Eur Respir J
1988, 1, 594–599

Assessment of thoracic gas volume by low-frequency ambient pressure changes in children

R. Peslin*, F. Marchal**, C. Gallina*, M. Oswald, J.P. Crance**

Assessment of thoracic gas volume by low-frequency ambient pressure changes in children. R. Peslin, F. Marchal, C. Gallina, M. Oswald, J.P. Crance.
ABSTRACT: The validity of a new method for measuring thoracic gas volume (TGV) was studied in 69 children, 4–16 yrs old, including twelve normal children and 57 children with an obstructive ($n=38$) or restrictive ($n=19$) respiratory disease. The method consisted of applying very slow (0.05 Hz) sinusoidal variations of ambient pressure around the body ($\Delta Pam = 40$ cmH_2O peak to peak) and studying the relationship between ΔPam and the resulting gas displacement at the mouth (Vaw): $TGVapc = P_B \cdot \Delta Vaw/\Delta Pam \cdot \cos\phi$, where P_B is barometric minus alveolar water vapour pressure and ϕ the phase angle between Pam and Vaw. Functional residual capacities derived from TGVapc (FRCapc) were compared to the values obtained by plethysmography (FRCplet) and by helium dilution (FRCdil). FRCapc did not differ significantly from FRCplet in either the entire group (1.75 ± 0.62 *l vs* 1.79 ± 0.45 *l*) or in the patient subgroups. However, with the new method a trend to slightly lower FRCs was seen in patients with the most obstruction ($p<0.05$). FRCdil was significantly lower than both FRCapc and FRCplet ($p<0.001$), particularly in children with obstruction. Significant correlations were found between the three methods ($p<0.001$). On the other hand, the method investigated requires that the subject breathe very regularly for a period of several minutes. This was rarely achieved, so that the reproducibility of the measurements was unacceptably low. At present, the method cannot be recommended for routine use in 4–16 yr old children.
Eur Respir J., 1988, 1, 594–599

* Unité 14 INSERM de Physiopathologie Respiratoire, 54500 Vandoeuvre-les-Nancy, France.
** Laboratoire d'Exploration Fonctionnelle de l'Hôpital d'Enfants du CHU Brabois, 54500 Vandoeuvre-les-Nancy, France.

Correspondence: R. Peslin, Unité 14 INSERM de Physiopathologie Respiratoire, c.o. No. 10, 54511 Vandoeuvre-les-Nancy cedex, France.

Keywords: Body plethysmography; Boyle's law; helium dilution method; lung volume measurements; respiratory mechanics.

Received: May 28, 1987; accepted after revision April 10, 1988.

It has recently been shown that thoracic gas volume (TGV) can be accurately measured in adults [1, 2] using a variant of Pflüger's gas expansion method [3]. It consists of applying very slow sinusoidal pressure changes around the entire body, *i.e.* varying ambient pressure, and measuring the relationship between the applied pressure and the resulting low-frequency component of gas flow at the mouth. The method has been shown to be in good agreement with body plethysmography in normal adults [1], and adult patients with chronic airway obstruction [2]. Its potential advantage over body plethysmography is that the measurements are made during quiet breathing, and do not require any special respiratory manoeuvre. As this could be a particularly useful feature in young subjects, we investigated the applicability and accuracy of the method in 4–16 yr old normal and abnormal children. The accuracy was assessed by comparison to the data obtained by body plethysmography, and/or by the helium dilution method; the reproducibility of the data obtained with the new technique was also evaluated.

Principle

The principle of the method has been described previously [1]. Briefly, when sinusoidal ambient pressure changes (ΔPam) are applied simultaneously at the airway opening and around the body, alveolar gas tends to equilibrate with the surrounding pressure, and is periodically compressed and expanded. This is achieved either by gas motion through the airways (Vaw) or by lung and chest volume changes (Vt), or both, depending on the respective mechanical impedances of the two pathways. At very low frequencies, such as 0.03–0.05 Hz, tissue impedance (Zt) is very much larger than airway impedance (Zaw), so that virtually all of the volume change takes place through the airways, and may be measured at the airway opening. Then, TGV may be derived, according to Boyle's law, from the following relationship:

$$TGV = (P_B - P_{H_2O}) \cdot \Delta Vaw/\Delta Pam \cdot \cos\phi \qquad (1)$$

where ΔVaw is the amplitude of the low-frequency component of Vaw, P_B and P_{H_2O} are barometric and alveolar water vapour pressure, respectively, and ϕ is the phase angle between the volume and the pressure sine waves. The latter is due to the fact that a small part of ΔPam is dissipated across airway resistance (Raw).

Materials and methods

The study was conducted in 69 children, 4–16 yr old. The group included twelve normal children (two girls) and 57 children who were classified on clinical grounds as presenting either an obstructive or a restrictive respiratory disease. The obstructive subgroup included 38 children (sixteen girls) with asthma, cystic fibrosis or bronchitis, and the restrictive subgroup 19 children (seven girls) with chest wall abnormalities or an interstitial lung disease. The biometric characteristics and the main functional data in the subgroups are shown in table 1. Children with obstructive diseases were characterized by a slightly decreased forced expiratory flow in one second/forced vital capacity (FEV_1/FVC) and increased specific airway resistance (sRaw). Children with restrictive disease had on average a lower FVC and FEV_1, with a normal FEV_1/FVC ratio, and a normal sRaw.

TGV measurements by ambient pressure changes (TGVapc) were made by seating the subject in a 410 *l* aluminium body chamber (a modified plethysmograph) connected to a large stroke-volume reciprocating pump. The pump achieved pressure swings around the subject of about 40 cmH_2O peak to peak at a frequency of 0.05 Hz. The subject wore a noseclip and breathed within the chamber through a Fleisch No. 1 pneumotachograph. Pam and the pressure drop across the pneumotachograph were measured with Validyne MP 45 transducers. The pressure and the flow signals were identically filtered to decrease the respiratory component of the flow, which was faster and much larger than the gas compression component (fig. 1), and digitized on-line with a sampling rate of 2.56 Hz. The measurements were made during quiet breathing and lasted five minutes (15 low-frequency cycles). At the end of that period a series of inspiratory capacity (IC) manoeuvres was recorded. Numerical processing of the data consisted of extracting the 0.05 Hz component of the signals by Fourier analysis and computing their amplitude ratio and phase angle. Then TGVapc was obtained

Table 1. – Biometric characteristics and functional data

	Normals n=12	Obstructive disease n=38	Restrictive disease n=19	Pno	Pnr	Por
Age yr	8.5±3.3	10.0±3.0	10.2±4.2	NS	NS	NS
Height cm	123.0±13.0	134.0±16.0	132.0±23.0	<0.05	NS	NS
Weight kg	24.2±6.4	30.4±10.9	32.4±16.9	<0.05	NS	NS
FVC % pred		92.7±16.9	78.9±18.9			<0.01
FEV_1 % pred		79.9±18.2	78.3±18.0			NS
FEV_1/FVC %		77.9±11.4	89.8±9.4			<0.001
sRaw $cmH_2O{\cdot}s^{-1}$	7.2±3.2	11.4±6.7	6.7±2.2	<0.01	NS	<0.001

Values are means±1 SD. Predicted values for FVC and FEV_1 are according to ZAPLETAL *et al.* [4]. Also shown is the statistical significance of the differences between normal and obstructive children (Pno), between normal and restrictive children (Pnr) and between obstructive and restrictive children (Por) by student's t-test; NS: not significant.

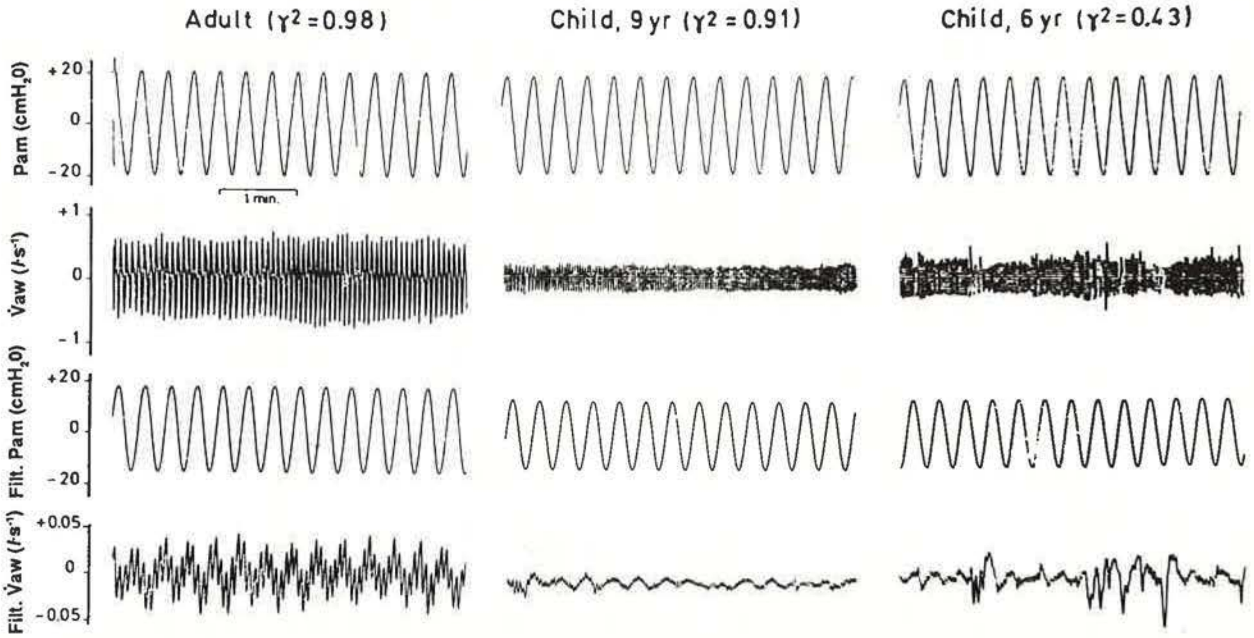

Fig. 1. Examples of recordings obtained in one healthy adult [1], and in two representative children. From top to bottom: unfiltered ambient pressure (Pam), unfiltered airways flow ($\dot{V}aw$), filtered pressure and filtered flow. Note the change in scale by a factor of 15 between unfiltered and filtered flow. Coherence functions (γ^2) are indicated.

according to equation 1. As TGVapc should represent the average lung volume during the measurement period, functional residual capacity (FRCapc) was derived by subtracting half a tidal volume from it; total lung capacity (TLCapc) was obtained by adding IC to FRCapc. The data were corrected to BTPS. Fourier analysis also provided the so-called coherence function γ^2 ($0 < \gamma^2 < 1$) which is an index of the signal to noise ratio of the relationship between the studied variables at the frequency of interest, and can be used to reject noisy data [5].

Plethysmographic determinations of lung volumes (FRCplet, TLCplet) were made in the same body chamber at a few minutes interval using the method of DU BOIS *et al.* [6]. Mouth pressure during airway occlusion and box pressure, as measured with Validyne MP 45 transducers, were digitized at a rate of 51.2 Hz and similarly processed by Fourier analysis [7]. The children were asked to support their cheeks with both hands during the measurements. The data from 2–4 panting manoeuvres were averaged. Satisfactory measurements were obtained in 61 subjects. FRC was also measured in 63 children using the standard helium dilution method (FRCdil).

In addition to inter-method comparisons, the reproducibility of TGVapc was evaluated separately in ten children with an obstructive disease and nine children with a restrictive disease. The measurements were repeated in the same conditions a few minutes apart. Finally, to assess whether TGVapc varied with the frequency of ambient pressure changes, measurements were made at both 0.05 and 0.03 Hz in 22 children, including 15 children with obstructive disease.

Statistical analysis of the data was made using standard linear regression and Student's t-test for paired data, where appropriate.

Results

Recordings obtained in two representative children and, for comparison, in one adult subject are shown in figure 1. The low-frequency component of airways flow, related to ambient pressure changes, is undetectable on the unfiltered signals. In the adult subject it can be seen quite clearly after low-pass filtering and amplification. This is also the case in one of the children, who breathed very regularly, although the amplitude of that component was more variable than in the adult and the coherence function a little lower. In the second child spontaneous breathing was rather irregular, both in frequency and amplitude. As a consequence the filtered flow was very noisy, and the coherence function very low. The distribution of γ^2 in the group is shown in figure 2. γ^2 averaged 0.72 ± 0.20. It was not correlated to age or to functional data. Values above 0.9, which are the rule in adults [1, 2], were seen in only a quarter of the subjects. A similar proportion of the children had values below 0.6, in which case TGV estimates are expected to be very unreliable [5, 8, 9]. Although this γ^2 threshold is somewhat arbitrary, we discarded those subjects and, in the following, have considered only the 52 children with $\gamma^2 > 0.6$.

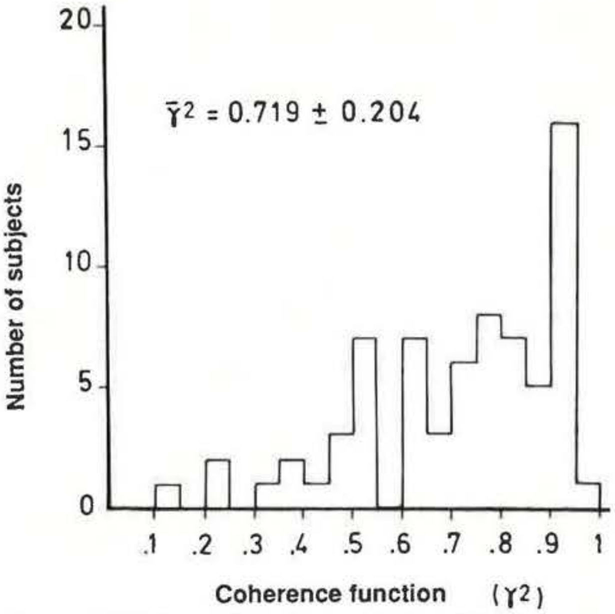

Fig. 2. Distribution of the coherence function (γ^2) in the group.

Functional residual capacities obtained by ambient pressure changes and by the two other methods are compared in table 2 and in figure 3. Considering the 39 children in whom TGV was assessed by the three

Table 2. – Functional residual capacities by the three methods

	All subjects n=39	Normals n=3	Obstructive disease n=23	Restrictive disease n=13
1. FRC apc *l*	1.75±0.62	1.64	1.78±0.59	1.73±0.76
2. FRCplet *l*	1.79±0.45	1.97	1.85±0.40	1.65±0.57
3. FRCdil *l*	1.50±0.52	1.57	1.47±0.43	1.53±0.71
p 1.2	NS		NS	NS
p 1.3	<0.001		<0.01	NS
p 2.3	<0.001		<0.001	NS

Values are means ± 1 SD. Subjects with $\gamma^2 > 0.6$ and studied by the three methods. p values are the statistical significances of the differences between methods by Student's t-test for paired data; comparisons between lines 1 and 2 (p 1.2), lines 1 and 3 (p 1.3) and lines 2 and 3 (p 2.3); NS: not significant.

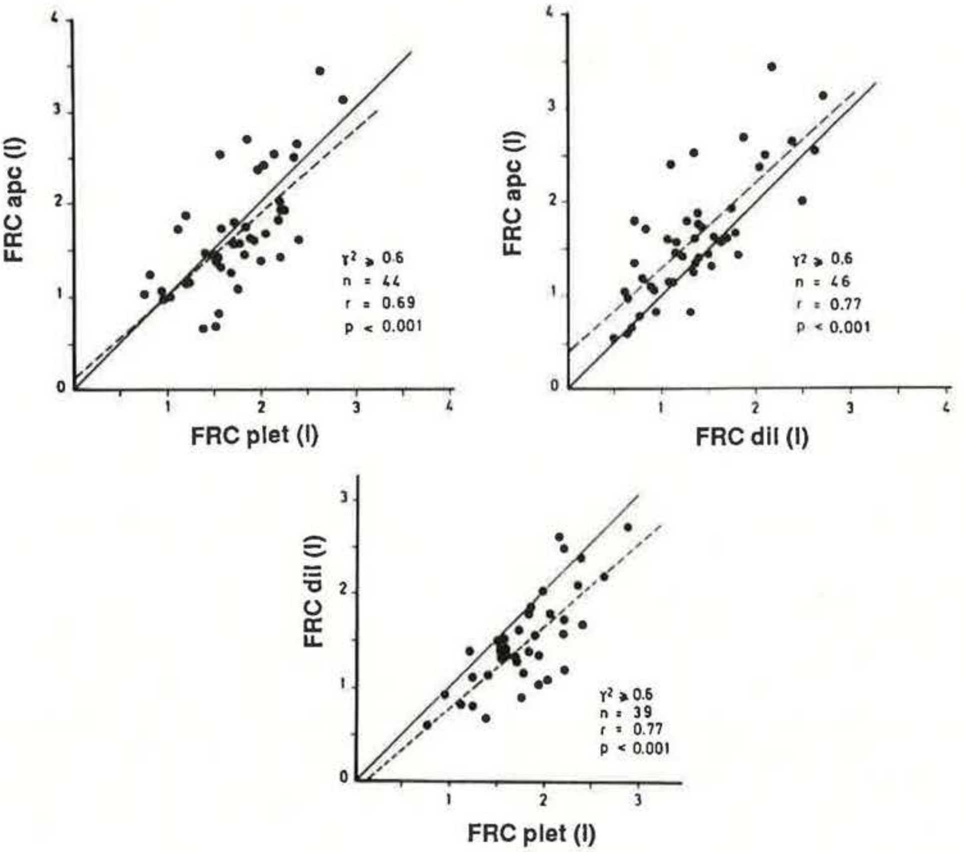

Fig. 3. Correlations between the functional residual capacities obtained by ambient pressure changes (FRCapc), by plethysmography (FRCplet) and by helium dilution (FRCdil). The identity lines (continuous) and regression lines (broken) are indicated.

methods (table 2), no significant difference was found between FRCapc and FRCplet, either in the entire group or in the patient subgroups. The mean values of FRCapc and FRCplet differed by only 2.3%. On the other hand, significantly lower values were found by helium dilution than by the other methods, and this was mainly the case for the obstructive patients.

Significant correlations ($p<0.001$) were found between FRCapc and the other two methods (fig. 3), as well as between FRCplet and FRCdil ($r=0.77$; $p<0.001$), but the relationships were not very close. Slightly higher correlation coefficients were obtained when comparing the total lung capacities ($r=0.82$ between TLCapc and TLCplet, 0.88 between TLCapc and TLCdil, 0.90 between TLCdil and TLCplet). Differences between the values obtained by ambient pressure changes and by plethysmography, irrespective of their sign, averaged 22.9% for FRC, and 17.2% for TLC. They were not correlated to the coherence function.

As the validity of the investigated method is based on the assumption that airways impedance is very small compared to tissue impedance, it was of interest to see whether inter-method differences, taken with their sign, were correlated to functional indices. Indeed, the relative differences between FRCapc and FRCplet were found to be correlated to some extent to both FEV_1/FVC ($r=0.315$; $p<0.05$) and FEV_1% predicted: FRCapc tended to be lower than FRCplet in the subjects with the most severe airway obstruction. The differences between FRCdil and FRCplet were also correlated to FEV_1/FVC ($r=0.39$; $p<0.05$), to FEV_1% predicted ($r=0.57$, $p<0.001$), and to FVC% predicted ($r=0.34$; $p<0.05$). No significant correlation with functional indices was found for the differences between FRCapc and FRCdil.

Repeated measurements of FRCapc at a few minutes interval in nineteen children revealed a very poor reproducibility. In the group as a whole, the difference between the two estimates averaged 34.3 ± 30.6%. In the twelve children with γ^2 values ≥ 0.6 for the two tests, it averaged 28.1 ± 24.4%; the large variability being due mainly to two children who had an FRC around one litre. Within-subject variability of FRC was much less with the plethysmographic method (7.5%) and with the gas dilution method (8.6%).

Discussion

The method investigated was in general well accepted and very few children complained of the tension in their eardrums. It did not appear necessary to use earplugs. The main difficulty was to have the child breathe regularly over a period of several minutes. This was not achieved in a number of cases (fig. 1, right) with, a noisy flow recording and a poor coherence function as a consequence. γ^2 is an index of causality between the studied variables, and is lowered if their relationship is non-linear or if the data are contaminated by noise [5]. The value of γ^2 is also a function of the number of data points in the Fourier analysis (here 256), and on the number of data blocks (here 5) which are summed. It follows that there is no direct relationship between γ^2 and the accuracy of the data. However, it has been demonstrated both theoretically and in practice that the reliability of the result is poor when γ^2 is low [8, 9]. In respiratory impedance measurements using a similar analysis, it is usual to discard the data when γ^2 is smaller than 0.9 or even 0.95 [5, 10, 11]. Had we used a threshold of 0.9, 52 of the 69 subjects would have been rejected. The decision to lower the threshold to 0.6, to exclude fewer subjects, was to some extent justified by the fact that the correlations between FRCapc and both FRCplet and FRCdil did not improve when the threshold was raised to 0.7 or even to 0.8. Also, as mentioned earlier, inter-method differences were not correlated to γ^2 when it was larger than 0.6. On the other hand, with this lower threshold, the within-subject variability of the measurements appeared to be unacceptably high, particularly in the children with a very low FRC. As only one child had a $\gamma^2 \geq 0.9$ for the two successive tests it is not possible to assess whether that condition would guarantee reproducible data.

In this study we observed that, on average, FRCapc did not differ significantly from FRCplet (table 2) and, also, that the method investigated tended to provide lower values than plethysmography in the children with most obstruction. This could in part be due to an overestimation of plethysmographic TGV due to the so-called upper airway artefact. The latter results from a small difference between alveolar and mouth pressure swings due to the combined effect of upper airway wall compliance and increased airway resistance [12, 13]. On the other hand, it could also be due to an underestimation of TGVapc if the ratio of airways and tissue impedance was not sufficiently low. Assuming that the effects of inertia are negligible at such low frequencies, the corresponding relative error (E) may be estimated on the basis of airway resistance, (Rt) and total tissue compliance (Ct):

$$E = \tau_1 \tau_2 \omega^2 / [\tau_1(\tau_1 + \tau_2)\ \omega^2 + 1] \qquad (2)$$

where $\tau_1 = Rt \cdot Ct$, $\tau_2 = Raw \cdot Ct$ and ω is the circular frequency ($\omega = 2\pi \cdot f = 0.314$ at 0.05 Hz). In a normal 10 yr old (140 cm) child $Ct \cong 0.05\ l \cdot cmH_2O^{-1}$ [14], $Raw \cong 4\ cmH_2O \cdot l^{-1} \cdot s$ [15] and, from forced oscillation data [11], Rt may be estimated to about $2\,cmH_2O \cdot l^{-1} \cdot s$. Then $\tau_1 \cong 0.1$ s, $\tau_2 \cong 0.21$ s, and TGV is expected to be underestimated by 0.2% at 0.05 Hz. As growth is characterized by a decrease in resistances and an increase in total compliance, the two time constants and the corresponding error are not expected to change much over the age range considered in this study. If either τ_1 or τ_2 were increased by a factor of 10, due to airway obstruction, increased tissue compliance, or increased tissue resistance, the error would still amount to only 2%. For the children with most obstruction seen in this study (sRaw increased by a factor of 5), who probably did not have overcompliant tissues, one could therefore expect that TGV would not be seriously underestimated due to an inadequate Zaw/Zt ratio. To test these theoretical predictions, TGVapc was measured in 22 children at the usual frequency of 0.05 Hz, and also at the lower frequency of 0.03 Hz, which should decrease the error in question. In the seven children with normal lung function or restrictive disease, FRCapc was not significantly smaller at 0.03 than at 0.05 Hz. In contrast, FRCapc was larger at 0.03 than at 0.05 Hz in the fifteen children with obstructive disease. The difference was not quite significant, but averaged 14% (1.75±0.8 *l vs* 1.53±0.53 *l*). This unexpectedly large difference points to the limitations of the monoalveolar model on which the above theoretical predictions are based. It suggests that, in some of the children, local obstruction may be much more severe than indicated by the global airway resistance with, as a consequence, a high local Zaw/Zt ratio and an underestimation of the gas volume behind the obstruction. It also suggests that a frequency of 0.05 Hz is inadequately high in the children with most obstruction.

From this study, we conclude that the method investigated presents serious limitations and cannot be recommended for routine pulmonary function testing in 4–16 yr old children. The main problem being that it requires the subject to breathe regularly, without pause or sighs, for several minutes; this is easily achieved by adults, but is difficult to accomplish for many children. As a consequence, the signal to noise ratio of the measurements is low and the data exhibit a large variability.

Acknowledgements: The authors are grateful to B. Clement for the typing and to M.C. Rohrer for the illustrations.

References

1. Peslin R, Duvivier C, Hannhart B, Gallina C. – Measurement of thoracic gas volume by low-frequency ambient pressure changes. *J Appl Physiol*, 1987, 62, 359–363.
2. Peslin R, Hannhart B, Duvivier C, Polu JM, Gallina C. – Thoracic gas volume measurements in chronic obstructive pulmonary disease by low-frequency ambient pressure changes. *Am Rev Respir Dis*, 1988, 137, 277–280.
3. Pflüger E. – Das pneumonometer. *Pflügers Arch*, 1882, 29, 244–246.
4. Zapletal A, Motoyama EK, van de Woestijne KP, Hunt VR, Bouhuys A. – Maximum expiratory flow-volume curves and airway conductance in children and adolescents. *J Appl Physiol*, 1969, 26, 308–316.
5. Michaelson ED, Grassman ED, Peters NR. – Pulmonary mechanics by spectral analysis of forced random noise. *J Clin Invest*, 1975, 56, 1210–1230.
6. DuBois AB, Botelho SY, Bedell GN, Marshall R, Comroe JH. – A rapid plethysmographic method for measuring thoracic gas

volume: a comparison with a nitrogen washout method for measuring functional residual capacity in normal subjects. *J Clin Invest*, 1956, 35, 322-326.

7. Peslin R, Gallina C, Rotger M. – Methodological factors in the variability of lung volume and airway resistance measured by plethysmography. *Bull Eur Physiopathol Respir*, 1987, 23, 323–327.

8. Franken H, Clement J, van de Woestijne KP. – Systematic and random errors in the determination of respiratory impedance by means of the forced oscillation technique: a theoretical study. *IEEE Trans Biomed Eng*, 1983, BME-30, 642–651.

9. Miller TK, Pimmel RL. – Standard errors on respiratory mechanical parameters obtained by forced random excitation. *IEEE Trans Biomed Eng*, 1983, BME-30, 826–832.

10. Nagels J, Landser FJ, van der Linden L, Clement J, van de Woestijne KP. – Mechanical properties of lungs and chest wall during spontaneous breathing. *J Appl Physiol: Respirat Environ Exercise Physiol*, 1980, 49, 408–416.

11. Peslin R, Gallina C, Teculescu D, Pham QT. – Respiratory input and transfer impedances in children 9–13 years old. *Bull Eur Physiopathol Respir*, 1987, 23, 107–112.

12. Bohadana AB, Peslin R, Hannhart B, Teculescu D. – Influence of panting frequency on plethysmographic measurements of thoracic gas volume. *J Appl Physiol: Respirat Environ Exercise Physiol*, 1982, 52, 739–747.

13. Rodenstein DO, Stanescu DC, Francis C. – Demonstration of failure of body plethysmography in airway obstruction. *J Appl Physiol: Respirat Environ Exercise Physiol*, 1982, 52, 949–954.

14. Sharp JT, Droz WS, Balagot RC, Baudelin WR, Danon J. – Total respiratory compliance in infants and children. *J Appl Physiol*, 1970, 29, 775–779.

15. Baran D, Englert M. – La conductance des voies aériennes chez l'enfant et l'adolescent normaux. *Bull Eur Physiopathol Respir*, 1971, 7, 125–135.

RÉSUMÉ: Nous avons étudié la validité d'une nouvelle méthode de mesure du volume des gaz intrathoraciques chez 69 enfants âgés de 4 à 16 ans, parmi lesquels 12 normaux et 57 malades atteints d'affection obstructive ($n = 38$) ou restrictive ($n = 19$) des voies respiratoires. La méthode consistait à appliquer des variations sinusoïdales très lentes (0.05 Hz) de pression ambiante autour du corps ($\Delta Pam = 40$ cmH$_2$O crête à crête) et à étudier les relations entre ΔPam et les déplacements gazeux qui en résultent au niveau de la bouche (Vaw): $TGVapc = P_B \cdot \Delta Vaw / \Delta Pam \cdot \cos\phi$, où P_B est la pression barométrique moins la pression de vapeur d'eau alvéolaire et ϕ l'angle de phase entre Pam et Vaw. Les capacités résiduelles fonctionnelles dérivées de TGVapc (FRCapc) ont été comparées aux valeurs obtenues par pléthysmographie (FRCplet) et par dilution de l'hélium (FRCdil). FRCapc n'a présenté aucune différence significative par rapport à FRCplet dans le groupe entier (1.75 ± 0.62 *l* *vs* 1.79 ± 0.45 *l*) ni dans les sous-groupes de patients. Toutefois, chez les enfants les plus obstructifs, on a trouvé une tendance à des valeurs légèrement plus basses de FRC avec la nouvelle méthode ($p < 0.05$). FRCdil apparaît significativement plus faible que FRCapc et FRCplet ($p < 0.001$), particulièrement chez les enfants obstructifs. Des corrélations significatives ont été trouvées entre les trois méthodes ($p < 0.001$). D'autre part, la méthode investiguée exige que le sujet respire très régulièrement pendant une période de plusieurs minutes. Dans beaucoup de cas, ceci n'est pas obtenu, de sorte que la reproductibilité des mesures est faible et inacceptable. Actuellement, la méthode ne peut pas être recommandée pour une utilisation de routine chez les enfants de 4 à 16 ans.