Eur Respir J 1997; 10: 2371–2375
DOI: 10.1183/09031936.97.10102371
Printed in UK - all rights reserved

European Respiratory Journal
ISSN 0903 - 1936

Comparison of helium dilution and plethysmographic lung volumes in pregnant women

F. García-Río, J.M. Pino-García, S. Serrano, M.A. Racionero, J.G. Terreros-Caro, R. Alvarez-Sala, C. Villasante, J. Villamor

Comparison of helium dilution and plethysmographic lung volumes in pregnant women. F. García-Río, J.M. Pino-García, S. Serrano, M.A. Racionero, J.G. Terreros-Caro, R. Alvarez-Sala, C. Villasante, J. Villamor. ©ERS Journals Ltd 1997.

ABSTRACT: The multibreath helium equilibration method is the technique recommended for routine measurement of static lung volumes in normal subjects. However, pregnancy could be an exception to this general rule, due to airway closure during the second half of gestation. The aim of this study was to compare the measurements of lung volumes by plethysmography and helium dilution during pregnancy.

Twenty three healthy women were studied at 12, 24 and 36 weeks of pregnancy, and 4 months postpartum. Total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV) were measured by multibreath helium equilibration (TLC_{He}, FRC_{He} and RV_{He}) and by plethysmography (TLC_{box}, FRC_{box} and RV_{box}).

Only at 36 weeks were there differences between the two methods. RV_{box} was significantly larger than RV_{He} (1.01±0.18 *vs* 0.77±0.21 L; $p<0.001$). FRC_{box} was larger than FRC_{He} (1.95±0.32 *vs* 1.60±0.32 L; $p<0.001$) and TLC_{box} was larger than TLC_{He} (4.83±0.52 *vs* 4.45±0.51 L; $p<0.05$). The 95% limits of agreement for differences between lung volumes measured by the two techniques (helium dilution - plethysmography) at 36 weeks were: -0.42 to -0.06 L for RV; -0.54 to -0.17 L for FRC; and -0.66 to -0.11 L for TLC.

We conclude that using the multibreath helium equilibration method to measure lung volumes in at-term pregnant women results in underestimation of functional residual capacity and total lung capacity.

Eur Respir J 1997; 10: 2371–2375.

Servicio de Neumología, Hospital Universitario La Paz, Madrid, Spain.

Correspondence: F. García-Río
Capitán Blano Argibay 26, 1° B
28029 Madrid
Spain

Keywords: Lung volume measurements
pregnancy
respiratory function tests
total lung capacity

Received: October 31 1996
Accepted after revision May 17 1997

Measurement of static lung volumes provides information about the mechanical properties of the ventilatory apparatus that may be of considerable importance in understanding the pathophysiological changes in patients with lung disease [1, 2].

Various procedures can be used to measure static lung volumes [2]. The two most widely used are multibreath helium equilibration and body plethysmography [1, 2]. Classically, it is accepted that in normal individuals and in patients with interstitial lung disease, these two techniques produce equivalent mean values [2–4], whereas the helium dilution method underestimates the absolute lung volumes in patients with obstructive lung disease to an extent that depends on the severity of airway obstruction [2, 3–5]. Pregnancy could be an exception to this general principle. It is well known that, when supine, some healthy pregnant women have hypoxaemia and an increase in the alveolar-arterial oxygen gradient [6–12]. These alterations have been attributed to airway closure during normal tidal breathing [13]. The existence of lung areas which communicate poorly with the central airways in pregnant women might result in a significant underestimation of true lung volumes measured by helium dilution as compared to plethysmography.

To examine this possibility, we have measured lung volumes by multibreath helium equilibration and plethysmography in normal pregnant women both during gestation and again postpartum.

Subjects and methods

Subjects

Twenty three healthy pregnant women without previous history of cardiovascular or respiratory diseases were studied. The subjects were aged 29±3 yrs (mean±SD), 159±4 cm in height and 58±7 kg in weight when non-pregnant. They were judged to be healthy by history, physical examination, electrocardiogram, basal spirometry, complete blood cell count and automated serum chemistry panel. All of the women had uncomplicated singleton pregnancies. Seventeen had no previous pregnancies, four had one, one had two, and one had three. Eleven of the women smoked. All volunteers were taking iron and/or vitamin supplements only.

Informed consent was obtained from all subjects, and the protocol was approved by the institutional Ethics Committee.

Methods

Study sessions were planned for weeks 12, 24 and 36 of pregnancy, and 4 months after childbirth for measurement in the nonpregnant state. Investigations commenced at the same time in the morning and in baseline conditions. Subjects were asked not to eat in the 4 h before the study. After a few minutes of adaptation to the mouthpiece, pulmonary function studies were started, with the subject seated in an upright position.

Spirometry was obtained by means of a pneumotachograph, and static lung volumes were measured both by body plethysmography and multibreath helium equilibration. In all subjects, pulmonary function tests were carried out by the same technician. The automated equipment (MasterLab 3.2; Jaeger, Würtzburg, Germany) used for all determinations was checked periodically following the European Respiratory Society guidelines [14]. Room temperature and barometric pressure were recorded twice daily with mean values of 22°C and 94.6±1.3 kPa (mean±SD), respectively.

After spirometry, lung volumes were determined using a constant-volume body plethysmograph. Thoracic gas volume (TGV) at the level of functional residual capacity (FRC_{box}) was measured while the subjects made gentle breathing movements against the shutter at a rate of <1 $L \cdot s^{-1}$. Corrections for not occluding the airway at a representative end-expiratory lung volume were made to obtain FRC_{box} [14]. Inspiratory capacity (IC) and expiratory reserve volume (ERV) were measured during the same manoeuvre from which FRC was determined. FRC_{box} was reported as the mean of three or more measurements which differed by less than 5% from the mean. Total lung capacity (TLC_{box}) was calculated by adding the mean FRC_{box} to the largest IC derived from a TGV which was within 5% of the mean. Similarly, residual volume (RV_{box}) was determined by subtracting the ERV from FRC_{box}. Airway resistance (R_{aw}) was computed from pressure and flow measurements breathing warm, moist air fulfilling body temperature, atmospheric pressure and saturation with water vapour (BTPS) conditions [15]. The frequency of panting was 2 Hz [14].

Thirty minutes after plethysmography, lung volumes were measured using the multibreath helium equilibration method, while the subjects were sitting in the body plethysmograph. The closed circuit was filled with a mixture of 10% He, 35% O_2 and the rest N_2. A helium heat conductivity analyser was employed. Oxygen was added to replenish the air taken up during rebreathing, and the CO_2 produced was removed by an in-line soda lime absorber. The helium equilibration was assumed to be complete when the concentration changed by less than 0.02% in 30 s [14]. The rebreathing started from the resting end-expiratory position and lasted 5–7 min. At the end of rebreathing, a number of IC and ERV manoeuvres were performed to calculate total lung capacity ($TLC_{He} = FRC_{He} + IC$) and residual volume ($RV_{He} = FRC_{He} - ERV$). Lung volumes by helium dilution were the mean of duplicate measurements.

Statistical analysis

The results are expressed as mean and standard deviation (SD). Statistical analysis was performed with BMDP (Classic release 7.0 (Statistical Solutions Ltd, Cork, Ireland). All data were analysed using an analysis of variance (ANOVA) for repeated measures. *Post-hoc* multiple comparisons were performed using the Bonferroni correction. Simple effects within each factor (lung volumes by plethysmography and helium dilution in each trimester) were analysed. A p-value of less than 0.05 was accepted as the minimum level of statistical significance [16]. Agreement between pairs of measurements (plethysmographic *vs* helium dilution) were analysed according to the methods described by BLAND and ALTMAN [17].

Results

Dynamic and static lung volumes and airway resistance for each trimester of pregnancy and after delivery are shown in table 1. No significant changes in forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio or R_{aw} were observed during pregnancy or postpartum. RV was significantly less at 36 than at 12 and 24 weeks and after delivery. FRC decreased progressively during pregnancy, the difference reaching statistical significance by week 24. An increase was noted after delivery. TLC was significantly greater at postpartum and at 12 and 24 weeks than at the end of pregnancy.

Only at 36 weeks were there significant differences between lung volumes measured by plethysmography and helium dilution. RV was greater when measured by plethysmography than by helium dilution (1.01±0.18 *vs* 0.77±0.21 L; p<0.001). Similar differences were found for FRC (1.95±0.32 *vs* 1.60±0.32 L; p<0.001) and TLC (4.83±0.52 *vs* 4.45±0.51 L; p<0.05). The mean differences in lung volumes (helium dilution minus

Table 1. – Lung function during pregnancy and statistical significance of the differences in value between the trimesters of pregnancy and between the plethysmographic and helium dilution methods of measurement

	Week 12	Week 24	Week 36	Postpartum
FVC L	3.45±0.43	3.58±0.32	3.50±0.37	3.52±0.31
FEV_1 L	3.19±0.38	3.17±0.28	3.08±0.33	3.15±0.31
FEV_1/FVC %	89±4	88±4	88±4	88±3
R_{aw} $kPa \cdot L^{-1} \cdot s$	0.26±0.09	0.24±0.08	0.26±0.10	0.32±0.11
RV_{box} L	1.27±0.24	1.25±0.21	1.01±0.18*¶§‡	1.37±0.37
RV_{He} L	1.21±0.24	1.14±0.21	0.77±0.21*¶§	1.23±0.26
FRC_{box} L	2.53±0.37	2.49±0.33*	1.95±0.32*¶§‡	2.69±0.37
FRC_{He} L	2.43±0.37	2.40±0.35	1.60±0.32*¶§	2.60±0.33
TLC_{box} L	5.01±0.57	5.12±0.39*	4.83±0.52*§#	5.08±0.53
TLC_{He} L	4.94±0.59	4.99±0.40	4.45±0.51*¶§	4.99±0.57

FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; R_{aw}: airway resistance; RV_{box}: plethysmographic residual volume; RV_{He}: helium dilution residual volume; FRC_{box}: plethysmographic functional residual capacity; FRC_{He}: helium dilution functional residual capacity; TLC_{box}: plethysmographic total lung capacity; TLC_{He}: helium dilution total lung capacity. Values are presented as mean±SD (n=23). *: p<0.05 *vs* postpartum; ¶: p<0.05 *vs* week 12; §: p<0.05 *vs* week 24; #: p<0.05 *vs* helium dilution method; ‡: p<0.001 *vs* helium dilution method.

Table 2. – Differences between lung volumes measured by helium equilibration and plethysmography during pregnancy

	RV L	FRC L	TLC L
Week 12	-0.07 (-0.21, 0.08)	-0.10 (-0.21, 0.02)	-0.07 (-0.19, 0.05)
Week 24	-0.12 (-0.30, 0.07)	-0.08 (-0.24, 0.07)	-0.13 (-0.26, 0.01)
Week 36	-0.24 (-0.42, -0.06)	-0.36 (-0.54, -0.17)	-0.38 (-0.66, -0.11)
Postpartum	-0.13 (-0.76, 0.50)	-0.09 (-0.33, 0.15)	-0.09 (-0.29, 0.10)

Values are presented as mean difference (helium equilibration minus plethysmography) and 95% limits of agreement in parenthesis. RV: residual volume; FRC: functional residual capacity; TLC: total lung capacity.

plethysmographic) and their 95% limits of agreement were calculated (table 2). At all time-points, the limits of agreement were wide, reflecting a great within-subject variability and method-related differences. The range of differences at 36 weeks for RV, FRC and TLC are illustrated in figure 1. At the end of pregnancy, the 95% limits of agreement for static lung volumes did not include zero. The lowest differences between the two techniques or 95% confidence intervals for the lower limit of agreement at 36 weeks were -0.13 to 0.01 L for RV, -0.24 to -0.10 L for FRC and -0.21 to -0.01 L for TLC. To evaluate the largest possible error, the 95% confidence intervals for the upper limit of agreement were also calculated. At 36 weeks, they were -0.49 to -0.26 L for RV, -0.62 to -0.47 L for FRC and -0.76 to -0.55 L for TLC. Therefore, in the third trimester of pregnancy, the multibreath helium equilibration method underestimated both FRC and TLC.

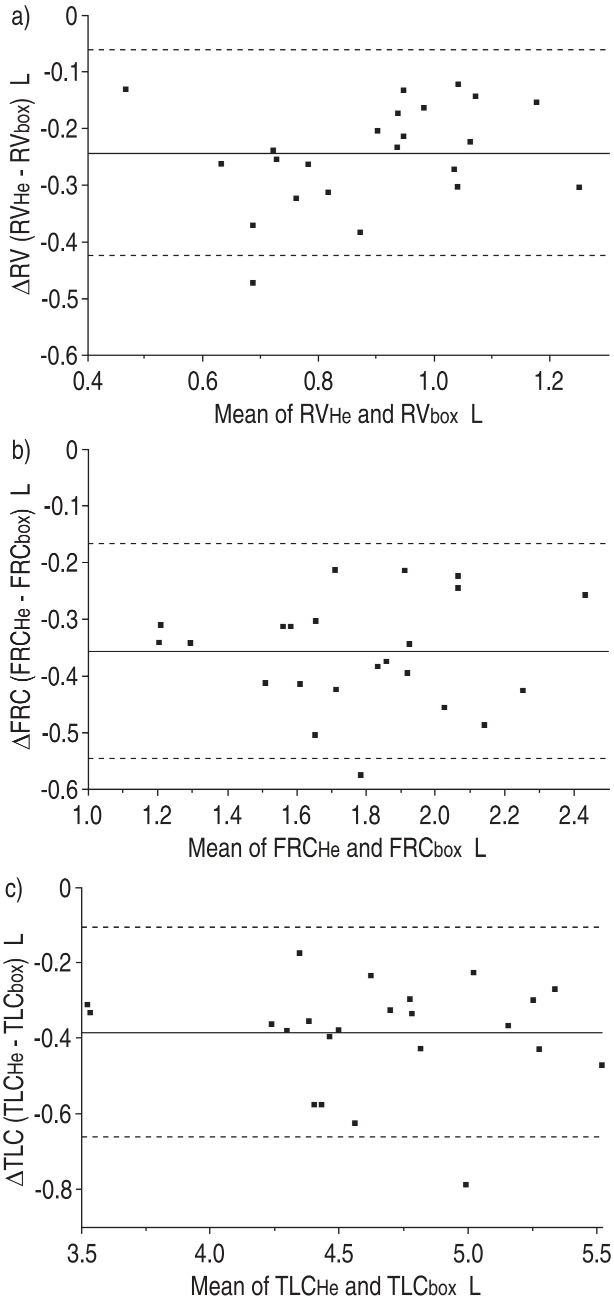

Fig. 1. – Differences (Δ) between lung volumes measured by plethysmography (RV_{box}, FRC_{box} and TLC_{box}) and multibreath helium equilibration (RV_{He}, FRC_{He} and TLC_{He}) plotted against the mean of the two values for: a) residual volume (RV); b) functional residual capacity (FRC); and c) total lung capacity (TLC), at week 36 of pregnancy. The continuous line represents the mean difference; the dashed lines represent 2 standard deviations around the mean.

Discussion

The results of the present study demonstrate that static lung volumes measured by helium dilution are lower than those measured by plethysmography during the third trimester of pregnancy.

As reported by others [18–20], we have not observed changes in dynamic lung volumes during pregnancy. The present results describing the evolution of static lung volumes are similar to previous reports [21–25]. We found a 27% decrease in FRC_{box} between postpartum and 36 weeks, which is similar to the decrements of 9.5 to 25% reported by other authors [7, 18, 21]. The fall in FRC at the end of pregnancy has been explained by the shift to the right of the chest wall pressure-volume curve [22]. Although some authors [24, 25] have reported that RV remains unchanged during pregnancy, others [7, 11, 18, 21] have found a 7–22% decrease of RV starting from the second half of gestation. We observed a 26% decrease in RV_{box} between week 36 of pregnancy and postpartum. In the present subjects, TLC_{box} was slightly (5%) diminished at term. This is in agreement with previous investigations that found minor changes of TLC in both directions [21]. The increase of the transverse diameter of the thorax, together with the unimpaired diaphragmatic function, causes the IC to increase in the second half of gestation [11]. The increase of IC is sufficient to compensate for the decrease of FRC, thus maintaining a constant TLC.

The comparison of lung volumes measured by plethysmography and helium dilution shows large differences at the end of pregnancy, principally in FRC and TLC. In some circumstances, the plethysmographic method induces errors in the measurement of lung volumes. In patients with high airway resistance, plethysmography may overestimate lung volume. In these subjects, the flow resulting from the motion of upper airway walls during panting may be responsible for a substantial pressure difference between mouth and alveoli [4, 26]. In the present subjects, no changes in airway resistance were noted during pregnancy (table 1). Moreover, the plethysmographic measurements were performed at a rate of <1 L·s^{-1} to minimize the overestimation of lung volume [27, 28]. Plethysmography may also overestimate thoracic gas volume in infants due to high compliance of extrathoracic airways [29], but this is not the case in adults [30].

The differences between the two methods could be attributed to an underestimation of lung volumes by the multibreath helium equilibration method. Airway closure at the end of pregnancy is well documented. In the last month of pregnancy, 50% of women show airway closure during normal ventilation [6]. Some authors [9, 10] have reported a slight increase in closing volume during pregnancy, which was attributed to an increase in lung water or to a change in the elastic properties of the lungs [10]. However, these studies failed to detect significant changes in lung volumes during pregnancy. In other studies [6, 7, 31, 32], no change in closing capacity was found throughout pregnancy, but the difference between closing capacity and FRC decreased as a consequence of a reduction in FRC. These changes may also explain airway closure during normal ventilation in the third trimester of pregnancy. Indirect evidence in support of premature airway closure during pregnancy is provided by measurements of oesophageal and gastric pressures [19], which are more positive in the third trimester of pregnancy than in postpartum. The resulting decrease in transpulmonary pressure could explain peripheral airway collapse.

Despite the absence of airway obstruction in the present subjects, the existence of poorly or nonventilated airspaces could induce an underestimation of lung volumes measured by helium dilution. Even in erect subjects, an increased airway closure (FRC and RV differences >150 mL at week 36) must induce hypoxaemia due to shunt, because the slight physiological hyperventilation of pregnancy would not undo the venous admixture in very poorly-ventilated or closed compartments [32, 33]. Other possible mechanisms to explain the difference between the two techniques are a change in transpulmonary pressure gradient [34], or changes in the pressure-volume characteristics of the lung [35].

In conclusion, it appears that the multibreath helium equilibration method underestimates lung volumes in the third trimester of pregnancy. Thus, the technique of choice to measure absolute lung volumes in healthy pregnant women should be body plethysmography. However, it should be remembered that to determine the lung volume accessible for gas exchange, the dilution method should be used.

Acknowledgements: The authors gratefully acknowledge the continuous technical assistance of A. Alvárez, P. Librán and C. Suárez.

References

1. Ries AL. Measurement of lung volumes. *Clin Chest Med* 1989; 10: 177–186.
2. Altose MD, Crapo RO, Wanner A. The determination of static lung volumes: report of the Section on Respiratory Pathophysiology. *Chest* 1984; 86: 471–474.
3. Miller RD, Offord KP. Roentgenologic determination of total lung capacity. *Mayo Clin Proc* 1980; 55: 694–699.
4. Paré PD, Wiggs BJR, Coppin CA. Error in the measurement of total lung capacity in chronic obstructive lung disease. *Thorax* 1983; 38: 468–471.
5. Burns CB, Scheinhorn DJ. Evaluation of single-breath helium dilution total lung capacity in obstructive lung disease. *Am Rev Respir Dis* 1984; 130: 580–583.
6. Bevan DR, Holdcroft A, Lohl L, McGregor WG, O'Sullivan JC, Sykes MK. Closing volume and pregnancy. *Br Med J* 1974; 1: 13–15.
7. Craig DB, Toole MA. Airway closure in pregnancy. *Can Anaesth Soc J* 1975; 22: 665–672.
8. Milne JA, Mills RJ, Howie AD, Pack AI. Large airways function during normal pregnancy. *Br J Obstet Gynaecol* 1977; 84: 448–451.
9. Garrard GS, Littler WA, Redman CWG. Closing volume during normal pregnancy. *Thorax* 1978; 33: 488–492.
10. Awe RJ, Nicotra MB, Newsom TD, Viles R. Arterial oxygenation and alveolar-arterial gradients in term pregnancy. *Obstet Gynecol* 1979; 53: 182–186.
11. Elkus R, Popovich J Jr. Respiratory physiology in pregnancy. *Clin Chest Med* 1992; 13: 555–565.
12. García-Río F, Pino-García JM, Alvarez-Sala R, Díaz-Lobato S, Casadevall J, Villasante C. Adaptación respiratoria durante el embarazo. *Arch Bronconeumol* 1995; 31: 172–180.
13. Fishburne JI. Physiology and disease of the respiratory system in pregnancy. *J Reprod Med* 1979; 22: 177–189.
14. Quanjer PhH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault J-C. Lung volumes and forced ventilatory flows. Report working party. Standardization of Lung Function Tests. European Coal and Steel Community. *Eur Respir J* 1993; 6: Suppl. 16, 5–40.
15. DuBois AB, Botelho SY, Comroe JH Jr. A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *J Clin Invest* 1956; 35: 327–335.
16. Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *Br Med J* 1983; 286: 1489–1493.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurements. *Lancet* 1986; i: 307–310.
18. Norregaard O, Schultz P, Ostergaard A, Dahl R. Lung function and postural changes during pregnancy. *Respir Med* 1989; 83: 467–470.
19. Contreras G, Gutiérrez M, Beroíza T, *et al*. Ventilatory drive and respiratory muscle function in pregnancy. *Am Rev Respir Dis* 1991; 144: 837–841.
20. Gilroy RJ, Mangura BT, Lavietes MH. Rib cage and abdominal volume displacements during breathing in pregnancy. *Am Rev Respir Dis* 1988; 137: 668–672.
21. Weinberger SE, Weiss ST, Cohen WR, Weiss W, Johnson TS. Pregnancy and the lung. *Am Rev Respir Dis* 1980; 121: 559–581.
22. Le Merre C, Préfaut Ch. Grossesse et fonction respiratoire. *Rev Mal Respir* 1988; 5: 249–254.
23. Ciappi G, Pistelli R, Valente S, Lini A, De Benedetto F, Moneta E. Mechanical properties of the thorax and airways in normal and obese pregnant women. *Bull Eur Physiopathol Respir* 1977; 13 (Suppl.): 85–86.
24. Berry MJ, McMurray RG, Katz VL. Pulmonary and ventilatory responses to pregnancy, immersion and exercise. *J Appl Physiol* 1989; 66: 857–862.
25. Alaily AB, Carrol KB. Pulmonary ventilation in pregnancy. *Br J Obstet Gynaecol* 1978; 85: 518–524.
26. Rodenstein DO, Stanescu DC. Frequency dependence

of plethysmographic volume in healthy and asthmatic subjects. *J Appl Physiol: Respirat Environ Exercise Physiol* 1983; 54: 159–165.

27. Shore SA, Huk O, Mannix S, Martin JG. Effect of panting frequency on the plethysmographic determination of thoracic gas volume in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1983; 128: 54–59.
28. Bégin P, Peslin R. Influence of panting frequency on thoracic gas volume measurements in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1984; 130: 121–123.
29. Brown R, Ingram JH Jr, McFadden ER Jr. Problems in the plethysmographic assessment of changes in total lung capacity in asthma. *Am Rev Respir Dis* 1978; 118: 685–692.
30. Rodenstein DO, Francis C, Stanescu DC. Airway closure in humans does not result in overestimation of plethysmographic lung volume. *J Appl Physiol: Respirat Environ Exercise Physiol* 1983; 55: 1784–1789.
31. Baldwin GR, Moorthi DS, Whelton JA, McDonnel KF. New lung functions and pregnancy. *Am J Obstet Gynecol* 1977; 127: 235–239.
32. Russell IF, Chambers WA. Closing volume in normal pregnancy. *Br J Anaesth* 1981; 53: 1043–1047.
33. Ang CK, Tan TH, Walters WAW, Wood C. Postural influence on maternal capillary oxygen and carbon dioxide tension. *Br Med J* 1969; 4: 201–203.
34. Mutoh T, Lamm WJE, Embree LJ, Hildebrandt J, Albert RK. Abdominal distension alters regional pleural pressures and chest wall mechanics in pigs *in vivo*. *J Appl Physiol* 1991; 70: 2611–2618.
35. Faridy EE. Pressure-volume characteristics of lungs of rats during pregnancy and postpartum. *Respir Physiol* 1981; 43: 43–58.