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Sequence of regional filling during a tidal breath in man

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GRANT, B. J. B., HAZEL A. JONES, AND J. M. B. HUGHES *Sequence of regional filling during a tidal breath in man.* J. Appl. Physiol. 37(2): 158–165. 1974.—Sequential portions of inspired gas were labeled with boluses of xenon 133 and inhaled at constant flow rates (0.1–1.0 $l \cdot s^{-1}$) from functional residual capacity. Twelve normal subjects were studied seated upright. The distribution of boluses injected at the mouth varied with flow rate; at 0.1 $l \cdot s^{-1}$ basal ventilation exceeded apical. At 0.4 $l \cdot s^{-1}$ base and apex ventilation was equal and at 1.0 $l \cdot s^{-1}$ apical ventilation exceeded basal. At comparable flow rates the distribution of boluses injected into the trachea was similar to those introduced at the mouth but when inhaled through 500 ml of added dead space, basal ventilation exceeded apical at all flow rates studied. Our results suggest that the distribution of inspired gas varies with flow rate over the first part of the tidal volume but becomes more independent of flow rate as inspiration continues. During normal tidal breathing the expired alveolar gas in the trachea and upper airways is distributed preferentially to the upper zones of the lungs on inspiration.

ventilation distribution; lung compliance; airway resistance; dead space; upper airways; trachea; regional gas exchange

THE ELASTIC PROPERTIES of the lung appear to play an important part in determining the distribution of inspired gas (12, 14). More recent studies have shown a different distribution at high inspiratory flow rates (9, 16), suggesting that there may be significant regional variations in airway resistance as well as parenchymal compliance. To what extent do these factors influence the distribution of various portions of the inspired tidal volume?

We have labeled different parts of the tidal volume with boluses of radioactive gas while subjects inhaled at constant flow rates over a range (0.1–1.0 $l \cdot s^{-1}$) found in normal breathing at rest. Up to the first one-third of tidal volume comprises dead space gas, of which half comes from the upper airways, common to both lungs. Although the distribution of dead space gas is important from the point of view of gas exchange (17) studies of the distribution of upper airways gas have not previously been reported.

METHODS

Twelve normal male volunteers were studied in the upright position. Details of physical characteristics, lung volumes, and overall airways resistance are given in Table 1.

We labeled different portions of the gas to be inspired, at FRC, by rapidly injecting 2.5 mCi of xenon 133 gas from a 5-ml syringe into one of three sites: *a*) into the trachea marking the early part of tidal volume, *b*) close to the mouth, or *c*) 500 ml from the mouth at the end of an added dead space to mark the gas inspired toward the end of a normal tidal volume. The tracheal boluses were injected through a catheter introduced into the trachea under fluoroscopic control. The radiopaque catheter was 40 cm long with an internal diameter of 1.2 mm. There were five to six side holes of 1 mm diameter near the tip which was sealed. Each subject sucked a 50-mg tablet of amethocaine hydrochloride 20 min before the insertion of the catheter and the upper airways were anesthetized with 2% lignocaine spray. The catheter was passed into the trachea and its tip positioned 3 or 4 cm above the carina. Two milliliters of 2% lignocaine solution were injected through the catheter for local analgesia. The subjects were free from discomfort and an additional dose of lignocaine was given through the catheter if necessary. The mouth boluses were injected through a needle with its tip in the center of tubing (internal diameter 2.15 cm) close to and directed toward the mouth. Boluses used to label later portions of the inspirate, toward the end of tidal volume, were injected through a needle at the end of a tube added to the mouthpiece tubing and of the same internal diameter. The needle for bolus injection into the added dead space was set in the center of the tubing with its shaft directed along the longitudinal axis. The end hole of the needle was closed off and the bolus delivered into the tubing as a narrow band through multiple side holes. The volume of tubing between this needle and the needle for mouth bolus injections was 500 ml.

Inspiratory flow was controlled by a regulating valve (10). The valve was accurate at settings of 0.1, 0.25, and 0.4 $l \cdot s^{-1}$ but at the high setting used (1 $l \cdot s^{-1}$), the control of airflow was less efficient. Without this valve it was difficult for our subjects to inspire at constant flow rates in a repeatable manner. Lateral mouth pressure was monitored by a differential pressure transducer (Sanborn 267B) coupled to a transducer converter (S.E. Labs, England). Subjects were given a visual display of mouth pressure to enable them to make light efforts (mouth pressure -15 cmH_2O) against the high valve resistance. At high flow rates, greater than 3 $l \cdot s^{-1}$, the regulating valve was not used. Instead, subjects inhaled as fast as possible through a Fleisch no. 4 pneumotachograph, coupled with a differential pressure transducer (Sanborn 270) and connected to the distal end of the mouthpiece or extension tubing. This arrangement allowed flow and volume from its integrated record to be monitored on an ultraviolet recorder (S.E. Labs) during tidal breathing.

TABLE . *Physical characteristics, lung volume (BTPS), and airways resistance*

Subj	Age, yr	Ht,	Wt, kg	FEV_1, liters	VC, liters	TLC, liters		
AF	29	175	72.9	3.9	4.8	6.9	1.5	0.16
MHe	39	185	72.7	4.8	5.7	8.1	0.8	0.24
PB	33	168	71.3	4.1	5.5	6.8	1.2	0.18
SS	29	176	70.7	4.1	5.1	6.3	0.8	0.30
HS	24	173	75.4	4.9	5.6	7.4	1.0	0.21
TC	25	188		5.6	7.0	9.5	1.0	0.19
MH	34	163	63.5	3.7	4.9	6.2	2.3	0.11
BG	27	179	72.3	4.1	6.1	8.1	1.0	0.17
RS	30	177	62.5	3.8	4.5	6.2	1.9	0.16
MG	29	178	67.6	4.5	5.1	6.0	0.5	0.46
HH	28	171	81.0	4.8	5.9	7.0	1.8	0.15
CMcG	27	180	67.7	5.3	6.0	7.5	0.8	0.26
NBP	38	187	76.0	5.2	6.1	8.1	1.4	0.16

FEV_1: forced expired volume in 1 s; VC: vital capacity; TLC total lung capacity; Raw: overall airways resistance at FRC, SGaw: specific airways conductance.

Before all measurements the subjects were asked to breathe normally. When a constant end expiratory level was achieved, they stopped breathing at end expiration and were connected through a tap to the regulating valve. The bolus was injected in one of the three sites described and the subjects inspired at a fixed flow rate. After at least 1 liter had been inhaled, the top was turned and subjects continued inspiration through a pneumotachograph until maximal lung inflation was reached. The lungs were then scanned from bottom to top with a pair of scintillation detectors placed anteriorly and posteriorly over each lung during a period of breath holding at total lung capacity for approximately 20 s. The scanning technique has been previously described (8). After bolus injections, 5 ml of gas were withdrawn through the catheter or needle before scanning the lungs to clear radioactivity from the lumen. The input to the regulating valve was from a spirometer. Flow rate was measured from its tracing on an ultraviolet recorder (S.E. Labs). Flow rates greater than 1 $l \cdot s^{-1}$, when boluses were inhaled from the trachea, were measured after 75 ml of inspiration since about half the anatomic dead space is situated between mouth and carina (13). Inspiratory capacity was computed as the sum of the volume change recorded from the spirometer and/or the integrated signal of the pneumotachograph.

At the end of each study the subjects rebreathed xenon 133 and air (concentration approximately 0.8 $mCi \cdot l^{-1}$) in closed circuit with a spirometer. After about 1 min, equilibration had been achieved and the lungs were scanned during a period of breath holding at TLC. All the scans of bolus distribution were related to the equilibration scan using the technique described by Ball et al. (4). To facilitate comparisons, these results were normalized so that 1.0 would be the value of ventilation per unit lung volume had distribution been uniform throughout the lung. The bottom of the lung was defined as the region where counts obtained during equilibration fell below 20% maximum. The values of ventilation per unit lung volumes for each region of right and left lungs were averaged.

The first six subjects in Table 1 were studied at flow rates of 0.1, 0.25, 0.4, and 1.0 $l \cdot s^{-1}$; the boluses were given at the mouth only. A comparison of boluses given at the mouth and through the trachea was made in five subjects (*HH, MH, RS, MG,* and *BG*). Four of the subjects (*HH, MH, RS,* and *BG*) were studied again on a later occasion to compare the distribution of boluses inhaled from the mouth and through the added dead space at 0.1, 0.4, and 1.0 $l \cdot s^{-1}$. In addition, these subjects and *CMcG* were give 1.2–1.8 mg atropine intravenously while lying horizontal to ensure uniform delivery of the drug to all lung regions. The distribution of boluses inhaled from the mouth at 0.1 $l \cdot s^{-1}$ was measured between 5 and 20 min later. The calculated radiation dosage to the lungs for each study was less than 150 mrad.

RESULTS

Figure 1 shows the mean results for 10 subjects of boluses inhaled from the mouth at 0.1, 0.4, and 1.0 $l \cdot s^{-1}$. The measured flow rate at the nominal value of 1.0 $l \cdot s^{-1}$ was 0.99 ± SE 0.04 $l \cdot s^{-1}$. At 0.1 and 0.4 $l \cdot s^{-1}$ the flow rate corresponded to its nominal value. The mean inspiratory capacity at 0.1 $l \cdot s^{-1}$ was 3.00 ± SE 0.15 liters, at 0.4 $l \cdot s^{-1}$ 3.12 ± SE 0.13 liters, and at 1.0 $l \cdot s^{-1}$ 3.00 ± SE 0.08 liters. Within any subject the largest difference of inspiratory capacity was 80 ml. Figure 1 shows how the distribution of gas varies with inspiratory flow rate. At 0.1 $l \cdot s^{-1}$ there is greater ventilation to the base than the apex. With increasing flow rate there is progressive reduction of ventilation to the basal regions and at 1.0 $l \cdot s^{-1}$ there is greater ventilation of the upper regions. The distribution of the bolus inhaled at 1.0 $l \cdot s^{-1}$ is somewhat similar to that obtained at maximal inspiratory flow rates (9). The first six subjects in Table 1 were also studied at 0.25 $l \cdot s^{-1}$ and the distribution was similar to that at 0.1 $l \cdot s^{-1}$. The majority of the change in distribution with flow rate occurs between 0.25 and 1.0 $l \cdot s^{-1}$ and predominately in the basal regions.

Distribution of tracheal gas. The distribution of boluses injected into the trachea was compared with that of boluses injected at the mouth at flow rates of 0.1 $l \cdot s^{-1}$ (Fig. 2) and 0.4 $l \cdot s^{-1}$ (Fig. 3). The mean inspiratory capacity at 0.1 $l \cdot s^{-1}$ was 2.80 ± SE 0.27 liters for mouth bolus injections

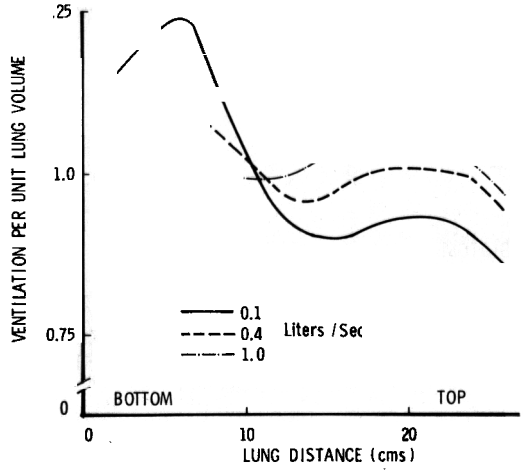

FIG. 1. Ventilation per unit lung volume plotted against lung distance for bolus injections at the mouth at 0.1, 0.4, and 1.0 $l \cdot s^{-1}$. Mean results for 10 subjects.

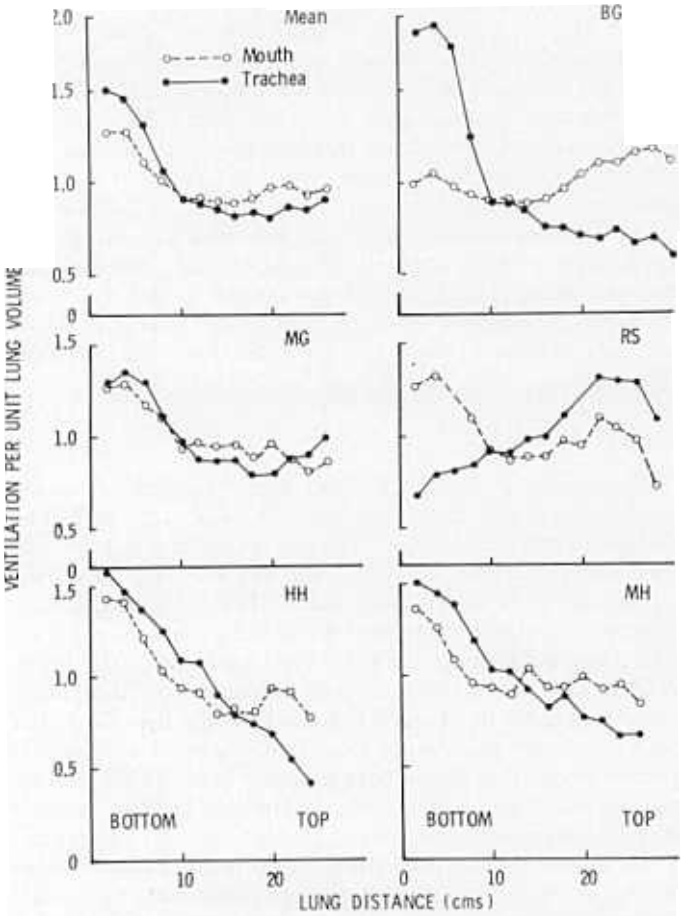

FIG. 2. Ventilation per unit lung volume at 0.1 $l \cdot s^{-1}$ for bolus injections at the mouth and through the tracheal catheter.

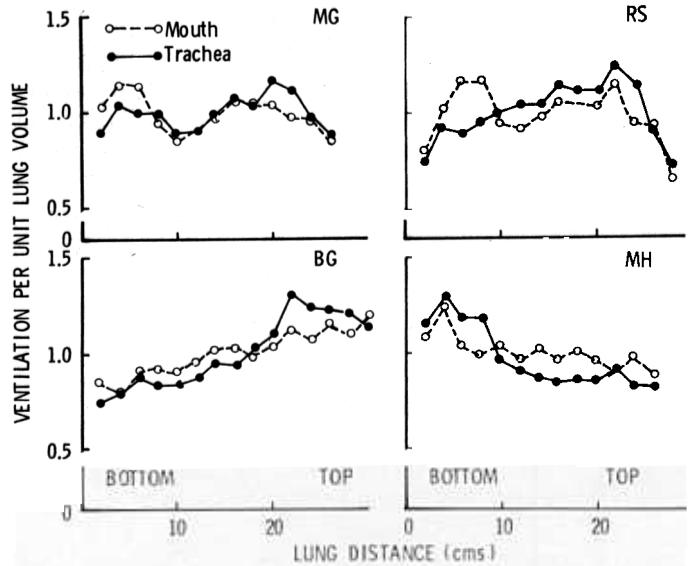

FIG. 3. Ventilation per unit volume at 0.4 $l \cdot s^{-1}$ for bolus injections at the mouth and through tracheal catheter.

and 2.87 ± SE 0.27 liters for tracheal bolus injections. The largest difference of inspiratory capacity within any one subject was 20 ml. The mean inspiratory capacity at 0.4 $l \cdot s^{-1}$ was 2.71 ± SE 0.27 liters for mouth bolus injections and 2.75 ± SE 0.26 liters for tracheal bolus injections. The largest difference of inspiratory capacity within any one subject was 54 ml. At 0.4 $l \cdot s^{-1}$ the distributions of mouth and tracheal boluses were similar but at 0.1 $l \cdot s^{-1}$ there were large differences in the pattern of distribution in two out of five subjects and the direction of the differences in *subjects BG* and *RS* varied.

Distribution of boluses from added dead space. For boluses inhaled through the added dead space at 0.1 $l \cdot s^{-1}$, ventilation per unit lung volume is more uniform compared with boluses inhaled from the mouth (Fig. 4). At 0.4 $l \cdot s^{-1}$ no significant differences were demonstrated between boluses inhaled from the mouth and through the added dead space (Fig. 5). The mean inspiratory capacity at 0.1 $l \cdot s^{-1}$ was 2.88 ± SE 0.29 liters for mouth bolus injections and 3.23 ± SE 0.19 liters for added dead space injections. The largest

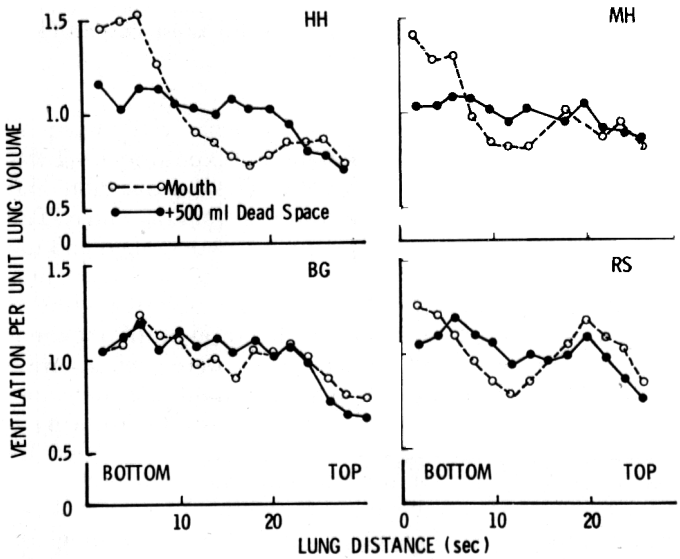

FIG. 4. Ventilation per unit lung volume at 0.1 $l \cdot s^{-1}$ for bolus injections at the mouth and into 500-ml added dead space.

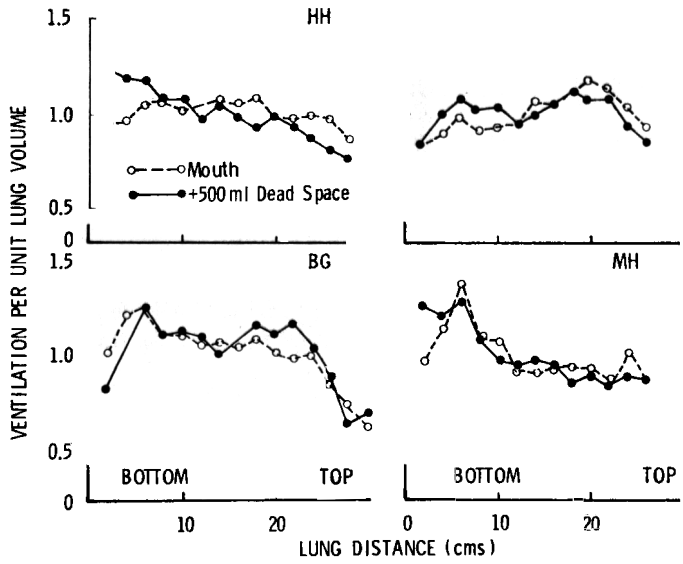

FIG. 5. Ventilation per unit lung volume at 0.4 $l \cdot s^{-1}$ for bolus injections at the mouth or into 500-ml added dead space.

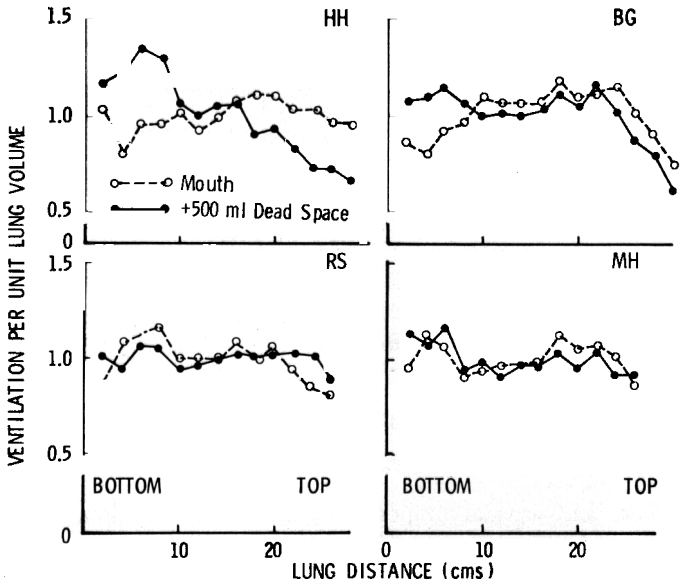

FIG. 6. Ventilation per unit lung volume at 1.0 $l \cdot s^{-1}$ for bolus injections at the mouth or into 500-ml added dead space.

difference of inspiratory capacity within any one subject was 34 ml. The mean inspiratory capacity at 0.4 $l \cdot s^{-1}$ was 3.17 ± SE 0.21 liters for mouth bolus injections and 3.04 ± SE 0.23 liters for added dead space injections. The largest difference of inspiratory capacity within any one subject was 19 ml.

The distributions obtained at 1.0 $l \cdot s^{-1}$ are shown in Fig. 6. The flow rate for mouth bolus injections was 1.04 ± SE 0.08 $l \cdot s^{-1}$ and mean inspiratory capacity was 3.03 ± SE 0.20 liters. The flow rate for added dead space injections was 0.95 ± SE 0.04 $l \cdot s^{-1}$ and mean inspiratory capacity was 2.95 ± SE 0.21 liters. The largest difference of inspiratory capacity within any one subject was 21 ml. In *subjects RS* and *MH* distribution of mouth boluses was fairly uniform and when boluses were inhaled through the added dead space, there was no demonstrable change. *Subjects HH* and *BG* showed a reduction in basal ventilation when boluses were inhaled from the mouth; when boluses were inhaled through the added dead space, basal ventilation increased significantly.

Effect of atropine. Atropine had no effect on the distribution of the bolus inhaled from the mouth at 0.1 $l \cdot s^{-1}$ in four out of five subjects studied (Fig. 7). The mean inspiratory capacity was 2.89 ± SE 0.22 liters before atropine and 3.29 ± SE 0.19 liters after atropine, the largest difference within any one subject being 19 ml. Two measurements of distribution were usually made after atropine injection but no difference between either measurement or the control scans was seen.

Effect of valve. The lateral mouth pressures developed during inspiration were displayed visually and subjects did not allow the pressure to fall below −15 cmH_2O. We have found the valve does not affect distribution provided light efforts are used (unpublished data). This is in agreement with the results of Martin et al. (11) who found that an added resistance of 183 $cmH_2O \cdot l \cdot s^{-1}$ had no effect on distribution of boluses inhaled slowly from residual volume. At 0.1 $l \cdot s^{-1}$ with 15 cmH_2O pressure drop across the valve, the external resistance is 150 $cmH_2O \cdot l \cdot s^{-1}$.

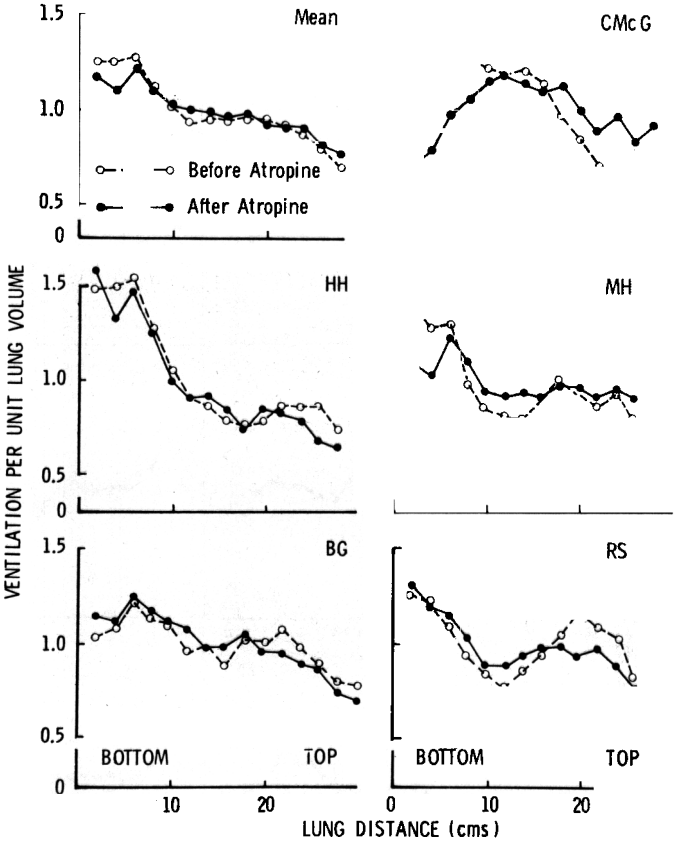

FIG. 7. Ventilation per unit lung volume at 0.1 $l \cdot s^{-1}$ for bolus injections at the mouth before and after atropine administration.

Effect of catheter. It is unlikely that the catheter provoked any changes in the subjects which would interfere with our results. Throughout the experiments all the subjects received adequate local anesthesia and there was little coughing or discomfort. The catheter provoked secretions which seemed to be mainly salivary and pharyngeal in origin. The distribution of boluses inhaled from the mouth compares favorably with other studies (see below).

DISCUSSION

Figure 8 summarizes the effect of flow rate on the distribution of different parts of the tidal volume inspired from FRC. For tracheal injections the distribution of boluses inhaled at 1.0 $l \cdot s^{-1}$ was not studied and the distribution at higher flow rates in the last seven subjects shown in Table 1 (*MH–NBP*) has been shown. Mean inspiratory capacity was 2.89 ± SE 0.24 liters and flow rate was 3.6 ± SE 0.3 $l \cdot s^{-1}$. The main points for discussion are *a*) the effect of flow rate on gas distribution, most marked for boluses given into the trachea or at the mouth, but almost absent for boluses inhaled from the 500-nl dead space, and *b*) the effect of bolus injection site at the same flow rate.

Factors affecting distribution of inspired gas. To achieve inspiratory flow ($\dot{V}$) a change in transpulmonary pressure (ΔP) is developed. This pressure is needed to overcome the elastic components of the lung primarily the alveoli, and the resistive elements of the lung, mainly the viscous resistance of the airways. Otis et al. (14) have expressed this relation-

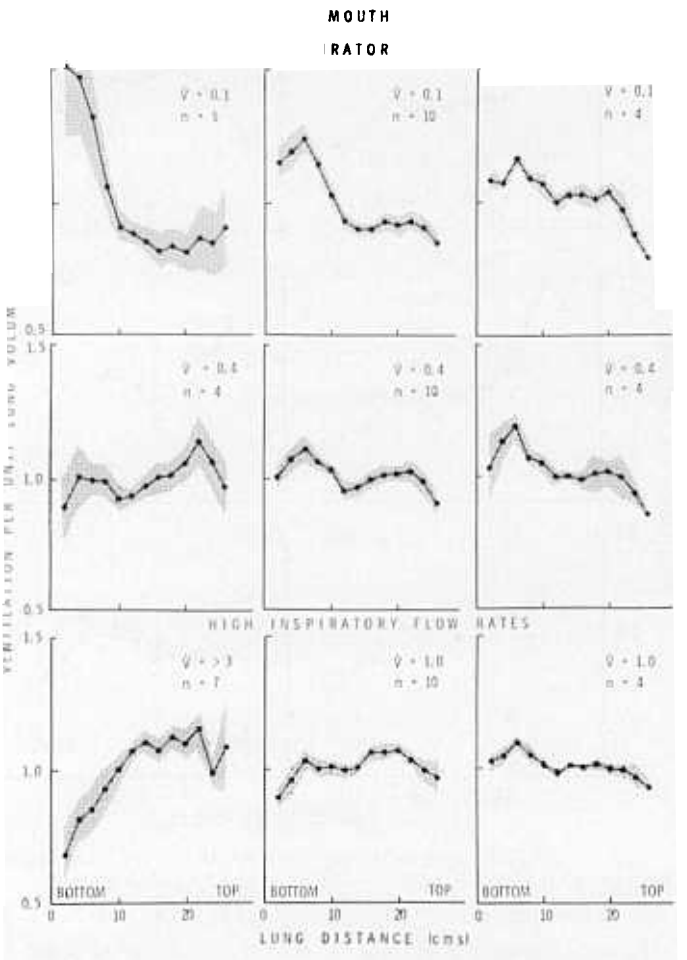

FIG. 8. Ventilation per unit lung volume at different flow rates and bolus injection sites (trachea, mouth, and +500-ml added dead space). Mean results with ±1 SE (shaded); n indicates the number of subjects in each graph, and $\dot{V}$, the flow rate in $l \cdot s^{-1}$.

ship in the following equation which, ignoring inertial effects, is

$$\Delta P = \Delta V/C + \dot{V}R \qquad (1)$$

When applied to bolus distribution, ΔV is the change in lung volume occurring while the bolus passes from its injection site to the site at which distribution is determined, ΔP is the change in transpulmonary pressure during this period, C is lung compliance, and R is lower airways resistance; $\Delta V/C$ is the elastic pressure drop and $\dot{V}R$ is the resistive pressure drop. Assuming that the volume (ΔV) between the site of bolus injection and the position in the airways where regional distribution is determined is the same for all lung regions

$$\frac{\Delta V}{\dot{V}} = \frac{\Delta Vr}{\dot{V}r} \qquad (2)$$

where ΔVr is the change in regional lung volume from the onset of inspiration until bolus distribution is determined and $\dot{V}r$ is the regional flow rate.

For any lung region (r), after substituting for ΔVr from *Eq. 2*, multiplying the second term ($\dot{V}r \cdot Rr$) by $\dot{V}/\dot{V}$ and rearranging, *eq. 1* becomes

$$\Delta Pr = \frac{\dot{V}r}{\dot{V}} (\Delta V/Cr + \dot{V}Rr) \qquad (3)$$

By subtracting *Eq. 3* from *Eq. 1* and rearranging

$$\frac{\dot{V}r}{\dot{V}} = \frac{(\Delta V/C + \dot{V}R) + (\Delta Pr - \Delta P)}{(\Delta V/Cr + \dot{V}Rr)} \qquad (4)$$

Assuming that ΔPr is the same for all lung regions (i.e., $\Delta Pr = \Delta P$) and converting $\dot{V}r/\dot{V}$ into the conventional units of ventilation per unit lung volume (Xr) by multiplying both sides of the equation by TLC/TLCr

$$Xr = \left[\frac{(\Delta V/C + \dot{V}R)}{(\Delta V/Cr + \dot{V}Rr)}\right] \frac{TLC}{TLC} \qquad (5)$$

where TLC is total lung capacity and TLCr is regional lung volume at total lung capacity. This expression shows that during a slow inspiration the distribution of a bolus can be explained on the basis of the elastic properties of the lung as $\dot{V}$ and so the resistive terms $\dot{V}R$ and $\dot{V}Rr$ are low. At FRC regional lung expansion increases with lung height and the greater basal ventilation is thought to be due to the relatively greater compliance of the lower zones (12). Because of the volume dependence of airways resistance (5) it is likely that the lung bases have a higher resistance than the upper zones. At high flow rates, $\dot{V}$ and the resistive terms $\dot{V}R$ and $\dot{V}Rr$ are increased; therefore distribution will be influenced to a greater extent by the resistive elements which will reduce basal ventilation.

Note that in *Eq. 5* ΔV and $\dot{V}$ do not by themselves have any influence on regional ventilation distribution; they merely contribute to the relative importance of C, Cr and R, Rr.

Effect of flow rate on mouth boluses. The effects of flow rate on the distribution of gas inhaled from the same lung volume could be explained by *1*) regional differences in driving pressure (i.e., $\Delta Pr \neq \Delta P$) with increasing flow rates and muscular effort, and *2*) a changing contribution of regional airway resistance and lung compliance to the regional impedence. Differences in ΔPr cannot be excluded but we tried to minimize muscular effort at different flow rates by having subjects monitor mouth pressure (Pmouth) so that -15 cmH_2O was not exceeded. At low flow rates (0.1 $l \cdot s^{-1}$) we have found that large efforts (Pmouth $>$ -50 cmH_2O) are needed before regional distribution changes. Measurements of changes of regional pleural pressure are difficult to make and the measurements in the literature (1, 6) are not strictly comparable to the situation we have studied.

The broad features of changes in the distribution of inspired gas can be explained on the basis of regional compliance and regional airway resistance (9, 12, 16). Pedley et al. (15) have extended the work of Otis et al. (14) and developed a mathematical model of ventilation in a two-lobe lung in the upright position taking into account the nonlinearity of the pressure-volume and pressure-flow relationships. They assumed that airways resistance was proportioned to local lung volume (i.e., a lower resistance in the more expanded upper lobe), and that there were no

differences in ΔPr. Their results in terms of apex-base differences are qualitatively similar to our findings and it is of interest that the major changes in distribution occurred at flow rates less than 1 $l \cdot s^{-1}$.

Changes in distribution with bolus injection site. At 0.4 $l \cdot s^{-1}$ and higher flow rates apical ventilation exceeded basal for tracheal injections (Fig. 8). This distribution was reversed when the bolus was inhaled through the 500-ml dead space and basal ventilation was greater than apical at all flow rates studied. With the added dead space the bolus reaches the lung at a higher lung volume and it is also more dispersed (see APPENDIX II). According to *Eq. 5*, ΔV is greater while resistance (R and Rr) and compliance (C and Cr) will be less because the bolus reaches the lung at a higher volume. Therefore gas distribution will be less dependent on flow rate and more influenced by the elastic elements of the lung.

Following this argument, bolus site should be of minor importance in determining the distribution of gas at 0.1 $l \cdot s^{-1}$ because lower airway resistance is almost negligible at this flow rate (19). The only major exception is that if ΔV is nearly zero, distribution may be resistive dependent even at this low flow rate (15). Only in one subject (*RS*, Fig. 2) was there any suggestion that this might be the case. Either the theory be assuming ΔPr is the same for all lung regions is incorrect or the marker gas in the lower trachea is not close enough to the site in the lung where bolus distribution is determined.

Figure 8 shows that distribution was not independent of injection site at 0.1 $l \cdot s^{-1}$ and various explanations will be considered. First, any effect of the inspiratory flow-regulating valve in causing transient variations in ΔPr can be discounted. Figure 9*A* compares the distribution of boli inhaled from the mouth in this study with those at comparable flow rates, but without a valve, from this laboratory (9) and elsewhere (7). We have made direct comparisons of distribution at 0.1 $l \cdot s^{-1}$ on and off the valve in several subjects and found no differences (unpublished data).

Second, a pure lung volume effect seems unlikely. In Fig. 9*B*, we have compared the distribution of boluses inhaled from the trachea and through the dead space with the distribution obtained by Dollfuss et al. (7) at 100 ml below and 700 ml above FRC. In the latter study flow rate was not controlled and boluses were given during a 5- to 10-s vital capacity maneuver starting from RV. For tracheal boluses (Fig. 9*B*), our results for regional ventilation are significantly different. To the extent that Dollfuss et al. (7) did not control flow rate they may have missed subtle variations in compliance distribution as lung volume changed. An alternative explanation is that the distribution of gas inspired at the onset of inspiration (tracheal boluses) is affected by phase differences in the force applied to lung regions by the chest wall muscles and diaphragm. This would lead to regional variations of ΔPr. Information on this point is difficult to obtain, as mentioned earlier. Daly and Bondurant (6) found a greater ΔP at the base compared with the upper zone of the lung. Bake et al. (3) found that tidal volume was not changed by varying the relative contributions of the rib cage and abdomen, but they did not use boluses and would have missed transients at the beginning of inspiration.

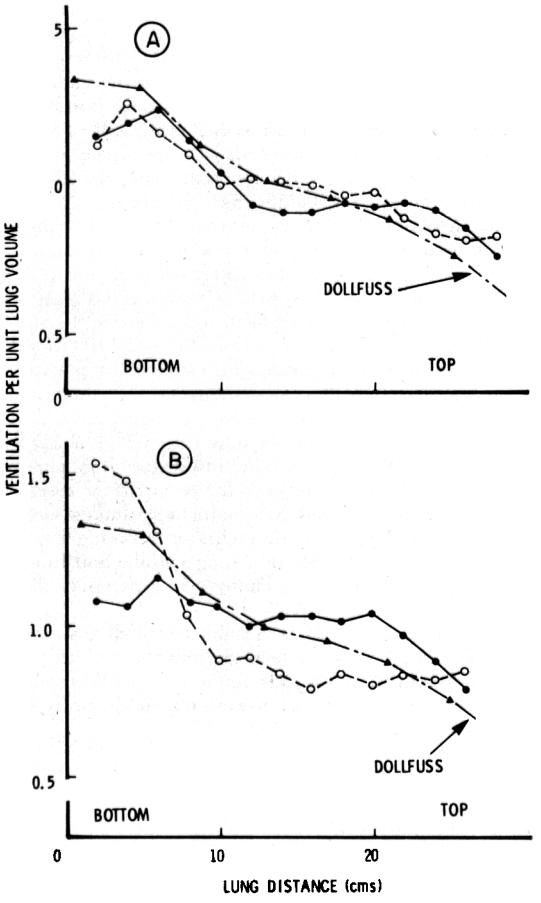

FIG. 9. A: distribution of ventilation for boluses inhaled from the mouth at FRC at 0.1 $l \cdot s^{-1}$ in this study (●——●), at 0.2 $l \cdot s^{-1}$ without a valve in a previous study (9) (○——○) and slowly (flow not specified) at 50% VC by Dollfuss et al. (7) (▲——▲). There are no significant differences. *B:* distribution of ventilation comparing Dollfuss' results for mouth boluses at 50% VC with this study for boluses inhaled from FRC at 0.1 $l \cdot s^{-1}$ given into the trachea (○——○) or 500-ml dead space (●——●).

Distribution of components of tidal volume during normal breathing. At a flow rate of 0.4 $l \cdot s^{-1}$ commonly achieved during normal tidal breathing, gas distribution varies with bolus injection site (Fig. 8). The tracheal bolus labels gas inhaled from the common dead space; this relatively hypoxic and hypercapnic gas (expired alveolar gas) is distributed to the upper zones. Since these regions are less well perfused and have high ventilation perfusion ratios (2) they are better equipped to take a higher proportion of dead space gas. Preferential distribution of dead space gas in this way may make alveolar P_{O_2} and P_{CO_2} more uniform throughout the lung than predicted previously (20).

APPENDIX I

Evaluation of Results

Many authors have expressed their results in ratios of apex/base difference but this is only valid when there is a linear relationship between ventilation per unit lung volume and lung distance. On many occasions, we have found that this is not the case. Clearly, if results are evaluated on this basis, not all the information available is utilized and this may lead to inaccuracies. This problem can be overcome by scanning over all the lung distance and comparing the mean results and standard errors in a group of subjects. Even this method may

shield significant differences within individual subjects because of considerable variation between subjects (see Fig. 2).

In the evaluation of our results, comparing the difference in regional distribution between two different maneuvers in the same subject, we have computed the average difference (d) of ventilation per unit lung volume, i.e., $\Sigma d/n$, where n is the number of regions. The signs have been ignored as we are not concerned with the direction of d only its magnitude. Since the mean of the two scans is 1, the average difference (α) is expressed as a percentage of the mean, $\alpha = \Sigma d/n \times 100\%$. During other experiments we have obtained two scans using the same maneuvers, scanning technique, and isotope dosages and computed αR to give a measure of repeatability where αR is the mean α of a pair of scans in a group of subjects. At 0.1 $l \cdot s^{-1}$ αR was 8.8% ± 3.4 SD for 16 pairs of scans obtained on separate occasions in 12 subjects. At maximal inspiratory flow rates αR was 7.2% ± 2.7 SD for 12 pairs of scans obtained on separate occasions in 9 subjects. For two scans obtained in one subject by different maneuvers, the results are judged significantly different if $\alpha > \alpha R + 2$ SD. For 0.1 $l \cdot s^{-1}$ $\alpha R + 2$ SD is 15.6% and for maximal inspiratory flow rates $\alpha R + 2$ SD is 12.6%. We have no repeatability data for other inspiratory flow rates but there appears to be little difference between the two extreme cases.

This empirical approach has two major advantages. Computation is simple and uses all the information without assuming any fixed relationship between ventilation per unit lung volume and lung distance. Because it is independent of any changes in pattern of distribution, this must be assessed visually.

The method of assessment of our results described above would tend to underestimate differences between scans as the majority of the control data was obtained in subjects unfamiliar with respiratory maneuvers. As a general rule, scans are usually significantly different if they only cross each other twice.

APPENDIX II

Bolus Spread in the Trachea

Measurements were made of the dispersal in the trachea of boluses injected at the mouth and through the 500-ml dead space. Inspirations were made at 0.1 and 1.0 $l \cdot s^{-1}$ with the tubing and flow-regulating valve already described. Radiation was detected with a gamma camera (Nuclear Enterprises (G.B.) Ltd., Edinburgh) with a shield used for thyroid scanning. Five milliliters of krypton 81^m gas produced from rubidium 81, was used as the radioactive marker gas, as it has a more suitable γ energy emission (190 keV) for the camera than xenon 133 (80 keV). The counting field in the neck was 12 x 8 cm and counts were recorded at 0.1- or 0.05-s intervals on a 100-channel multiscaler (Laben, Milan). Figure 10 plots these data for boluses inhaled from the mouth and through the 500-ml dead space at 1.0 $l \cdot s^{-1}$. From these curves mean transit times (MTT) were calculated from the formula $MTT = \Sigma c \cdot t / \Sigma c$, where c = radioactive counts for each time interval and t = time relative to zero time. For boluses inhaled through the 500-ml dead space, points on the descending limb of the curve were plotted on semilogarithmic paper and an extrapolation to background level made. The product of MTT and flow rate gives the volume of gas in which the bolus was distributed on its passage through the trachea. Values for MTT and dispersed volume are given in Table 2. Dispersion of the bolus as it passes through the trachea increases with mean flow rate and with distance from the site of injection. Experimental and theoretical studies by Taylor (18) have shown that dispersion in turbulent flow through pipes depends on *a*) tube length and *b*) a coefficient of diffusion, representing a combination of the velocity gradient over the tube cross section and molecular diffusion in a radial direction. For the same tube diameter and fluid density and viscosity, the diffusion coefficient will be greater at higher flow rates. Our results are in agreement qualitatively with those of Taylor (18), but since minor degrees of curvature increase the dispersion greatly a quantitative comparison between the complex geometry of the upper airways and straight or coiled pipes is not possible. The practical point is that the peak concentration of the bolus arrives at a time determined by the mean flow rate and the volume between the injection site and the trachea. Dispersion around this frame of reference means that up to 30% of the bolus inhaled at 1 $l \cdot s^{-1}$ through the added dead space arrives in the trachea relatively later and at a lung volume some 500 ml higher than expected in the absence of dispersion. At lower flows and for mouth boluses the effect of dispersion is much less (Table 2).

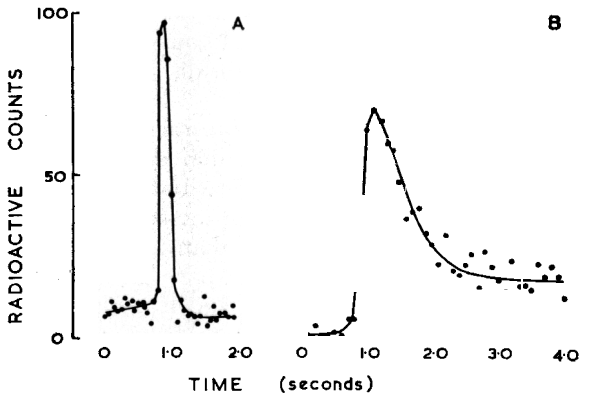

FIG. 10. Radioactive counts at 0.05-s (*A*) and 0.1-s (*B*) intervals plotted against time for boluses inhaled at 1.0 $l \cdot s^{-1}$ from FRC given at the mouth (*A*) or into the 500-ml dead space (*B*). Note the greater dispersal when the bolus is injected further from the trachea.

TABLE 2. *Mean transit time and dispersion volume for boluses of ^{81m}Kr inhaled from the mouth or through a 500-ml dead space*

Bolus Injection	Flow rate, $l \cdot s^{-1}$	MTT, s	Dispersion vol,
Mouth	0.1	0.76	76
Mouth	1.0	0.25	250
500-ml dead space	0.1	2.65	265
500-ml dead space	1.0	1.0	000

MTT: mean transit time.

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