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# Assisted Mechanical Ventilation Using Elastic Unloading: A Study in Cats with Normal and Injured Lungs[1]

ANDREAS SCHULZE, PETER SCHALLER, ANDERS JONZON, AND GUNNAR SEDIN

*Department of Pediatrics and Department of Physiology and Medical Biophysics, Uppsala University, Uppsala, Sweden [A.S., P.S., A.J., G.S.]; Children's Hospital, Dresden Medical Academy, Dresden, Germany [A.S.]; and Institute for Biomedical Engineering, Dresden Medical Academy, Dresden, Germany [P.S.]*

**ABSTRACT. Elastic unloading [otherwise known as negative ventilator compliance ($C_v$) or proportional assist ventilation] is a new mode of assisted mechanical ventilation. The ventilator continuously measures the volume of spontaneous breathing (V) and adjusts the pressure at the airway opening in proportion to V. The quotient of pressure above the baseline end-expiratory level per unit of V (the gain of the assist) is constant at any point in time and can be preset. The apparatus used for this study can also generate elastic loading (positive $C_v$) by decreasing the pressure at the airway opening in proportion to V. This might be useful during the weaning process. This study compares measured values of total compliance of the combined lung-respirator system ($C_{tot}$) with values predicted according to theory, where $1/C_{tot} = 1/C_v + 1/C_l$ with $C_l$ being the lung compliance. Respiratory mechanical data were derived from esophageal pressure and airflow in eight anesthetized, intubated, spontaneously breathing cats. Different $C_v$ levels were set on the ventilator both before and after lung injury with xanthine oxidase. The difference (mean ± SD) between the measured and predicted $C_{tot}$ was 1.4 ± 21.4% (healthy lungs) and −11.6 ± 14.1% (injured lungs) during unloading and 2.5 ± 7.5% (healthy lungs) during elastic loading. An elevation of $C_{tot}$ decreased the expiratory airflow. Tidal volume increased slightly in healthy lungs and arterial $P_{CO_2}$ decreased. We conclude that the effects of $C_v$ on the total compliance of the combined lung-respirator system can accurately be predicted. (*Pediatr Res* 34: 600–605, 1993)**

### Abbreviations

**$C_l$, lung compliance**
**CPAP, continuous positive airway pressure**
**$C_{tot}$, total compliance of the combined lung-ventilator system**
**$C_v$, ventilator compliance**
**ETT, endotracheal tube**
**$P_{ao}$, pressure at the airway opening**
**V, volume of spontaneous breathing**
**$\dot{V}$, airflow of spontaneous breathing**
**$PaCO_2$, arterial carbon dioxide tension**

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Correspondence: Andreas Schulze, M.D., McMaster University, HSC, Dept. Pediatrics, Room 4G40, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5.
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Impaired $C_l$ is often the major mechanical handicap causing respiratory failure during CPAP therapy. The use of controlled mechanical ventilation as an alternative in early lung disease stages or during recovery may, however, additionally damage lungs. Barotrauma is supposed to be more severe if the ventilator pressure levels and timing are inappropriately adjusted. Therefore, it might be helpful to enable a ventilator in its CPAP mode to counterbalance an elevated elastic recoil of the lung (*i.e.* to counterbalance decreased $C_l$) in a quantitative manner and always in tight synchrony with spontaneous breathing activity. This can be described as unloading of the elastic part of the work of breathing in patients connected to a ventilator generating a negative $C_v$. Elastic unloading might be of direct clinical relevance in stiff lungs. On the other hand, elastic loading may also be clinically useful for respiratory muscle training and during the weaning process. A patient who tolerates short periods of elastic loading appropriately is probably ready to be weaned from ventilation.

The aim of this study was to demonstrate the effects of different amounts of $C_v$ on the $C_{tot}$. $C_{tot}$ is the real elastic load placed on respiratory muscles during spontaneous breathing via a ventilator. Another objective was to assess the pattern of breathing and other parameters of pulmonary function when $C_{tot}$ is manipulated.

## MATERIALS AND METHODS

*Ventilator.* Technical details of the ventilator have been described elsewhere (1–5). The apparatus uses sensors to record $P_{ao}$ and $\dot{V}$ directly where the ETT is connected. The $P_{ao}$ signal is fed into a rapid negative feedback control loop (Fig. 1, circuit 2). Any desired $P_{ao}$ profile over time can be generated by the pneumatic system when the feedback loop controllers are guided accordingly. At CPAP mode, $P_{ao}$ is kept constant over time at a

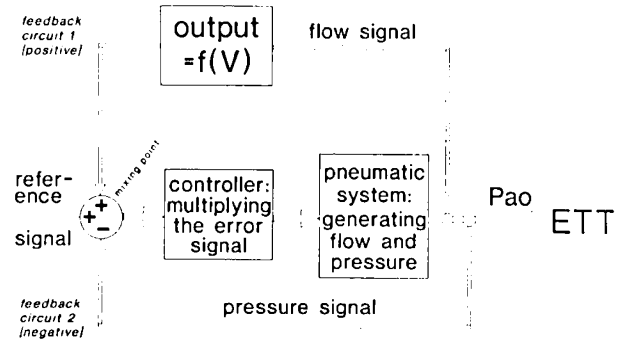


Fig. 1. Feedback system of a ventilator for elastic loading or unloading of spontaneous breathing. The $P_{ao}$ depends on a reference signal and V. For further explanation, see text.

positive pressure level. This level is determined by the reference signal only, *i.e.* feedback circuit 1 is inactivated during CPAP. To generate negative or positive $C_v$ (elastic unloading or loading), the transformed volume signal of spontaneous breathing (V, integral of $\dot{V}$) is additionally fed into the mixing point (Fig. 1). This results in $P_{ao}$ deviations from the end-expiratory baseline proportional to the instantaneously inhaled V. The degree and the direction of the $P_{ao}$ change per unit of V depends on the algorithm used to transform the volume signal in feedback circuit 1. For this study, multiplication by a constant factor of either sign was used. Therefore, the ratio $\Delta P_{ao}$ per unit of V was constant at any point in time over the volume range of spontaneous breathing (linear $C_v$). To start the loading or unloading mode, the operator sets two parameters at the ventilator front panel: *1*) the reference signal to set the end-expiratory pressure level; and *2*) the transformation factor (gain) for the volume signal in feedback circuit 1 to set the ratio $\Delta P_{ao}$ per unit of V. This ratio characterizes the elastance of the ventilator. The inversed ratio is the $C_v$.

Figure 2 shows a $P_{ao}$ profile with a positive (Fig. 2*A*, elastic loading) and negative (Fig. 2*B*, elastic unloading) $C_v$. A dummy lung with a neonatal ETT and an elastic, corrugated bag was used for this test. Spontaneous inspiration was simulated just by stretching the bag. Releasing tension on the bag allowed for passive expiration.

*Hypothesis.* The animal's lung is connected in series via the ETT to the ventilator, and therefore,

$$\frac{1}{C_{tot}} = \frac{1}{C_l} + \frac{1}{C_v} \tag{1}$$

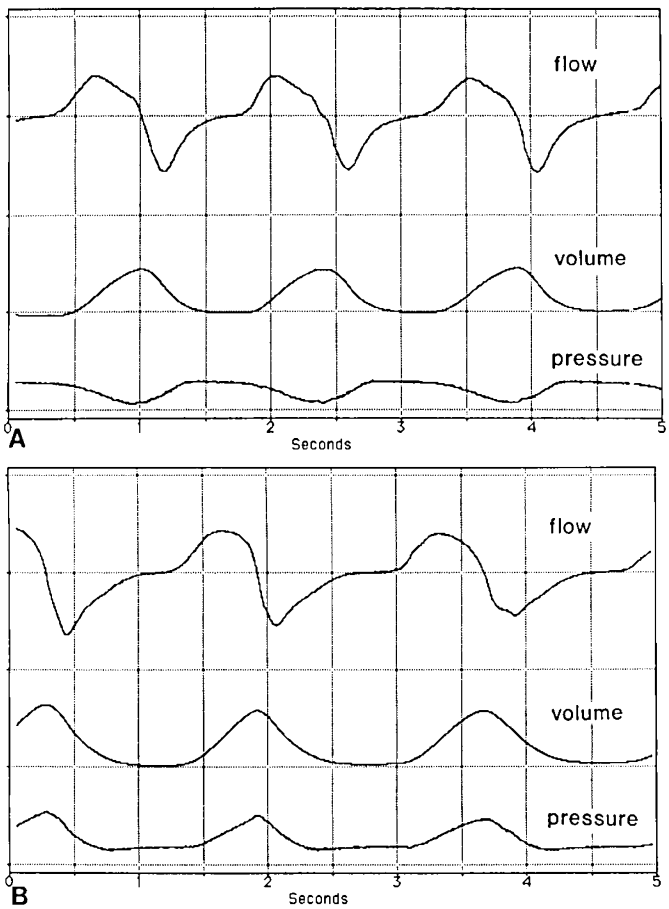


Fig. 2. $\dot{V}$, V, and $P_{ao}$ with positive (elastic loading, *A*) and negative (unloading, *B*) $C_v$. The ventilator was connected to a mechanical lung model that simulates spontaneous breathing. Arbitrary units of the signals are plotted over time.

Rearranging equation 1 yields:

$$\frac{1}{C_{tot}} = \frac{1}{C_l}\left(1 + \frac{C_l}{C_v}\right) \tag{2}$$

This gives

$$C_{tot} = C_l \frac{1}{1 + \frac{C_l}{C_v}} \tag{3}$$

This relationship between $C_{tot}$ and $C_v$ (equation 3) is graphically depicted as a solid line in Figure 3. Illustrating the theoretically expected quantitative effect of $C_v$ (*x* axis) on the total elastic load placed on spontaneous breathing activity (*y* axis), it constitutes the basic hypothesis of this study.

Because each cat had its own individual $C_l$, both $C_{tot}$ and $C_v$ were normalized to $C_l$ in each experimental run. This enabled us to include the data from all animals within one diagram (Fig. 3).

*Respiratory mechanics measurement.* A commercially available system for evaluation of lung mechanics in infants (PeDS, Medical Associated Services Inc., Hatfield, PA) was used to measure the effects of different settings of $C_v$ on $C_{tot}$.

The original Fleisch 00 pneumotach was replaced by a pneumotachometer with less dead space and resistance but equivalent dynamic properties (6). This sensor was interposed between the ETT and the ventilator's connector piece.

Esophageal pressure was recorded, referenced to atmospheric pressure, to give the total compliance and resistance data instead of that of the lung alone, which would have been calculated with esophageal pressure measurement against $P_{ao}$. The esophageal balloon was 40 mm long and 7.5 mm in diameter with a flat frequency response up to 5 Hz. The second port of the differential pressure transducer was opened to the atmosphere. The balloon was connected to an 8 French catheter and positioned in the lower part of the esophagus until the largest pressure swing

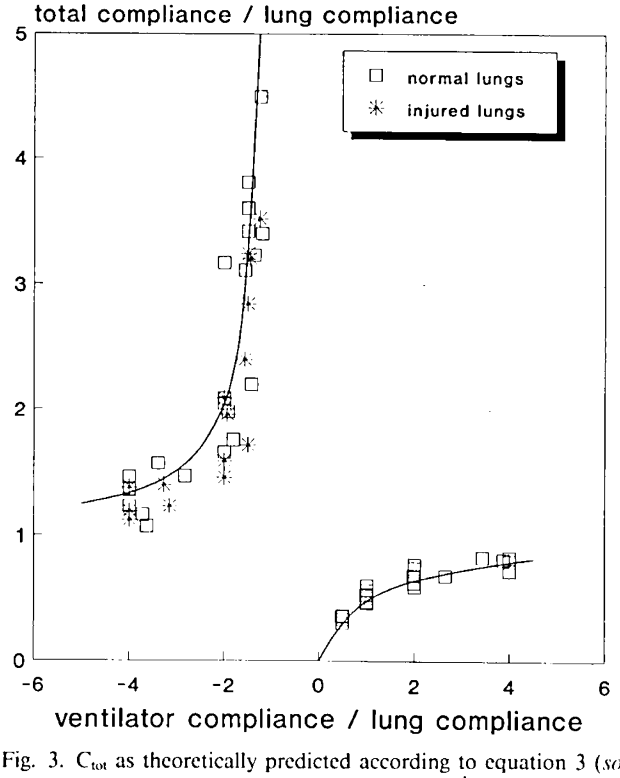


Fig. 3. $C_{tot}$ as theoretically predicted according to equation 3 (*solid line*) and as measured from esophageal pressure and $\dot{V}$ tracings in healthy (*squares*) and xanthineoxidase-injured (*asterisks*) lungs against $C_v$. All values are normalized for the baseline $C_l$. Negative $C_v$ represents elastic unloading; positive $C_v$ is elastic loading.

occurred. The validity of the esophageal balloon technique was checked using an airway occlusion technique before each experimental run (7).

Among others, the following variables were calculated by the PeDS program: total dynamic compliance, total resistance, inspiratory resistance, expiratory resistance, inspiratory and expiratory peak airflow, respiratory frequency, and inspiratory time.

*Study protocol.* Eight adult cats (mean body weight 2.74 kg, range 2.3–3.2 kg) were initially anesthetized with chloroform followed by i.v. administration of 20 mL of 0.72% chloralose (E. Merck AG, Darmstadt, Germany). Additional doses of chloralose were given regularly during the experiments. A mixture containing two thirds 10% glucose and one third bicarbonate (50 mg/mL) was given continuously i.v. at a rate of 6.4 mL/h with an infusion pump throughout the experiments. The cats were orally intubated with a 3.5-mm inner diameter ETT. A medial incision was made in the pretracheal region and a ligature was tied around the trachea to prevent leakage around the ETT.

Measurements of respiratory mechanics were started while in CPAP mode with 0.2 kPa of constant pressure at the ETT connector. No variations in $P_{ao}$ occurred at this point during tidal breathing and therefore the ventilator's resistance was zero and its compliance was infinite in this mode. Thus, recording of esophageal pressure and $\dot{V}$ during spontaneous breathing in this situation allowed us to calculate the mechanical parameters of the lung itself. These lung compliance, lung resistance, and other parameters were defined as baseline.

Thereafter, we applied four different amounts of positive $C_v$ in descending order, *i.e.* periods of stepwise increased elastic loading in each cat. The values of $C_v$ used were selected according to the individual cat's $C_l$: $C_v$ was successively set to approximately 4 times, 2 times, 1 times, and 0.5 times $C_l$. According to equation 3, this should result in $C_{tot}$ values of $0.8 \times C_l$, $0.66 \times C_l$, $0.5 \times C_l$ and $0.33 \times C_l$.

Elastic unloading was then performed using again four steps of $C_v$ set at approximately −4 times, −2 times, −1.5 times, and −1.25 times $C_l$. The corresponding expected $C_{tot}$ values were $1.33 \times C_l$, $2 \times C_l$, $3 \times C_l$, and $5 \times C_l$ (equation 3).

To document the effect of negative $C_v$ in injured lungs, the four steps of elastic unloading were repeated after intratracheal instillation of 1 mL of xanthine and 1 mL of hypoxanthine solution (8–11) in five of the eight cats. A period of at least 30 min was allowed after the instillation procedure for the animals to stabilize before the measurements of $C_l$ were performed. This new baseline value was then used to set the different levels of unloading.

Both loading and unloading modes were used with a positive end-expiratory pressure of 0.2 kPa. At least 10 consecutive breathing cycles were recorded and calculated for each ventilator setting.

*Statistics.* To evaluate the effects of changes in $C_{tot}$ on resistance, airflow, tidal volume, respiratory frequency, and $PaCO_2$, data were plotted against a logarithmic scale of $C_{tot}$. Logarithmic transformation was used because $C_{tot}$ increased nonlinearly with $C_v$ and the variance of the measured $C_{tot}$ also increased with higher $C_{tot}$ (Fig. 3). Linear regression analysis was performed using the method of least squares to obtain the line of best fit for each animal separately. This is shown for the parameters expiratory resistance, peak expiratory flow, tidal volume, and $PaCO_2$ in Figures 5 and 6. Two-tailed *t* tests were done to evaluate whether the mean of the slopes of the regression lines across all individual animals was significantly different from zero. This analysis was performed separately for the data from healthy and injured lungs. Two-tailed *t* tests were used to assess the baseline mechanical parameters before and after lung injury (Table 1).

## RESULTS

As confirmed with the mechanical test lung, the ventilator kept $P_{ao}$ constant with the CPAP mode of breathing. There were neither variations in $P_{ao}$ proportional to $\dot{V}$ nor variations in $P_{ao}$ proportional to V, *i.e.* apparatus resistance was zero and apparatus compliance was infinite. With elastic loading and unloading, the pattern of $P_{ao}$ imitated the V pattern and no changes in $P_{ao}$ proportional to $\dot{V}$ occured (Fig. 2).

*Qualitative Characteristics of Esophageal Pressure, $\dot{V}$, and V Signals with Elastic Unloading.* With partial elastic unloading, the esophageal pressure drop necessary to generate a given amount of tidal volume was lower than during baseline measurements (Fig. 4*A*, left and middle tracings, top and bottom panel). The corresponding esophageal pressure-volume loops (Fig. 4*B*, left and middle upper loop) are characterized by a steeper slope with the unloading mode. This indicates the elevation of $C_{tot}$. Improving $C_{tot}$ by unloading uniformly affected the expiratory flow-volume-time characteristics. With unloading, expiratory peak flow decreased and the decay rate of $\dot{V}$ over time was diminished (Fig. 4*A*, middle panel; *B*, lower panel). As a result, volume was expired more slowly and the slope of the expiratory $\dot{V}$-V loop was reduced (Fig. 4*B*, lower panel). This demonstrates the prolonged time constant of the system (product of $C_{tot}$ and resistance) with elastic unloading.

Further increase in the degree of the elastic unloading resulted in a further increase in the slope of the pressure-volume loop until it was perpendicular. In this situation of infinite $C_{tot}$, *i.e.* when the negative $C_v$ completely balances the positive $C_l$, there remains only a resistive load on spontaneous breathing activity. With decreasing the negative $C_v$ in amount even more, the pressure-volume loops move to the left of the vertical, which gives them a negative slope. Thus, the elastic retraction forces of the lung were overcompensated, leading to negative $C_{tot}$. There was a dramatic sudden change in the pattern of breathing with overcompensation. Both total cycle duration and tidal volume increased considerably. The pressure-volume loops changed their direction and turned clockwise (Fig. 4*A* and *B* right columns).

*Quantitative Findings. Baseline respiratory parameters with infinite $C_v$.* Table 1 gives the means ± SD of all individual baseline respiratory parameters as measured with zero ventilator resistance and infinite $C_v$ before starting the loading-unloading experiments. "Baseline" $C_l$ was significantly lower after administration of xanthine oxidase. All other changes after xanthine oxidase did not reach the level of significance.

*Effect of $C_v$ on $C_{tot}$.* The measured $C_{tot}$ changed in a hyperbolic way by the selection of $C_v$ in accordance with the hypothesis (Fig. 3). Table 2 gives the mean differences between measured $C_{tot}$ values and $C_{tot}$ as predicted according to equation 3.

*Effect of $C_v$ on resistance and $\dot{V}$.* With increasing $C_{tot}$, we found a significant decrease in total resistance both in normal and injured lungs. This was mainly due to a decrease in expiratory resistance, whereas inspiratory resistance did not change significantly (Table 3, Fig. 5).

These changes in resistance with elastic loading and unloading paralleled the changes in the $\dot{V}$ pattern. Peak expiratory $\dot{V}$ decreased with increasing $C_{tot}$, but peak inspiratory $\dot{V}$ remained unchanged (Table 3, Fig. 5).

*Effect of $C_v$ on pattern of spontaneous breathing.* The pattern of breathing in cats with normal lungs was characterized by a slight increase in tidal volume with elevating $C_{tot}$, whereas the respiratory rate did not change significantly. This resulted in an increase in minute ventilation and, as expected, the $PaCO_2$ was lower with unloading (Table 3, Fig. 6). Inspiratory time did not change significantly with the amount of elastic load. Significant effects on tidal volume, respiratory rate, and $PaCO_2$ were not found in cats with injured lungs.

## DISCUSSION

We studied the *in vivo* applicability of an infant ventilator system designed to generate negative or positive internal compliance. The rationale of this concept is that the respiratory system and the ventilator—when interconnected by an ETT—both con-

Table 1. *Baseline respiratory parameters before starting loading/unloading experiments in healthy lungs and after tracheal instillation of xanthine oxidase (mean ± SD)*

| | Healthy lungs ($n = 8$) | Xanthine oxidase–injured lungs ($n = 5$) | $p$ |
|---|---|---|---|
| Lung compliance (mL/kPa) | 53.3 ± 9.16 | 45.8 ± 10.4 | <0.05 |
| Lung resistance (kPa/L/s) | 5.26 ± 1.07 | 5.64 ± 1.50 | NS |
| Inspiratory resistance (kPa/L/s) | 6.29 ± 1.83 | 5.40 ± 3.19 | NS |
| Expiratory resistance (kPa/L/s) | 4.19 ± 1.31 | 5.58 ± 1.78 | NS |
| Peak inspiratory flow (L/min) | 1.95 ± 0.72 | 1.86 ± 0.11 | NS |
| Peak expiratory flow (L/min) | 3.02 ± 0.74 | 3.00 ± 0.44 | NS |
| Respiratory frequency (L/min) | 11.7 ± 2.68 | 12.9 ± 2.88 | NS |
| Tidal volume (mL) | 12.6 ± 2.74 | 11.6 ± 2.36 | NS |
| Inspiratory time (s) | 2.01 ± 0.43 | 1.69 ± 0.36 | NS |
| $Paco_2$ (kPa) | 6.37 ± 0.71 | 6.98 ± 0.37 | NS |

tribute to the $C_{tot}$ (according to equation 3). This $C_{tot}$ imposes the elastic workload on the respiratory muscles. Conventional ventilators in CPAP mode usually behave with infinite or very high compliance, *i.e.* the pressure at the endotracheal tube level either does not change at all with the tidal volume or decreases a little with inspiring volume from the system. Therefore, $C_{tot}$ equals $C_I$ (see equation 3) and the elastic work of breathing increases with a decrease in $C_I$ on those ventilators. $C_{tot}$ can achieve higher ("better") values than $C_I$ only when $C_V$ is negative. That implies an instantaneous increase in $P_{ao}$ proportional to the inspired volume and results in unloading of the elastic work of spontaneous breathing. In other words, with a negative $C_V$ the elastic work of breathing is shared between respiratory muscles and the ventilator.

*Effect of $C_V$ on $C_{tot}$.* Our study was not done just to validate the theory of elastic unloading. This is not necessary because the assumptions and corollaries are physically correct and proven in a "bag in bottle" lung model (3). However, it seemed necessary to demonstrate that the technical system meets our theoretical expectations when used for elastic loading and unloading *in vivo*. If so, the measured $C_{tot}$ should be close to the theoretically calculated $C_{tot}$. This is shown in Figure 3 for both normal and injured lungs. It demonstrates that in an *in vivo* situation the negative $C_V$ can be adjusted accurately enough within a range where $C_{tot}$ is at least 3 to 4 times higher than $C_I$. Beyond this range, the relationship between $C_{tot}$ and $C_V$ becomes critically steep so that a very small change in ventilator compliance can cause a tremendous increase in $C_{tot}$. The situation is potentially dangerous when $C_{tot}$ approaches infinity, *i.e.* when the pressure-volume loops become perpendicular or even rotated to the left (negative $C_{tot}$). In this situation, the elastic retraction forces of the lung are overcompensated. This results in an unstable behavior because the negative $C_V$ mode is a positive feedback loop: a small increase in volume generates an elevated pressure high enough to produce in turn a further increase in volume, thus filling the lungs with more and more volume. At some point, the ongoing inflation will be stopped when the lungs become critically overinflated and the (nonlinear) $C_I$ decreases, finally overwhelming the (linear) negative $C_V$ (Fig. 4*A* and *B*, right panels).

There are several options to avoid this hyperinflation in case of inadvertent elastic overcompensation. The operator must have possibilities to set an upper tidal volume and/or upper $P_{ao}$ limits. When reaching a limit, the ventilator could immediately return to the end-expiratory pressure level allowing a fast expiration without negative $C_V$. Unloading could then be started again with the next inspiration. Another alternative would be to hold the $P_{ao}$ at the upper limit until a decrease in volume is initiated by spontaneous expiration. If exhalation is accompanied by the same negative $C_V$, expiration will be very slow because of the high $C_{tot}$ and therefore long time constant near elastic overcompensation. Thus, either the ventilator should automatically increase the negative $C_V$ in amount or the user should be requested to do it manually.

These options to prevent hyperinflation and to prevent expiration from being too slow can easily be integrated in the software of the ventilator system used. The question as to which is most practical remains to be answered. We also have not yet studied systematically the pattern of breathing with either limiting mechanism in place.

*Effect of $C_V$ on resistance and $\dot{V}$.* The decrease in expiratory resistance with elastic unloading (Fig. 5) cannot be attributed to any resistive properties of the ventilator because the ventilator resistance was kept at zero throughout these experiments. Airway resistance rises at higher levels of $\dot{V}$. Therefore, the decrease in expiratory resistance is likely to be due at least in part just to the lower expiratory $\dot{V}$ at higher levels of $C_{tot}$ (Fig. 4*A* and *B*, left and middle panel; Fig. 5). Another reason might be that the higher pressure exerted during expiration by the negative $C_V$ with unloading keeps the airways better expanded and thereby lowers the expiratory resistance. In contrast, peak inspiratory $\dot{V}$ and inspiratory resistance did not change significantly.

*Effect of $C_V$ on pattern of breathing.* Efforts to study the effect of elastic loading and unloading on the pattern of spontaneous breathing have previously been hampered by technical difficulties. Most authors used rigid containers of different sizes to provide the load but were unable to adjust the load gradually or to unload respiration. Our findings agree with previous reports showing a decrease in tidal volume with elastic loading in cats (12), human adults (13), and human infants (14, 15). Our study was not designed to evaluate the effect of elastic unloading on $Paco_2$ homeostasis, and therefore the results given in Table 3 and Figure 5 should be considered with caution. Moreover, there was a broad scattering of the baseline $Paco_2$ values (Table 1). However, it seems to be justified to conclude from Figure 6 that minute ventilation is reduced with elastic loading at the expense of higher arterial $CO_2$ levels. This might be interpreted as an attempt of the respiratory system to prevent respiratory muscle fatigue when confronted with the load at the expense of maintaining a normal $Paco_2$.

On the other hand, elastic unloading increased tidal volume in normal lungs. The same tendency was found in diseased lungs but did not reach significance statistically, most likely because of the small sample size (Table 3). Whether it may induce some mild sustained hyperventilation in normal lungs as Figure 6 suggests remains to be further studied. This question, however, seems not to be of clinical relevance. We basically do not want to unload healthy lungs but aim to handle low-compliance lungs in a way that leads to elastic properties of the combined lung-ventilator system within the normal range of the lung compliance.

To our knowledge, two other groups have been working on the concept of respiratory mechanical unloading (16–20). Whereas earlier studies focused on physiologic effects of unloading, Younes *et al.* (19, 20) recently reported on a pilot clinical application of the technique (called proportional assist ventilation) in adults. Their apparatus generates mechanical unloading

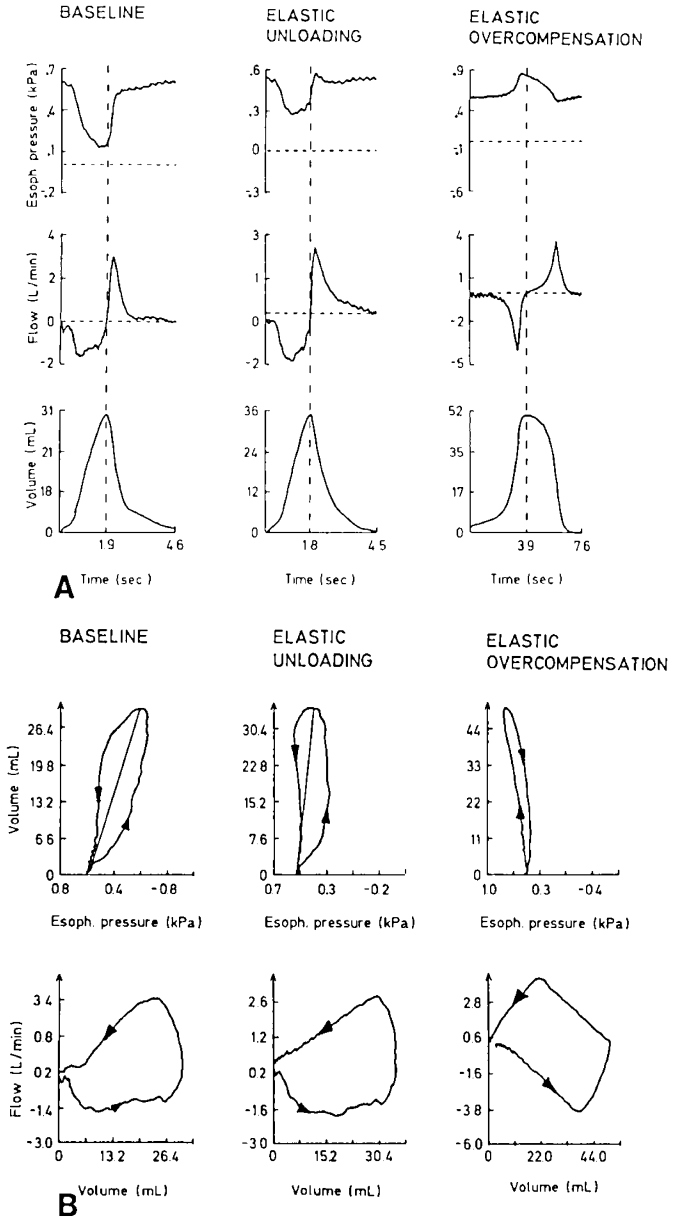


Fig. 4. *A*, Esophageal pressure (measured against atmosphere), airflow, and tidal volume over time for three single cycles of spontaneous breathing. Baseline was recorded with an infinite $C_v$ and therefore characterizes the elastic properties of the lung itself. *Middle* and *right panel* show partial compensation of lung elasticity and overcompensation, respectively. *B*, Corresponding pressure-volume and flow-volume loops of the breaths shown in *A*. Note the different scales. For further explanation, see text.

Table 2. *Differences between measured and calculated* $C_{tot}$ *(mean ± SD)*

| | Measured − calculated $C_{tot}$ (%)* | |
|---|---|---|
| | Loading | Unloading |
| Healthy lungs | 2.5 ± 7.5 ($n$ = 31) | 1.4 ± 21.4 ($n$ = 23) |
| Injured lungs | | −11.6 ± 14.1 ($n$ = 15) |

* The differences are given in percent of the calculated $C_{tot}$·$C_{tot}$ values are multiples of the baseline $C_1$ ($C_{tot}/C_1$), and therefore they do not have a dimension.

Table 3. *Effect of* $C_{tot}$ *on lung function parameters**

| | Normal lungs ($n$ = 8) | | | Injured lungs ($n$ = 5) | | |
|---|---|---|---|---|---|---|
| Parameter | $\bar{b}$ | SD | $p$ | $\bar{b}$ | SD | $p$ |
| Rtot | −1.30 | 0.78 | <0.01 | −1.06 | 0.61 | <0.02 |
| Rexp | −1.46 | 1.00 | <0.01 | −2.66 | 1.55 | <0.02 |
| Rinsp | −0.03 | 0.76 | NS | 0.44 | 0.55 | NS |
| Peak expiratory $\dot{V}$ | −1.28 | 0.72 | <0.01 | −0.93 | 0.47 | <0.02 |
| Peak inspiratory $\dot{V}$ | 0.07 | 0.17 | NS | 0.16 | 0.21 | NS |
| Tidal volume | 0.84 | 0.59 | <0.01 | 1.64 | 1.34 | NS |
| Respiratory frequency | 0.38 | 0.89 | NS | −0.75 | 0.74 | NS |
| $P_{ACO_2}$ | −0.63 | 0.42 | <0.01 | −0.50 | 0.45 | NS |

* Mean and SD of the regression line slopes ($\bar{b}$, SD) are shown. Rtot, total resistance; Rexp, expiratory resistance; Rinsp, inspiratory resistance. Regression lines were calculated for the relationship between a lung function parameter and the logarithm of $C_{tot}$ in $n$ individual animals. $p$ indicates the probability that the parameter of interest does not change with $C_{tot}$ (two-tailed $t$ test with null hypothesis: b = 0).

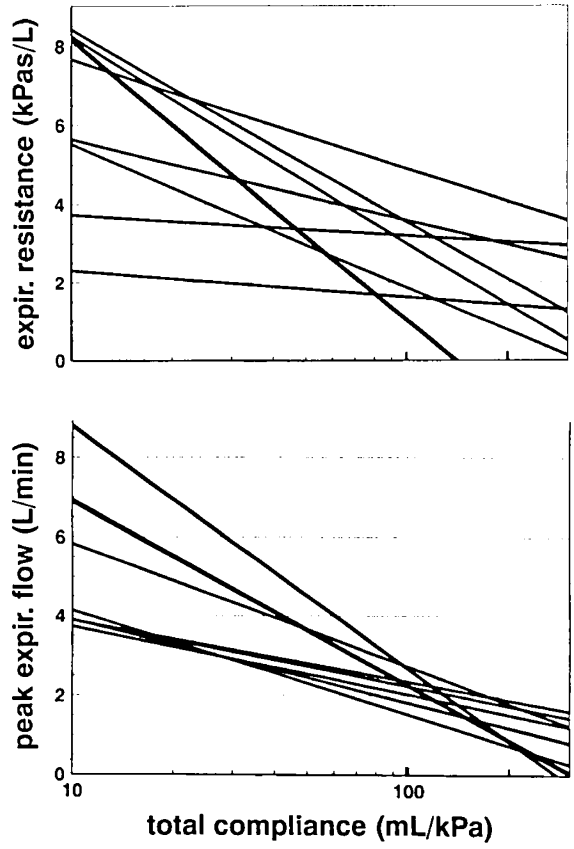


Fig. 5. Expiratory resistance and expiratory peak airflow *vs* $C_{tot}$. Regression lines for eight cats without lung injury are shown.

during inspiration and expiration takes place against a constant positive pressure. When other modes of mechanical ventilation become necessary, the patient has to be connected to a conventional ventilator.

Our system was constructed as an all-purpose infant ventilator. In addition to the conventional patterns of mechanical ventilation and high-frequency oscillation (4), it can provide resistive (5) and elastic unloading (3) as a specific type of assisted ventilation. At this latter mode, the ventilator serves to compensate impaired resistive and/or elastic properties of the lung. Consequently, the patient's diaphragm works on a lung-ventilator system with the mechanical properties of a normal lung. The patient can set the main parameters of the breathing pattern, *i.e.* flow, volume, and timing, using his own neuromuscular system.

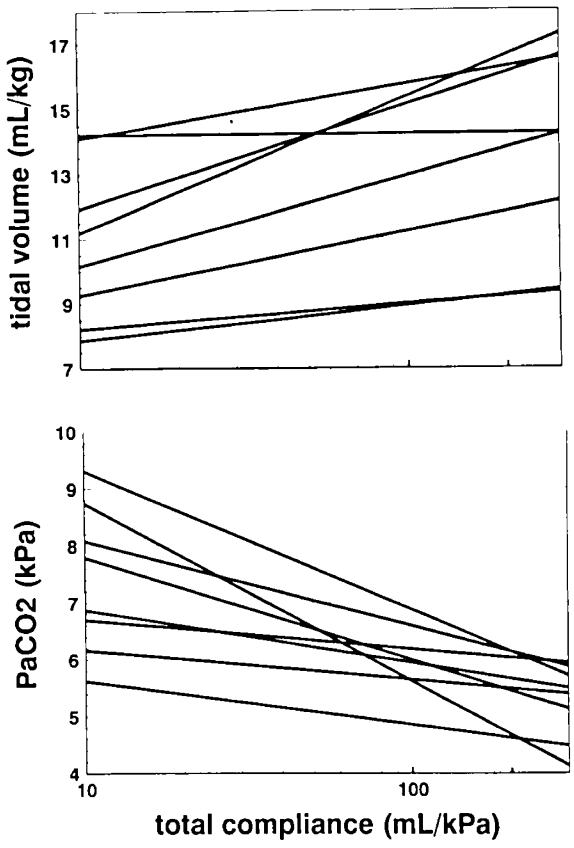


Fig. 6. Tidal volume and $Paco_2$ *vs* $C_{tot}$. Regression lines for eight cats without lung injury are shown.

This is different from recently developed modes for triggered ventilation that synchronize the patient's "internal" onset of inspiration and the beginning of the mechanical cycle with a fairly short response time. Those systems still deliver a preset mechanical pattern fixed at least with respect to inspiratory time, peak inspiratory pressure, or tidal volume. Therefore, they cannot avoid discrepancies between the "internal breathing pattern generator" and the pattern of the machine.

Elastic unloading appears to be a useful form of assisted mechanical ventilation in our experimental setup. However, several important aspects remain to be studied before this system can be introduced in the clinical setting. For example, the performance of the technique has not been studied with leaks around the ETT. The effect of elastic and resistive overcompensation (which may occur inadvertantly) on the regulation of breathing and cardiovascular parameters is unknown. In addition, clinical pilot studies should benefit from a more advanced ventilator technology with possibilities to apply nonlinear $C_x$ characteristics and to monitor the breathing pattern closely.

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REFERENCES

1. Schaller P 1982 Patent "Beatmungsgerät" DD A 61 M 16/00:212186, Berlin, Germany
2. Schaller P 1983 Patent "Beatmungsgerät" DD A 61 H 31/00:221364, Berlin, Germany
3. Schaller P, Schulze A 1991 A ventilator generating a positive or negative internal compliance. Ups J Med Sci 96:219–234
4. Schulze A, Schaller P, Gehrhardt B, Mädler H-J, Dinger J, Gmyrek D, Winkler U, Nitzsche H, Mehler HJ 1989 High frequency oscillatory and conventional mechanical ventilation in experimental surfactant deficiency: a study using a new infant ventilator technique. Z Erkr Atmungsorgane 172:272–281
5. Schulze A, Schaller P, Gehrhardt B, Mädler H-J, Gmyrek D 1990 An infant ventilator technique for resistive unloading during spontaneous breathing. Results in a rabbit model of airway obstruction. Pediatr Res 28:79–82
6. Schaller P, Mädler H-J, Schulze A, Böhme B, Leupold W 1985 Ein Lamellen-Spirorezeptor für die Pneumotachographie bei Frühgeborenen und Säuglingen. Z Klin Med 40:947–949
7. Beardsmore CS, Helms P, Stocks J, Hatch DJ, Silverman M 1980 Improved esophageal balloon technique for use in infants. J Appl Physiol 49:735–742
8. Saugstad OD, Hallman M, Becher G, Oddoy A, Lachmann B 1984 Protective effect of superoxide dismutase on severe lung damage caused by xanthine oxidase. Pediatr Res 18:802(abstr)
9. Saugstad OD 1985 Oxygen radicals and pulmonary damage. Pediatr Pulmonol 1:167(abstr)
10. Lachmann B, Saugstad OD, Klein J, Erdmann W 1987 Acute respiratory failure induced by tracheal instillation of xanthine oxidase, its prevention and therapy by exogenous surfactant instillation. Adv Exp Med Biol 215:351–354
11. Saugstad OD, Becher G, Grossmann M, Merker G, Oddoy A, Lachmann B 1987 Acute and chronic effects of xanthine oxidase on lung thorax-compliance in guinea pigs. Intensive Care Med 13:30–32
12. Miserocchi G, Milic-Emili J 1976 Effect of mechanical factors on the relation between rate and depth of breathing in cats. J Appl Physiol 41:277–284
13. Poon C-S 1989 Effects of inspiratory elastic load on respiratory control in hypercapnia and exercise. J Appl Physiol 66:2400–2406
14. Boychuk RB, Seshia MMK, Rigatto H 1977 The immediate ventilatory response to added inspiratory elastic and resistive loads in preterm infants. Pediatr Res 11:276–279
15. Fox RE, Kosch PC, Feldman HA, Stark AR 1988 Control of inspiratory duration in premature infants. J Appl Physiol 64:2597–2604
16. Poon CS, Ward SA 1986 A device to provide respiratory-mechanical unloading. IEEE Trans Biomed Eng 33:361–365
17. Poon CS, Ward SA, Whipp BJ 1987 Influence of inspiratory assistance on ventilatory control during moderate exercise. J Appl Physiol 62:551–560
18. Younes M, Bilan D, Jung D, Kroker H 1987 An apparatus for altering the mechanical load on the respiratory system. J Appl Physiol 62:2491–2499
19. Younes M 1992 Proportional assist ventilation, a new approach to ventilatory support. Am Rev Respir Dis 145:114–120
20. Younes M, Puddy A, Roberts D, Light RB, Quesada A, Taylor K, Oppenheimer L, Cramp H 1992 Proportional assist ventilation. Results of an initial clinical trial. Am Rev Respir Dis 145:121–129