

Time Course and Mechanisms of Lung-volume Increase with PEEP in Acute Pulmonary Failure

Jeffrey A. Katz, M.D.,* Gerard M. Ozanne, M.D.,* Steven E. Zinn, M.D.,* H. Barrie Fairley, M.B., B.S.†

To determine the effects of a step change in end-expiratory pressure on functional residual capacity (FRC) and lung-thorax compliance (C_{LT}), 10 cm H₂O positive end-expiratory pressure (PEEP) was applied in eight patients who needed mechanical ventilation for acute pulmonary failure. Of the total change in FRC, 66 ± 5.3 per cent (mean \pm SEM) was complete within the next breath, and 90 per cent change was achieved in 4.6 ± 1.4 breaths (24 ± 6.4 sec). There was no statistically significant difference between times to 90 per cent FRC change with application and with removal of PEEP. In another 13 patients, PEEP was increased in 5 cm H₂O steps from 3 to 18 cm H₂O. Mean FRC at 3 cm H₂O PEEP was 1.51 ± 0.20 l (55 \pm 7.0 per cent predicted supine value). Mean C_{LT} did not change significantly until 18 cm H₂O PEEP was reached, at which point it decreased ($P < 0.005$). The static compliance derived from change in FRC ($\Delta FRC/\Delta PEEP$) increased with increments of PEEP ($P < 0.05$) compared with the initial level. At PEEP levels of 8 and 13 cm H₂O, mean FRC was larger than would be predicted from mean C_{LT} ($P < 0.005$), but it was not significantly different at 3 cm H₂O PEEP. The lung component accounted for 62 ± 3.7 per cent of the lung-thorax compliance difference. These data define a time-dependent increase in lung volume that resembles pressure-volume hysteresis in normal man. Possible mechanisms include surface tension changes, recruitment of nonventilated lung, and stress relaxation of lung and chest wall. This study may explain the greater efficiency of PEEP compared with large tidal-volume ventilation in increasing P_{aO_2} in patients with acute pulmonary failure. (Key words: Lung; acute respiratory failure; compliance; functional residual capacity. Ventilation: positive end-expiratory pressure.)

A POSITIVE END-EXPIRATORY PRESSURE (PEEP), applied during mechanical ventilation, may improve pulmonary oxygen exchange in patients with acute pulmonary failure (APF) when large tidal volumes are ineffective.^{1,2} Although PEEP causes an increase in functional residual capacity (FRC), the mechanisms responsible for this improvement in oxygen exchange have been incompletely defined.^{3,4}

When PEEP is applied, two possible time courses exist for the increase in lung volume. First, the increase may occur within one breath by elastic ex-

pansion of already open alveoli⁵ and by prevention of collapse of unstable alveoli at end-expiration.^{3,6} This increase could be predicted by a lung-thorax compliance (C_{LT}) value derived from the linear portion of a whole C_{LT} curve. Second, PEEP may result in an additional increase in lung volume by overcoming forces that require a longer inflation time than occurs during one tidal inspiration. This might involve surface tension changes, stress relaxation, and recruitment of alveoli remaining collapsed during a tidal inspiration. Thus, the full increase in FRC with PEEP would take several breaths and would be larger than that predicted by the C_{LT} .^{6,7} This second mechanism could account for the difference between the effects of PEEP and large-tidal-volume ventilation on pulmonary oxygen exchange.

The purpose of this study was to determine whether these two mechanisms exist, and the relative contributions of lung and chest wall.

Methods

We studied 21 patients who needed mechanical ventilation for APF, 16 men and five women, 21-73 years of age (mean 45 years). The study was approved by our Committee on Human Research, and informed consent was obtained for each patient. Pulmonary failure had followed massive trauma in 11, a major surgical procedure in four, and either a metabolic or an infectious process in the remainder.

ABBREVIATIONS

APF	= acute pulmonary failure
C_{CW}	= chest-wall compliance
C_{FRC}	= change in FRC per change in end-expiratory pressure
C_L	= lung compliance
C_{LT}	= lung-thorax (lung and chest wall) "static" tidal volume compliance
FRC	= functional residual capacity
$P(A-a)O_{2,0.5}$	= alveolar-to-arterial partial pressure difference at 50 per cent inspired oxygen
$P_{aw} \dot{V}$	= end-inspiratory plateau airway pressure
PEEP	= positive end-expiratory pressure
TLC	= total lung capacity
V_E	= expired tidal volume
$\Sigma \Delta V_E$	= cumulative expired tidal volume change
ΔV	= time-dependent volume increase

* Assistant Professor of Anesthesia.

† Professor of Anesthesia.

Received from the Department of Anesthesia, University of California, San Francisco, San Francisco General Hospital, San Francisco, California. Supported in part by Grant #GM240223. Accepted for publication June 30, 1980. Presented in part at the annual meeting of the American Society of Anesthesiologists, San Francisco, October 23, 1979.

Address reprint requests to Dr. Katz: Department of Anesthesia, San Francisco General Hospital, Room 3S40A, 1001 Potrero Avenue, San Francisco, California 94110.

All patients were in stable condition with respect to cardiopulmonary variables and were studied at least 24 hours after institution of mechanical ventilation.

All patients were ventilated with a volume- or time-preset ventilator (Monaghan 225 or Siemens Servo 900B). There was no spontaneous respiratory activity during the study period. Tidal volume was adjusted to 14 ± 0.2 per cent total lung capacity (TLC) as predicted from height and age.⁸ The inspiratory flow, respiratory frequency, and inspired oxygen concentration were held constant throughout the study period. Fractions of inspired oxygen ranged from 0.45 to 0.5 (hereafter referred to as F_{IO_2} 0.5). Patients were in the supine position when studied.

TIME COURSE OF LUNG-VOLUME CHANGE WITH PEEP

Two separate study protocols were followed. In all instances, maneuvers designed to produce an end-expiratory pressure change were made during an inflation phase. This was to ensure that the entire expired tidal volume (V_E) of the next breath reflected the step change in PEEP. In eight patients, a PEEP sequence of 3, ‡ 13, and 3 cm H_2O was applied, with a 10-min period at each level of PEEP. Before and after each step change, breath-by-breath V_E and end-inspiratory plateau airway pressure (P_{aw} \dot{I}) were measured. Cumulative net loss or gain of V_E was assumed to reflect net gain or loss in lung volume, respectively (see calculations below). The FRC was measured before and 10 min after each change in PEEP, so that a comparison with the estimated lung-volume change could be made.

In three patients selected randomly from the original eight, the effect of lung-volume history was evaluated by repeating these measurements after two hyperinflations to an end-inspiratory airway pressure greater than 50 cm H_2O .

In 13 additional patients, PEEP was increased in 5 cm H_2O steps from 3‡ to 8, 13, and 18 cm H_2O ; measurements of FRC, P_{aw} \dot{I} , and V_E were made after each step change (see measurements below). In ten of these patients, an esophageal balloon was *in situ*, and esophageal pressure was also measured.

MEASUREMENTS

Airway and esophageal pressures (P_{aw} and P_{es}) were measured and recorded simultaneously using Statham P23DB and PM131TC pressure transducers and a Gould recorder. Esophageal pressure was measured with a nasogastric esophageal balloon⁹ (National Catheter Corporation) 10 cm long and 3.8 cm in cir-

cumference. The tip of the balloon was placed in the mid-esophagus^{10,11} by passing the balloon into the stomach, then withdrawing it 10 to 15 cm after the top portion of the balloon had entered the esophagus, as evidenced by a negative deflection on the esophageal trace with a spontaneous inspiration. In patients incapable of spontaneous inspiration, the position was verified radiographically by a radiopaque marker in the tip of the balloon. The balloon was evacuated, then inflated with 0.6 ml of air.^{12,13}

Each expired breath was collected in a reservoir bag surrounded by a second bag. During the next inspiration, the outer bag was pressurized, ejecting the mixed expired gas at constant flow through a heated Fleisch pneumotachygraph. It was integrated for V_E , recorded on a Gould recorder, and stored in a computer. The V_E was corrected linearly by the computer, which compared the viscosity of the expired gas mixture with the viscosity of the pneumotachygraph calibrating gas. All respiratory gases were measured by mass spectrometry (Medspect II).

Functional residual capacity was determined by a simultaneous exchange (wash-in, wash-out) of two insoluble gases, argon (Ar) and nitrogen (N_2), utilizing the breath-by-breath mixed expired collection system. Each patient was connected to one of two parallel bag-in-box systems that was in turn powered by his own ventilator. One bag was filled with N_2/O_2 and the other with Ar/O_2 (same F_{IO_2}). Full equilibration of inspiratory and mixed expired gas concentrations with one of the two parallel bag-in-box systems (*e.g.*, N_2/O_2) was achieved. Then, by turning a valve at end-expiration, the patient's ventilator was turned to the other bag-in-box system (*e.g.*, Ar/O_2), and argon was washed in while N_2 was washed out. Each exchange resulted in two FRC determinations, and the average of these was considered the FRC for that exchange. In a previous study of 65 such exchanges, the mean difference between wash-in and wash-out curves of FRCs was found to have a standard deviation of 84 ml. We used this criterion to determine an acceptable exchange (*i.e.*, no leak). Two such exchanges were made 8 and 15 min after a change in PEEP. Stability within patients is demonstrated by comparing the mean FRC of all first exchanges (1.86 l), by *t* test for paired data, with the mean FRC of all second exchanges (1.85 l). No significant difference existed between these values. The standard deviation of the first exchange minus the second was 85 ml ($n = 83$).

CALCULATIONS

Lung-thorax compliance (C_{LT}), $V_E/\Delta P_{aw}$, and its components lung compliance (C_L), $V_E/\Delta(P_{aw} - P_{es})$,

‡ 3 cm H_2O PEEP was used as the initial level, since most ventilators do not return to zero end-expiratory pressure.

and chest-wall compliance (C_{CW}), $V_E/\Delta P_{es}$, were derived from the pressure differences between the end of a period of zero end-inspiratory flow of 1.2 sec and end-expiration. Data from ten breaths were averaged to derive each value. The FRC compliance (C_{FRC}) was derived by dividing the change in FRC by the increment in PEEP ($\Delta FRC/\Delta PEEP$). Statistical manipulations of compliance values were handled as their reciprocal (elastance), in order to reflect a more linear distribution of elastic recoil circumstances.

Alveolar-to-arterial oxygen partial pressure difference at 50 per cent inspired oxygen, $P(A-a)O_{2.0.5}$, was calculated assuming

$$PA_{O_2} = PI_{O_2} - PA_{CO_2}/R$$

where PA_{O_2} is the calculated ideal alveolar oxygen partial pressure, PI_{O_2} is the partial pressure of inspired oxygen, PA_{CO_2} is equal to arterial blood P_{CO_2} , and R is assumed equal to 0.85.

Total volume change ($\Sigma\Delta V_E$) is the cumulative expired tidal volume change after the application or removal of 10 cm H₂O PEEP, and was calculated as follows. A steady-state V_E (corrected for compression secondary to application of PEEP) and P_{aw} were derived from an average of breaths 21 to 30 and 31 to 40 occurring after a step change in PEEP. Steady-state was tested by averaging V_E from breaths 21 to 30 (822 ± 28 ml) and comparing the result with the average for breaths 31 to 40 (823 ± 29 ml). There was no statistically significant difference between these means. Each V_E that was recorded after a change in PEEP was subtracted from this steady-state V_E . This difference in expired tidal volume was then totaled to give a value reflecting the total lung-volume increase or decrease.

An index of the time-dependent component of lung volume increase (ΔV) was calculated from the mean data by comparing end-inspiration and end-expiration at constant pressure (fig. 1). To make this comparison when volume data points were not available at the same pressure, the lung volume measured

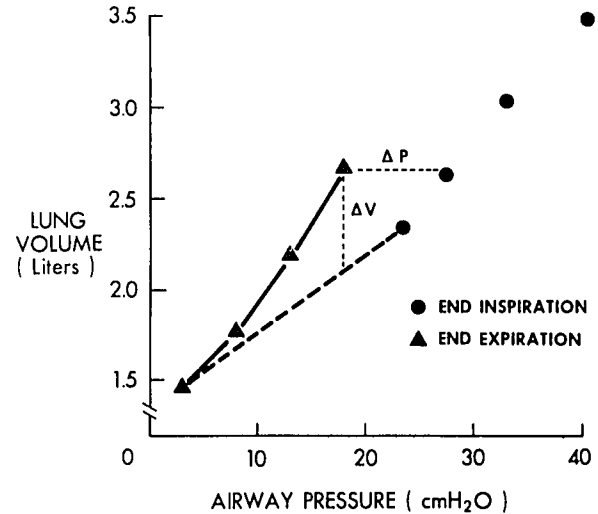


FIG. 1. Pressure-volume data of the lung-thorax (fig. 3). The ΔV and ΔP represent the time-dependent volume and pressure changes calculated at 18 cm H₂O PEEP. These are the differences between (interpolated) end-inspiration and end-expiration at either the same pressure or the same lung volume.

at end-inspiration was interpolated from the C_{LT} line obtained at 3 cm H₂O end-expiratory pressure (fig. 1). This interpolation may be supported by linear data for sequential increases in end-inspiratory pressure within a tidal volume range of 30 per cent of TLC.^{14,15}

Predicted supine FRC was assumed to be equal to 80 per cent of the predicted sitting value.^{8,10}

Data are presented as mean \pm SEM.

Results

EFFECTS OF PEEP ON FRC AND TIME COURSE OF VOLUME CHANGE

At 3 cm H₂O PEEP, mean FRC was 1.51 ± 0.20 l (55 ± 7.0 per cent predicted supine); it increased with each 5 cm H₂O increment of PEEP (table 1).

The mean sum of the total breath-by-breath V_E

TABLE 1. Mean (\pm SE) Compliance, FRC, and $P(A-a)O_{2.0.5}$ at Different Levels of Positive End-expiratory Pressure (PEEP) (n = 13)

	Positive End-expiratory Pressure			
	3 cm H ₂ O	8 cm H ₂ O	13 cm H ₂ O	18 cm H ₂ O
$P(A-a)O_{2.0.5}$ (torr)	180 ± 13	173 ± 13	$159 \pm 14^{*†}$	$147 \pm 14^{*†}$
FRC(l)	$1.51 \pm .20^{\ddagger}$	$1.80 \pm .24^{\ddagger}$	$2.21 \pm .27^{\ddagger}$	$2.68 \pm .32^{\ddagger}$
E_{LT} (cm H ₂ O/l)	24.2 ± 2.3	23.4 ± 2.4	24.6 ± 2.5	$30.4 \pm 3.7^{\S}$
C_{LT} (ml/cm H ₂ O)	41 ± 4.0	43 ± 4.5	41 ± 4.2	$33 \pm 4.1^{\S}$

* Significant difference compared with 3 cm H₂O, $P < 0.05$.

† Significant difference compared with 8 cm H₂O, $P < 0.05$.

‡ Significant difference compared with all other PEEP levels, $P < 0.001$.

§ Significant difference compared with 3, 8, 13 cm H₂O, $P < 0.005$.

$P(A-a)O_{2.0.5}$ = alveolar-to-arterial partial pressure difference of 50 per cent inspired oxygen; FRC = functional residual capacity; E_{LT} = lung-thorax elastance; C_{LT} = lung-thorax compliance. Statistical analysis by analysis of variance, with differences between groups detected by Newman-Keuls test.

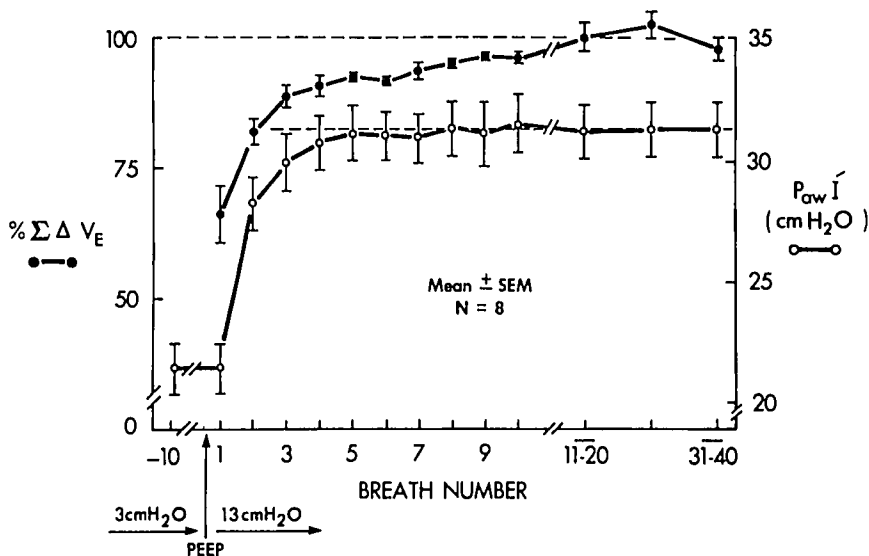


FIG. 2. Cumulative expired tidal volume changes ($\Sigma \Delta V_E$) and airway plateau pressure ($P_{aw} \bar{I}$) after a 10 cm H₂O increase in PEEP. The breath immediately preceding the increase in PEEP is at baseline $P_{aw} \bar{I}$. During that inflation, the expiratory circuit is adjusted to 13 cm H₂O PEEP (indicated by the vertical arrow). The next expiration (breath 1) is decreased and reflects a gain in lung volume by the patients. Breath 2 is then the first to be initiated from PEEP, and this is reflected by an increase in $P_{aw} \bar{I}$.

($\Sigma \Delta V_E$) (703 ± 51 ml) was not statistically significantly different from the mean ΔFRC (699 ± 59 ml) after the application or removal of 10 cm H₂O PEEP. After an increase of 10 cm H₂O PEEP, 66 \pm 5.3 per cent of the total lung-volume change was complete within the first breath, and 90 per cent change was achieved in 4.6 ± 1.4 breaths (24 ± 6.4 sec) (fig. 2). Prior hyperinflation of the lung in three patients did not alter these findings (table 2). On removal of PEEP, 73 ± 7.9 per cent of the total volume change was complete within the first breath, and 90 per cent change was achieved in 3.1 ± 0.6 breaths (16 ± 3.2 sec). There was no significant difference between times to 90 per cent volume change with application and with removal of PEEP.

EFFECT OF PEEP ON COMPLIANCE

With increments of 5 cm H₂O PEEP, the mean C_{LT} did not change significantly until 18 cm H₂O of PEEP was reached, at which point it decreased ($P < 0.005$) (fig. 3, table 1). The C_{FRC} increased with increments of PEEP ($P < 0.05$) (fig. 3, table 3). At PEEP levels of 8 and 13 cm H₂O, the corresponding mean C_{FRC} was larger than the mean C_{LT} ($P < 0.005$),

TABLE 2. Effect of Prior Hyperinflation on Functional Residual Capacity and Lung-Thorax Compliance

	Positive End-expiratory Pressure				
	Pre-hyperinflation		Post-hyperinflation		
	3 cm H ₂ O	13 cm H ₂ O	3 cm H ₂ O	3 cm H ₂ O	13 cm H ₂ O
Functional residual capacity (l)					
Patient 1	1.91	2.81	1.96	1.90	2.92
Patient 2	1.50	2.16	1.45	1.40	2.02
Patient 3	.75	1.33	.79	.81	1.35
Lung-thorax compliance (ml/cm H ₂ O)					
Patient 1	59	45	63	64	45
Patient 2	47	41	46	46	40
Patient 3	43	44	43	42	44

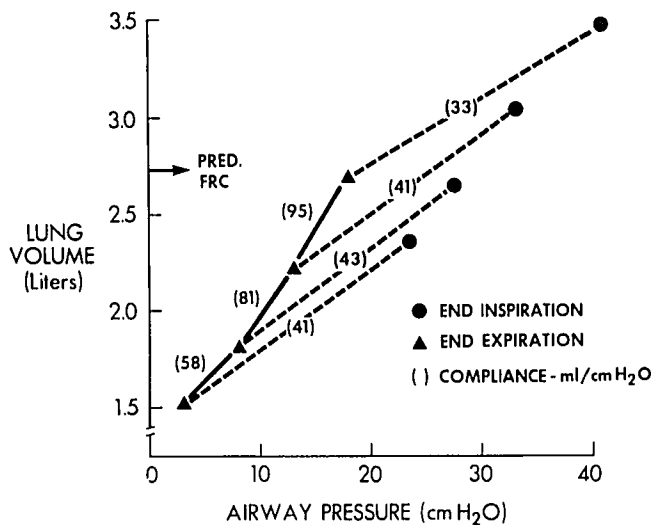


FIG. 3. Mean lung-thorax pressure-volume data of 13 patients: measured FRCs and end-expiratory pressures (\blacktriangle); end-inspiratory lung volumes and airway plateau pressures (\bullet). Dashed lines and numbers in parentheses are the mean lung-thorax (tidal volume) compliance at individual levels of PEEP. The solid line connecting the triangles and the corresponding compliance numbers are the C_{FRC} .

TABLE 3. Lung-Thorax (C_{LT}) and FRC Compliances (C_{FRC}) at Different Levels of Positive End-expiratory Pressure (PEEP) (Mean \pm SE, $n = 13$)

PEEP (cm H ₂ O)	C_{LT} (ml/cm H ₂ O)	C_{FRC} (ml/cm H ₂ O)	Significance
3	41 \pm 4.0	58 \pm 10	N.S.
8	43 \pm 4.5	81 \pm 12*	$P < 0.005$
13	41 \pm 4.2	95 \pm 11†	$P < 0.001$

* $P < 0.05$ compared with 3 cm H₂O.

† $P < 0.005$ compared with 3 cm H₂O.

Statistical analysis by analysis of variance, with difference between groups detected by Newman-Keuls test.

but they were not significantly different at 3 cm H₂O PEEP (table 3). Thus, at the same lung volume there was a difference between end-inspiratory and end-expiratory pressure data (fig. 1). At these comparable lung volumes (referenced to the FRC maintained by 18 cm H₂O PEEP), the pressure difference between the end-inspiratory and end-expiratory data was distributed across both the lungs and the chest wall, with the lung component accounting for 62 \pm 3.7 per cent of the total lung-thorax change (fig. 1, table 4).

Conversely, a volume difference existed between end-inspiration and end-expiration at the same pressure (fig. 1). At 18 cm H₂O, this volume difference (ΔV_{18}) was 38 \pm 2.6 per cent of the total FRC change, and this corresponded to the 34 per cent of volume change that was observed to have occurred after the first breath following a step change in PEEP. In addition, ΔV_{18} correlated directly with C_{LT} measured at 3 cm H₂O PEEP ($r = 0.81$, $P < 0.001$, fig. 4). Consistent with the significant increase in C_{FRC} at higher PEEP levels is the increase in ΔV at 18 cm H₂O PEEP (table 5).

EFFECT OF PEEP ON OXYGENATION

The mean $P(A-a)O_{2_{0.5}}$ decreased progressively with each increment of 5 cm H₂O PEEP (table 1). For each patient's pressure-volume data, the additional volume (ΔV_{18}) maintained by PEEP at 18 cm H₂O correlated inversely with the associated improvement in $P(A-a)O_{2_{0.5}}$ from 3 to 18 cm H₂O PEEP ($r_s = -0.7$, $P < 0.05$).

TABLE 4. Mean (\pm SE) Pressure Difference Between End-inspiratory and End-expiratory Data* ($n = 10$)

Mean Pressure Difference (ΔP , cm H ₂ O \pm SE)		
Lung	Chest Wall	Lung-Thorax
4.67 \pm 0.68	2.60 \pm 0.22	7.27 \pm 0.77

* Calculations made at FRC achieved by 18 cm H₂O PEEP.

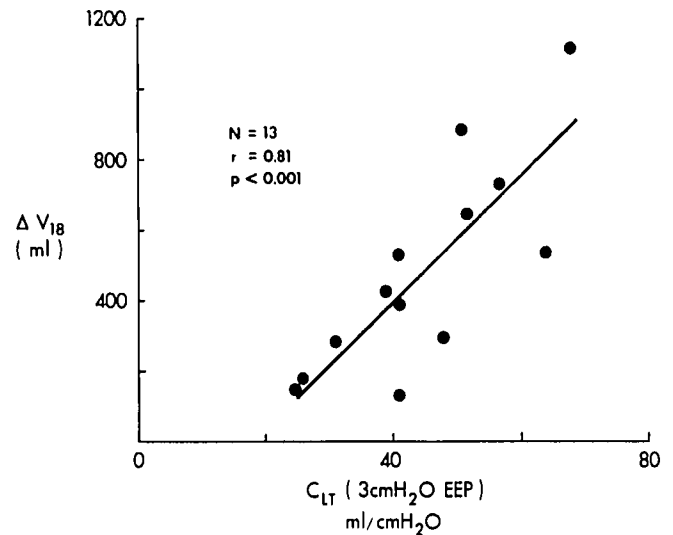


FIG. 4. Relationship of time-dependent volume calculated at 18 cm H₂O to the lung-thorax compliance at 3 cm H₂O end-expiratory (EEP).

Discussion

Our data demonstrate that increases in FRC after changes in end-expiratory pressure are larger than would be expected from the C_{LT} , due to a time-dependent component in lung-volume change. The data support two general mechanisms by which lung volume increases with PEEP. First, the volume increase occurs as a result of expansion of open alveoli and the prevention of terminal air space collapse during expiration. The breath-by-breath data support this (fig. 2). The increase in lung volume (volume retained by the patient) on the first breath after application of PEEP is directly proportional to the elasticity of the lung open during the end-inspiratory pause (proportional to C_{LT} , $r = 0.97$). Second, there is an additional increase in lung volume that occurs more slowly. It is this additional volume (ΔV) that results in the observed hysteresis-like effect. We chose to characterize this effect in terms of a single sampling point, *i.e.*, the absolute volume difference between that measured at end-expiration and that at end-in-

TABLE 5. Time-dependent Volume Increases (ΔV) with Increments in Positive End-expiratory Pressure (PEEP) (Mean \pm SE, $n = 13$)

	Positive End-expiratory Pressure		
	3 \rightarrow 8 cm H ₂ O	8 \rightarrow 13 cm H ₂ O	13 \rightarrow 18 cm H ₂ O
ΔV (ml)	63 \pm 37	161 \pm 44	246 \pm 38*

* Significant compared with (3 \rightarrow 8), $P < 0.005$.

Statistical analysis by analysis of variance, with differences between groups detected by Newman-Keuls test.

spiration at a constant pressure, 18 cm H₂O (ΔV_{18}).^{15,16} The presence of this ΔV is supported by the breath-by-breath P_{aw} \dot{V} (fig. 2), which shows a progressive rise, as might be expected with constant tidal volumes delivered from a progressively increasing end-expiratory volume. The P_{aw} \dot{V} reaches a plateau in four to five breaths after a change in PEEP. This pressure change is consistent with the 90 per cent change in lung volume at that time.

Falke *et al.*⁶ demonstrated that the static compliance equivalent to our C_{FRC} increased with PEEP, which was correlated with an improvement in $P(A-a)O_2$. This is consistent with our findings. They attributed this increase in compliance to recruitment of terminal airspaces. We agree, but suggest other mechanisms that might account for a significant proportion of the observed volume increase.

Tidal volume, FRC, and volume history have all been shown to affect hysteresis.¹⁴ Three theories have been advanced to explain this phenomenon.¹⁵ These include surface tension changes, presumably as a result of pulmonary surfactant, stress relaxation (a viscoplastic property whose definition is a time-dependent decrease in transrespiratory pressure at constant lung volume), and recruitment of collapsed alveoli. The data presented in this study do not allow us to define which of these factors is responsible for the observed changes.

In our study, tidal volume is standardized at 14 per cent total lung capacity (TLC), a clinically applicable tidal volume. The presence of an opening pressure phenomenon and recruitment of collapsed alveoli is supported by the lack of difference in C_{FRC} or C_{LT} at the lower PEEP levels, and by the significant increases in C_{FRC} and ΔV at 18 cm H₂O (tables 3 and 5).¹⁷⁻¹⁸ These changes at the higher levels are also consistent with results of previous studies of surface tension changes^{14,19} and stress relaxation.^{20,21}

The effects of increments of PEEP on C_{LT} and C_{FRC} are distinctly different (table 3, fig. 3). The increase in C_{FRC} may be related to recruitment of lung previously not ventilated during each tidal volume. The decrease in C_{LT} at 18 cm H₂O PEEP while lung is recruited may be explained by over-expansion at end-inspiration of open gas spaces relative to recruitment of lung volume at end-expiration. This situation may lead to an increased physiologic dead space, impaired distribution of pulmonary blood flow, and/or reduced cardiac output.³ The mean pressure-volume data (fig. 3) indicate that lung volume is larger at end-expiration than at end-inspiration at the same pressure. The harmful effects of over-expansion of lung at end-inspiration might be avoided by using PEEP to recruit nonventilated lung at end-expiration, while mini-

mizing the end-inspiratory pressures by decreasing tidal volume. We have no data as to the effect of this maneuver on pulmonary oxygen exchange.

The effect of volume history was examined in three patients. In standardizing volume history, lungs are usually inflated to TLC two to three times and then the measurement or respiratory maneuver is commenced. The static compliance in normal man and animals has been shown to increase after such maneuvers by as much as 30 to 50 per cent.^{22,23} The mechanism proposed for this increase is either recruitment of collapsed alveoli or a change in surface tension.²²⁻²⁴ This effect is transient, with the compliance values returning to baseline over several breaths,^{23,25} and is primarily seen with ventilation at low tidal volumes. Relatively small reversible compliance changes are seen when large tidal volumes are used.^{15,26} In this study, we found no effect on the static pressure-volume data (table 2) and the breath-by-breath lung volume changes in three patients following hyperinflation. Two possible explanations exist. First, an average delay of six to eight breaths occurred between hyperinflation and FRC measurement. Second, intrinsic parenchymal disease in these patients would probably cause alveolar instability and thus, without PEEP, recruited lung would not be sustained. These data imply a very transient effect, if any, on compliance by periodic sighs or hyperinflation, and are in agreement with results of a prior study of patients with acute pulmonary failure.²⁷

Our index of the time-dependent component of FRC increase (ΔV_{18}) correlated directly with the C_{LT} at 3 cm H₂O PEEP (fig. 4). This suggests that the measured hysteresis effect was larger in more compliant lungs, and is consistent with Permutt and Martin's data for normal man.¹⁶ They found hysteresis (described as a volume difference at constant pressure) to be related to the size of vital capacity.

In this study, we found both the lung and the chest wall were involved in the hysteresis-like effect. The partition of the pressure difference at comparable lung volumes into chest wall and lung components rests upon measurements of esophageal pressure with the subject in the supine position. The absolute pressures that were measured were abnormally positive and therefore inaccurate.²⁸ This is probably due to the weight of the heart and mediastinal contents.²⁹ It is commonly felt that a change in esophageal pressure validly represents change in pleural pressure, even in the supine position, except at extremes of vital capacity (less than 20 per cent or more than 80 per cent vital capacity).^{10,29,30} In this study, separation of the lung and chest-wall pressure-volume relationships was made only at one lung volume, 18 cm H₂O

PEEP (mean 81 per cent of predicted supine FRC), and therefore might reliably separate the two components of the total lung-thorax pressure change. That both the lung and the chest wall were involved and that the lung component was larger are consistent with previously reported findings in animals and normal man.^{20,31} Chest-wall hysteresis is probably due to stretching the skeletal muscles and ligaments, both of which are known to show hysteresis.²⁰ In addition, viscous resistance of abdominal contents may add to the chest-wall effect.

The two different methods of measuring compliance employed in this study might explain the observed hysteresis-like effect. A redistribution of ventilation to lung compartments with a long time constant would be reflected in the measured FRC, but might not be reflected in the breath-by-breath compliance value if dynamic or flow-resistive factors were present. The C_{LT} (breath-by-breath) is a quasi-static measurement; in this study a period of zero flow of 1.2 sec at end-inspiration was used for this calculation. The pressure decay from the peak inspiratory pressure to the end-inspiratory pressure plateau is exponential. At an airway resistance of 1.5 cm H₂O/l/sec and a C_{LT} of 100 ml/cm H₂O, the time constant would be 0.15 sec. Thus, an inflation hold of 1.2 sec is generally believed to be adequate, even in abnormal lungs, to obtain a compliance value that would be in general agreement with a static measurement and allow enough time for redistribution of air.^{32,33} In this study, the volume retained on the first breath after the application of 10 cm H₂O PEEP (average expiratory time 3.0 sec) was directly proportional to the C_{LT} (1.2 sec), and this suggests that the commonly considered dynamic factors were not present. From the data presented we cannot exclude the possibility that the differences in C_{LT} and C_{FRC} (the measured ΔV) may be explained by a slow compartment of ventilation through collateral channels.

Data on the contribution of pulmonary blood volume to compliance are conflicting.^{34,35} The contribution of this effect to the overall observed hysteresis cannot be quantitated from this study.

We conclude that in patients with acute pulmonary failure lung volume may be increased by PEEP by two mechanisms. First, PEEP may stretch already open alveoli and prevent collapse of those that are unstable at end-expiration. Second, there may be an additional time-dependent increase in lung volume which resembles pressure-volume hysteresis in normal man. Three mechanisms for this hysteresis are cited and discussed. The increases and decreases of lung volume that follow application and removal of 10 cm H₂O PEEP have a time course of less than

1 min. Both lung and chest-wall factors are involved in the phenomenon, with the lung component predominating. There is no sustained effect from hyperinflation on C_{LT} or FRC. We believe these data explain the observation that PEEP may increase PaO₂ in patients with acute pulmonary failure when large-tidal-volume ventilation fails to do so.

The authors gratefully acknowledge the technical assistance of Patrick D. Pangburn, R.R.T., and the editorial advice of Pauline Snider.

References

1. Ashbaugh DG, Petty TL, Bigelow DB, et al: Continuous positive-pressure breathing (CPPB) in adult respiratory distress syndrome. *J Thorac Cardiovasc Surg* 57:31-41, 1969
2. Kumar A, Falke KJ, Geffin B, et al: Continuous positive-pressure ventilation in acute respiratory failure: effects on hemodynamics and lung function. *N Engl J Med* 283: 1430-1436, 1970
3. Suter PH, Fairley HB, Isenberg MD: Optimum end-expiratory airway pressure in patients with acute pulmonary failure. *N Engl J Med* 292:284-289, 1975
4. McIntyre RW, Laws AK, Ramachandran PR: Positive expiratory pressure plateau: improved gas exchange during mechanical ventilation. *Can Anaesth Soc J*:16:477-486, 1969
5. Powers SR Jr, Mannal R, Neclerio M, et al: Physiologic consequences of positive end-expiratory pressure (PEEP) ventilation. *Ann Surg* 178:265-272, 1973
6. Falke KJ, Pontoppidan H, Kumar A, et al: Ventilation with end-expiratory pressure in acute lung disease. *J Clin Invest* 51:2315-2323, 1972
7. Newell JC, Shah DM, Dutton RE, et al: Pulmonary pressure-volume relationships in traumatized man. *J Surg Res* 26: 114-119, 1979
8. Bates DV, Macklem PT, Christie RV: *Respiratory Function in Disease. An Introduction to the Integrated Study of the Lung.* Second edition. Philadelphia, W. B. Saunders, 1971, p 93
9. Leatherman NE: An improved balloon system for monitoring intraesophageal pressure in acutely ill patients. *Crit Care Med* 6:189-192, 1978
10. Milic-Emili J, Mead J, Turner JM: Topography of esophageal pressure as a function of posture in man. *J Appl Physiol* 19:212-216, 1964
11. Macklem PT: Procedures for Standardized Measurements of Lung Mechanics; and Leith DE, Mead J: Principles of Body Plethysmography. National Heart and Lung Institute, Division of Lung Diseases. Bethesda, Maryland, November 1974
12. Milic-Emili J, Mead J, Turner JM, et al: Improved technique for estimating pleural pressure from esophageal balloons. *J Appl Physiol* 19:207-211, 1964
13. Lemen R, Benson M, Jones JC: Absolute pressure measurements with handdipped and manufactured esophageal balloons. *J Appl Physiol* 37:600-603, 1974
14. Bachofen H, Hildebrandt J: Area analysis of pressure-volume hysteresis in mammalian lungs. *J Appl Physiol* 30:493-497, 1971
15. Radford EP Jr: Static mechanical properties of mammalian

- lungs, *Handbook of Physiology. Section 3: Respiration. Volume 1.* Edited by WO Fenn, H Rahn. Washington, D. C., American Physiological Society, 1964, pp 429-449
16. Permutt S, Martin HB: Static pressure-volume characteristics of lungs in normal males. *J Appl Physiol* 15:819-825, 1960
 17. Anthonisen NR: Effect of volume and volume history of the lungs on pulmonary shunt flow. *Am J Physiol* 207:235-238, 1964
 18. Nielson D, Olsen DB: The role of alveolar recruitment and de-recruitment in pressure-volume hysteresis in lungs. *Resp Physiol* 32:63-77, 1978
 19. Mead J, Whittenberger JL, Radford EP Jr: Surface tension as a factor in pulmonary pressure volume hysteresis. *J Appl Physiol* 10:191-196, 1957
 20. Sharp JT, Johnson FN, Goldberg NB, et al: Hysteresis and stress adaptation in the human respiratory system. *J Appl Physiol* 23:487-497, 1967
 21. Marshall R, Widdicombe JG: Stress relaxation of the human lung. *Clin Sci* 20:19-31, 1961
 22. Mead J, Collier C: Relation of volume history of lungs to respiratory mechanics in anesthetized dogs. *J Appl Physiol* 14:669-678, 1959
 23. Ferris BG Jr, Pollard DS: Effect of deep and quiet breathing on pulmonary compliance in man. *J Clin Invest* 39:143-149, 1960
 24. Williams JV, Tierney DF, Parker HR: Surface forces in the lung, atelectasis, and transpulmonary pressure. *J Appl Physiol* 21:819-827, 1966
 25. Egbert LD, Laver MB, Bendixen HH: Intermittent deep breaths and compliance during anesthesia in man. *ANESTHESIOLOGY* 24:57-60, 1963
 26. Bendixen HH, Hedley-Whyte J, Laver MB: Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. *N Engl J Med* 269:991-996, 1963
 27. Housley E, Louzada N, Becklake MR: To sigh or not to sigh. *Am Rev Respir Dis* 101:611-614, 1970
 28. Mead J, Gaensler EA: Esophageal and pleural pressures in man, upright and supine. *J Appl Physiol* 14:81-83, 1959
 29. van de Woestijne KP, Trop D, Clément J: Influence of the mediastinum on the measurement of esophageal pressure and lung compliance in man. *Pflügers Arch* 323:323-341, 1971
 30. Gillespie DJ, Lai Y-L, Hyatt RE: Comparison of esophageal and pleural pressures in the anesthetized dog. *J Appl Physiol* 35:709-713, 1973
 31. Butler J: The adaptation of the relaxed lungs and chest wall to changes in volume. *Clin Sci* 16:421-433, 1957
 32. Bone RC: Diagnosis of causes for acute respiratory distress by pressure-volume curves. *Chest* 70:740-746, 1976
 33. Suter PM, Fairley HB, Isenberg MD: Effect of tidal volume and positive end-expiratory pressure on compliance during mechanical ventilation. *Chest* 73:158-162, 1978
 34. Goldberg HS, Mitzner W, Adams K, et al: Effect of intrathoracic pressure on pressure-volume characteristics of the lung in man. *J Appl Physiol* 38:411-417, 1975
 35. Gray BA, McCaffree DR, Sivak ED, et al: Effect of pulmonary vascular engorgement on respiratory mechanics in the dog. *J Appl Physiol* 45:119-127, 1978