

# Volume and time dependence of respiratory system mechanics in normal anaesthetized paralysed humans

E. D'Angelo\*, M. Tavola\*\*, J. Milic-Emili<sup>†</sup>

*Volume and time dependence of respiratory system mechanics in normal anaesthetized paralysed humans. E. D'Angelo, M. Tavola, J. Milic-Emili. ©ERS Journals Ltd 2000.*

**ABSTRACT:** The purpose of the present investigation was to assess the effect of large tidal volumes and mean lung volumes on the viscoelastic properties of the respiratory system in normal humans; and to verify if in this case the results could be satisfactorily described by a simple linear viscoelastic model of the respiratory system.

Twenty-eight subjects (7 females), aged 14–28 yrs, were studied before orthopaedic surgery on the lower limbs. None were obese, or had clinical evidence of cardiopulmonary disease. The interrupter conductance and the viscoelastic constants of the respiratory system were assessed using the rapid end-inspiratory airway occlusion method during mechanical ventilation with tidal volumes up to 3 L and applied end-expiratory pressures up to 23 cmH<sub>2</sub>O.

It was found that the interrupter conductance increased linearly with lung volume over a larger range than used previously; and the viscoelastic resistance and time constant did not change over the entire range of tidal volumes and end-expiratory pressures studied.

In conclusion, in normal anaesthetized, paralysed subjects a simple linear viscoelastic model satisfactorily described the viscoelastic behaviour of the respiratory system over the whole range of volume studied.

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The rapid end-inspiratory occlusion method has been used extensively to assess respiratory mechanics both under normal and pathological conditions. In normal anaesthetized, paralysed, mechanically ventilated humans, a large proportion of the total respiratory system resistance was found to reflect pressure dissipation within the pulmonary and chest wall tissues, *i.e.* tissue resistance, and could be satisfactorily explained by a simple linear viscoelastic model of the respiratory system [1–3]. While it has long been recognized that airway resistance decreases progressively with increasing lung volume [4], the effect of large volume changes on the resistance of lung and chest wall tissues has, as yet, not been investigated in normal humans. In patients with acute respiratory distress syndrome (ARDS), however, tissue resistance has been found to increase markedly by augmenting lung volume with application of positive end-expiratory pressure (PEEP) up to 15 cmH<sub>2</sub>O [5]. Under these conditions, the simple linear viscoelastic model of the respiratory system failed to fully describe the observed results of respiratory mechanics. In the absence of comparable studies in normal subjects, it remains to be seen whether this is the consequence of changes in tissue viscoelastic behavior due to lung injury or to excessive distension of the functional lung units.

The purpose of the present investigation was to assess in normal anaesthetized, paralysed humans the effect of large tidal volumes and mean lung volumes (PEEP up to 23 cmH<sub>2</sub>O) on the viscoelastic properties of the respiratory

system, and to verify if in these cases the results could still be satisfactorily described by a simple linear viscoelastic model [1–3].

## Materials and methods

Twenty-eight patients (7 females) undergoing general anaesthesia for orthopaedic surgery on the lower limbs were studied before the intervention. Their mean±SD age, weight, and height were 20±4 yrs (range: 14–28), 63.8±8.5 kg, and 172±9 cm, respectively. None were obese, or had a history or clinical evidence of cardiopulmonary disease. The investigation was approved by the institutional ethics committee and informed consent was given by each subject.

Thirty to forty minutes prior to anaesthesia, the subjects were premedicated with diazepam (0.2 mg·kg<sup>-1</sup> intramuscular). Anaesthesia and muscle relaxation were induced with intravenous thiopental sodium (5–7 mg·kg<sup>-1</sup>) and pancuronium bromide (0.1 mg·kg<sup>-1</sup>), respectively. The subjects were transtracheally intubated with a Mallinkrodt cuffed endotracheal tube (ET tube; 8–8.5 mm internal diameter (ID), 30–36 cm long) and mechanically ventilated in supine position (Siemens 900C Servoventilator, Berlin, Germany). Anaesthesia was maintained with isoflurane (0.8–1% in 60% N<sub>2</sub>O, balance O<sub>2</sub>) and muscle relaxation with additional aliquots of pancuronium bromide (0.04 mg·kg<sup>-1</sup>).

Flow ( $\dot{V}$ ) was measured with a heated pneumotachograph (Fleisch no. 2, Lausanne, Switzerland) connected to the breathing circuit *via* a cone and to a differential pressure transducer (Statham 270, Hewlett-Packard, Cupertino, CA, USA). The response of the pneumotachograph, which was calibrated with the experimental gas mixture, was linear over the experimental range of flows. Tracheal pressure ( $P_{tr}$ ) was measured with a pressure transducer (Hewlett-Packard 1290A) connected to a polyethylene catheter (1.5 mm ID, 50 cm long) with two or three side holes near its closed tip, which jutted 3–4 cm out from the ET tube into the trachea. Oesophageal pressure ( $P_{oes}$ ) was measured with a similar transducer connected to a thin walled latex balloon (8 cm long) filled with 0.5–1 mL of air through a polyethylene catheter (2 mm ID, 120 cm long). Transpulmonary pressure ( $P_L$ ) was obtained as  $P_{tr} - P_{oes}$ . With this recording system, pressure measurements were not affected by phase shift or alteration in amplitude up to 20 Hz. The above variables were recorded both on a four channel pen recorder (Hewlett-Packard 7754B; Hewlett Packard) and sampled at 200 Hz by a 12-bit analogue-to-digital converter to be stored on a personal computer for subsequent data analysis. Changes in lung volume were then obtained by numerical integration of the digitized flow signal.

Tests were carried out both with zero PEEP (ZEEP) and PEEP; the latter was applied by water immersion of a large tube connected to the expiratory port of the ventilator. Two levels of PEEP were used:  $9 \pm 2$  and  $23 \pm 2$  cmH<sub>2</sub>O. The changes in end-expiratory lung volume with PEEP were computed as the mean of the changes measured at the onset of its administration and after its removal. With the higher PEEP level, the changes in volume were 0.1–0.2 L larger after the removal of PEEP ( $p < 0.02$ ), whereas no significant difference was observed with the lower PEEP level.

The heart rate (range: 80–121 min<sup>-1</sup>), systemic arterial pressure (range: 100–124 mmHg) and oxygen saturation (>97%) were continuously monitored together with the electro-cardiogram. The end-tidal carbon dioxide tension in arterial blood ( $P_{a,CO_2}$ ) (Datex Normocap, Datex, Helsinki, Finland) was similar with ZEEP and the lower level of PEEP ( $37 \pm 2$  versus  $37 \pm 2$  mmHg) but was significantly lower ( $32 \pm 3$  mmHg;  $p < 0.02$ ) at the higher PEEP level.

#### Procedure and data analysis

The baseline ventilator settings consisted of a fixed tidal volume ( $V_T$  range: 0.47–0.76 L), and fixed respiratory frequency which ranged 10–13 min<sup>-1</sup> among subjects and was chosen to maintain normocapnia while breathing on ZEEP. The subjects were connected to the ventilator by a single length of standard low-compliance tubing (2 cm ID, 110 cm long), and the humidifier was removed. A normally open solenoid valve (closing time 10–15 ms), placed between the Y connector and the pneumotachograph, could be activated to produce an end-inspiratory pause (5–6 s in duration). Tests were accepted if 4–5 s after occluding the airways at end-inspiration,  $P_{tr}$  remained essentially constant, taking into account the small change expected from continuing gas exchange [6, 7]. Intrinsic PEEP was absent in all subjects, as flow became nil at end-expiration.

Two different procedures were carried out: 1) in 13 subjects on ZEEP, test breaths were performed by chan-

ging intermittently both  $\dot{V}'_I$ , from basal setting to values ranging 0.2–1.3 L·s<sup>-1</sup>, and  $V'_T$ , from basal setting to values ranging 0.44–3.3 L; and 2) in 15 subjects on ZEEP and two levels of PEEP, test breaths were performed by changing  $\dot{V}'_I$  intermittently from basal setting to values ranging 0.2–1.3 L·s<sup>-1</sup> while keeping  $V'_T$  constant ( $0.61 \pm 0.05$  L).

Respiratory mechanics was assessed by means of the rapid airway occlusion method, as previously described in detail [1, 2]. Briefly, end-inspiratory airway occlusions were followed by a rapid initial drop in  $P_{tr}$  ( $P_{max} - P_1$ ), and by a slow decay of both  $P_{tr}$  and  $P_{oes}$  ( $P_1 - P_{st}$ ) to an apparent plateau value. These plateau pressures, computed as the mean values recorded during the interval 4–5 s after the occlusion, were taken to represent the quasi-static endinspiratory elastic recoil pressure of the respiratory system ( $P_{st,rs}$ ) and chest wall ( $P_{st,w}$ ), respectively. The rapid pressure drops in  $P_{tr}$  divided by the flow preceding the occlusion yield the interrupter resistance of the respiratory system ( $R_{int,rs}$ ). The slow pressure drops in  $P_{tr}$  and  $P_{oes}$  divided by the flow preceding the occlusion yield the additional resistance of the respiratory system ( $\Delta R_{rs}$ ) and chest wall ( $\Delta R_w$ ), respectively. Viscoelastic parameters were computed by fitting the values of  $\Delta R$  measured for different durations of inflation ( $t_i$ ) and  $t_i$  with the function [1].

$$\Delta R = R_{visc} \times (1 - e^{-t_i/\tau_{visc}}) \quad (1)$$

where  $R_{visc}$  and  $\tau_{visc}$  are viscoelastic resistance and time constant, respectively, viscoelastic elastance ( $E_{visc}$ ) being  $R_{visc}/\tau_{visc}$ . Finally,  $P_{st,rs}$  and  $P_{st,w}$  were divided by the inflation volume to obtain the quasi-static elastances of the respiratory system ( $E_{st,rs}$ ) and chest wall ( $E_{st,w}$ ), respectively. For the lung the various parameters were computed as difference between the corresponding values pertaining to the respiratory system and chest wall.

Values are mean  $\pm$  SD, unless stated otherwise. Regression analysis was performed using the least-square method and analysis of variance. Comparison was made by means of a paired t-test, and  $p \leq 0.05$  was accepted as statistically significant.

## Results

### Effects of changes in tidal volume

Figure 1 shows the average static inflation  $V$ - $P$  curves of lung and chest wall obtained by changing intermittently  $V'_T$  during baseline ventilation on ZEEP in 13 subjects. Pressures are expressed as changes relative to the end-expiratory values on ZEEP. Since on ZEEP static end-expiratory  $P_{tr}$  was always nil, the sum of the lung and chest wall pressures at any given volume represents the pressure of the respiratory system. The inflation  $V$ - $P$  curve of the lung was S-shaped, the curvature at low  $\Delta V$  being mainly due to the fact that three of the 13 subjects exhibited a clearcut "knee" [8].

The interrupter resistance of the respiratory system did not change significantly with  $V'_T$ : hence, for a given subject and  $V'_T$ , the interrupter conductance ( $G_{int,rs} = 1/R_{int}$ ) could be represented by a single value. Figure 2 shows the relationship of  $G_{int,rs}$  to the inflation volumes at which  $G_{int,rs}$  was measured. A significant ( $p < 0.01$ ) linear

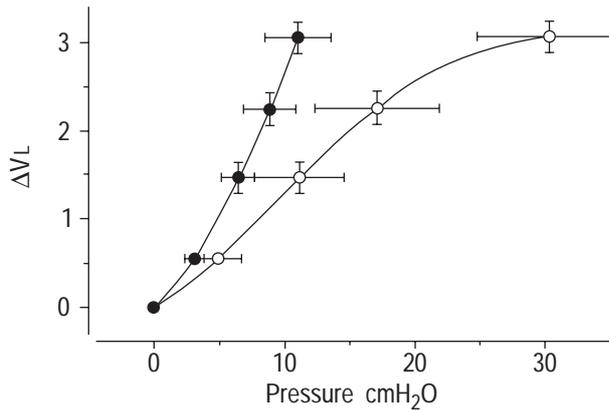


Fig. 1. – Relationship between lung volume above functional residual capacity ( $\Delta V$ ) and changes in quasi-static end-inspiratory pressure of lung ( $\circ$ ) and chest-wall ( $\bullet$ ) in 13 normal subjects. Bars: sd. Data pertaining to lung and chest wall were fitted by means of a fourth and second degree polynomial function, respectively.

relationship ( $G_{int,rs}=a+b\Delta V$ ) was obtained. The average values of the coefficients  $a$  and  $b$  of the 13 subjects were  $0.63\pm 0.17$  L  $\text{cmH}_2\text{O}^{-1}\cdot\text{s}^{-1}$  and  $0.12\pm 0.08$   $\text{cmH}_2\text{O}^{-1}\cdot\text{s}^{-1}$ , respectively. On an individual basis, that relationship was significant in all but three subjects in whom  $G_{int,rs}$  decreased at the highest inflation volume.

Figure 3 depicts the relationships of  $\Delta R_{rs}$ ,  $\Delta R_w$  and  $\Delta RL$  to  $t_i$  obtained in one subject. A unique function in the form of Equation 1 adequately described the data obtained with different  $V_T$  ( $p<0.001$ ), allowing computation of  $R_{visc}$  and  $\tau_{visc}$ . The average data from the 10 subjects are shown in figure 3, while their mean values of  $R_{visc}$  and  $\tau_{visc}$  for the respiratory system, lung, and chest wall are reported in table 1. In the three subjects who exhibited a clearcut "knee" in the static inflation  $V$ - $P$  curve of the lung, two distinct functions, both in the form of Equation 1, fitted the data of  $\Delta R_{rs}$  and  $\Delta RL$  versus  $t_i$  obtained with the lower and with the three larger  $V_T$ , whilst a unique function applied to  $\Delta R_w$  versus  $t_i$  (fig. 4).  $V_T$  dependency affected only  $R_{visc,rs}$  and  $R_{visc,L}$  ( $p<0.05$ ), whereas  $\tau_{visc}$  was independent of  $V_T$  (table 1).

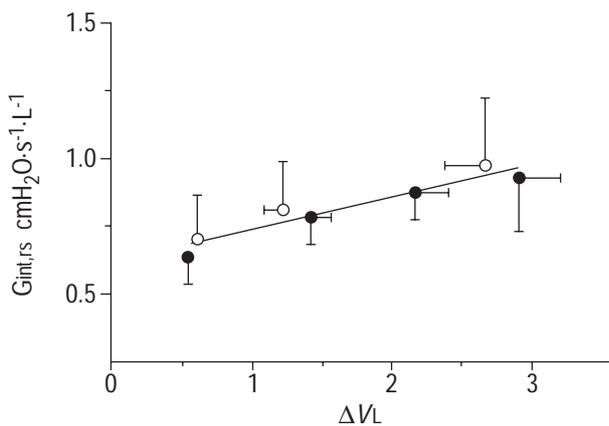


Fig. 2. – Relationship between interrupter conductance of respiratory system ( $G_{int,rs}$ ) and lung volume above functional residual capacity ( $\Delta V$ ) in 13 subjects ventilated on ZEEP with different tidal volumes ( $\bullet$ ), and in 15 subjects ventilated with a fixed tidal volume ( $0.61\pm 0.05$  L) on ZEEP and PEEP of 9 and 23  $\text{cmH}_2\text{O}$  ( $\circ$ ). Bars: sd. The regression equation was computed pooling the data of the 28 subjects,  $r=0.96$ ;  $p<0.001$ .

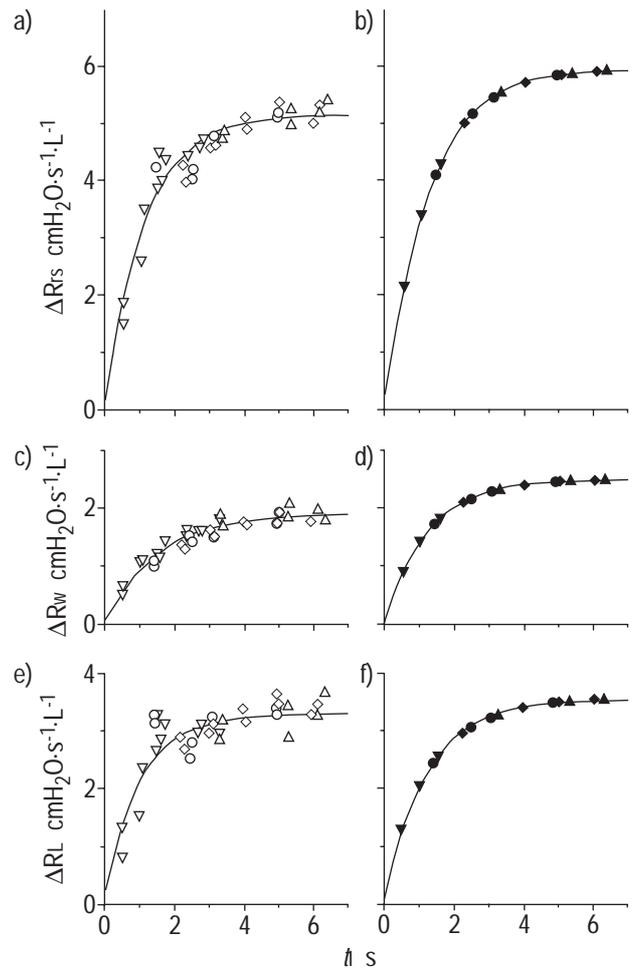


Fig. 3. – Relationships of additional resistance ( $\Delta R$ ) of a) the respiratory system (rs), b) chest wall (w) and c) lung (L) to duration of inspiration ( $t_i$ ) at different tidal volumes ( $\nabla$ : 0.54;  $\circ$ : 1.56;  $\diamond$ : 2.32;  $\triangle$ : 3.21;  $\blacktriangledown$ : 0.58;  $\bullet$ : 1.39;  $\blacklozenge$ : 2.22; and  $\blacktriangle$ : 3.09) obtained in experiments of figure 1. Representative subject (a, c and e) and average relationships of 10 subjects (b, d and f) the lung inflation  $P$ - $V$  curve of whom did not present a clearcut "knee" at low volumes.

#### Effects of changes in end-expiratory volume

In 15 subjects, application of a PEEP of 9 and 23  $\text{cmH}_2\text{O}$  increased the end-expiratory lung volume by  $0.61\pm 0.10$  and  $2.08\pm 0.29$  L, respectively. Figure 5 shows the average quasi-static  $V$ - $P$  curves of lung and chest wall obtained with fixed  $V_T$  ( $0.61\pm 0.05$  L) on ZEEP and the two levels of PEEP. The average values of quasi-static elastance of respiratory system ( $E_{st,rs}$ ), lung ( $E_{st,L}$ ), and chest wall ( $E_{st,w}$ ) over the fixed  $V_T$  at different levels of PEEP are reported in table 2. While  $E_{st,w}$  increased with increasing PEEP,  $E_{st,rs}$  and  $E_{st,L}$  decreased with the lower PEEP, but increased with the higher PEEP.

Both on ZEEP and PEEP,  $R_{int,rs}$  was independent of  $V_T$ . With PEEP  $R_{int,rs}$  decreased relative to ZEEP (table 2). Figure 2 depicts the relationship of  $G_{int,rs}$  to the end-inspiratory lung volume at which conductance was measured. A significant ( $p<0.01$ ) linear relationship ( $G_{int,rs}=a+b\Delta V$ ) was obtained. The average values of the coefficients  $a$  ( $0.68\pm 0.30$  L· $\text{cmH}_2\text{O}^{-1}\cdot\text{s}^{-1}$ ) and  $b$  ( $0.14\pm 0.10$   $\text{cmH}_2\text{O}^{-1}\cdot\text{s}^{-1}$ ) were similar to those obtained in the 13

Table 1. – Viscoelastic resistance ( $R_{\text{visc}}$ ) and time constant ( $\tau_{\text{visc}}$ ) of respiratory system, lung, and chest wall in anaesthetized, paralysed subjects ventilated with various tidal volumes ( $V_T$ ) at zero end-expiratory pressure

Subjects n	$V_T$ L	Respiratory system		Lung		Chest wall	
		$R_{\text{visc}}$ $\text{cmH}_2\text{O}\cdot\text{s}\cdot\text{L}^{-1}$	$\tau_{\text{visc}}$ s	$R_{\text{visc}}$ $\text{cmH}_2\text{O}\cdot\text{s}\cdot\text{L}^{-1}$	$\tau_{\text{visc}}$ s	$R_{\text{visc}}$ $\text{cmH}_2\text{O}\cdot\text{s}\cdot\text{L}^{-1}$	$\tau_{\text{visc}}$ s
10	0.47–3.10	$5.97\pm 0.80$	$1.29\pm 0.38$	$3.56\pm 0.53$	$1.37\pm 0.49$	$2.51\pm 0.85$	$1.20\pm 0.23$
3	0.48–0.56	$6.97\pm 0.48$	$1.58\pm 0.19$	$4.35\pm 0.24$	$1.54\pm 0.38$	$2.65\pm 0.33$	$1.36\pm 0.15$
3	0.80–3.13	$6.04\pm 0.30^*$	$1.67\pm 0.32$	$3.63\pm 0.20^*$	$1.65\pm 0.41$	$2.40\pm 0.31$	$1.36\pm 0.09$

Values presented as mean $\pm$ SD and refer to 10 subjects in whom  $R_{\text{visc}}$  was independent of  $V_T$  and to three subjects in whom this was in part not the case. \*: different from lower  $V_T$  ( $p<0.05$ ).

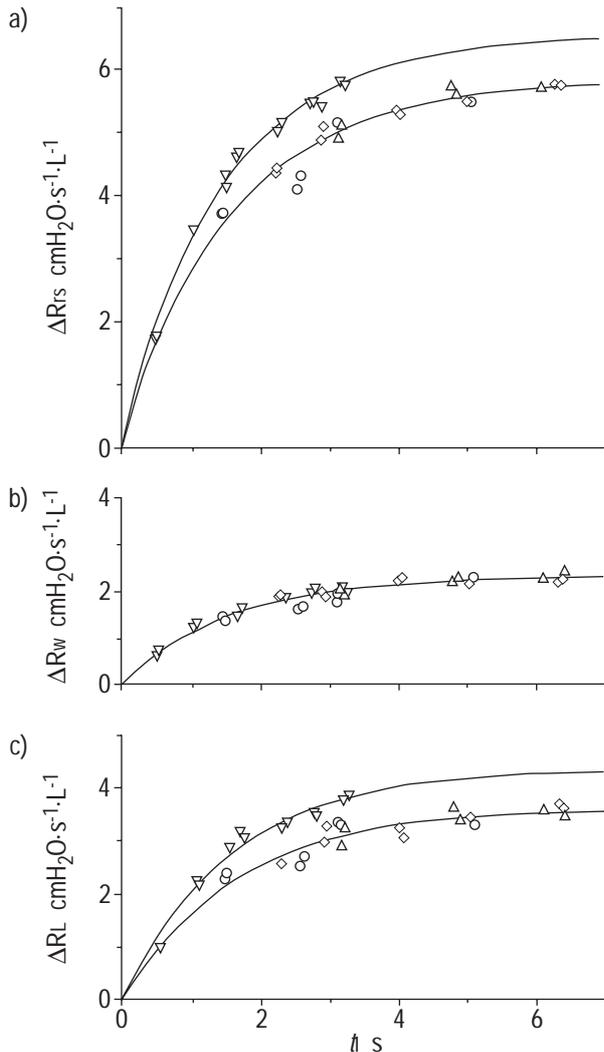


Fig. 4. – Relationships of additional resistance ( $\Delta R$ ) of a) respiratory system (rs), b) chest wall (w) and lung (L), to duration of inspiration ( $t$ ) obtained in one subject ventilated on ZEEP with various tidal volumes ( $V_T$ ;  $\nabla$ : 0.54;  $\circ$ : 1.56;  $\diamond$ : 2.32; and  $\triangle$ : 3.21. The lung inflation  $P$ - $V$  curve of this subject showed a clearcut "knee" at low volumes. Data pertaining to the respiratory system and lung obtained with the lowest  $V_T$  ( $\nabla$ ) and with the other three  $V_T$  were fitted separately to Equation 1 to derive  $R_{\text{visc}}$  and  $\tau_{\text{visc}}$  (mean $\pm$ SE), whereas all data pertaining to chest wall could be fitted to a unique function. For both respiratory system and lung,  $\tau_{\text{visc}}$  did not differ significantly with inflation volume, whereas  $R_{\text{visc}}$  did, ( $R_{\text{visc}}=6.42\pm 0.18$  and  $5.7\pm 0.08$  and  $\tau_{\text{visc}}=1.48\pm 0.09$  and  $1.59\pm 0.09$  for  $\Delta R_{\text{rs}}$ ,  $R_{\text{visc}}=2.18\pm 0.04$  for  $\Delta R_w$ , and  $R_{\text{visc}}=4.22\pm 0.21$  and  $3.48\pm 0.08$  for  $\Delta R_L$ ).

subjects ventilated on ZEEP with different  $V_T$ . On an individual basis, that relationship was significant in all but four subjects. In the latter individuals  $G_{\text{int,rs}}$  increased between ZEEP and the lower PEEP, but decreased with the larger PEEP.

Figure 6 depicts the relationships of  $\Delta R_{\text{rs}}$ ,  $\Delta R_w$  and  $\Delta R_L$  to  $t$  obtained on ZEEP and PEEP in a representative subject and the average relationships for the 15 individuals. In all subjects these relationships closely fitted Equation 1 ( $p<0.001$ ). Table 3 reports the average values of  $R_{\text{visc}}$  and  $\tau_{\text{visc}}$  for the respiratory system, lung, and chest wall obtained at different levels of PEEP. Both  $R_{\text{visc}}$  and  $\tau_{\text{visc}}$  of the respiratory system, lung, and chest wall did not change significantly with the changes in lung volume due to PEEP. The average values of the viscoelastic constants (table 3) were similar to those obtained in the experiments with different  $V_T$  on ZEEP (table 1).

## Discussion

The main new finding of the present study is that in normal anaesthetized, paralysed subjects the linear viscoelastic model originally proposed by MOUNT [9] explains satisfactorily the stress adaptation behaviour of the lung and chest wall over a wide range of inflation volumes (up to 3 L) and pressures (up to 30  $\text{cmH}_2\text{O}$ ).

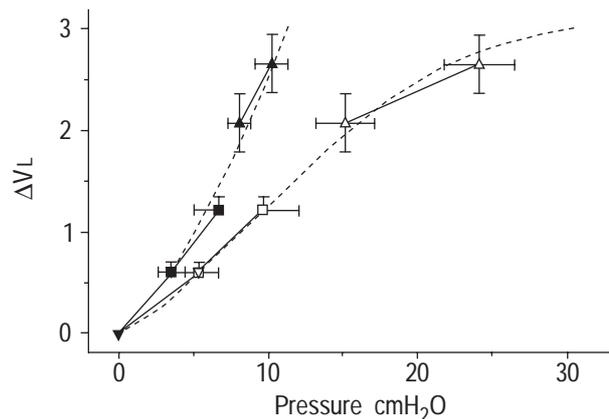


Fig. 5. – Relationships between lung volume above functional residual capacity ( $\Delta V$ ) and corresponding changes in quasi-static pressure of lung ( $\circ$ ) and chest wall ( $\bullet$ ) measured at the end-expiratory and end-inspiratory volume in 15 normal subjects ventilated with a fixed tidal volume ( $0.61\pm 0.05$  L) 0 ( $\nabla$ ,  $\blacktriangledown$ ), 9 ( $\square$ ,  $\blacksquare$ ) and 23 ( $\triangle$ ,  $\blacktriangle$ )  $\text{cmH}_2\text{O}$  end-expiratory pressure. Dotted lines are corresponding relationships from figure 1. Bars: sd.

Table 2. – Quasi-static elastance ( $E_{st}$ ) of respiratory system (rs), lung (L), and chest wall (w), and of interrupter resistance of respiratory system ( $R_{int,rs}$ ) in 15 anaesthetized, paralysed subjects ventilated with fixed tidal volume ( $0.61 \pm 0.05$  L) at different levels of peak end-expiratory pressure (PEEP)

PEEP cmH <sub>2</sub> O	$E_{st,rs}$ cmH <sub>2</sub> O·L <sup>-1</sup>	$E_{st,L}$ cmH <sub>2</sub> O·L <sup>-1</sup>	$E_{st,w}$ cmH <sub>2</sub> O·L <sup>-1</sup>	$R_{int,rs}$ cmH <sub>2</sub> O·s <sup>-1</sup> ·L <sup>-1</sup>
0	14.6±3.3	8.7±2.4	5.8±2.0	1.4±0.3
9±2	12.2±3.8*	7.2±2.5 <sup>†</sup>	5.0±2.0*	1.3±0.3 <sup>‡</sup>
23±2	18.9±3.4*	15.3±2.6*	3.6±1.3*	1.1±0.2*

Values are presented as mean±SD. \*: p<0.001; <sup>†</sup>: p<0.01; <sup>‡</sup>: p<0.05, compared with PEEP=0.

### Quasi-static volume-pressure curves

As expected, the slope of the  $V$ - $P$  curves of the chest wall increased progressively with increasing lung volume, whilst the  $V$ - $P$  curves of the lungs were S-shaped (fig. 1). Except in three subjects, the lower inflection point ("knee") was slight, indicating that there was little or no small airway closure and/or atelectasis [10, 11]. This is supported by the fact that at the same lung volume the end-expiratory  $P_L$  on PEEP of 9 cmH<sub>2</sub>O was not significantly lower than the end-inspiratory  $P_L$  on ZEEP ( $5.3 \pm 1.3$  versus  $5.7 \pm 1.4$  cmH<sub>2</sub>O). In contrast, in a previous investigation [12], these pressures were significant-

tly larger on ZEEP ( $\Delta P_L = 0.6 \pm 0.3$  cmH<sub>2</sub>O), suggesting that PEEP had resulted in larger alveolar recruitment or larger stress relaxation [13]. However, likely because of stress relaxation, both end-expiratory  $P_L$  and  $P_w$  on PEEP of 23 cmH<sub>2</sub>O were substantially lower than the values expected on the basis of the inflation  $V$ - $P$  curves (fig. 5).

On ZEEP, the values of  $E_{st,rs}$ ,  $E_{st,L}$  and  $E_{st,w}$  obtained at baseline  $V_T$  (table 2) were essentially the same as those previously found in similar experiments on normal subjects [2] in which  $E_{st,L}$  and  $E_{st,w}$  amounted to  $8.2 \pm 1.7$  and  $6.3 \pm 1.1$  cmH<sub>2</sub>O·L<sup>-1</sup>. With PEEP of 9 cmH<sub>2</sub>O there was a significant decrease in  $E_{st,rs}$ ,  $E_{st,L}$  and  $E_{st,w}$  (table 2), in line with previous results obtained with PEEP of 8 and 10 cmH<sub>2</sub>O [12, 14]. With PEEP of 23 cmH<sub>2</sub>O both  $E_{st,rs}$  and  $E_{st,L}$  increased significantly relative to corresponding values on ZEEP, while  $E_{st,w}$  was markedly decreased (table 2). There are no previous data for such high levels of PEEP in normal subjects. The changes in  $E_{st,L}$  and  $E_{st,w}$  with PEEP in table 2 reflect the corresponding quasi-static  $V$ - $P$  curves (fig. 5).

SHARP *et al.* [15] were the only ones to assess quasi-static  $V$ - $P$  curves of normal anaesthetized, paralysed subjects over a large volume range as in the present study. While the  $V$ - $P$  curves of the chest wall were similar to those in figure 1, the  $V$ - $P$  of the lung were linear and shifted to the left. However, in the study of SHARP *et al.* [15] the lungs were held inflated for 10 s at a tracheal pressure of 40 cmH<sub>2</sub>O before measurements: this should reduce atelectasis and small airway closure, which are thought to contribute to the "knee" at low inflation volumes [8]. The subjects were also older in the study of SHARP *et al.* (mean age: 47 yrs) and taller (mean height: 177 cm): owing to the age related loss of lung elastic recoil, the upper inflection point in the  $P$ - $V$  curve should be less marked than in young subjects [16], while the greater TLC and lower EL in taller individuals should allow accommodation of greater absolute volumes before reaching the upper inflection point of the  $P$ - $V$  curve. Also in the study of SHARP *et al.* [15]  $V$ - $P$  curves were obtained by a sequence of stepwise lung inflations that lasted ~30 s: during this time there could be an artefactual decrease in lung volume due to continuing gas exchange, which was minimized in the present study because the  $P$ - $V$  curves were constructed by inflating intermittently the lungs with different volumes.

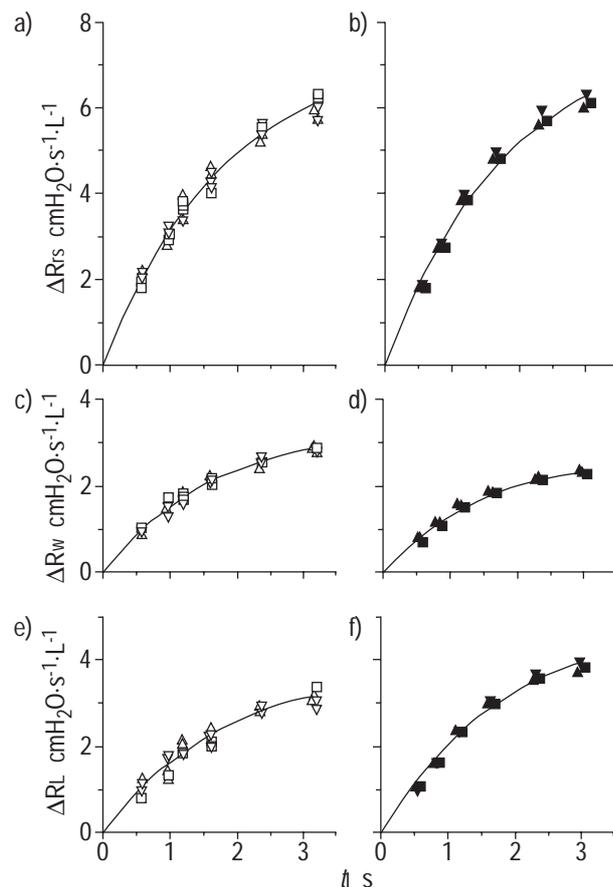


Fig. 6. – Relationships of additional resistance ( $\Delta R$ ) of a, b) respiratory system (rs), c, d) chest wall (w) and e, f) lung (L), to duration of inspiration ( $t$ ) obtained in the same experiments as figure 4. Representative subject and average relationships of 15 subjects. Positive end-expiratory pressure values are:  $\Delta$  and  $\blacktriangle$ : 23 cmH<sub>2</sub>O;  $\square$  and  $\blacksquare$ : 9 cmH<sub>2</sub>O;  $\nabla$  and  $\blacktriangledown$ : 0 cmH<sub>2</sub>O.

### Interrupter resistance

$R_{int,rs}$  did not change with  $V_T$ , independent of the end-inspiratory lung volume. This is in line with the findings of JONSON *et al.* [3] and D'ANGELO *et al.* [12], but contrasts

Table 3. – Viscoelastic resistance ( $R_{\text{visc}}$ ) and time constant ( $\tau_{\text{visc}}$ ) of respiratory system, lung, and chest wall in 15 anaesthetized, paralysed subjects ventilated with fixed tidal volume ( $0.61 \pm 0.05$  L) at different levels of positive end-expiratory pressure (PEEP)

PEEP cmH <sub>2</sub> O	Respiratory system		Lung		Chest wall	
	$R_{\text{visc}}$ cmH <sub>2</sub> O·s·L <sup>-1</sup>	$\tau_{\text{visc}}$ s	$R_{\text{visc}}$ cmH <sub>2</sub> O·s·L <sup>-1</sup>	$\tau_{\text{visc}}$ s	$R_{\text{visc}}$ cmH <sub>2</sub> O·s·L <sup>-1</sup>	$\tau_{\text{visc}}$ s
0	6.43±2.83	1.31±0.36	4.26±2.51	1.43±0.70	2.46±1.05	1.25±0.37
9±2	6.33±3.05	1.32±0.21	4.06±2.58	1.38±0.55	2.58±0.99	1.24±0.33
23±2	6.17±3.16	1.34±0.21	3.72±2.07	1.39±0.59	2.67±0.85	1.30±0.36
Overall	6.28±2.75	1.32±0.24	4.01±2.29	1.39±0.50	2.57±0.93	1.27±0.31

Values are presented as mean±SD.

with earlier results [1, 2] showing a significant, though small, increase of  $R_{\text{int,rs}}$  with increasing  $V'$ . This discrepancy is probably due to methodological differences: in the earlier study a subtraction technique was used to correct for the resistance of the endotracheal (ET) tube, whilst in the other studies tracheal pressure was directly measured, and it has been shown that the ET tube resistance *in situ* may differ from that *in vitro* [17].

The present study provides for the first time the relationship of  $G_{\text{int,rs}}$  with lung volume ( $\Delta V$ ) up to 3 L above functional residual capacity (FRC). This relationship was linear and independent of the way  $\Delta V$  were obtained (fig. 2). However, in three of the subjects studied with increasing  $V_T$  and in four of the subjects studied at various levels of PEEP with fixed  $V_T$ ,  $G_{\text{int,rs}}$  actually decreased at the highest  $\Delta V$ . The nature of this phenomenon, which has also been observed in some patients with ARDS [14, 18], is unknown; it is possible that at high lung volumes the longitudinal stretching of large airways induces a decrease in calibre and/or viscous dissipations within the chest wall tissues are increased [19].

### Viscoelastic properties

The slow decay of pressure after the end-inspiratory occlusion should essentially reflect viscoelastic behaviour, since pendelluft, which could also contribute to that decay, is irrelevant in normal lungs [20, 21]. In all subjects and conditions, the viscoelastic behaviour of the chest wall could be described by a unique relationship (Equation 1). The same applies to the lung, except for three subjects in whom, during lung inflation of 0.5 L from ZEEP,  $R_{\text{visc,L}}$  was 15–20% larger than with higher inflation volumes. In contrast, in the same three subjects  $\tau_{\text{visc}}$  was independent of inflation volume. These subjects were the ones who exhibited a clearcut "knee" on the quasi-static inflation  $V$ - $P$  curve of the lung. This "knee" is consistent with recruitment of atelectatic lung units [10] or reopening of small airways. Under these conditions the functional lung volume is reduced, and hence, for a given  $V_T$ , the expansion of the units that are still functional is greater than would be obtained if all units were functional. Assuming uniform viscoelastic properties within the lung, a reduction in functional lung units should cause a proportional increase in  $R_{\text{visc}}$  with no change in  $\tau_{\text{visc}}$ . Thus the increase of  $R_{\text{visc,L}}$  with the smallest  $V_T$  would imply a 15–20% reduction in functional lung units. However, there is no direct evidence that such a reduction in functional lung units was actually present in these three subjects, whose age ranged 14–25 yrs. In older indi-

viduals a substantial decrease in functional lung units may be present as a result of increased closing capacity and reduction in FRC during anaesthesia [10, 18].

Previous studies on normal anaesthetized, paralysed subjects, in whom viscoelastic constants were assessed using the end-inspiratory airway occlusion method, were limited to smaller lung volumes [1–3, 12, 14]. In 42 normal subjects, at inflation volumes up to 1 L above FRC, the values of  $R_{\text{visc}}$  ( $3.7 \pm 1.2$  and  $2 \pm 0.7$  cmH<sub>2</sub>O·s<sup>-1</sup>·L<sup>-1</sup>) and  $\tau_{\text{visc}}$  ( $1.23 \pm 0.32$  and  $1.21 \pm 0.31$  s) for the lung and chest wall were independent of lung volume and not significantly different from the corresponding values obtained in the present investigation (tables 1 and 3). The fact that, on average,  $\tau_{\text{visc}}$  in the latter study was slightly longer is probably related to the greater range, nearly three times, of  $t_i$  used in the present study. This allowed extension of the observations towards the flat portion of the  $\Delta R$ - $t_i$  relationship (fig. 3 and 4), which is implicit in the viscoelastic model described by Equation 1.

Stress adaptation ( $P_1$ - $P_{\text{st}}$ ) after lung inflations from 0.5–3 L above FRC has been investigated in 12 normal anaesthetized, paralysed subjects by SHARP *et al.* [15]. In line with the present results, they found that: 1) the time course of stress adaptation is essentially monoexponential with time constants ( $\tau_{\text{visc}}$ ) in the range 1.1–2 s that are independent of inflation volume and only slightly shorter for the chest wall than the lung; and 2) stress adaptation was greater in the lung than chest wall, independent of inflation volume. Conversely, SHARP *et al.* [15] found that stress adaptation of lung and chest wall tissues increased, though moderately, with the largest inflation volumes. According to Equation 1 this may either indicate that  $R_{\text{visc}}$  increased with inflation volume, since  $\tau_{\text{visc}}$  remained unchanged, or reflect the fact that the duration of inflation increased with increasing  $\Delta V$ . Indeed in the study of SHARP *et al.* [15] lung inflations were accomplished manually with a supersyringe, without fixing the duration of inflation, except for keeping it <1 s. An additional limitation in comparing the results of the present study with those of SHARP *et al.* [15] is related to differences in the inspiratory flow waveform. Indeed, the pressure stored in the viscoelastic elements at end-inflation, and hence the amount of stress adaptation, should also vary with the inspiratory flow waveform [22].

In the model of MOUNT [9], a single Kelvin body confers viscoelastic behaviour to the respiratory system and its component parts. In contrast, HILDEBRANDT [23], on the basis of stress relaxation data obtained in isolated cat lungs, proposed a model in which the viscoelastic compartment is made by linear viscoelastic material

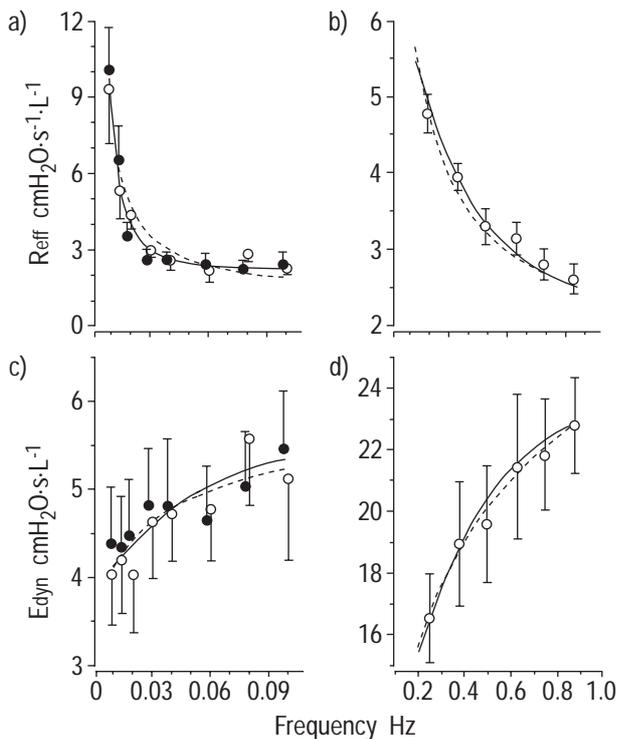


Fig. 7. – Relationships of frequency to a, b) effective resistance ( $R_{\text{eff}}$ ) and c, d) dynamic elastance ( $E_{\text{dyn}}$ ) of lung (a, c, data from ref. 19) and respiratory system (b, d data from ref. 21) in normal awake, seated subjects. Bars: SE. Lung  $R_{\text{eff}}$  and  $E_{\text{dyn}}$  measured with constant-flow ( $\circ$ ) and constant-volume inputs ( $\bullet$ ). Average data were fitted with the equations pertaining to Hildebrandt's model (Equation 2; - - -) and Mount's model (Equation 3; —).

with a continuous distribution of time constants, the mechanical analogue being represented by a number of Kelvin bodies arranged in parallel. Indeed, when assessed over extended periods, the time course of the pressure decay that occurs after a step change in volume ( $\Delta V$ ) could be represented by  $P(t) = (A - B \log t) \Delta V$ , where  $A$  is the elastance 1 s after the step change and  $B$  a parameter proportional to tissue resistance. Clearly, this approach cannot be used *in vivo*. Both models by HILDEBRANDT [23] and MOUNT [9] can be used, however, to interpret low-frequency input impedance data. With the former model, the effective resistance ( $R_{\text{eff}}$ ) and dynamic elastance ( $E_{\text{dyn}}$ ) during sinusoidal volume oscillations are given by [24].

$$R_{\text{eff}} = R_1 + R_{\text{tis}} = R_1 + 0.683B/\omega; E_{\text{dyn}} = A + B(0.25 + \log \omega) \quad (2)$$

where  $R_1$  represents viscous resistance, like  $R_{\text{int}}$  in the model of MOUNT [9],  $R_{\text{tis}}$  is tissue viscance,  $\omega$  angular frequency, and  $A$  and  $B$  are constants. For this model the corresponding equations [2] are

$$\begin{aligned} R_{\text{eff}} &= R_{\text{int}} + R_{\text{visc}}/(1 + \omega^2 \cdot \tau_{\text{visc}}^2); \\ E_{\text{dyn}} &= E_{\text{st}} + E_{\text{visc}} \cdot \omega^2 \cdot \tau_{\text{visc}}^2 / (1 + \omega^2 \cdot \tau_{\text{visc}}^2) \end{aligned} \quad (3)$$

Both models have been shown to describe equally well the respiratory impedance of normal dogs 0.125–0.75 Hz

[25]. As shown in figure 7, the same holds for impedance data obtained in the low-frequency range on normal seated, awake subjects in previous studies using the forced oscillation method [24, 26].

Human studies concerned with volume dependence of respiratory impedance at low frequencies are scarce and limited to the normal  $V_T$  range. While effective resistance and  $E_{\text{dyn,L}}$  of the lungs appears to be independent of  $V_T$  [24, 27, 28],  $E_{\text{dyn,rs}}$  and, in some cases,  $R_{\text{eff,rs}}$  were found to decrease with increasing  $V_T$  at constant frequency [28]. This is not in contrast with the present results which show volume independence of both lung and chest wall viscoelastic properties (fig. 3 and 6). Indeed that alinearity could reflect in part the volume dependence of viscous resistance and quasi-static elastance (fig. 1 and 2), which are included in  $R_{\text{eff}}$  and  $E_{\text{dyn}}$  (see above), or it could be predominantly associated with chest wall tissue plasticity [27, 28]. Plastoelastic pressure dissipation cannot in fact be detected by the present approach, as it becomes manifested only when the direction of volume changes is reversed.

In ARDS patients the simple linear viscoelastic model of the respiratory system failed to fully describe viscoelastic behaviour [5]. The present results suggest that this should be due to disease-related lung injury rather than overdistension of functional lung units. In fact, in the present study the end-inspiratory  $P_{\text{st,L}}$  averaged 30 cmH<sub>2</sub>O (fig. 1). According to the 1993 Consensus Conference of the American College of Chest Physicians, maximal inspiratory transalveolar pressure should not exceed 30–35 cmH<sub>2</sub>O during each tidal cycle [29].

In conclusion, the results obtained in normal anaesthetized, paralysed subjects by means of the rapid end-inspiratory occlusion method, show that the viscoelastic behaviour of the respiratory system at large inflation and mean lung volumes is satisfactorily described by the simple linear viscoelastic model of MOUNT [9], while alinearities are due to volume dependence of interrupter resistance and quasi-static elastance of the respiratory system. The Mount model also adequately described the impedance data obtained in previous studies [24, 26] on normal awake humans with the forced oscillation method. In anaesthetized paralysed humans the rapid end-inspiratory occlusion method is technically easier to implement than the forced oscillation method, which involves major methodological problems.

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