Post-mortem lung volumes

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ABSTRACT   The volumes of 78 adult human lungs at necropsy after fixation with intrabronchial 10% formaldehyde at a transpulmonary pressure of 25 cm of water (VL) were similar to their total lung capacity (TLC) as assessed radiologically (Vx). Corrected for stature, VL and Vx did not increase with age in non-emphysematous lungs, nor did the ratio of VL to Vx (VL/Vx) change with age. VL and Vx relative to body length increased with emphysema, and the increase even occurred in lungs from men with trivial or equivocal amounts of emphysema. Thus alteration of the mechanical properties of the lung may precede the appearance of obvious emphysema. VL/Vx was not affected by the presence or severity of emphysema. The right lung formed 53% of VL with a range of 49–58% in apparently normal lungs. The amount of air in 13 human lungs at necropsy averaged 61% of TLC with a wide variation, indicating that this is not a useful point at which to measure lung dimensions. It is concluded that the volume of lungs fixed with formaldehyde at a transpulmonary pressure of 25 cmH_2O closely approximates to total lung capacity.

The volume to which the lung is inflated may affect the dimensions of structures within it, and it is therefore important to indicate this volume when making quantitative measurements of lung structure. During life the volumes can be expressed in terms of total lung capacity (TLC) or other lung volumes. Once the lung is removed from the thorax, however, referral lung volumes are unclear since it is not certain that an apparently fully inflated lung or a lung inflated to a large transpulmonary pressure will correspond to TLC in vivo. For example, with increasing age or with emphysema changes in the elastic properties of the lung might lead to unnaturally large volumes in excised lungs compared to TLC in life, which may be determined by limitation of chest wall expansion rather than lung stiffness. Various techniques have been used to inflate lungs at necropsy—for example, expansion to apparent full inflation (Moolten, 1935; Leopold and Gough, 1957), to an estimated 0·75 of full inflation (Weibel and Vidone, 1961), to the size of a thorax at necropsy (Hartroft and Macklin, 1943; McLean, 1956), or to standard transpulmonary pressures (Heard, 1960; Sweet *et al*, 1961; Wright, 1961). The last is perhaps the most commonly used, but since this is often accomplished by fluid fixation in a partially degassed lung, it is not clear to what lung volume in life lungs prepared in this way may

correspond. On the one hand, fluid will reduce surface forces and perhaps result in overdistension at conventional distending transpulmonary pressures of 20–30 cmH_2O, while on the other hand, fixatives may harden lung tissue and produce tissue shrinkage and thus smaller lung volumes.

This study was designed to examine the relation between lung volumes fixed at a standard transpulmonary pressure of 25 cmH_2O using 10% formaldehyde to lung volumes during life, and to examine the effect of age and emphysema on post-mortem lung volumes. It also gives information about the relative volumes of the right and left lung and of the volume of the lung at necropsy.

Materials and methods

The material was selected from 475 necropsies performed on subjects 20 years of age or older. As assessed from the necropsy report and from histological sections of the lung, all lungs with chronic lung disease, except for chronic bronchitis or emphysema or both, were rejected, as were lungs with acute lung disease thought severe enough to affect lung distensibility. The chief causes were pneumonia, oedema, and infarction. and the assessment was subjective and difficult since lungs are seldom free from any acute disease at necropsy. This exclusion was done without

knowledge of the lung volume data. All lungs were distended for at least 14 hours at a constant transpulmonary pressure of 25 cm of 10% formaldehyde. Lungs that were observed to leak at the time of inflation or that appeared inadequately inflated at the completion of the inflation process were excluded. A paper-mounted whole-lung section was prepared from the mid-sagittal slice (Gough and Wentworth, 1958). For comparison of ante-mortem radiological lung volumes with post-mortem lung volumes, patients who had good quality anteroposterior and lateral radiographs taken at a standard distance (3 m tube-to-film distance with a 15 cm air gap) and free from acute and chronic disease, were used. The criteria for exclusion and the interval between radiological examination and death have been described elsewhere (Thurlbeck and Simon, 1978). Seventy-eight cases were deemed adequate for study.

Lung volumes (VL) at the end of fixation were measured by water displacement. The amount of emphysema was assessed in the lungs from the paper-mounted whole-lung sections, using a standard panel of grading pictures (Thurlbeck *et al*, 1970a) in which the extent and severity of emphysema is graded on an arbitrary scale of 0 (no emphysema) to 100 (severest grade of emphysema recorded in the series). Each paper-mounted whole-lung section was scored by three observers (M S Dunnill, R C Ryder, and W M Thurlbeck) and the score assigned to the lung was the mean of the three observers. Lungs were then placed in one of nine emphysema groups depending on the score of the lung. Group 0 consisted of lungs with an average score of zero (that is, thought to be free from emphysema by each of the three observers) and the other groups are indicated in table 1. For analysis of some of the data, groups 2 and 3 and groups 4–8 were combined. The first category consists of lungs with mild but obvious emphysema and the latter consists of patients with moderate and severe emphysema. Examples of the varying grades of emphysema have been published elsewhere (Thurlbeck *et al*, 1970a).

Table 1 *Emphysema severity groups*

Group	Average emphysema score
0	0
1	1–5
2	6–15
3	16–25
4	26–35
5	36–45
6	46–55
7	56–65
8	> 65

Radiological total lung capacity was measured using the technique of Harris *et al* (1971) and this volume will be referred to subsequently as Vx. Before necropsy, some of the bodies were hoisted on a block and tackle with a loop placed under the arms and radiographs were taken in the PA and lateral position with a 3 m tube-to-film distance and a 15 cm air gap. Radiological lung volumes were then determined by the method of Harris *et al* (1971).

Results and discussion

VL (lung volume at the end of fixation in distension with formaldehyde at a transpulmonary pressure of 25 cmH$_2$O) and Vx (radiographically determined total lung capacity) are compared in fig 1. The relation is significant (r = +0·80, P<0·001) and
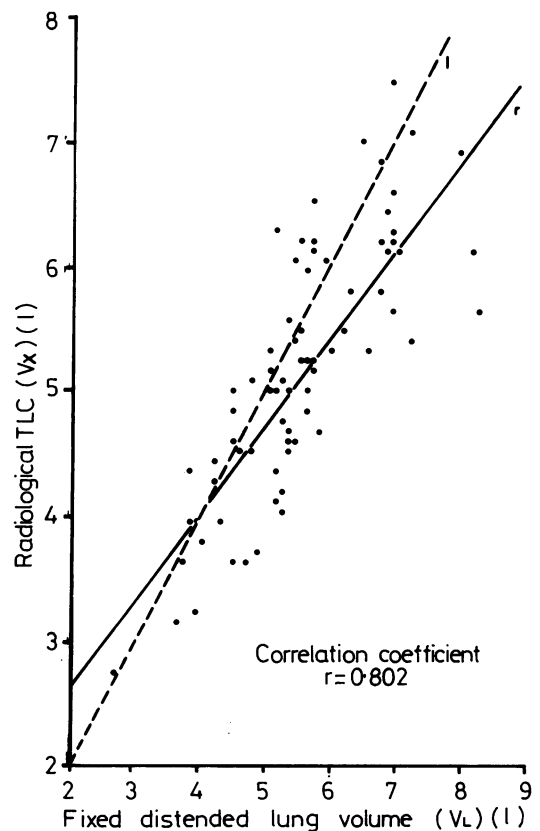

Fig 1 *Radiological lung volume (Vx) and volume of lung after fixation at a transpulmonary pressure of 25 cmH₂O (VL) are closely related (r = +0·80), but VL is usually larger than Vx. I is identity line and r regression line.*

it is apparent that for any lung VL is usually greater than Vx. This is to be expected since VL is the sum of TLC plus volume of tissue and Vx is a measurement of air within the lung and specifically excludes tissue. On the average, VL is 8% larger than Vx and is close to what would be expected from TLC plus volume of tissue, which is about 10–12·5% of VL (Weibel and Vidone, 1961).

The ratio of VL/Vx was the same in men as in women and was not related to age in either sex in patients without emphysema (r = −0·22, p > 0·05 in men; r = −0·04, p > 0·05 in women; r = +0·03, p > 0·05 for both sexes). The ratio of VL/Vx in various emphysema categories is shown in table 2 and VL/Vx is unrelated to the amount of emphysema in the lung (r = −0·11, p > 0·05 in men; r = −0·18, p > 0·05 in women; r = −0·15 for both sexes). The lack of relationship of the ratio to both emphysema and age is surprising since it is generally agreed that loss of recoil, especially at high lung volumes, is a characteristic feature of emphysema and age (Turner *et al*, 1968; Park *et al*, 1970; Boushy *et al*, 1971; Gibson *et al*, 1976; Knudson *et al*, 1977). Since the lungs were distended post-mortem at a pressure greater than can be generated in many old subjects or patients with emphysema, one would have anticipated that VL would be larger than TLC in life and that the ratio of VL/Vx would increase with age and emphysema. The data suggest that VL and TLC in life are closely related even in old and emphysematous subjects .

The effect of age on VL and Vx was also assessed in patients without emphysema (group 0) by comparing age with lung volumes normalised for stature by dividing by the cube of body length

(BL³), and this showed a similar, surprising result. Both VL/BL³ and Vx/BL³ were not statistically-related to age (table 3), whereas it might have been anticipated that VL/BL³ could increase with age, reflecting the decreased elastic recoil of the lungs. In other words, maximum distensibility as measured by Vx and VL did not increase with age. In contrast there is evidence for an increase in both VL and Vx with emphysema (fig 2). Interestingly, the increase in VL/BL³ and Vx/BL³ is significant (t = 2·43 and t = 2·70 respectively; p < 0·05) in the male patients in group 1 as well as in the other grades compared with those in
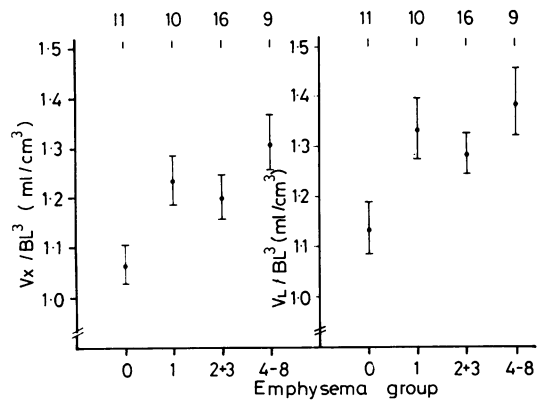

Fig 2 *Ratio of* Vx *and* VL *to cube of body length* (BL³) *increases significantly in emphysematous lungs in men. Numbers in each group are indicated above; and mean ±1 SE indicated. Group 0: no emphysema, group 1: "trace" or equivocal emphysema, groups 2 and 3: mild emphysema, and groups 4–8: moderate and severe emphysema.*

Table 2 *Number of subjects in each group and various relations of* VL *to* Vx *in patients with varying degrees of emphysema with comparisons of individual lung volumes*

	No emphysema	Group 1 (score 1–5)	Mild emphysema (score 6–25)	Moderate and severe emphysema (Score > 25)
No of patients	22	19	24	13
Age (yr)	51·5 ± 3·2	56·42 ± 3·06	59·25 ± 2·27	65·15 ± 3·56
VL/Vx	1·08 ± 0·03	1·08 ± 0·03	1·11 ± 0·02	1·04 ± 0·04
VRL/VLL	1·15 ± 0·02	1·13 ± 0·02	1·14 ± 0·02	1·11 ± 0·02

VRL = Volume of right lung. VLL = Volume of left lung. (± 1 standard error is indicated).

Table 3 *Correlation coefficients between age and* Vx *and* VL *corrected for stature in patients without emphysema*

Comparison	Men (11)	Women (11)	Men and women (22)
VL/BL³ and age	−0·306	−0·331	−0·305
Vx/BL³ and age	−0·143	−0·433	−0·291

group 0. (For V_L/BL^3, t=2·25, P<0·05 for patients with mild emphysema and t=2·99, P<0·01 for patients with moderate to severe emphysema. For V_X/BL^3, t=2·21, P<0·05 for mild emphysema and t=3·75, P<0·01 for patients with moderate and severe emphysema.) The increase in group 1 is surprising as the emphysema in these cases is equivocal or trivial (so-called "trace" emphysema). When such lungs are rescored they are randomly scored as either no emphysema or trace emphysema and there is considerable inter-observer variation as to the presence or absence of emphysema in these lungs (Ryder *et al*, 1969; Thurlbeck *et al*, 1969). It is apparent, however, that the maximum distensibility of the lungs of this group, as assessed by V_L and V_X, is abnormal. A similar trend is present in lungs from women but is not significant. It is difficult to account for the increase in V_L and V_X on the basis of the trivial or equivocal changes of alveolar wall destruction used as the criterion for the recognition of emphysema. Probably the scleroproteins throughout the lung have been altered, suggesting that the destructive lesions of emphysema and maximum lung distensibility have proceeded independently. Since the increase in maximum distensibility of the lungs occurs in lungs with equivocal emphysema and is about as pronounced as in those with obvious emphysema, changes in mechanical properties may precede the lesions of emphysema. Similar changes in V_L were indicated in a previous study (Thurlbeck, 1967) but this was observed in more obviously emphysematous lungs (corresponding to groups 2 and 3). In that paper it was argued that the observed increase in inter-alveolar wall distance seen in mildly emphysematous lungs was due to an increase in V_L because of an increase in maximum distensibility of the lungs, rather than destruction of alveolar tissue. Changes in elastic properties were also present in patients whose lungs showed mild emphysema in the present study. In these patients the emphysema is obvious and would be recognised by most observers, but once again the changes seem too trivial to account for obvious changes in elastic properties. The lesions are in general mild, and only a small proportion of the lung is affected by emphysema.

The changes in lung volume in patients with "trace" and "mild emphysema" may account for the changes in the mechanical properties of the lung described with age in living subjects. Patients with these grades of emphysema are older than subjects without emphysema (table 2). Since these grades of emphysema are unlikely to be detected in life, these subjects might well be included in clinical studies as non-emphysematous older subjects.

It could be that distension with 10% formaldehyde has an effect on the lung brought about by fixation that somehow parallels the change in maximum distensibility of the lung in life, although it is not easy to conceive of such a mechanism. Degassed lungs shrink 6·1% after fixation with 4% formaldehyde (Fukaya and Martin, 1969), but there is considerably more shrinkage when formalin steam is used to distend and fix lungs (Weibel and Vidone, 1961). It may be that liquid formalin fixes as distension proceeds, that coincidentally the fixed volume is close to V_X and TLC, and the volume of *air*-distended lung outside the chest may be larger than it situ. To explain the lack of difference between V_L and V_X in the conditions when air distended lung volume might be much larger outside the chest (in old age and emphysema), it would be necessary to postulate either more rapid fixation or greater shrinkage in these lungs.

The average ratio of volume of right to left lung (V_{RL}/V_{LL}) was 1·13 (standard deviation 0·10) and thus the right lung constituted 53·1% of V_L (table 2). The range of V_{RL}/V_{LL}, however, was 0·96–1·39 in lungs in group 0 and 1. Put another way, the right lung formed 49–58% of V_L in apparently normal lungs. This variation was larger than anticipated and suggested that it is unwise to extrapolate from one lung in morphometric studies. The amount of emphysema does not affect V_{RL}/V_{LL} suggesting that the amount of emphysema and its effect on lung volume is generally similar in both lungs.

Post-mortem radiological volume (V_{PM}) averaged 61% (range 39–77%) of V_X in the 13 patients in whom this volume was available. All of the patients had at least some emphysema, and there was no statistically significant relation (r=+0·39, P>0·05) between the amount of emphysema and the proportion that V_{PM} formed of V_X. Five of the patients were in group 1 and four were in group 2. Changes in functional residual capacity (FRC) and TLC are slight in patients with these amounts of emphysema (Thurlbeck *et al*, 1970b). Calculations from the age and sex of the patients and known changes in FRC and TLC with emphysema suggest that FRC would be about 67% of TLC in this group of patients as a whole. Thus values for V_{PM} are roughly similar to, but show a much wider variation than, predicted FRC. This wide variation makes this volume an unsuitable one at which to make stereological measurements.

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Correction

Tattersall, S F, *et al*. Lung distensibility and airway function in intermediate alpha$_1$-antitrypsin deficiency (Pi MZ). *Thorax*, 1979, **34**, 642.

The legend for fig 3 should read . . . (a) 12 Pi MZ and (b) 12 Pi M subjects.

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