	50	5.0	4.1	Exsmoker
ED	M	44	1.77	92	4.6	3.3	Pipe smoker
HM	M	29	1.77	71	5.3	4.4	Smoker
DH	F	32	1.62	58	3.8	3.2	Exsmoker
MH	M	44	1.69	64	5.0	3.9	Nonsmoker
JC	M	43	1.76	73	6.2	5.0	Nonsmoker
DW	M	44	1.76	72	6.0	4.8	Nonsmoker
PB	M	34	1.77	75	6.0	4.7	Nonsmoker
TA	M	32	1.82	83	5.9	4.7	Nonsmoker

VC, vital capacity; FEV_1, forced expired volume in 1 s.

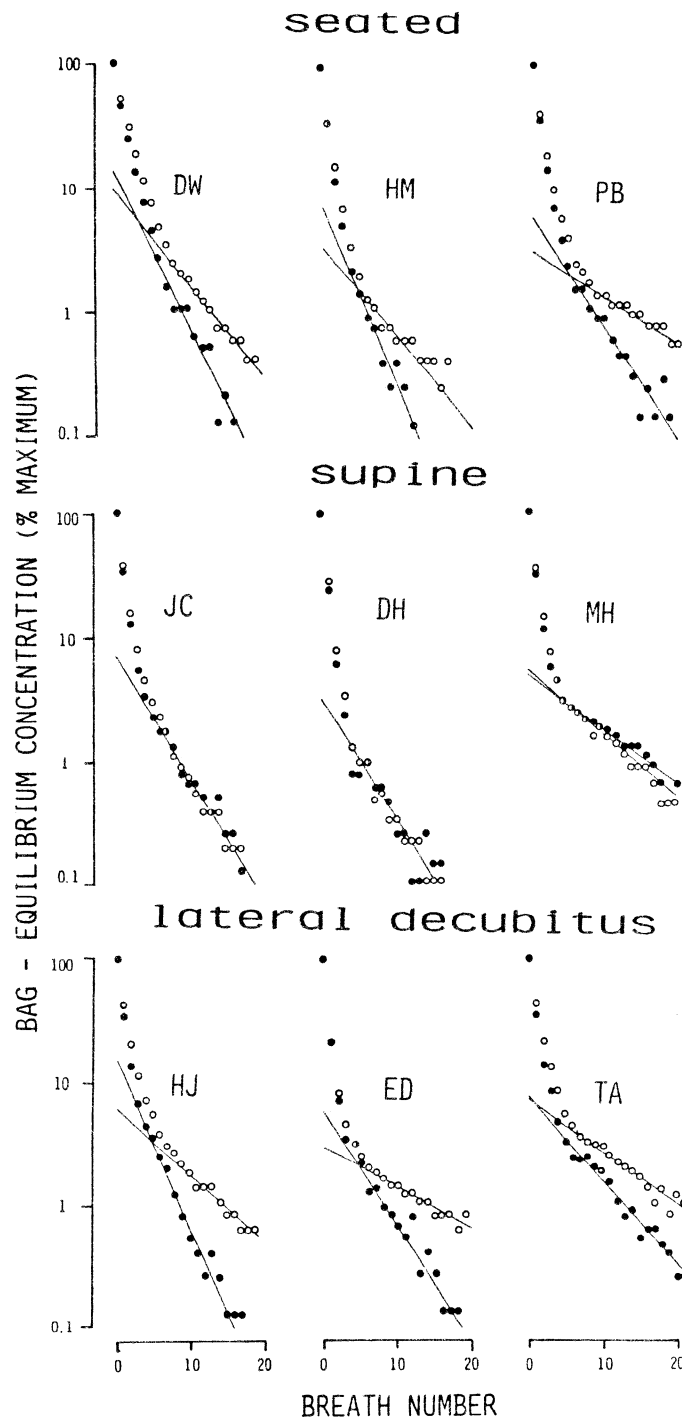

FIG. 1. Examples from all subjects of He (*closed circles*) and SF_6 (*open circles*) mixing in various postures. From these plots rate of mixing (λ) (breaths^{-1}) was calculated as exponential of final mixing phase. n_{99} (breaths) was taken as point on *abscissa* at which this final slope intersected 1% on *ordinate*.

TABLE 2. *Number of breaths for He and SF_6 to reach n_{99} when breathing from a relaxed end-expiratory volume*

Subj	Seated			Supine			Lateral Decubitus		
	n_{99} He	n_{99} SF_6	FRC, liters	n_{99} He	n_{99} SF_6	FRC, liters	n_{99} He	n_{99} SF_6	FRC, liters
HJ	6.2	10.0	3.50	7.4	8.9	2.80	8.5	14.4	3.09
	7.1	12.8	3.35	8.0	10.0	2.81	9.0	16.8	2.91
ED	7.5	8.8	2.52	13.2	13.2	1.84	8.0	14.0	2.36
				11.7	10.8	1.74	9.3	18.0	2.32
HM	5.8	7.2	3.50	8.8	8.0	2.01	9.1	12.6	2.45
	5.9	6.7	2.67	6.8	6.0	2.01	7.9	11.3	2.49
DH	5.4	5.4	2.07	6.7	4.9	1.73	6.5	6.5	1.69
	5.6	5.8	2.24	5.0	5.0	1.57	6.3	7.5	1.69
MH	9.6	9.6	4.09	15.2	14.0	2.80	7.0	12.8	2.33
	12.0	11.9	3.93	11.6	16.2	2.89	9.6	17.8	2.25
JC	11.6	16.7	5.43	9.0	9.6	3.06	10.0	17.8	3.36
	12.6	21.0	5.41	8.6	8.6	2.75	12.4	20.2	3.62
DW	9.8	14.4	4.69	10.1	18.4	3.30	16.8	22.4	3.60
	9.1	13.0	4.30	10.0	14.9	3.33	17.6	25.8	4.01
PB	10.4	12.0	5.58	8.6	8.0	2.43	10.6	17.6	2.98
	8.7	13.2	5.97	6.8	6.8	2.23	10.0	15.4	2.92
TA	5.6	8.2	3.59	6.3	6.3	2.72	12.7	19.8	3.11
	6.2	8.9	3.44	6.4	7.4	2.56			
Mean	8.2	10.9	3.90	8.9	9.8	2.48	10.1	15.9	2.78
±SD	±2.4	±4.0	±1.16	±2.6	±3.9	±0.54	±3.1	±4.8	±0.64

n_{99}, 99% equilibrium; FRC, functional residual capacity.

TABLE 3. *Slopes of final phase of mixing for He and SF_6 and ratio of slopes when breathing from FRC*

Subj	Seated			Supine			Lateral Decubitus		
	Slope, breaths^{-1} He	Slope, breaths^{-1} SF_6	Slope ratio	Slope, breaths^{-1} He	Slope, breaths^{-1} SF_6	Slope ratio	Slope, breaths^{-1} He	Slope, breaths^{-1} SF_6	Slope ratio
HJ	0.170	0.120	1.42	0.227	0.172	1.32	0.317	0.126	2.52
	0.172	0.083	2.07	0.213	0.170	1.25	0.249	0.085	2.93
ED	0.326	0.219	1.49	0.158	0.158	1.00	0.217	0.074	2.93
				0.179	0.197	0.91	0.216	0.072	3.00
HM	0.332	0.164	2.02	0.213	0.214	1.00	0.199	0.046	4.33
	0.297	0.161	1.84	0.318	0.356	0.89	0.185	0.132	1.40
DH	0.314	0.314	1.00	0.230	0.235	0.98	0.197	0.197	1.00
	0.244	0.266	0.92	0.224	0.224	1.00	0.166	0.177	0.94
MH	0.178	0.195	0.91	0.098	0.117	0.84	0.187	0.085	2.20
	0.146	0.182	0.80	0.149	0.112	1.33	0.192	0.073	2.63
JC	0.136	0.104	1.31	0.227	0.209	1.08	0.244	0.116	2.10
	0.128	0.074	1.72	0.225	0.225	1.00	0.265	0.119	2.23
DW	0.392	0.135	2.90	0.168	0.087	1.93	0.126	0.082	1.54
	0.284	0.174	1.63	0.185	0.092	2.01	0.159	0.093	1.71
PB	0.192	0.101	1.90	0.293	0.323	0.91	0.213	0.124	1.72
	0.188	0.086	2.18	0.513	0.513	1.00	0.225	0.114	1.97
TA	0.233	0.122	1.91	0.258	0.258	1.00	0.160	0.099	1.62
	0.239	0.122	1.96	0.204	0.212	0.96			
Mean	0.233	0.154	1.65	0.227	0.215	1.13	0.207	0.107	2.16
±SD	±0.077	±0.064	±0.53	±0.085	±0.101	±0.32	±0.044	±0.037	±0.82

FRC, functional residual capacity.

function of breath number. There are significant differences between the λ for He and SF_6 in the seated ($P < 0.001$) and lateral decubitus ($P < 0.001$) postures not but in the supine position. The ratio of λ_{He} to λ_{SF_6} in all postures is also shown. In Fig. 2 the mean value for $\lambda_{He}/\lambda_{SF_6}$ for each pair of measurements is shown for all

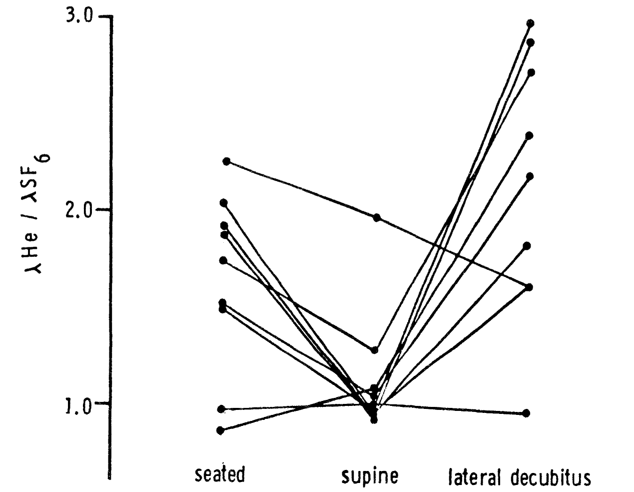

FIG. 2. Ratio of rate constants for He and SF_6 for all subjects in all postures when breathing from a relaxed end-tidal volume. Each *point* represents mean of 2 values and *lines* link values for each subject.

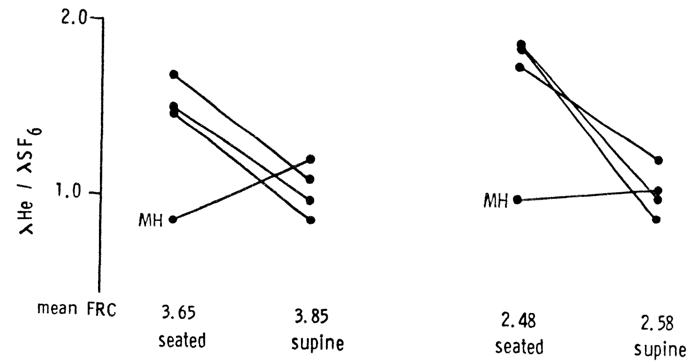

FIG. 3. Ratio of rate constants for He and SF_6 in 4 subjects breathing at a low volume seated and a high volume supine. *Lines* link these values to those made during rebreathing from a relaxed end-expiratory volume in each posture. Behavior of *subject MH* was different from others.

subjects in the three postures. The solid lines indicate the changes within each subject. Note that one subject (*DH,* Table 3) demonstrated no difference between mixing for He and SF_6 in any posture.

The results for He and SF_6 at a volume higher than FRC supine and a volume lower than FRC seated are shown in Fig. 3. The ratio of λ_{He} to λ_{SF_6} at these volumes is compared with the same ratio obtained from the measurements made rebreathing from a normal FRC in the same postures. One subject (*MH*) showed no He-SF_6 mixing difference nor any variation of the λ ratio with change in volume or posture. The subjects in whom a He-SF_6 mixing difference was present seated but absent supine also showed no changes in the λ ratio with changes of lung volume in either posture.

In situations where there were no differences in mixing during the final phase of the rebreathe, there were always initial differences between the two gases, which lasted over the first few breaths. Figure 4 shows the breath-by-breath ratio of He to SF_6 concentrations, normalized to the ratio in the bag. Figure 4 (top) shows the data for *subject DH,* in whom no difference in the final phase of mixing could be demonstrated in any posture; over the first few breaths there is clearly a He-SF_6 difference, which disappears before equilibrium is reached. *Subject*

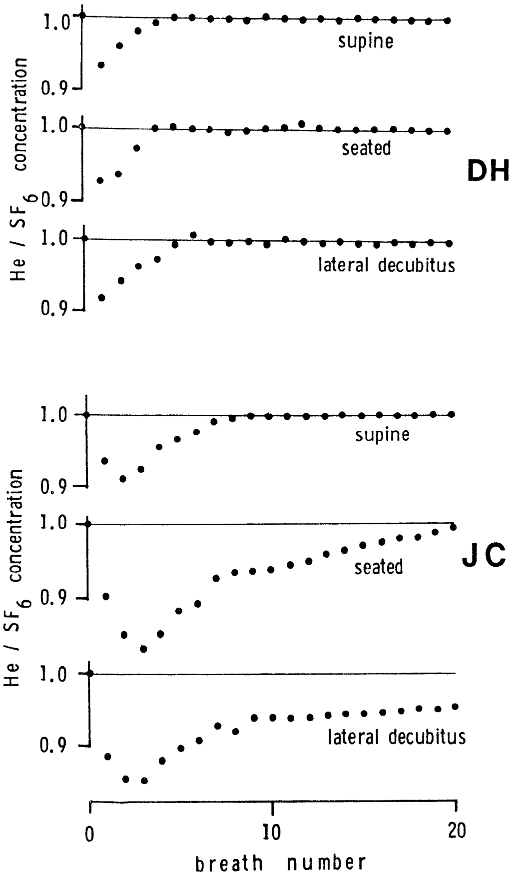

FIG. 4. Breath-by-breath He/SF_6 concentration ratios in each posture in 2 subjects. Note change in ratio over first few breaths, which is independent of presence or absence of mixing differences in final phase (see text).

JC, who was more typical of the group as a whole with He-SF_6 differences in the final phase of mixing in both seated and lateral decubitus postures but absent supine, shows differences over the first few breaths in all postures. The magnitude of these differences over the first few breaths is greatest in the seated position, although the final phase of mixing is faster than in the lateral decubitus posture.

DISCUSSION

Criticism of methods. By the use of Ar/N_2 (15) a serious artifact of closed-circuit equilibration techniques, falsely high values of insoluble gas concentrations caused by volume shrinkage, was overcome. There was no difficulty in defining the plateau values. Thus the approach to equilibrium was measured with a high degree of confidence. The advantage of a small bag volume is twofold. Tidal volume is maintained constant for each breath, and mixing of gases is measured in the normal tidal volume range. The flow weighting of the inspired gas gives a faithful representation of the fractional composition of the previous expiration and is independent of variations of concentration that occur during expiration (the sloping alveolar plateau). The relatively high dead space (instrumental plus anatomical)-to-tidal volume ratio delayed alveolar mixing during the initial phase of mixing but did not influence the final phase.

Theory. Certain features of the approach to equilibrium between the bag (including dead space) and "fast" and "slow" alveolar compartments are of interest. As shown in Fig. 1, there is an initial rapid phase (I) followed by a second phase (II), which is virtually monoexponential. In simple mathematical models of a bag connected to up to five alveolar compartments in parallel, the slope of phase II is always effectively monoexponential even with a tidal volume dispersion of 20:1 (13). As with the classical analysis of open-circuit washout, the final phase is related to the dispersion of tidal volume and its zero time intercept to the dispersion of alveolar volume. This had been predicted by Visser (35) and Nye (23, 24). The intuitive explanation for the monoexponential final phase is that during rebreathing all compartments are interdependent and feed each other. This behavior is easier to analyze than the multiexponential curves seen in the open-circuit washout.

Influence of dead space. The effective dead space of the lungs increases with gas density (17, 18) as does the Bohr dead space (31). In the rebreathing situation we have shown by mathematical modeling the final phase of mixing is independent of the anatomical and instrumental dead space (13). The initial fast phase of mixing is influenced by these dead spaces and the initial He-SF_6 differences (Fig. 4) confirm previous work that dead space increases with increasing molecular weight (18). The He-SF_6 differences shown in the seated and lateral decubitus postures must be due to a diffusion-dependent process at a more peripheral level; the absence of He-SF_6 differences in the supine posture implies that the anatomic and instrumental dead spaces (common to all postures) do not influence the final mixing phase.

Interregional inhomogeneity. Changes of posture are known to alter the distribution of ventilation and volume between lung regions. Lillington et al. (19) measured N_2 clearance of the right and left lungs in the supine and lateral decubitus postures. Clearance overall was 40% slower in the lateral position; this was caused by the uppermost lung receiving a smaller tidal volume (−30%) at a higher FRC (+40%) than the same lung when supine. The tidal volume and FRC of the lower lung was similar in both positions. All lungs had an alinear clearance (intrapulmonary inhomogeneity), but the within-lung mixing inefficiency was unaffected by posture or local FRC.

Through the use of radioactive gases and external counting techniques, vertical gradients of FRC and ventilation have been examined in several postures (1, 16, 22). A summary of these results is presented in Table 4. Vertical gradients of end-expiratory volume (FRC_r/TLC_r) are similar in all postures. Vertical differences in ventilation per lung volume ($\dot{V}/V_A$) are more marked in lateral decubitus and supine postures. From the regional studies no clear picture emerges to explain the large He-SF_6 change between supine and lateral decubitus, since gradients of FRC and $\dot{V}/V_A$ are similar in both postures. A special feature of the lateral decubitus posture is the discontinuity between the two lungs caused by the mediastinum (11, 34). It is also possible that bronchospirometry by eliminating a dead space common to both

TABLE 4. *Interregional differences of expansion and $\dot{V}/V_A$ in upper and lower lungs and top and bottom lung regions*

Position	FRC_r/TLC_r			$\dot{V}/V_A$, $l \cdot min^{-1} \cdot l^{-1}$		
	Top	Bottom	Top/bottom	Top	Bottom	Top/bottom
Seated	0.60	0.35	1.71	0.86	1.10	0.78
Supine	0.58	0.35	1.66	0.55	1.38	0.40
Lateral decubitus	0.60	0.32	1.88	0.91	2.16	0.42

FRC_r/TLC_r, regional functional residual capacity-to-total lung capacity ratios; $\dot{V}/V_A$, ventilation per unit volume; NB frequency, 9–15 min^{-1}; tidal volume, 800–1,000 ml. See Refs. 1, 15, 21.

lungs, exaggerates the interlung differences in the lateral posture.

Intralobar and intra-acinar differences. Uneven ventilation within lobes in humans is well recognized, both from sampling with fine catheters during N_2 washout (32) and from radioisotope clearance curves (9, 28). Recently, the asymmetry of path lengths within the acinus has been proposed as one of the mechanisms responsible for uneven ventilation (26). Nevertheless, others feel that acinar asymmetry plays a relatively minor role (3). It is unlikely that inhomogeneity at a local level is responsible for the postural differences in gas mixing efficiency, since the most marked differences between He and SF_6 were found in the lateral decubitus position, which has a distribution of resting lung volumes very similar to that supine (Table 4) where no He-SF_6 difference could be demonstrated. The distribution of pathway lengths are likely to be similar in these two positions.

Influence of frequency. The relatively high frequency (1 Hz) of our rebreathing maneuver may emphasize the effect of uneven time constants between lung units and decrease the efficiency of alveolar mixing as a whole. Forkert et al. (10) showed a decrease in the efficiency of insoluble gas washout with increase of frequency within lung regions (by external counting) compared with total lung washout (measured at the mouth). They concluded that this effect was due to inequalities of time constants in the periphery, inasmuch as the gradient of regional washouts remained constant. In addition, they failed to demonstrate any diffusion dependence with change of frequency using 80% SF_6–20% O_2 washout mixtures. In contrast, we have demonstrated in closed circuit that the reduction in mixing efficiency with increasing frequency is greater for SF_6 than for He (14). It is possible that frequency may enhance the effects shown by changes in posture, but because all maneuvers were carried out at the same frequency, it cannot be the cause.

Influence of pulmonary surface pressure. Distribution of gas in the lungs is determined by pressure differences along the conducting pathways. These differences are generated by the pressure applied at the lung surface. Gravity acting on the lung and abdominal mass together with the shape of the lung within the chest are the chief determinants of the static pleural pressure gradient down the lung (22). Because of the elastic properties of the lung the same change in pressure will cause a different change in local tidal volume at different levels down the lung. This in itself will affect the mixing of gas and influences the slope of the alveolar plateau (2, 5).

In dogs, the weight of the heart influences the vertical distribution of transpulmonary pressures (12). This is caused by distortion of the lung parenchyma supporting the heart. In humans, the heart may be held more firmly and its interaction with pleural surface pressures may be less. Nevertheless, the mediastinum is displaced in the lateral decubitus posture, so it is possible that the weight of the heart and other tissues alter the vertical gradients of surface pressure between the supine and lateral decubitus postures. Therefore, despite their similar vertical heights and resting lung volumes differences in mixing efficiency may result.

The use of different muscles for breathing will, by altering the shape of the chest, alter the pattern of applied pleural surface pressure. Conscious use of either diaphragm or intercostal muscles alters the distribution both of inspired gas and the slope of the alveolar plateau (29). Positive-pressure ventilation in anesthesized paralyzed subjects demonstrated marked differences in lung washout compared with that in awake subjects for similar reasons (4, 27). It is known that change in posture is usually accompanied by the use of different muscles during normal breathing (30); in the supine posture, the diaphragm is the major contributor and in the erect posture, the intercostals. In our study, it is possible that change in posture induced such a change during the rebreathing maneuver. Nevertheless, we have been unable to demonstrate any change in mixing efficiency for He or SF_6 either by the voluntary use of different muscles or by performing the maneuver with both arms raised above the head. As this latter maneuver alters both the shape of the chest and the mechanical advantage of the muscles, without effect on gas mixing efficiency, further investigation of other factors is being pursued.

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