

# Decreasing size of cardiogenic oscillations reflects decreasing compliance of the respiratory system during long-term ventilation

Michael Lichtwarck-Aschoff,<sup>1</sup> Bela Suki,<sup>2</sup> Anders Hedlund,<sup>1</sup> Ulf H. Sjöstrand,<sup>1</sup> Agneta Markström,<sup>1</sup> Rafael Kawati,<sup>1</sup> Göran Hedenstierna,<sup>3</sup> and Josef Guttmann<sup>4</sup>

Departments of <sup>1</sup>Surgical and <sup>3</sup>Medical Sciences, Uppsala University, 751 05 Uppsala, Sweden; <sup>2</sup>Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215; and <sup>4</sup>Department of Anaesthesiology and Critical Care Medicine, Freiburg University, 79085 Freiburg, Germany

Submitted 18 May 2003; accepted in final form 22 October 2003

**Lichtwarck-Aschoff, Michael, Bela Suki, Anders Hedlund, Ulf H. Sjöstrand, Agneta Markström, Rafael Kawati, Göran Hedenstierna, and Josef Guttmann.** Decreasing size of cardiogenic oscillations reflects decreasing compliance of the respiratory system during long-term ventilation. *J Appl Physiol* 96: 879–884, 2004. First published October 24, 2003; 10.1152/jappphysiol.00532.2003.—Part of the energy produced by the heartbeat is transferred to the lung and promotes intrapulmonary gas mixing. It is likely that this transmission in the form of local mechanical disturbances affects and reflects respiratory mechanics. The effects of the cardiogenic oscillations were studied in seven piglets during 7 h of monotonous mechanical ventilation. During the 1st h of ventilation, every heartbeat triggered a noticeable transient increase in lung volume of 14 ml (95% confidence interval = 10–17 ml). After 7 h, the increase in lung volume due to heartbeat significantly decreased to 7 ml (95% confidence interval = 2–9 ml,  $P < 0.05$ ). During the course of ventilation, overall lung compliance and gas exchange were progressively compromised. We conclude that 1) sufficient mechanical energy is transferred from the beating heart to the lung to increase lung volume, and 2) the ability of the heartbeats to help increase lung volume is reduced during long-term ventilation, which reflects the changes in lung compliance.

heart-lung interaction; cardiac cycle; heart motion

CARDIOGENIC OSCILLATIONS on the volume-pressure (V-P) curves of the lung reflect a transfer of mechanical energy from the beating heart to the lungs. As a result of this energy transfer, intrapulmonary gas mixing is enhanced. A related aspect of the heart-lung coupling is the potential impact of local mechanical disturbances induced by the heartbeats on respiratory mechanics (1). Cardiogenic oscillations might have a diagnostic application. Their appearance on the V-P curve is affected by and reflects the conditions of energy transmission, that is, the elastic and resistive properties of the respiratory system. Consequently, Bijaoui and coworkers (1) used cardiogenic oscillations to assess mechanical lung output impedance. The heartbeats, generated by a natural “in-built” oscillator, potentially offer a tool for analyzing respiratory mechanics without disturbing ongoing ventilation.

Our aim was to evaluate the increase in lung volume induced by cardiogenic oscillations on the inspiratory V-P curve during long-term mechanical ventilation. Because the compliance of the respiratory system decreases during monotonous ventilation, we assumed that the cardiogenic oscillations would equally decrease and, hence, that their size would reflect the change in the compliance of the lung. In piglets with healthy

lungs, we found that the disturbances or “kicks” in the pleural space induced by the beating heart were strong enough to significantly increase lung volume and that this effect was attenuated by long-term mechanical ventilation.

## MATERIALS AND METHODS

After approval of the Ethics Committee, this study was conducted in conformity with the National Institutes of Health guidelines in the laboratories of the Department of Surgical Sciences, University of Uppsala.

**Study protocol.** The lungs of seven piglets ( $25.0 \pm 1.5$  kg) were ventilated for 7 h at constant settings. Measurements for mechanics (data acquisition period = 2 min) were taken after a 30-min stabilization period and in the prone position every 15 min. At the end of the protocol, the animals were killed with potassium chloride.

In four animals, before long-term ventilation, additional measurements were performed with 1) the endotracheal tube disconnected from the ventilator and complete muscle paralysis, i.e., with the airways open to the atmosphere but without the animals breathing on their own, and 2) during a 10-s end-expiratory hold at 0 cmH<sub>2</sub>O positive end-expiratory pressure (PEEP) with the endotracheal tube connected to the ventilator, also with muscle paralysis.

In one animal, short-term ventilation was applied at 0, 6, 10, and 15 cmH<sub>2</sub>O PEEP, each for 15 min.

**Ventilator settings.** Inspiratory flow was constant (0.2 l/s), inspiration-to-expiration ratio was 1:1, ventilatory frequency was 20 min<sup>-1</sup>, end-expiratory pressure (PEEP) and flow were zero, tidal volume (V<sub>T</sub>) was 13 ml/kg [ $6.2 \pm 1$  kPa arterial P<sub>O</sub><sub>2</sub> (Pa<sub>O</sub><sub>2</sub>),  $7.38 \pm 0.4$  arterial pH], and fraction of inspired O<sub>2</sub> was 1.0. To standardize lung volume history, volume-controlled ventilation was applied for 1 min before initiation of long-term ventilation, with PEEP set to 15 cmH<sub>2</sub>O and V<sub>T</sub> doubled.

**Anesthesia and monitoring.** Ketamine (20 mg·kg<sup>-1</sup>·h<sup>-1</sup>) and morphine (0.5 mg·kg<sup>-1</sup>·h<sup>-1</sup>) produced a light level of anesthesia; neuromuscular block was achieved by administration of pancuronium bromide (0.25 mg·kg<sup>-1</sup>·h<sup>-1</sup>). The level of anesthesia was assumed appropriate, because hemodynamics could be kept stable at the postinduction level and neither signs of spontaneous respiratory activity [as determined from esophageal pressure (P<sub>es</sub>) tracings] nor pain reflex muscular or autonomic nerve activity induced by intermittent pinching of the paw could be detected. ECG signals were obtained from a standard V<sub>5</sub> lead. Intravascular catheters were surgically placed for the collection of blood for arterial and mixed venous blood-gas analysis (model ABL5 analyzer and OSM3 hemoximeter, Radiometer, Copenhagen, Denmark) and measurement of central venous, pulmonary arterial (via the external jugular vein), and aortic pressures (via the carotid artery). The position of the catheters was confirmed by pressure

Address for reprint requests and other correspondence: M. Lichtwarck-Aschoff, Department of Anesthesiology, Klinikum Augsburg, D-86009 Augsburg, Germany (E-mail: m.lichtwarck-aschoff@t-online.de).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

tracing. Cardiac output was determined by thermodilution. Derived variables were calculated according to standard formula.

**Data acquisition.** Ventilation was applied through an endotracheal tube (ID 8, Mallinckrodt, Athlone, Ireland) by a ventilator (Servo 300, Siemens-Elma, Solna, Sweden). Pes, airway pressure, and flow were measured with a monitor (model CP100, Bicore Monitoring Systems, Irvine, CA) placed between the tracheal tube and the Y piece of the ventilator circuit. Data were sampled at 200 Hz with AcqKnowledge software (version 3.2.7, BioPac System, Santa Barbara, CA).

**Analysis of mechanics.** Airway pressure at the Y piece (Paw), Pes, and flow were measured. Transpulmonary pressure (Ptp) was calculated as  $P_{tp} = P_{aw} - P_{es}$ , and volume was calculated by integration of flow.

A straight line was fitted to the inspiratory  $V_T$ -Paw and  $V_T$ -Ptp curves, and the overall compliance of the respiratory system (Crs) and the overall compliance of the lung were determined from the slope of the straight-line fit. The quasi-static compliance of the respiratory system was also determined (using a 5-s end-inspiratory and end-expiratory hold).

To assess the effects of the heartbeats on the V-P curves, a straight line was fit to the first 40 data points (corresponding to 200 ms) of the V-P curve immediately after a cardiogenic oscillation using the least squares method. In most cases, we observed a sudden increase in volume after a heartbeat, which we attributed to a regional lung volume gain due to the heartbeat kick. The volume gains were determined as the volume difference (or difference in intercepts) between the straight-line fits to the post- and pre-heartbeat segment.

**Data presentation and statistics.** If not otherwise indicated, values are means  $\pm$  SD or 95% (lower to upper) confidence interval (CI). Differences in time-related variables were assessed using repeated-measures ANOVA with the Student-Newman-Keuls post hoc test. Variables were assessed for potential association by regression analysis. Statistical significance was assumed with  $P \leq 0.05$ .

## RESULTS

**Impact of cardiogenic oscillations on respiratory mechanics.** With the airways open to the atmosphere (endotracheal tube disconnected) and without respiratory muscle activity, each heartbeat induced a transient peak of gas flow entering the lung that coincided with atrial systole. A second gas flow transient, coinciding with ventricular systole, was followed by an expiratory trough, coinciding with diastole (Fig. 1A). The gas volume transfer corresponded to 20 ml (95% CI = 17–26 ml) in both directions. The delay between the QRS complex and the onset of inspiratory flow was 36 ms (95% CI = 30–39 ms).

With the airways closed to the atmosphere (endotracheal tube connected) again at end expiration and with muscle paralysis (Fig. 1B), changes in Paw were also regularly coupled to the heartbeats: Paw started to increase 140 ms (95% CI = 110–164 ms) after the QRS complex.

When the ventilator delivered a constant inspiratory flow (Fig. 2), the same modulating effect of the heartbeats on the flow vs. time and pressure vs. time plots could still be seen. An inspiratory flow transient coincided with atrial and ventricular systole, while the diastolic trough disappeared in the flow oscillations caused by flow-regulating valves in the ventilator (Fig. 2A). In the Paw-time plot, the heartbeat-induced inspiratory flow transients were immediately followed by a deceleration of the Paw, appearing as a deviation from its linear increase and causing concavity in the Paw curve (“cardiac kicks”; arrows in Fig. 2B). The time during which the Paw increase was slowed after a heartbeat was  $\sim$ 50 ms.

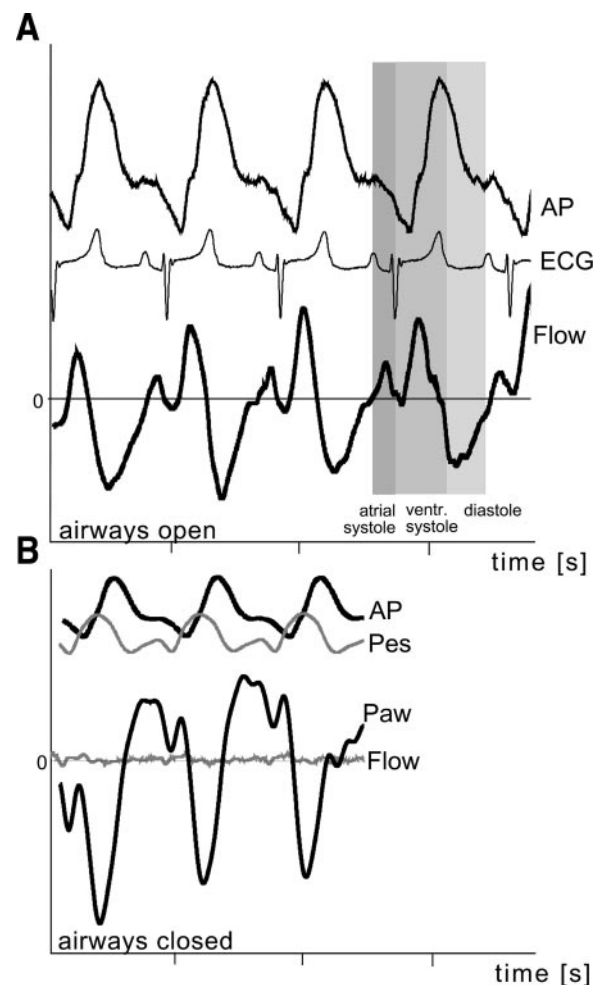


Fig. 1. Heartbeat-induced pressure and flow in a representative animal. **A:** airways open to atmosphere (with endotracheal tube disconnected and without respiratory muscle activity). AP, systemic arterial pressure. Part of the cardiac cycle is shown in shaded boxes. Flow corresponds to a volume of 20 ml per heartbeat. Flow that is positive with respect to the zero line represents flow into the lung; flow that is negative with respect to the zero line represents flow out of the lung. **B:** airways closed to the atmosphere (with the endotracheal tube connected) at an end-expiratory hold without respiratory muscle activity. Values for esophageal pressure (Pes), airway pressure (Paw), and gas flow are arbitrary units.

If the compliance of the respiratory system is constant and the ventilator delivers a constant inspiratory flow, the V-Paw relation should be a straight line with the same slope as its initial segment (i.e., the segment from start until  $c_1$ , slope  $I$  in Fig. 3). Instead, there are distinctive heartbeat-induced sudden volume gains ( $c_1$ ,  $c_2$ , and  $c_3$  in Fig. 3) on the V-Paw relation. These cardiac kicks shift the volume to a higher level with a minimal increase in Paw (Fig. 2) and Pes (Fig. 3). After a cardiac kick, the volume continues to increase, now in a more steady way (see segments after  $c_1$ - $c_2$  and  $c_2$ - $c_3$  in Fig. 3), until the next cardiac kick. Those segments of the V-Paw curve between the cardiac kicks are, however, not perfectly linear. Rather, volume increases at a reduced rate from  $c_1$  to  $a_1$ , and this rate is accelerated between  $a_1$  and  $c_2$ . Again, in the  $c_2$ - $c_3$  segment, volume increases in a slightly slower fashion from  $c_2$  to  $a_2$  and increases more

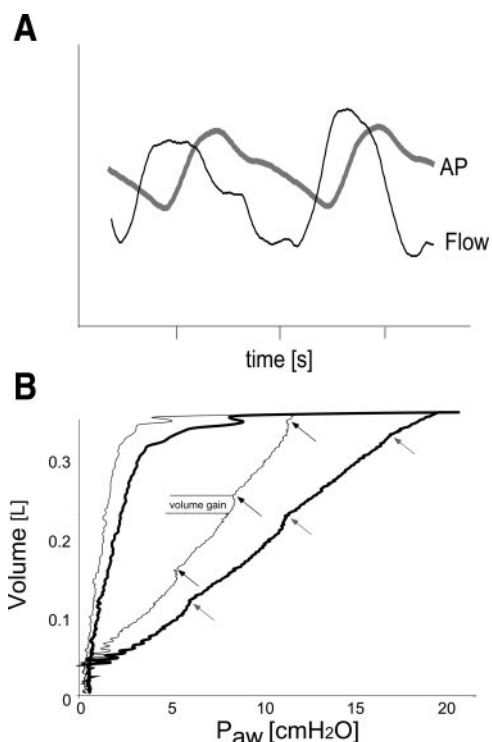


Fig. 2. Heartbeat-induced gas flow and lung volume during constant-flow mechanical inflation in a representative animal. *A*: systemic AP and gas flow in arbitrary units during a constant-flow mechanical inspiration without respiratory muscle activity. Both traces are smoothed with a moving average (period = 20 data points). *B*: plot of lung volume vs.  $P_{aw}$  at the beginning of the experiment (thin loop) and after 7 h of ventilation (thick loop). Arrows denote heartbeat-induced volume gain at nearly constant pressure.

rapidly from  $a_2$  to  $c_3$ . These small fluctuations in volume increase coincide roughly with the time during which the ventricles fill (ventricular diastole + atrial systole). During this period,  $P_{es}$  rises, and the increase in lung volume is slowed ( $c_1$ - $a_1$  and  $c_2$ - $a_2$ ). During the ventricular ejection phase (most pronounced during rapid ejection),  $P_{es}$  decreases and volume increases more rapidly ( $a_1$ - $c_2$  and  $a_2$ - $c_3$ ).

At the beginning of the experiment (Figs. 3*B* and 4*A*), the first heartbeats induced a lung volume gain of 14 ml (95% CI = 10–17 ml), while at the end of the 7-h experimental period (Fig. 4*B*), volume gain per heartbeat was 7 ml (95% CI = 2–9 ml,  $P \leq 0.05$ ; Table 1). The volume gain was associated with Crs, which continuously decreased from 27 to 21 ml/cmH<sub>2</sub>O ( $P \leq 0.05$ , beginning vs. end of the experiment; see Fig. 5 for the regression analyses; for detailed statistics see Tables 1 and 2).

When PEEP was increased stepwise from 0 to 15 cmH<sub>2</sub>O, the volume gain per cardiogenic oscillation decreased progressively, and it was abolished at 15 cmH<sub>2</sub>O PEEP.

**Hemodynamics.** Stroke volume index remained at its initial level of 38 ml·beat<sup>-1</sup>·m<sup>-2</sup> throughout the experiment. Left ventricular stroke work index increased from 53 to 63 ml·beat<sup>-1</sup>·m<sup>-2</sup>·mmHg<sup>-1</sup>.

**Blood gases.**  $P_{aO_2}$  showed a small but significant decrease during the experiment (from 76 to 74 kPa,  $P \leq 0.05$ ; Fig. 6, Table 1), while the tendency for arterial  $P_{CO_2}$  to increase was statistically not significant.

## DISCUSSION

The main result of this study was that heartbeats induced a regular pattern in gas flow and airway pressure and, thereby, were able to generate sufficient disturbance to result in significant lung volume gains that were accompanied by a short increase in intratidal compliance. Crs and  $P_{aO_2}$  decreased and arterial  $P_{CO_2}$  tended to increase with time, as observed elsewhere (2–5, 8, 9, 12). Despite unchanged cardiac stroke volume, the lung volume gain induced by the cardiogenic oscillations decreased together with overall compliance and time. The size of the gain, thus, reflected the mechanical conditions of the respiratory system during uninterrupted monotonous ventilation.

*How do the heartbeats induce repetitive lung volume gains?* Few data exist that allow assumptions about the mechanisms involved in producing cardiogenic oscillations. Using the dynamic spatial reconstructor, Hoffman and Ritman (6) found a

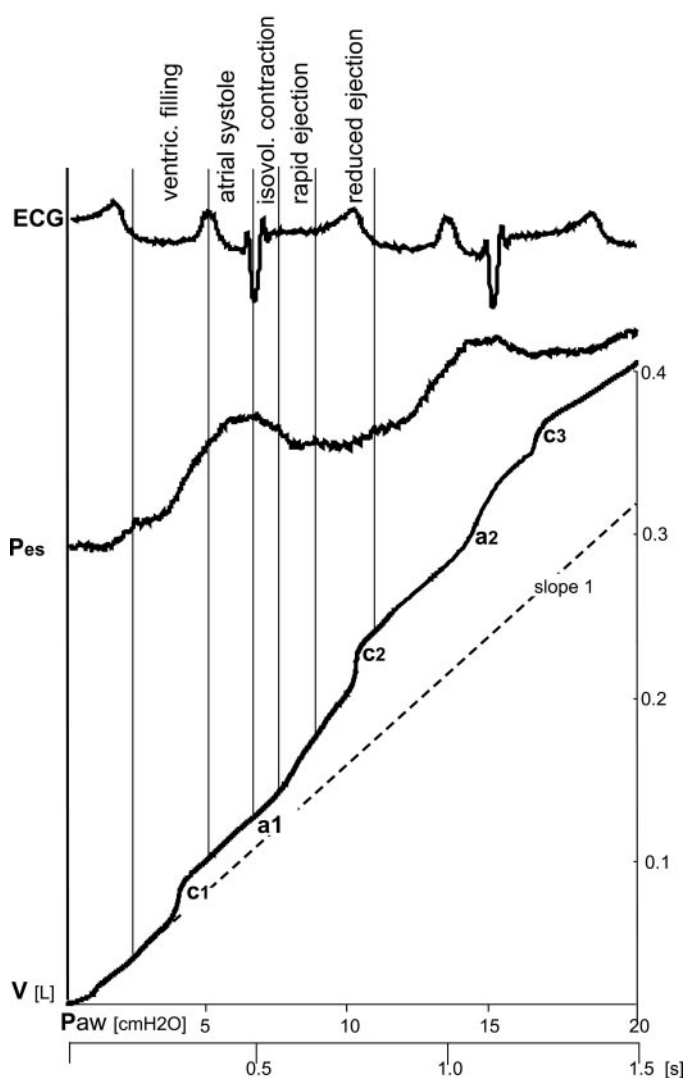


Fig. 3. Changes in  $P_{es}$  and  $P_{aw}$  in relation to phases of the cardiac cycle during constant-flow mechanical inflation in a representative animal. ECG (ventricular filling, atrial systole, isovolumic contraction, rapid ejection, and reduced ejection),  $P_{es}$ , and lung volume (V) are plotted vs.  $P_{aw}$ . ECG and  $P_{es}$  are expressed in arbitrary units and lung volume in liters. Time course of  $P_{aw}$  is also indicated.

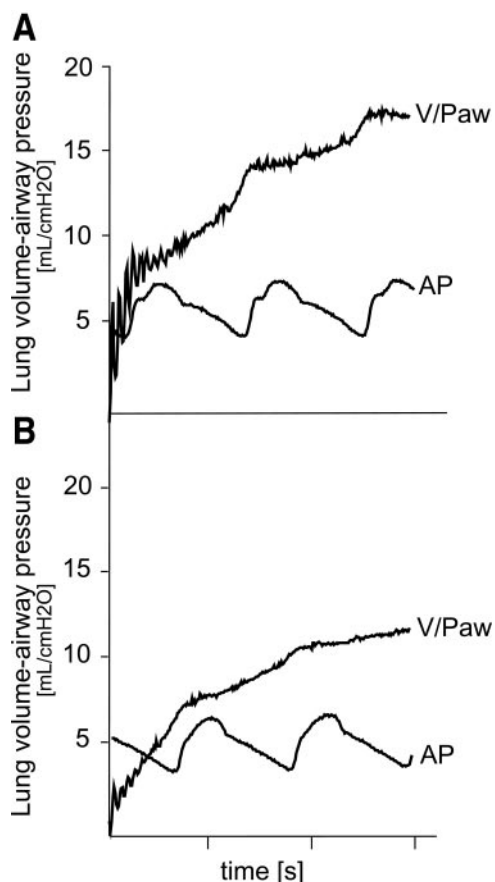


Fig. 4. Slope of inspiratory V-Paw curves during ventilation in a representative animal at the beginning of the experiment (A) and after 7 h of monotonous ventilation (B). AP (in arbitrary units) is also shown. On the V-Paw plot, heartbeats induced a rapid upward shift of intratidal compliance, which is more pronounced at low lung volume in early inspiration (A vs. B).

2–5% reduction in total heart volume between end diastole and end systole, and this small cardiac volume shift could act as a pump adding lung volume. Flow and pressure changes were regularly coupled to cardiac systole and diastole (Figs. 1–3) with and without constant-flow mechanical inflation. This regular coupling does, however, not allow us to conclude that it is the shift in cardiac volume that induces the gain in lung volume. It is equally possible, and indeed more likely, that most of the lung volume change is due to the rapid pressure swings caused by the contraction of the heart and not necessarily by its volume change. The amount of lung volume that

Table 1. *Effects of cardiogenic oscillations on respiratory system mechanics*

	60 min	420 min
PaO <sub>2</sub> , kPa	76 (74.9–78.1)	74* (71.0–77.8)
PaCO <sub>2</sub> , kPa	5.83 (5.23–6.42)	6.01 (5.4–6.63)
SVI, ml·beat <sup>-1</sup> ·m <sup>-2</sup>	38 (32.0–43.8)	40 (35.6–45.1)
Overall Crs, ml/cmH <sub>2</sub> O	27 (22–31)	21* (15–26)
V <sub>card</sub> (1st beat), ml	13.5 (10.4–16.6)	6.5* (2.4–9.2)

Values are means, with 95% confidence intervals in parentheses. PaO<sub>2</sub> and PaCO<sub>2</sub>, arterial PO<sub>2</sub> and PCO<sub>2</sub>; SVI, stroke volume index; Crs, respiratory system compliance; V<sub>card</sub>, heartbeat recruited lung volume. \*Significantly different ( $P \leq 0.05$ ) from 60 min.

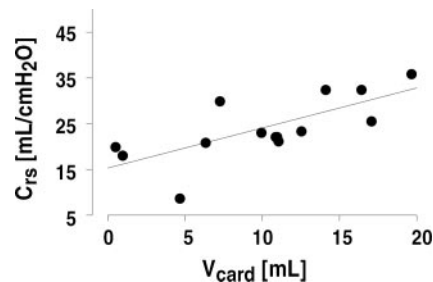


Fig. 5. Regression analysis for overall compliance of the respiratory system (Crs) vs. heartbeat-recruited lung volume (V<sub>card</sub>):  $Crs = 15.2 + 0.87 \times V_{card}$  (ml/cmH<sub>2</sub>O) ( $R = 0.73$ ,  $R^2 = 0.52$ ,  $P \leq 0.01$ ). Values are means of 3 consecutive breaths for each animal.

is added by the cardiogenic oscillations does not appear to depend on the timing of the heartbeat within the inspiratory period. It seems, therefore, that the heartbeats merely trigger a process that results in repetitive lung volume gain. The amount of the added volume should depend on the strength of the heartbeat-generated kicks and how these kicks are transmitted to the underlying alveolar region. To the extent that the heart can be considered locally as a mechanical pump generating pressure swings in the pleural space, the local pressure in the lung due to a kick should be proportional to the regional compliance of the lung. When the magnitude of this pressure kick is larger than the opening pressures of airways and alveoli in that region, one or more airways pop open, triggering perhaps an avalanche-like process (11), which eventually leads to a noticeable lung volume increase visible on the V-Paw curve (10).

*Potential mechanical effects of heartbeats on the lung.* The above interpretation of lung volume gains is supported by the following arguments. The V-P trace becomes nearly vertical immediately after a heartbeat (Figs. 2–4). This suggests that the total lung volume was suddenly increased without a corresponding increase in Paw. It is unlikely that this volume increase occurs by pure elastic expansion of the lung, because, in that case, Paw would have to increase as well. If, however, the added volume suddenly enters a new lung region hitherto collapsed (or one in which a lower pressure prevails), Paw does not necessarily increase. The situation is conceptually similar to slowly inflating a system that contains a large chamber connected to a much smaller chamber via a valve. Initially, the valve is closed, and the pressure in the small chamber is much lower than the pressure in the large chamber. If the valve is suddenly opened, air rushes from the large chamber to fill up the small chamber until the pressure becomes homogeneous in the whole system. Because the same amount of air is redistributed in a larger volume, the total pressure can decrease. However, if the source inflating the large chamber is strong enough and the second chamber is much smaller than the first, air will be drawn from the source while the pressure in the two chambers stays essentially the same as before the valve was opened. In our case, the source corresponds to the mechanical ventilator, and the opening of the valve corresponds to the heartbeat-induced reopening of a small collapsed region of the lung. A consequence of this mechanism is that the newly reopened region immediately becomes inflated and pressurized so that it remains open and stable even after the heartbeat. A similar vertical increase in volume without an increase in

Table 2. Respiratory variables during 7 h of monotonous ventilation

Time	Peak Inspiratory Pressure, cmH <sub>2</sub> O	End-Inspiratory Pause Pressure, cmH <sub>2</sub> O	Mean Paw, cmH <sub>2</sub> O	Overall Crs,st, ml/cmH <sub>2</sub> O
Start	20±3.5	13.7±2.2	7±0.6	26.7±4.6
60 min	19±2.9	15.3±1.8	6.5±0.5	24.5±6.5
120 min	20±4.5	16.4±2.3	7.0±1.0*	22.8±6.3
180 min	21±2.6	16.3±1.2*	7.2±0.5*	24.1±2.3*
240 min	21±3.0	17.6±2.3*	7.4±0.5*	21.4±5.6*
300 min	21±2.6	17.1±1.6*	7.2±0.5*	21.3±5.3*
360 min	22±2.8*	17.8±2.1*	7.4±0.5*	21.1±5.3*
420 min	22±3.0*	17.7±2.2*	7.4±0.5*	20.9±5.3*

Values are means ± SD. Paw airway pressure; Crs,st, static Crs. \*Significantly different from start ( $P \leq 0.05$ ).

pressure can be observed during the first inflation of degassed lungs, and this phenomenon has been quantitatively modeled on the basis of airway opening (7).

We have no independent data to support our interpretation, and other interpretations are equally possible. It could be argued, for example, that the recruited lung volume seems to be derecruited on the subsequent expiration. This is suggested by the fact that every inspiration is accompanied by a new sequence of volume gains. We emphasize that, because of the normal variability of heartbeat frequency mediated among others by respiratory sinus arrhythmia, the heartbeats continuously change position on subsequent inspirations. This implies that different lung areas are affected from beat to beat (rather

than the same areas being recruited and derecruited all the time). Moreover, in four animals, we measured the V-Paw curves 1 s after the heart was stopped. It is unlikely that, 1 s after the heart is stopped, intrapulmonary blood volume would have increased such that it would significantly reduce lung compliance. In these animals, we did not observe any sudden lung volume increases during ventilation, and lung compliance was 20% lower at end inspiration when the heart was stopped. Further support of heartbeat-induced recruitment comes from the PEEP studies. Immediately after induction of anesthesia and, hence, probably with some parts of the lungs collapsed, ventilation at 0-cmH<sub>2</sub>O PEEP was applied, and the heartbeats always resulted in lung volume increments. Increasing PEEP, however, progressively reduced lung volume gains due to the cardiac oscillations. This was probably due to the fact that the increasing levels of PEEP gradually reduced the amount of lung volume collapse at end expiration and also increased the stiffness of the lung. At the maximum PEEP of 15 cmH<sub>2</sub>O, the lung was stiff and there was not much lung volume left for intratidal recruitment, which in turn resulted in complete disappearance of cardiac kicks from the V-Paw curve.

It might be argued that the volume increments in Figs. 2–4 are plotted against Paw and, hence, do not show the actual changes in Ptp. We cannot fully eliminate the possibility that the cardiac kicks merely generate transient lung volume increases due to the heart sucking in a small amount of gas during systole and subsequently expelling it during diastole. However, examining the data in Fig. 3 more closely, we would like to emphasize the following. If the heart indeed increases and decreases lung volume, then during inspiration, lung volume should increase at a constant rate, and this increase should be cyclically modulated by the heart's emptying and filling. In other words, the rate of increase of lung volume should be somewhat larger during systole and slightly smaller during diastole. This is actually observed in Fig. 3. From  $c_1$  to  $a_1$ , as well as from  $c_2$  to  $a_2$  (coinciding approximately with the diastolic filling phases), the increase in lung volume is slowed; from  $a_1$  to  $c_2$  and from  $a_2$  to  $c_3$  the increase in lung volume is augmented by the suctionlike effect of the emptying heart (systolic rapid and reduced ejection phase, respectively). These changes are also reflected in the course of Pes. Thus the cyclic emptying and filling of the heart is in tight temporal correspondence with the small interbeat fluctuations in lung volume ( $c_1$ - $a_1$  vs.  $a_1$ - $c_2$ ) around a linear increase during inspiration. The sudden increases in lung volume at  $c_1$ ,  $c_2$ , and  $c_3$ , however, are not connected in the same way to the phases of cardiac emptying and filling. Instead, they appear after the end of cardiac emptying, and, in contrast to the volume changes

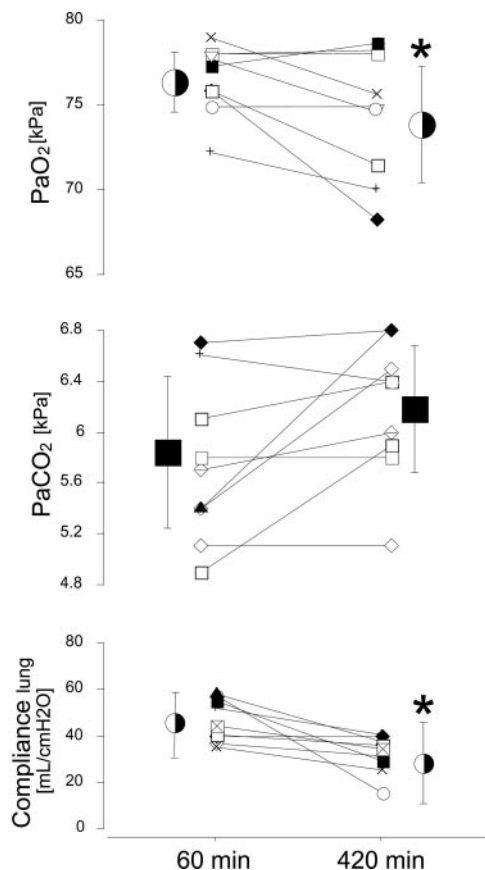


Fig. 6. Individual arterial  $\text{PO}_2$  ( $\text{PaO}_2$ ) and  $\text{PCO}_2$  ( $\text{PaCO}_2$ ) and lung compliance values during monotonous ventilation at 1 h after beginning and at the end of the experiment (420 min). Symbols denote individual animals. Large symbols at right and left denote means (with 95% confidence interval). \*Significantly different from 60 min.

corresponding to the sucking-expelling action of the heart, those volume jumps are more pronounced and the volume gain is not lost or reversed on subsequent filling of the heart. Those jumps interrupt the linear increase in volume, and they result in an almost parallel shift in the V-Paw curve. This means that there is a permanent increase in volume. Therefore, each heartbeat results in a parallel shift in lung volume that, at end inspiration, produces a total volume increase of ~75 ml compared with the predicted volume based on the slope of the first V-Paw segment (*slope 1*). Additionally, had there been no shifts superimposed on the increase in lung volume, the pressure would have increased faster than the volume due to the elastic nonlinearity of the lung at higher lung volumes and, if anything, the V-Paw curve would deviate downward from *slope 1*. These considerations therefore support our hypothesis that the sudden jumps in volume along the V-Paw curve are a result of regional lung volume recruitment induced by the rhythmic contraction of the heart.

*Cardiogenic oscillations reflect overall mechanical properties of the respiratory system.* Irrespective of the above discussion, there was a strong association between Crs and the volume of the cardiogenic oscillations. We found that Crs and lung compliance gradually and continuously decreased during monotonous ventilation (Fig. 5, Tables 1 and 2), an observation that was first made by Mead and Collier (8) in isolated lungs. Despite a constant pressure output, in terms of constant stroke volume and left ventricular stroke work, cardiogenic oscillations became smaller in magnitude with time, because an increasing part of the energy produced by the contracting heart dissipated in overcoming the reduced Crs. Thus the lung volume gain per heartbeat was also time dependent. Whatever mechanism is behind the decrease in overall compliance (loss of lung volume, stiffening of lung tissue and/or chest wall, and/or changes in the air-liquid interface), the flattening of the cardiogenic oscillations reflects the increasing stiffness of the lung. This makes the study of cardiogenic oscillations a potential tool for noninvasive analysis of respiratory mechanics (1).

In conclusion, our data suggest that, depending on the overall mechanical conditions of the respiratory system, cardiogenic oscillations can induce significant lung volume gains. We speculate that the sudden gains in lung volume are due to recruitment induced by heart contraction. By the end of 7 h of monotonous mechanical ventilation, the lung becomes so stiff

that the cardiogenic oscillations result in much smaller volume gain, which is accompanied by a deterioration of gas exchange. The flattening of the cardiogenic oscillations reflects the increasing stiffness of the lung, making cardiogenic oscillations a potential tool for noninvasive analysis of respiratory mechanics.

#### ACKNOWLEDGMENTS

We thank Jason H. T. Bates and Eric A. Hoffman for helpful criticism, insight, and unselfish teaching related to this work, and Anders K. Nordgren for constant and skillful assistance in performing the experiments.

#### GRANTS

This study was supported by grants from the Laerdal Foundation for Acute Medicine (Stavanger, Norway), Swedish Medical Research Council Grant 5315, and the Lions Cancer Foundation (Uppsala, Sweden).

#### REFERENCES

1. Bijaoui E, Baconnier PF, and Bates JH. Mechanical output impedance of the lung determined from cardiogenic oscillations. *J Appl Physiol* 91: 859–865, 2001.
2. Cereda M, Foti G, Musch G, Sparacino ME, and Pesenti A. Positive end-expiratory pressure prevents the loss of respiratory compliance during low tidal volume ventilation in acute lung injury patients. *Chest* 109: 480–485, 1996.
3. Egbert LD, Laver MB, and Bendixen HH. Intermittent deep breaths and compliance during anesthesia in man. *Anesthesiology* 24: 57–60, 1963.
4. Ferris B and Pollard D. Effect of deep and quiet breathing on pulmonary compliance in man. *J Clin Invest* 39: 143–149, 1960.
5. Fletcher ME, Ewert M, Stack C, Hatch DJ, and Stocks J. Influence of tidal volume on respiratory compliance in anesthetized infants and young children. *J Appl Physiol* 68: 1127–1133, 1990.
6. Hoffman EA and Ritman EL. Intracardiac cycle constancy of total heart volume. *Dyn Cardiovasc Imaging* 1: 199–205, 1988.
7. Horie T and Hildebrandt J. Volume history, static equilibrium, and dynamic compliance of excised cat lung. *J Appl Physiol* 33: 105–112, 1972.
8. Mead J and Collier C. Relation of volume history of lung to respiratory mechanics in anesthetized dogs. *J Appl Physiol* 14: 669–678, 1959.
9. Popow C and Simbruner G. Influence of tidal volume on the compliance of the respiratory system in mechanically ventilated newborn infants. *Wien Klin Wochenschr* 101: 323–326, 1989.
10. Suki B, Alencar AM, Tolnai J, Asztalos T, Petak F, Sujeer MK, Patel K, Patel J, Stanley HE, and Hantos Z. Size distribution of recruited alveolar volumes in airway reopening. *J Appl Physiol* 89: 2030–2040, 2000.
11. Suki B, Barabasi AL, Hantos Z, Petak F, and Stanley HE. Avalanches and power-law behaviour in lung inflation. *Nature* 368: 615–618, 1994.
12. Watson WE. Some observations on dynamic lung compliance during intermittent positive-pressure respiration. *Br J Anaesth* 34: 153–157, 1962.