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EFFECT OF POSTURE ON INTER-REGIONAL DISTRIBUTION OF PULMONARY VENTILATION IN MAN

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Abstract. Regional ventilation per unit alveolar volume ($\dot{V}/V_A$) and regional lung expansion (FRC_R/TLC_R) were measured in twelve normal male human subjects in seated, supine, lateral decubitus and prone postures using a gamma camera and inhalation of the radioactive gases $^{81}Kr^m$ (half-life 13 sec) and $^{85}Kr^m$ (half-life 4.4 h). FRC_R/TLC_R decreased from superior to inferior in all postures except prone where it was uniform; $\dot{V}/V_A$ increased from superior to inferior except in the prone position where it was uniform. In the horizontal axis FRC_R/TLC_R and $\dot{V}/V_A$ were uniformly distributed except for cranial to caudal gradients (with lower values caudally) in supine and lateral decubitus postures. In the prone posture $\dot{V}/V_A$ tended to be higher in caudal lung zones.

Krypton-81m	Regional lung volume
Krypton-85m	Regional ventilation
Posture	Regional lung function

Assessment of regional pulmonary ventilation using radioactive gases has often involved determination of the distribution of radioactivity in the lung during breath-holding (Ball *et al.*, 1962; Milic-Emili *et al.*, 1966; West and Dollery, 1960). In 1975, Fazio and Jones introduced steady-state inhalation of the 13 sec half-life radioactive gas $^{81}Kr^m$ as a method of imaging, with a gamma camera, the distribution of ventilation in the lung during tidal breathing. The $^{81}Kr^m$ steady-state count distribution images so obtained reflect total regional flow rather than flow per unit volume (Amis and Jones, 1980); this paper utilizes a method for measuring regional ventilation per unit alveolar volume ($\dot{V}/V_A$) using a longer-lived radioactive gas $^{85}Kr^m$ in addition to $^{81}Kr^m$ (Amis *et al.*, 1978, 1980).

Gravity is thought to be a major determinant of the distribution of ventilation in the lung (Milic-Emili *et al.*, 1966); thus alterations in body position profoundly

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affect the function of various lung regions. Most studies of this subject, however, have been performed under quasi-static conditions (Kaneko et al., 1966) which may not reflect the distribution of ventilation under dynamic conditions (Bake et al., 1974; Grant et al., 1974). Recent reports also suggest that the pattern of respiratory muscle action employed during breathing may profoundly affect the distribution of inspired gas in the lung (Roussos et al., 1976a,b; Chevrolet et al., 1979).

In this paper we report studies on the regional distribution of lung volume and ventilation per unit alveolar volume ($\dot{V}/V_A$) during tidal breathing in five different body positions. A companion paper (Amis et al., 1984) presents results for the regional distribution of pulmonary perfusion per unit alveolar volume and the associated topography of ventilation perfusion ratios in the same postures.

Theory

The theoretical basis for the use of steady-state inhalation of $^{81}Kr^m$ to quantitate regional ventilation has been discussed previously (Amis and Jones, 1980; Fazio and Jones, 1975). Briefly, during the steady-state inhalation of any relatively insoluble inert radioactive gas the amount of tracer present in any lung region remains constant with time. Under these conditions the rate of arrival of isotope in a lung region must be equal to its rate of removal. Thus, in a ventilated and perfused lung compartment:

$$\dot{V}_I C_I = \dot{V}_E C_L + \lambda N + \alpha \dot{Q} C_L \tag{1}$$

where $\dot{V}_I$ is the inspiratory flow into the compartment, C_I is the concentration of tracer in the inspired gas, $\dot{V}_E$ is the expiratory flow from the compartment, C_L is the concentration of tracer in the compartment, λ is the appropriate decay constant, N is the number of atoms of tracer in the compartment, α is the solubility coefficient for the gas in blood and $\dot{Q}$ is the blood flow through the compartment.

In the case of inhalation of isotopes of Krypton, removal by blood flow may be neglected because of Krypton's low solubility ($\alpha = 0.045$ ml gas STPD/ml blood at 37 °C and 760 mm Hg; Yeh and Peterson, 1965).

Therefore, rewriting eq. (1) and substituting N/V_A for C_L where V_A is the alveolar volume of the lung region:

$$\dot{V}_I C_I = (N/V_A)\ \dot{V}_E + \lambda N \tag{2}$$

i.e.

$$N = \dot{V}_I C_I/(\dot{V}_E/V_A) + \lambda \tag{3}$$

The terms $\dot{V}_I$ and $\dot{V}_E$ are very nearly the same since they differ only to the extent that the respiratory exchange ratio differs from one. Thus:

$$N = \dot{V}C_I/(\dot{V}/V_A) + \lambda \tag{4}$$

where $\dot{V} = \dot{V}_I = \dot{V}_E$. In order to relate the number of radioactive gas atoms in the compartment to external counts detected over the chest a further factor (K_{81}) is required:

$$N_{t81} = K_{81} \cdot [\dot{V}C_I/(\dot{V}/V_A) + \lambda] \tag{5}$$

where N_t is the externally detected count rate.

Thus, during a steady-state inhalation of Krypton-81m the amount of isotope present in any lung region is determined by a balance between its rate of arrival (*via* inspiratory flow) and its rate of removal (*via* ventilatory washout and radioactive decay).

To the extent that radioactive decay dominates the removal process regional count rates will be largely determined by regional inspiratory flow. Since the decay constant for Krypton-81m is 3.2 min^{-1} at normal ventilatory levels regional count rates during steady-state inhalation of $^{81}Kr^m$ are dominated by regional ventilation (Fazio and Jones, 1975). This relationship will not hold at higher turnover rates as the ventilatory washout process overrides radioactive decay resulting in equilibration between inspired and alveolar concentrations of radioactive gas. In this case, regional count rates will merely reflect regional volume.

Regional count rates during $^{81}Kr^m$ inhalation reflect total inspired ventilation of the region (Amis and Jones, 1980). In practice this approaches inspired alveolar ventilation because the lung regions studied consist mainly of alveoli. The volume of lung involved in any particular region of the image will affect the counts obtained over that region as also occurs with the single-breath ^{133}Xe technique (Ball *et al.*, 1962). In this study, $^{85}Kr^m$ was inhaled as a volume marker and ventilation per unit lung volume was calculated from the ratio of the count rates obtained with $^{81}Kr^m$ and $^{85}Kr^m$.

The radionuclide $^{85}Kr^m$ is the metastable state of Krypton-85 (^{85}Kr) to which it decays by isomeric transition with a half-life of 4.4 h emitting beta particles and 150 KeV (74% of disintegrations) and 305 KeV gamma rays. For this study $^{85}Kr^m$ was produced in the M.R.C Cyclotron at Hammersmith Hospital by 16 MeV deuteron irradiation of stable Krypton-84 (Clark and Buckingham, 1975). In the case of inhalation of $^{85}Kr^m$, λ is 0.002625 min^{-1} and can be neglected; thus, from eq. (5):

$$N_{t85} = K_{85} \cdot V_A \cdot C_{I85} \tag{6}$$

where the subscript 85 refers to values for $^{85}Kr^m$ inhalation.

The effects of CI are eliminated for both $^{81}Kr^m$ inhalation and $^{85}Kr^m$ inhalation by expressing regional count rates as a fraction of total lung field count rates.

$$\frac{(N_{t81})_R}{(N_{t81})_T} = \frac{\dot{V}_R}{\dot{V}_T}\left[\frac{(\dot{V}/VA)_T + \lambda}{(\dot{V}/VA)_R + \lambda}\right]\frac{(K_{81})_R}{(K_{81})_T} \tag{7}$$

and

$$\frac{(N_{t85})_R}{(N_{t85})_T} = \frac{(VA)_R\,(K_{85})_R}{(VA)_T\,(K_{85})_T} \tag{8}$$

where the subscript R refers to a regional value, the subscript T a total lung field value, and λ is the decay constant for $^{81}Kr^m$ (3.2 min^{-1}).

An index (in arbitrary units) for ventilation per unit alveolar volume may be obtained by division of eqs. (7) and (8), assuming that the regional/total attenuation coefficient ratio (K_R/K_T) is similar for $^{81}Kr^m$ and $^{85}Kr^m$. This has been confirmed in a lung model (Amis and Jones, 1980), *i.e.*

$$\frac{(N_{t81})_R/(N_{t81})_T}{(N_{t85})_R/(N_{t85})_T} = \left[\frac{(\dot{V}/VA)_R + \lambda}{(\dot{V}/VA)_T + \lambda}\right]\frac{(\dot{V}/VA)_R}{(\dot{V}/VA)_T} \tag{9}$$

By rearranging eq. (9):

$$(\dot{V}/VA)_R = \lambda\left[\frac{(N_{t85})_R/(N_{t85})_T}{(N_{t81})_R/(N_{t81})_T}\cdot\left\{1 + \frac{\lambda}{(\dot{V}/VA)_T}\right\} - 1\right] \tag{10}$$

It is possible to solve eq. (10) for $(\dot{V}/VA)_R$ if two steady-state count distribution images are obtained; one with $^{81}Kr^m$ inhalation and one with $^{85}Kr^m$ inhalation and their relationship calibrated with a value for $(\dot{V}/VA)_T$. In this study the initial slope of the clearance curve for both lungs together obtained following inhalation equilibrium with $^{85}Kr^m$ was used to estimate $(\dot{V}/VA)_T$.

Regional counts recorded during an equilibration with $^{85}Kr^m$ are related to regional alveolar volume in the same way as they would be for other relatively long-lived radioactive gases. It is therefore also possible to use $^{85}Kr^m$ to measure regional distribution of volume in the lung in terms of the ratio of regional functional residual capacity to regional total lung capacity (FRC_R/TLC_R) as has been previously described using Xenon-133 (Milic-Emili *et al.*, 1966).

Methods

Subjects. Table 1 lists the characteristics of 14 healthy adult male human subjects, in whom radioactive gas studies were performed in one or two of the following postures: upright (seated), left and right lateral decubitus (LLD and RLD), supine, and prone. All subjects were volunteers, free of signs and symptoms of respiratory disease, who had given informed consent for the study. Ethical permission was obtained from the Medical School and Hospital Ethical Committee

TABLE 1

Anthropometric data of subjects undergoing radioactive gas studies (all male)* and postures in which they were studied. U = upright, S = supine, P = prone, RLD = right lateral decubitus, LLD = left lateral decubitus. FEV_1 = force expiratory volume in one second; NM = not measured.

Subject	Age (yr)	Height (cm)	Weight (kg)	Total lung capacity (L)	Vital capacity (L)	FEV_1 (L)	Posture
1	30	180	82	6.74	5.3	4.75	P LLD
2	28	173	79	6.75	5.2	4.2	LLD
3	29	180	74	7.5	5.7	4.7	LLD
4	30	194	93	7.8	6.25	5.35	U RLD
5	26	181	67	6.85	5.5	5.0	LLD
6	44	177	68	7.7	5.0	3.9	S RLD
7	34	179	61	NM	6.2	4.5	S U
8	34	185	85	7.4	5.3	4.2	P
9	35	175	69	NM	5.8	4.5	P LLD
10	30	179	57	7.1	5.0	4.4	P
11	31	175	83	7.44	4.9	4.1	P
12	29	172	68	5.7	4.5	4.0	S
13	40	167	63	6.17	4.9	3.95	LLD S
14	36	181	97	7.05	6.25	4.8	S RLD

* All subjects except 1,5,11 are nonsmokers.

and the MRC Radioisotope Committee. Out of a total of 21 studies $\dot{V}/V_A$ was measured in 13 studies while regional lung volume distribution was assessed in 8 studies. Subjects 13 and 14 had ventilation perfusion ratio studies only (Amis *et al.*, 1984). A diagram of the experimental arrangement is given in fig. 1 of the accompanying paper (Amis *et al.*, 1984).

Radioactive gas technique. Subjects were placed in front of a large-field gamma camera (Jumbo GCA 202, Toshiba, Tokyo, Japan) fitted with a medium-energy collimator and linked to a digital computer (Nova 1220, Data General Corp., Southboro, MA, U.S.A.). Information from the camera was recorded on magnetic discs (model 848-12 CDC, London, U.K.) for later replay and processing. Data could be collected as an accumulated count distribution image (static mode) or as a series of 4-sec frames under dynamic conditions (dynamic mode).

Subjects studied upright were seated with their back to the camera in a specially

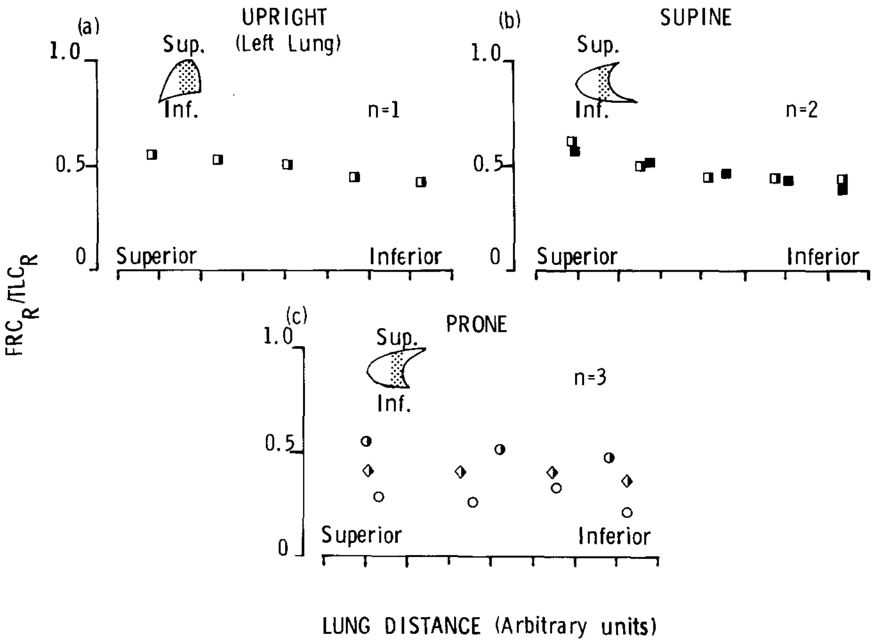

Fig. 1. Vertical distribution of regional functional residual capacity (FRC_R) as a proportion of regional total lung capacity (TLC_R) in (a) upright, (b) supine and (c) prone postures. Shaded areas on lung diagrams denote lung region analysed; n = number of subjects; different symbols represent individual subjects.

designed chair. For studies involving lateral decubitus postures subjects lay on a bed with their back to the camera face. In the supine and prone postures the subject's left side was placed against the camera.

Subjects breathed through a mouthpiece to which was attached a pneumotachograph (Fleisch No. 2, Gould Inc., Cleveland, OH, U.S.A.) connected to a pressure transducer (No. 390, Elema Schönander, Fack, Sweden) whose signal was fed through an amplifier to an ultraviolet multichannel recorder (No. 3006, S.E. Labs, Feltham, U.K.). This flow signal was electrically integrated to give tidal volume. Initial calibration of these signals was achieved with a flow generator, rotameter and 1 L syringe.

The pneumotachograph was joined to a large bore three-way tap, one arm of which was attached to a T-piece connected by wide bore tubing to an extractor fan which pumped gas to waste outside of the laboratory. The other arm of the T-piece was open to room air. The third arm of the three-way tap was attached to a nonrebreathing valve connected in closed circuit with a lead shielded spirometer and soda lime CO_2 absorber. Instrumental dead space, measured by water displacement, was approximately 200 ml when the subject was breathing on open circuit and about 100 ml on closed circuit. The functional instrumental dead space during open circuit breathing was, however, probably much less than 200 ml because of the bias flow provided by the extractor fan.

A potentiometer on the spirometer provided a signal of tidal volume to the multichannel recorder. The spirometer was equipped with two ports, one through which $^{85}Kr^{m}$ was initially added to the spirometer and then subsequently used to add oxygen at a rate equivalent to gas absorption from the circuit during rebreathing. The second port was used to obtain gas samples for measurement of $^{85}Kr^{m}$ concentrations. A well counter (Castle NE 5502, Nuclear Enterprises, Edinburgh, U.K.) and digital ratemeter (M5-183A Ekco-electronics, Southend-on-Sea, U.K.) were used to detect radiation from these gas samples. The spirometer was filled with air, oxygen and sufficient $^{85}Kr^{m}$ to ensure a final lung concentration of around 1 mCi/L. Oxygen was added to keep its concentration in the system around 20%. The system was mixed, a gas sample taken and a measurement of $^{85}Kr^{m}$ concentration was made in the well counter.

A stream of air (*ca.* 1 L/min), used to elute $^{81}Kr^{m}$ from its parent ^{81}Rb in a generator, reached the subject *via* a port near the mouthpiece and mixed with inspired room air inhaled *via* the T-piece. During a preliminary inhalation of $^{81}Kr^{m}$ the position of each subject was adjusted to give an optimum image in the gamma camera. Once positioned, subjects were instructed not to move. A system of two lights, fixed in position and focused on points marked on the subject's chest, monitored any movement. Measurement of tidal volume and respiratory rate commenced. Inhalation of $^{81}Kr^{m}$ was restarted; once a steady state was achieved (after 6–10 breaths) a static count distribution image was obtained containing around 250 000 counts; this took 1–2 min depending on the activity level of the generator. The $^{81}Kr^{m}$ inhalation was then stopped and residual radioactivity allowed to decay to room background. For the measurement of lung volume the subject was switched into the closed circuit spirometer system at functional residual capacity (FRC) and inhaled to total lung capacity (TLC) before breath-holding for 20 sec while the resulting count distribution was recorded. A number of deep breaths were then taken in order to equilibrate rapidly with the $^{85}Kr^{m}$ in the spirometer circuit. This was followed by a second inhalation to TLC and a further breathhold of 20 sec. The subject then returned to normal breathing and after sufficient counts were accumulated to define an equilibration plateau of activity, he was switched out of the circuit. Room air was breathed while the clearance of $^{85}Kr^{m}$ from the lung was monitored until counts over the lung were less than 10% of initial count rate. The time taken for the rebreathing and washout maneuver was usually 6–7 min. A final gas sample was taken from the spirometer and counted in the well counter. The above procedure was appropriately modified when subjects were involved in only a partial study, *e.g.* when FRC_R/TLC_R was not measured. The estimated absorbed radiation dose to the lungs of experimental subjects was 130 mrad per posture studied.

Data processing. From dynamic recordings of 4-sec frames during the equilibration plateau obtained with $^{85}Kr^{m}$, sufficient frames were added to produce a static image of approximately 250 000 counts reflecting the distribution of lung volume.

The ventilation count distribution image was already stored for analysis.

A normalizing region was chosen on the volume image using a light pen. This was typically a rectangular region enclosing the total lung field. Two rectangular vertical strips were chosen for analysis. These strips fell within areas on the image which contained counts greater than 20% peak count.

In the upright posture, strips were taken centrally down each lung. In horizontal postures, one vertical strip was situated cranial to the heart, the other just cranial to the diaphragm. Cranial–caudal (*i.e.* horizontal) strips were chosen down the center of the upper and lower lung in lateral decubitus postures, while superior and inferior horizontal strips were chosen in the other postures. These strips were divided into 5–15 subregions. The exact same subregions were chosen on both ventilation and volume count distribution images and normalized count ratios calculated according to eqs. (7) and (8).

For dynamic analysis of $^{85}Kr^m$ clearance from the total lung field a semilogarithmic plot of activity *vs* frame number was produced and a line fitted by eye to the initial slope of the curve. The specific ventilation of the total lung field $(\dot{V}/V_A)_T$ was estimated from the slope of this line and included in the calculation of regional $\dot{V}/V_A$ from the normalized count ratios (eq. 10).

In order to compare the distribution of function in the lungs of subjects of different size, breathing at different overall levels of ventilation, the results for each region were expressed as a fraction of the area-weighted mean of the distribution of which they formed a part. Although the technique provides a measure of $(\dot{V}/V_A)_R$ in absolute units, comparisons between subjects are expressed more conveniently in normalized values. These indices were plotted against lung distance (arbitrary units) which was normalized by making the strip length equal for all subjects. No absolute lung distances were measured. In order to analyse vertical and horizontal differences all data points in the superior or cranial 20–30% of the lung distance were compared with data points falling in the inferior or caudal 20–30% of the lung using Student's *t* distribution (Mendenhall, 1969).

In addition, regional $\dot{V}/V_A$ (arbitrary units) was also calculated from the initial slope of the regional $^{85}Kr^m$ clearance curves. We intended to compare values so obtained with those measured by the combination of $^{81}Kr^m$ and $^{85}Kr^m$. However, as the computer treated these analyses separately it was not possible to be certain that the regions chosen were identical for the two estimates. In addition, larger regions were chosen for the clearance analysis in order to improve the statistical quality of the clearance curves. Our comparison has therefore been confined to an analysis (paired difference test – Mendenhall, 1969) of the superior/inferior and cranial/caudal ratios obtained with the two techniques.

Regional FRC/TLC ratios were calculated for the larger regions used for the regional clearance analysis using the $^{85}Kr^m$ concentrations measured in the samples taken from the spirometer (after decay and background correction) and the count rates recorded during the breath-holding maneuvers (Milic-Emili *et al.*, 1966).

Results

Data presentation. The regional distribution of FRC_R/TLC_R and $\dot{V}/VA$ found in the five postures studied are presented as individual data points for each subject in figs. 1–4. Pooled results (mean ± 1 SD) for values found over the superior or cranial (lateral in upright) 20–30% of the lung compared to the inferior or caudal (medial in upright) 20–30% of the lung together with values for total lung field FRC/TLC and $\dot{V}/VA$ ($^{85}Kr^m$ washout) are shown in table 2. Since results for both vertical lung strips were similar in all horizontal postures, only the caudal lung strip results are given. Similarly, for the horizontal strips in upright and prone postures only the superior strip is reported. Data is presented for both inferior and superior horizontal strip analyses in the supine posture. In lateral decubitus postures horizontal strips were taken across the middle of each lung while in the upright posture vertical and horizontal analysis was confined to the left lung since results were similar in both lungs.

Vertical distribution of FRC_R/TLC_R. In the upright and supine postures FRC_R/TLC_R decreased from superior to inferior by 24–32% (fig. 1 a,b) in contrast to the prone posture where FRC_R/TLC_R was more uniformly distributed (fig. 1c). In

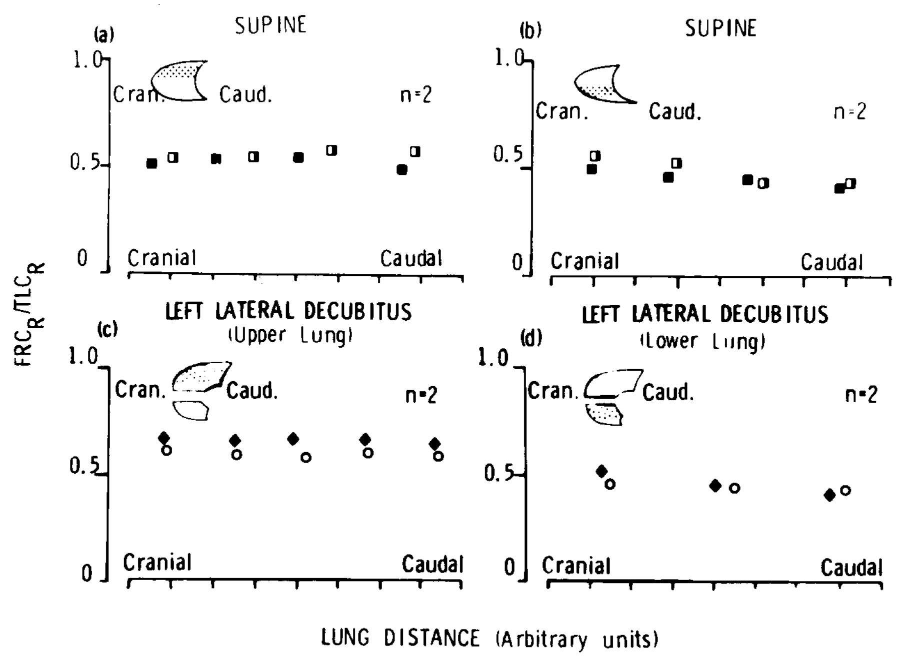

Fig. 2. Horizontal distribution of FRC_R/TLC_R in supine, (a) superior analysis (b) inferior analysis, and left lateral decubitus, (c) upper and (d) lower lung. Symbols as in fig. 1. Note that upper and lower lung values are normalized within each lung, thus upper – lower lung differences have been suppressed in this figure.

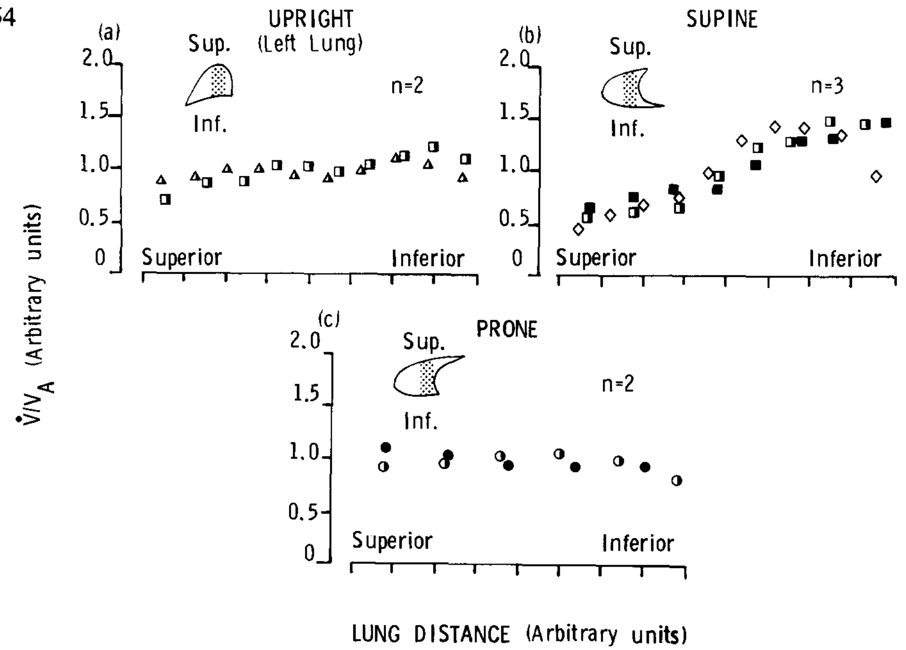

Fig. 3. Vertical distribution of ventilation per unit volume in the (a) upright, (b) supine and (c) prone postures. Symbols as in fig. 1.

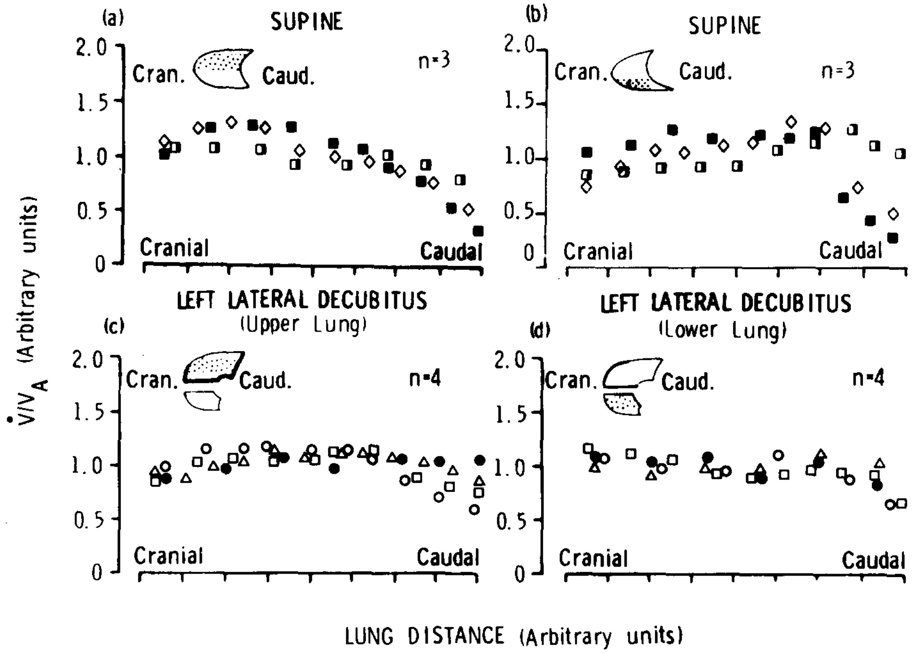

Fig. 4. Horizontal distribution of ventilation per unit volume in supine, (a) superior analysis, (b) inferior analysis, and left lateral decubitus posture, (c) upper and (d) lower lung. Symbols as in fig. 1. Note that upper and lower lung values are normalized within each lung, thus upper – lower lung differences have been suppressed in this figure.

left lateral decubitus the FRC_R/TLC_R was calculated for each lung separately, being 0.58 for the upper and 0.43 for the lower lung, *i.e.* an upper/lower ratio of 1.35; a similar result was found in RLD (upper/lower ratio 1.31). FRC_R/TLC_R tended to decrease by 5–12% down the upper lung in lateral decubitus postures and by 12–16% down the lower lung (table 2), although neither of these changes reached statistical significance.

Horizontal distribution of FRC_R/TLC_R. There was no change in FRC_R/TLC_R across the left lung in the upright posture (table 2) and in the supine posture FRC_R/TLC_R was uniformly distributed in superior zones. In inferior zones FRC_R/TLC_R was about 24% lower caudally than cranially, although this change did not reach significance at the 5% level (fig. 2a,b). In the prone posture lung volume was relatively uniformly distributed in both vertical and horizontal directions (table 2). In lateral decubitus postures, FRC_R/TLC_R was uniformly distributed along a horizontal axis in the upper lung (fig. 2c, table 2) but tended to decrease by 15–16% from cranial to caudal in the lower lung (fig. 2d).

Vertical distribution of $\dot{V}/V_A$. In the upright posture $\dot{V}/V_A$ increased significantly by about 28% from superior to inferior down the left lung (fig. 3a). The increase in $\dot{V}/V_A$ from superior to inferior was considerably greater (151%) in the supine posture (fig. 3b), while in the prone position $\dot{V}/V_A$ was fairly uniformly distributed (fig. 3c).

Lateral decubitus postures were characterized by a higher $\dot{V}/V_A$ in the lower lung compared to the upper lung (upper/lower ratio 0.39–0.49). Within the upper lung $\dot{V}/V_A$ tended to increase from superior to inferior by about 22–31% (table 2); this change achieved significance in LLD. Within the lower lung the increase was more variable (about 23% in LLD and 43% in RLD); statistical significance was not achieved in either posture. The smaller increase in LLD was associated with a decrease in $\dot{V}/V_A$ near the inferior border of the lung.

Horizontal distribution of $\dot{V}/V_A$. In the upright posture $\dot{V}/V_A$ was relatively uniformly distributed across both lungs but some lower values were found at the medial border on the left (table 2). In the supine posture $\dot{V}/V_A$ decreased significantly by 43% from cranial to caudal along a superior strip while inferiorly $\dot{V}/V_A$ increased from cranial to caudal to a point three quarters of the way along the lung before decreasing again near the diaphragm (fig. 4 a, b). For the prone posture $\dot{V}/V_A$ increased significantly by 38% from cranial to caudal. In lateral decubitus postures $\dot{V}/V_A$ was fairly uniformly distributed in the upper lung while cranial to caudal decreases were noted in the lower lung (fig. 4c, d; table 2); this change was significant in LLD.

Distribution of $\dot{V}/V_A$ measured by $^{85}Kr^m$ clearance. Results obtained for the vertical and horizontal distribution of $\dot{V}/V_A$ using the regional clearance of $^{85}Kr^m$ are

TABLE 2

Comparison of pooled values (mean ± 1 SD) for regional lung expansion (FRC_R/TLC_R) and ventilation per unit alveolar volume ($\dot{V}/V_A$) found over the superior or cranial 20–30% of the lung compared to the inferior or caudal 20–30% of the lung in the five postures studied. Also shown are total lung field values for each posture including $\dot{V}/V_A$ measured from the $^{85}Kr^m$ clearance phase of the study. Superior and inferior horizontal analyses are shown for the supine posture and separate vertical and horizontal analyses for each lung in decubitus postures; horizontal analyses in the upright posture are lateral to medial over the left lung. n = number of subjects.

Posture	Vertical distribution			
	FRC_R/TLC_R		$\dot{V}/V_A$ (arbitrary units)	
	Superior	Inferior	Superior	Inferior
Upright (left lung)	0.55	0.42	0.86 ±0.1	1.0$^{\infty}$ ±0.1
(n)	(1)	(1)	(2)	(2)
Supine	0.60 ±0.03	0.41$^{\infty}$ ±0.01	0.55 ±0.07	1.33$^{\infty}$ ±0.19
(n)	(2)	(2)	(3)	(3)
Prone	0.42 ±0.13	0.36 ±0.14	1.03 ±0.11	0.95 ±0.08
(n)	(3)	(3)	(2)	(2)
Left lateral decubitus (upper lung)	0.62 ±0.03	0.59 ±0.06	0.83 ±0.07	1.01$^{\infty}$ ±0.14
Left lateral decubitus (lower lung)	0.44 ±0.01	0.39 ±0.04	0.90 ±0.10	0.96 ±0.06
(n)	(2)	(2)	(4)	(4)
Right lateral decubitus (upper lung)	0.70	0.62	0.70 ±0.05	0.92 ±0.12
Right lateral decubitus (lower lung)	0.49	0.41	0.78 ±0.25	1.10 ±0.09
(n)	(1)	(1)	(2)	(2)

* Superior lung strip.

$^{+}$ Inferior lung strip.

$^{\infty}$ Significant differences at 5% level or below.

Horizontal distribution				Total lung field	
FRC_R/TLC_R		$\dot{V}/V_A$ (arbitrary units)		FRC/TLC	$\dot{V}/V_A$ ($L \cdot min^{-1} \cdot L^{-1}$)
Cranial or lateral (upright)	Caudal or medial (upright)	Cranial or lateral (upright)	Caudal or medial (upright)		
0.48	0.48	1.06	0.83	0.5	1.48
		±0.04	±0.11		±0.35
(1)	(1)	(2)	(2)	(1)	(2)
0.53*	0.53*	1.15*	0.66*$^{\infty}$	0.53	1.43
±0.01	±0.05	±0.09	±0.23	±0.01	±0.30
0.53^{+}	0.41^{+}	0.94^{+}	0.74^{+}		
±0.05	±0.01	±0.13	±0.35		
(2)	(2)	(3)	(3)	(2)	(3)
0.40	0.41	0.84	1.13$^{\infty}$	0.36	1.46
±0.07	±0.14	±0.07	±0.18	±0.10	±0.30
(3)	(3)	(2)	(2)	(3)	(2)
0.63	0.60	0.96	0.84	0.58	0.92
±0.04	±0.03	±0.10	±0.16		±0.40
0.48	0.40	1.10	0.84$^{\infty}$	0.43	1.89$^{\infty}$
±0.04	±0.01	±0.07	±0.15		±0.43
(2)	(2)	(4)	(4)	(2)	(4)
0.66	0.63	0.99	0.77	0.67	0.88
		±0.09	±0.16		±0.22
0.54	0.46	0.98	0.83	0.51	2.27$^{\infty}$
		±0.13	±0.10		±0.19
(1)	(1)	(2)	(2)	(1)	(2)

TABLE 3

$\dot{V}/V_A$ in arbitrary units (mean ± 1 SD) for superior and inferior, cranial and caudal or lateral and medial lung regions in normal human subjects (n = number of subjects) as measured by the regional clearance of $^{85}Kr^m$.

Posture	Superior	Inferior	Cranial	Caudal
Upright (n = 2)	0.68 ± 0.07	1.34 ± 0.08$^{\infty}$	1.08 ± 0.03* 1.11 ± 0.23†	0.93 ± 0.05* 0.95 ± 0.15†
Supine (n = 3)	0.73 ± 0.25	1.32 ± 0.14$^{\infty}$	0.87 ± 0.13^{+}	1.11 ± 0.13^{+}
Prone (n = 2)	0.98 ± 0.03	1.03 ± 0.05	1.05 ± 0.04	0.95 ± 0.03
Left lateral decubitus (upper lung) (n = 5)	0.94 ± 0.06	1.06 ± 0.06$^{\infty}$	0.93 ± 0.09	0.91 ± 0.12
Left lateral decubitus (lower lung) (n = 5)	0.80 ± 0.04	1.17 ± 0.05$^{\infty}$	1.00 ± 0.14	0.98 ± 0.1
Right lateral decubitus (upper lung) (n = 2)	1.0 ± 0	1.02 ± 0.11	1.14 ± 0.07	0.97 ± 0.06
Right lateral decubitus (lower lung) (n = 2)	0.83 ± 0.01	1.16 ± 0$^{\infty}$	1.01 ± 0.09	0.92 ± 0.12

* Left lung, lateral to medial analysis.
† Superior horizontal strip analysis (n = 2).
$^{+}$ Inferior horizontal strip analysis.
$^{\infty}$ Significant difference at 5% level or below.

shown in table 3. Significant vertical gradients of $\dot{V}/V_A$ were found in upright, supine, LLD and RLD but not in prone. In RLD $\dot{V}/V_A$ tended to increase from superior to inferior within the lower lung but this gradient did not reach significance at the 5% level. $\dot{V}/V_A$ increased from the top lung to the bottom lung in both lateral decubitus postures (table 2). No significant horizontal gradients of $\dot{V}/V_A$ were detected. Pooled superior/inferior and cranial/caudal ratios obtained for each posture with $^{85}Kr^m$ washout were not significantly different from those found with $^{81}Kr^m/^{85}Kr^m$.

Discussion

Critique of methods

Steady-state administration of $^{81}Kr^m$ has usually been analysed in terms of a single-compartment lung model (Fazio and Jones, 1975; Harf *et al.*, 1978). A theoretical discussion of the limitations and implications of this approach in terms of the quantitative use of $^{81}Kr^m$ as a flow tracer in the lung has been presented previously (Amis and Jones, 1980).

The use of $^{85}Kr^m$ as a volume marker for comparison with $^{81}Kr^m$ as a flow tracer was first described by Jones *et al.* (1978) and Amis *et al.* (1978). These radionuclides have very different half-lives (13 sec for $^{81}Kr^m$ and 4.4 h for $^{85}Kr^m$) but similar gamma-emission energy levels. Subject movement during, or especially between, the accumulation sequentially of ventilation and volume count distribution images can lead to random or systematic errors in the calculation of regional $\dot{V}/V_A$. In the present study, subjects kept as still as possible; movement was monitored with a system of lights focused on points on the subject's chest. A special problem related to movement exists around the edges of the lung, particularly adjacent to the diaphragm. Since the count distribution image is accumulated continuously over many respiratory cycles, the degree of lung excursion (*i.e.* tidal volume) should ideally be identical for the ventilation and volume weighted images. The largest deviation from scan to scan occurred in the supine posture where the ratio of mean tidal volume during $^{81}Kr^m$ administration to that during $^{85}Kr^m$ inhalation was 0.65. Although differences were less in other postures, in some subjects and postures regional $\dot{V}/V_A$ may be poorly defined around the lung edges.

Krypton-81m is not a pure flow tracer. Equation (5) shows that when ventilation is high and $\dot{V}/V_A$ is greater than λ the regional $^{81}Kr^m$ count rate reflects increasingly the distribution of V_A rather than $\dot{V}$. Theoretically, the relationship between N_r ($^{81}Kr^m$) and $\dot{V}_r$ is reasonably linear up to a $\dot{V}/V_A$ of 2.5 $L \cdot min \cdot L^{-1}$, flattening out at higher levels of ventilation. This relationship has been confirmed experimentally by Arnot *et al.* (1981) in which the distribution of ^{13}N washout and $^{81}Kr^m$ steady-state counts were compared in dogs artificially ventilated at different levels of tidal volume and frequency. Equation (10) and the use of whole-lung $^{85}Kr^m$ washout takes this alinearity into account. In addition, total-lung $\dot{V}/V_A$ from $^{85}Kr^m$ washout never exceeded 2.3 $L \cdot min \cdot L^{-1}$.

A separate problem is whether inspired $^{81}Kr^m$ has the same distribution in the periphery of the lung as a tracer with a longer half-life such as ^{133}Xe or ^{13}N. Because of its 13 sec half-life, the peripheral parts of alveolar units ventilated in series might have a lower concentration of $^{81}Kr^m$ if the transit time was prolonged and allowed a significant amount of radioactive decay to occur. In other words, the volume of distribution of $^{81}Kr^m$ may not be the same as that for $^{85}Kr^m$ (Amis and Jones, 1980). Modell and Graham (1982) have estimated overall end expiratory volume in dogs, anaesthetized and artifically ventilated – from tidal volume and the total maximum/minimum $^{81}Kr^m$ count rate ratio during gated acquisitions –

and found a 40% underestimation of lung volume. These measurements rest on the assumption that the system is well mixed, but after only 13 sec there will still be many *parallel* inhomogeneities of ventilation in such lungs leading to regional variations in $^{81}Kr^m$ concentration. Although *serial* inhomogeneities in the lung periphery may invalidate the simple steady-state equation for gases of very short half-life, the effects in normal subjects are likely to be very small and difficult to detect with available technology. This problem merits further study. Nevertheless, in the context of the present study, the regional differences of $\dot{V}/V_A$ measured from the washout of long half-life tracer ($^{85}Kr^m$) were similar to those obtained with the short half-life ($^{81}Kr^m$) steady-state technique.

Comparison of $^{81}Kr^m$ and $^{85}Kr^m$ count rates detected over the lung implies similar counting geometry for gamma emissions from the two isotopes. Amis and Jones (1980) have shown that attenuation coefficients for the 190 KeV energy peak of $^{81}Kr^m$ and the 150 KeV of $^{85}Kr^m$, as measured in a lung model, differ only by about 6%.

Vertical distribution of regional lung volume

In the upright and supine postures the vertical gradients of lung volume were similar to those previously reported (Kaneko *et al.*, 1966; Milic-Emili *et al.*, 1966) except that regional expansion was more uniform in the prone posture. Assuming uniform mechanical properties of the lung (Ishikawa *et al.*, 1964; Sutherland *et al.*, 1968; Berend *et al.*, 1980), the vertical gradient of pleural pressure at FRC must be reduced in the prone posture.

Upper and lower lungs in lateral decubitus postures were treated separately; the superior to inferior difference was about the same in each lung but there was a step change in volume between lungs. As an explanation for this discontinuity the weight of the mediastinum or transmission of abdominal pressure *via* the diaphragm may compress the lower lung. This is consistent with the work of Roussos *et al.* (1976a, 1977b) who have demonstrated that in lateral decubitus postures alterations in tension of the diaphragm affect the vertical distribution of lung volume through modification of the vertical pleural pressure gradient and displacement of the mediastinum

Horizontal distribution of regional lung volume

The absence of systematic differences in expansion between lung regions at the same vertical height in the upright posture agrees with previous work (Milic-Emili *et al.*, 1966; Sutherland *et al.*, 1968). In the supine posture there have been conflicting reports (Bake *et al.*, 1967; Grassino *et al.*, 1975; Kaneko *et al.*, 1966) concerning the distribution of lung volume along the horizontal axis. The present finding of a uniform horizontal distribution of lung volume in superior regions but a decrease in caudal relative to cranial expansion in inferior regions may explain the discrepancies in previous studies where the counters have been placed above and below rather than at the side of the chest.

In lateral decubitus postures there have also been conflicting reports concerning horizontal gradients of lung volume (Demedts, 1978; Kaneko *et al.*, 1966) and in the present analysis a horizontal gradient appeared only in the lower lung. Previous workers (Bake *et al.*, 1967; Demedts, 1978) have suggested that horizontal gradients may be explained by non-uniform mechanical properties of the human lung but no such differences have been demonstrated (Sutherland *et al.*, 1978; Berend *et al.*, 1980) in human studies. Since these gradients depend on vertical height within the thoracic cavity, it seems more likely that they reflect modification of the distribution of forces acting on the lung surface, *i.e.* a non-uniform distribution of pleural pressure in the horizontal direction. The inferior zone horizontal gradient may be associated with the transmission of abdominal pressure to inferior caudal lobes and the weight of mediastinal contents.

Vertical distribution of regional ventilation per unit alveolar volume

In the supine posture the vertical gradient of $\dot{V}/V_A$ was more pronounced than in the upright posture. Increased ventilation in inferior regions in this posture has been demonstrated previously under quasi-static conditions (Kaneko *et al.*, 1966) but with a less steep gradient. The vertical distribution of inspired gas in this posture may depend on the level of preinspiratory lung volume suggesting that dependent zone airway closure is influencing ventilation distribution in supine subjects (Préfaut and Engel, 1981). The FRC/TLC ratio was somewhat higher in our supine subjects than usual (Agostoni and Mead, 1964) and closing capacity, although not measured, would not be expected to have exceeded the end expiratory level. Given an overall FRC of about 53% TLC the gradient of $\dot{V}/V_A$ supine (fig. 3) is compatible with those of Préfaut and Engel (1981).

In the prone posture ventilation has been reported to increase from superior to inferior (Kaneko *et al.*, 1966), but the more uniform distribution of $\dot{V}/V_A$ found in the present study is consistent with the homogeneous distribution of regional lung volume.

In lateral decubitus postures, upper lung $\dot{V}/V_A$ was only half of that of the lower lung (table 2) in general agreement with a number of authors who have mainly studied the right lateral decubitus posture under quasi-static conditions (Demedts, 1978; Kaneko *et al.*, 1966; Roussos *et al.*, 1977a). The discontinuity in $\dot{V}/V_A$ between upper and lower lungs is in keeping with the similar discontinuity in regional lung volume. However, the difference in $\dot{V}/V_A$ between upper and lower lung seems more than can be explained by the gradient of regional lung volume. The difference in expansion between superior and inferior lung regions in the upright posture was about 13% TLC_R and the superior/inferior ventilation ratio (0.78) was of the same order. The difference in resting lung volume between upper and lower lung in the lateral decubitus postures was 15–16% TLC_R, *i.e.* similar to the erect posture, but the associated superior to inferior ventilation ratio was 0.39–0.49. Thus, the effects of regional lung volume alone cannot determine the regional distribution of ventilation in lateral decubitus postures.

Chevrolet *et al.* (1979) have shown that the vertical distribution of ventilation in lateral decubitus postures is profoundly influenced by the pattern of respiratory muscle action. With a relaxed diaphragm inspired gas is distributed uniformly between lungs but with natural breathing or with enhanced motion of the diaphragm and abdomen, the lower lung is the better ventilated. Transdiaphragmatic pressure was not monitored in this study but the pattern of regional ventilation found in decubitus postures suggests inspiration was performed predominantly through diaphragmatic contraction.

Horizontal distribution of ventilation per unit alveolar volume
The absence of systematic horizontal gradients of $\dot{V}/V_A$ in the upright posture agrees with previous work (Newhouse *et al.*, 1968). In the supine posture, the horizontal distribution of inspired gas has been reported to be greater in cranial regions at FRC, uniform at 40% of vital capacity and reversed at 60% (Engel and Préfaut, 1981). In the present study at FRC the horizontal distribution of $\dot{V}/V_A$ was non-uniform, depended on the vertical height in the lung, and showed a sudden decrease near the diaphragm (see fig. 4). Decreased ventilation of caudal lung regions in man in the supine posture has been confirmed by other investigators under completely different conditions of measurement (Bynum *et al.*, 1976; Engel and Préfaut, 1981) and it may be related to the difference between closing capacity and FRC suggesting that airway closure contributes to the horizontal ventilation gradient (Engel and Préfaut, 1981). Nevertheless, the present study is the first in which counting has been done from the lateral aspect enabling horizontal strips of lung to be analysed at different vertical levels. In the prone posture $\dot{V}/V_A$ was higher near the diaphragm similar to findings at 60% VC in supine (Engel and Préfaut, 1981). In lateral decubitus postures $\dot{V}/V_A$ tended to be lower near the diaphragm but movement artifact cannot be excluded since it occurred in both upper and lower lung and therefore at two different lung volumes. There are uncertainties concerning the horizontal distribution of inspired gas in this posture with reports that it is uniform (Kaneko *et al.*, 1966) or greater in cranial regions (Demedts, 1978).

Distribution of $\dot{V}/V_A$ measured with $^{81}Kr^m/^{85}Kr^m$ and $^{85}Kr^m$ clearance
In general the distribution of $\dot{V}/V_A$ was similar with the two techniques. Slight disagreements occurred sometimes in horizontal postures near the diaphragm (zone of tidal diaphragmatic excursion artifact). Significant vertical gradients of $\dot{V}/V_A$ were detected with $^{85}Kr^m$ clearance analysis but not with $^{81}Kr^m/^{85}Kr^m$ in LLD and RLD (lower lung). In both cases $\dot{V}/V_A$ calculated from the steady-state data tended to increase from superior to inferior but did not achieve significance at the 5% level. Differences in horizontal $\dot{V}/V_A$ gradients between the two techniques in LLD (lower lung) and prone may be explained by the different sizes of lung regions chosen for analysis. Since larger regions were used for the clearance analysis one washout region incorporates 2 to 3 steady-state regions. Examination of fig. 4, for example, indicates that the volume weighted mean $\dot{V}/V_A$ of the caudal 2 to 3 regions

in LLD (lower lung) may not be very different from that for the cranial 2 to 3 regions. This emphasizes that in any study of linear topography the size of the detected gradient will depend on the number and size of regions analysed. When superior/inferior and cranial/caudal ratios were pooled there were no significant differences between the two techniques.

Determinants of regional pulmonary volume and ventilation

In 1966 Milic-Emili *et al.* proposed a model based on a lung with uniform mechanical properties, a vertical pleural pressure gradient determined by its weight and a uniform change in pleural pressure to explain the distribution of inspired gas during quasi-static breathing maneuvers. Models developed to explain the distribution of inspired gas using the time constant theory (Otis *et al.*, 1956; Pedley *et al.*, 1972) make similar assumptions. More recently it has been shown, through the effects of varying inspiratory flow rate (Sybrecht *et al.*, 1976) and selective use of different respiratory muscle groups (Chevrolet *et al.*, 1981; Dosman *et al.*, 1981; Roussos *et al.*, 1976a,b, 1977b), that the change in pleural pressure which occurs during inspiration may not be uniform over the surface of the lung in all circumstances. We have recently shown that the distribution of $\dot{V}/V_A$ is altered in patients with bilateral diaphragmatic paralysis in horizontal postures (Amis *et al.*, 1980).

Studies of the distribution of ventilation in anesthetized paralyzed subjects with mechanical ventilation (APMV) have also highlighted the role of the respiratory muscles, especially the diaphragm, in stabilizing and expanding the respiratory system. An increase in ventilation to non-dependent lung zones, persisting over a wide range of inspiratory flow rates, has been shown to occur during APMV, particularly in lateral decubitus postures (Rehder *et al.*, 1972, 1977, 1981; Chevrolet *et al.*, 1978). Although effects on dependent zone compliance and airway closure have been implicated (Bindslev *et al.*, 1981; Hedenstierna *et al.*, 1981), other evidence suggests an effect of altered patterns of expansion of the respiratory system (Rehder *et al.*, 1977; Jones *et al.*, 1979).

In lateral decubitus and supine postures the dependent part of the diaphragm has the greatest tidal excursion in non-paralyzed subjects. APMV results in a cephalad shift of the lower portion of the diaphragm, where abdominal pressure is greatest, and a shift of the maximum tidal excursion to the non-dependent part (Froese and Bryan, 1974). Chevrolet *et al.* (1978) trained conscious subjects to relax during intermittent positive presence ventilation (IPPB). In the lateral decubitus posture, the upper/lower ventilation ratio during IPPB was 0.95 compared with 0.61 during normal breathing, a result similar to studies in paralyzed subjects. It is of interest that APMV has less effect on the distribution of ventilation in the supine or seated postures (Rehder *et al.*, 1977) and no effect in the prone (suspended) position (Rehder *et al.*, 1978). These findings suggest similarities of expansion of the respiratory system during APMV in some postures but not in others.

The present study has demonstrated that during tidal breathing around FRC the distribution of ventilation is similar to that predicted by the model of Milic-

Emili *et al.* (1966) in the upright, supine and lateral decubitus positions but not in the prone position. In addition the large vertical gradients of $\dot{V}/V_A$ found in supine and lateral decubitus postures may reflect additional influences on the distribution of inspired gas. Since diaphragmatic movement is greater in dependent zones in these postures (Froese and Bryan, 1974) it is possible that effects of posture on patterns of movement of the respiratory muscles are determining a distribution of pleural pressure change during tidal breathing which influences the distribution of inspired gas.

Changes of posture have been shown to be associated with alterations in the pattern of tidal excursion of rib-cage and abdomen during quiet breathing (Vellody *et al.*, 1978) indicating that effective muscle action may be applied to move the rib-cage in some postures which is not applied in other postures. Potential mediators for this effect include alterations in abdominal compliance, with resultant changes in the efficiency with which the diaphragm expands the rib-cage (Goldman and Mead, 1973), and alterations in the resting position of various respiratory muscles on their intrinsic length–tension relationships.

In addition to effects on diaphragmatic movement posture has been shown to alter the relative activity of a number of other respiratory muscle groups including the serratus anterior (Reid *et al.*, 1976) scalene, sternocleidomastoid, parasternal intercostal muscles and abdominal oblique (Druz and Sharp, 1981). During quiet breathing normal human subjects show electromyographic evidence of tonic or phasic abdominal muscle contraction while standing and sitting but not while supine (Loring and Mead, 1982).

Finally, the model of Milic-Emili *et al.* (1966) does not explain the presence of horizontal (isogravity) gradients of lung volume or ventilation. Findings in the present study and those reported by other indicate that horizontal gradients of function are present in human subjects during tidal breathing in some horizontal postures. While changes of overall lung volume can change the gradients, elucidation of all the mechanisms associated with these distributions requires further investigation. It is apparent that the distribution of regional lung expansion and inspired gas during tidal breathing is determined by a number of complex influences whose interaction may be substantially modified by posture.

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