

Functional residual capacity in healthy preschool children

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Functional residual capacity in healthy preschool children. J.H. Pauwels, H.P. Van Bever, K.N. Desager, M.J. Willemen, W.L. Creten, K.J. Van Acker, P.A. Vermeire. ©ERS Journals Ltd 1996.

ABSTRACT: The purpose of this study was to evaluate the feasibility of routine functional residual capacity (FRC) measurements in healthy preschool children aged 2.7–6.4 yrs. Furthermore, accuracy and reproducibility were investigated and normal values were collected.

A mass-produced closed-circuit helium dilution device (rolling seal) was used. Selection of the 113 healthy children (from the 571 measured) was based on an extensive personal and family history questionnaire and on clinical examination before measurements were performed.

With three successive attempts it was possible to achieve at least two reproducible measurements in 73% of the children (repeatability coefficient 95.3 mL). The main problems were leakage at the corner of the mouth and irregular breathing pattern. The mean time to perform a measurement was 113 s. Mean FRC was significantly higher in boys than in girls: 778 versus 739 mL for a body length of 110 cm ($p < 0.05$). FRC correlated with height (H) ($r = 0.69$), weight (W) ($r = 0.56$), age (A) ($r = 0.62$) and all three combined ($r = 0.70$): $FRC = -534.89 + 1.84 \times W$ (kg) $+ 10.07 \times H$ (cm) $+ 2.51 \times A$ (months). When a power or exponential function was used to describe FRC as a function of height, the results were not superior to the linear regression ($r = 0.69$): FRC (mL) = $-766.2 + 13.8 \times H$ (cm) ($r = 0.69$) or FRC (L) = $0.620 \times H$ (m)^{2.03} ($r = 0.69$) or FRC (mL) = $99.5 \times e^{0.018 \times H}$ (cm) ($r = 0.69$). Among these, we recommend the power function because it will better fit broader height ranges.

Reliable functional residual capacity measurements can be routinely performed in preschool children with a mass-produced device. Reference values were collected for children 95–125 cm in height.

Eur Respir J., 1996, 9, 2224–2230.

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Keywords: Functional residual capacity preschool children

Received: December 22 1995
Accepted after revision July 5 1996

Chronic respiratory diseases, such as bronchial asthma, often start in early childhood and may persist into adult life [1, 2]. There are indications that lung function abnormalities may precede the occurrence of respiratory symptoms [3, 4]. Taking into consideration the increasing morbidity of asthma in children, there is therefore a need for reliable equipment that allows evaluation of lung function in young children [5].

Several procedures have been described for the measurement of lung function in infants, usually when under sedation [5, 6]. In the 2–5 yrs age group, however, only a limited number of procedures are possible. One of the techniques which can be applied in this age group is the determination of functional residual capacity (FRC), which requires only the passive co-operation of the child [7, 8]. In previous studies of FRC in preschool children, it has already been demonstrated that FRC measurements can be performed in that age group [7–9]. There remains, however, much discrepancy between the few prediction equations available, and further modelling is needed to assess the potential influence of gender, weight, posture and age [10]. In the present study, a large group

of healthy children was measured using a mass-produced device with a new generation helium (He) analyser permitting us to assess breath-by-breath sampling, resulting in very strict He stabilization criteria. The feasibility and reproducibility of routine FRC measurements was evaluated in preschool children. Reference values for children 95–125 cm in height were collected.

Patients and methods

A written invitation to participate in the study was sent to the parents of all 726 preschool children in a suburb of Antwerp. There was no heavy industry in the neighbourhood. In an accompanying questionnaire, information was sought about the child's general and respiratory health and medical history, and the respiratory history of the relatives. Consent was obtained for 651 children (90%), but of these 55 (8%) were absent when the FRC measurements were performed in the kindergarten: overall 596 children, aged 2.7–6.4 yrs (mean 4.8 yrs), were investigated. These measurements took place

from autumn 1993 until spring 1994. In each child, weight and height were recorded and clinical investigation, including heart and lung auscultation and inspection of the skin for eczema, was performed just before the measurements. A child was categorized as healthy when the personal and family history was negative for chronic respiratory symptoms, eczema or other allergic disorders, when there was no history of prematurity, pneumonia, bronchiolitis or laryngitis, in the absence of systemic disease or heart disease, and when the clinical examination was normal [11].

FRC was measured twice in all but 45 children, with an interval of at least 10 min. In the 45 children, three measurements were performed in order to assess the improvement in success rate if an additional (extra-time consuming) attempt to measure FRC was made. Biological variability was assessed by investigating 10 children at the same hour in the morning on two consecutive days, and 10 others with an interval of 1 week. For measurement of FRC, the children were seated on a height-adjustable chair, with their back stretched and their hands on their knees. Connection to the spirometer was made through a mouthpiece (paediatric size, Jaeger, Germany, or Vacumed, USA) protected by an antibacterial filter (Pall Pro-tec®) and with clipped nose. Correct position of the child was enforced by the limited flexibility of the mouthpiece. Leakage at the mouth or nose was checked carefully by visual inspection of the child's lips and nose and by reviewing all breathing patterns for drifts of the end-expiratory volume level.

FRC was measured with a prototype of the new Masterscreen CS-FRC device, designed for use in preschool children (Jaeger, Germany and Mijnhardt, The Netherlands). This device uses the multiple breath He equilibration method with closed-circuit (rolling seal). A small dead space is achieved by reducing the length and diameter of the tubing to a minimum and by the use of external tubes with 2 cm diameter. The volume of the bell can be adapted to the child's lung volume within a range of 250 mL to 10 L. During each measurement, data corrected for body temperature, pressure and saturation (BTPS), BTPS factor, dead space volume, initial He concentration, bell volume, inspiratory and expiratory volume during each breath and He concentration during each breath, were stored for analysis. The dead space of the system (bell + internal and external tubing + filter + mouthpiece) varies between 2.24 and 2.42 L (mean 2.31 L). The bell volume of the dry spirometer was set at 1 L and the combined volume of mouthpiece and filter was 69 mL. The pressure sensor had a measuring range of 80–115 kPa; the dynamic resistance was $<0.1 \text{ kPa}\cdot\text{L}^{-1}\cdot\text{s}$ at $10 \text{ L}\cdot\text{s}^{-1}$; the blower capacity was used in the $180 \text{ L}\cdot\text{min}^{-1}$ setting; oxygen concentration during measurement was maintained at $20.9\pm 0.5\%$; and soda lime was used for CO_2 absorption.

Because of the high technical requirements inherent to lung function testing in young children, a number of possible errors were evaluated. Thus, the theoretical error due to mismatching between the child's lung volume and the bell volume was calculated. Assuming a lung volume of 0.4 L in a 3 year old girl at the 5th percentile for height [7, 8], and considering that the dead space volume of the device, the mouthpiece and the bell is 2.31 L, 0.069 L and 1 L, respectively, the ratio of the

child's lung volume to the volume of the entire device is 0.12. This is below the generally accepted minimum value of 0.3. But taking into account that, within the volume range which is used, the He analyser has a maximal error of 0.01 vol %, the overall theoretical error clearly remains below 10%, and is, therefore, acceptable [12, 13]. The accuracy and the precision of the measurement of a 0.5 L volume at a start bell volume of 1 L were 0.8% (mean 504 mL, range 494–514 mL) and 1% or 5 mL, respectively. The response time and the accuracy of the He analyser were less than 150 ms and 0.01 vol %, respectively.

External conditions were measured directly by the sensors of the apparatus and BTPS corrections were automatically performed using standard formulae [12]. Volume and dead space determination were calibrated every day, and pressure and temperature measurements by the apparatus on the first day of every week. In accordance with the European Respiratory Society (ERS) guidelines, He stabilization was defined as a dilution of less than 0.02% over 30 s, which was automatically traced [12]. However, whereas in these guidelines He sampling is performed every 15 s, we sampled He during each breath, which resulted in a mean of 13 samples (range 7–24) during 30 s and, therefore, a much more precise evaluation of stabilization. Mean tidal volume (VT) and respiratory frequency (fR) during the 30 s of FRC measurement were calculated by computer.

Statistical analysis

For statistical analysis, all the results were processed using the CSS Statistica® package from Statsoft (1991). Variability was assessed by calculating the repeatability coefficient as adopted by the British Standards Institution [14]. This coefficient is defined as the standard deviation of the differences between two measurements in the same child. For the intersubject variability, the mean coefficient of variation (based on absolute values) for all FRC values was calculated. For regression equations, multiple linear regression analysis and nonlinear estimates for exponential and power functions were used. For the regression equation of FRC on height, the confidence limits for the theoretical curve and the prediction limits for the experimental data were calculated (see Appendix for details). Percentiles of the predicted values are also given. Sex differences were investigated using covariance analysis. All data were checked for assumption of normality with the Kolmogorov-Smirnov or Chi-squared test. Differences were considered significant when the probability of erroneously rejecting the zero hypothesis was below 5%.

The study was approved by the Hospital Ethics Committee. Written informed consent was obtained from the parents.

Results

In order to evaluate the feasibility of routine FRC measurements in preschool children, co-operation and technical success rates were determined in 596 children for whom written informed consent was obtained and

who were present at the moment of measurement. Full co-operation was obtained in 571 (96%) of the 596 children: 21 refused to co-operate and four attempted the measurement only once. Co-operation was independent of age. Measurement of FRC was performed twice in 526 children, and in 45 children three measurements were performed. At least one technically acceptable measurement was achieved in 73%. Both measurements were technically acceptable in 51%. In the 45 children measured three times, in order to assess improvement of success rate, the success rate did indeed increase, as at least two reproducible results were obtained in 73% instead of 51%. However, because of time restrictions, only two measurements were performed in the other children. The two major practical problems were leakage at the mouth (72% of the missing data), and irregular breathing pattern resulting in a difference of more than 10% between two FRC measurements (28% of the missing data). The technical success rate was lower in the 3 year olds as compared to the 5 year olds, but this was not statistically significant.

Of the 596 children who were initially selected for the study, only 167 (28%) could be considered as healthy as defined previously. Of these 167 children, 54 were excluded (21 because there was a leak during both measurements, 19 because there was a leak during one measurement, 11 because their breathing pattern was very irregular resulting in >10% difference, and three because they did not co-operate). Therefore, the data (discussed below) used to obtain normal values are those from the remaining 113 children. In order to control for any possible bias by excluding the measurements which differed by more than 10% of single measurements, these excluded measurements were pooled and compared with those from the 113 children. This resulted in a non-significant difference ($p=0.83$). However, they were not included in order to keep the quality standards and the criteria of being healthy as high as possible [10]. There was also no age difference between the 54 excluded and the 113 included children. After exclusion, there were 58 boys and 55 girls remaining, all Caucasian, mean age 4.8 yrs (range 2.7–6.4 yrs), mean height 110.2 cm (range 92.5–126.0 cms), and mean weight 19.6 kg (range

Table 1. – Time needed for FRC measurement, FRC values during first and second measurement, difference between first and second FRC measurement, tidal volume and respiratory frequency during both measurements

	Mean	Min	Max	SD
Time 1 s	116	52	261	48
Time 2 s	110	46	315	50
FRC 1 mL	770	463	1075	136
FRC 2 mL	759	412	1077	152
Difference	40	2	93	26
V_T 1 mL	337	181	1099	186
V_T 2 mL	336	164	798	156
f_R 1 br·min ⁻¹	26	17	40	5
f_R 2 br·min ⁻¹	28	16	50	8

FRC: functional residual capacity; V_T : tidal volume; f_R : respiratory frequency; br·min⁻¹: breaths per minute; Min: minimum; Max: maximum; 1: first measurement; 2: second measurement.

13.0–29.0 kg). In none of these children was the weight above the 97th percentile.

The time needed for the whole FRC procedure during each of the two measurements, the FRC values in millilitres, the differences between two FRC measurements, the tidal volume and the respiratory frequency during 30 s of He stabilization, are presented in table 1. The He stabilization reached a mean of 0.012% (± 0.004) over 30 s.

For assessment of the intrasubject variability, the repeatability coefficient between both FRC measurements in all 113 subjects was calculated: it amounted to 95.3 mL. As can be seen from figure 1, all differences are within 2 SD of the mean difference (being almost 0, as expected). When the measurements which differed by >10% (due to irregular breathing patterns and, thus, considered as technically unacceptable) were included, a repeatability coefficient of 126 mL was obtained. Biological variability was assessed by measuring FRC in 10 children on two consecutive days at the same hour, and in 10 others with an interval of 1 week. Repeatability coefficients were again calculated, using the mean FRC of both measurements on the two different occasions. This

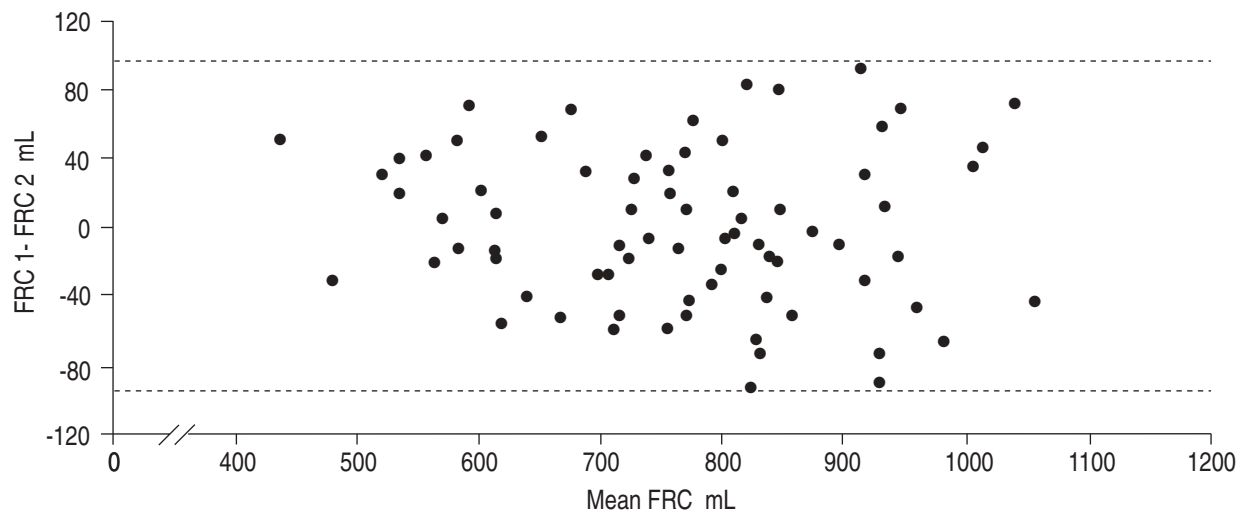


Fig. 1. – Difference versus the mean of the two functional residual capacity (FRC) measurements in each child, in order to evaluate repeatability [14]. The broken lines represent the $2 \times$ SD.

Table 2. – Regression equations for FRC as a function of height (H), weight (W) and age (A)

x-axis	Regression equation for FRC mL	SEE	r	p-value
Height cm	$FRC = -766.199 + 13.837 \times H$	105.7	0.691	<0.001
Height boys	$FRC = -735.710 + 13.733 \times H$	99.9	0.730	<0.001
Height girls	$FRC = -817.852 + 14.123 \times H$	110.5	0.666	<0.001
Weight (kg)	$FRC = 259.954 + 25.741 \times W$	121.7	0.556	<0.001
Age (months)	$FRC = 287.409 + 8.116 \times A$	114.9	0.623	<0.001
H×W×A	$FRC = -534.885 + 1.84 \times W + 10.07 \times H + 2.51 \times A$	238.8	–	=0.027

FRC: functional residual capacity; SEE: standard error of estimate; r: Pearson correlation coefficient.

resulted in a repeatability coefficient of 118 mL on two consecutive days and of 121 mL with an interval of 1 week. In the first case, only one difference fell outside the 2 SD zone of the mean, whereas in the second case three differences fell outside this zone. For the inter-subject variability, the mean coefficient of variation (based on absolute values) for all FRC values was used; it was 13.9%.

Table 2 shows the regression equation of FRC on age, weight, height and the combination of age, weight and height. All the regression equations were highly significant ($p < 0.001$), except for that of height × weight ×

age, which was significant at the 5% level ($p < 0.05$). Multiple regression of FRC on height, weight and age revealed that only the beta-value for height reached statistical significance ($p < 0.01$). The FRC values were significantly different in boys and girls when covariance analysis was used with height as covariant ($F = 3.97$; $p < 0.05$); mean FRC was 778 mL in boys measuring 110 cm and 739 mL in girls of the same height. As the best correlation was found between FRC and height, the 90, 95 and 97% prediction limits for our experimental data, and the 95% confidence limits for the regression of FRC on height for each gender are given in figure 2. The

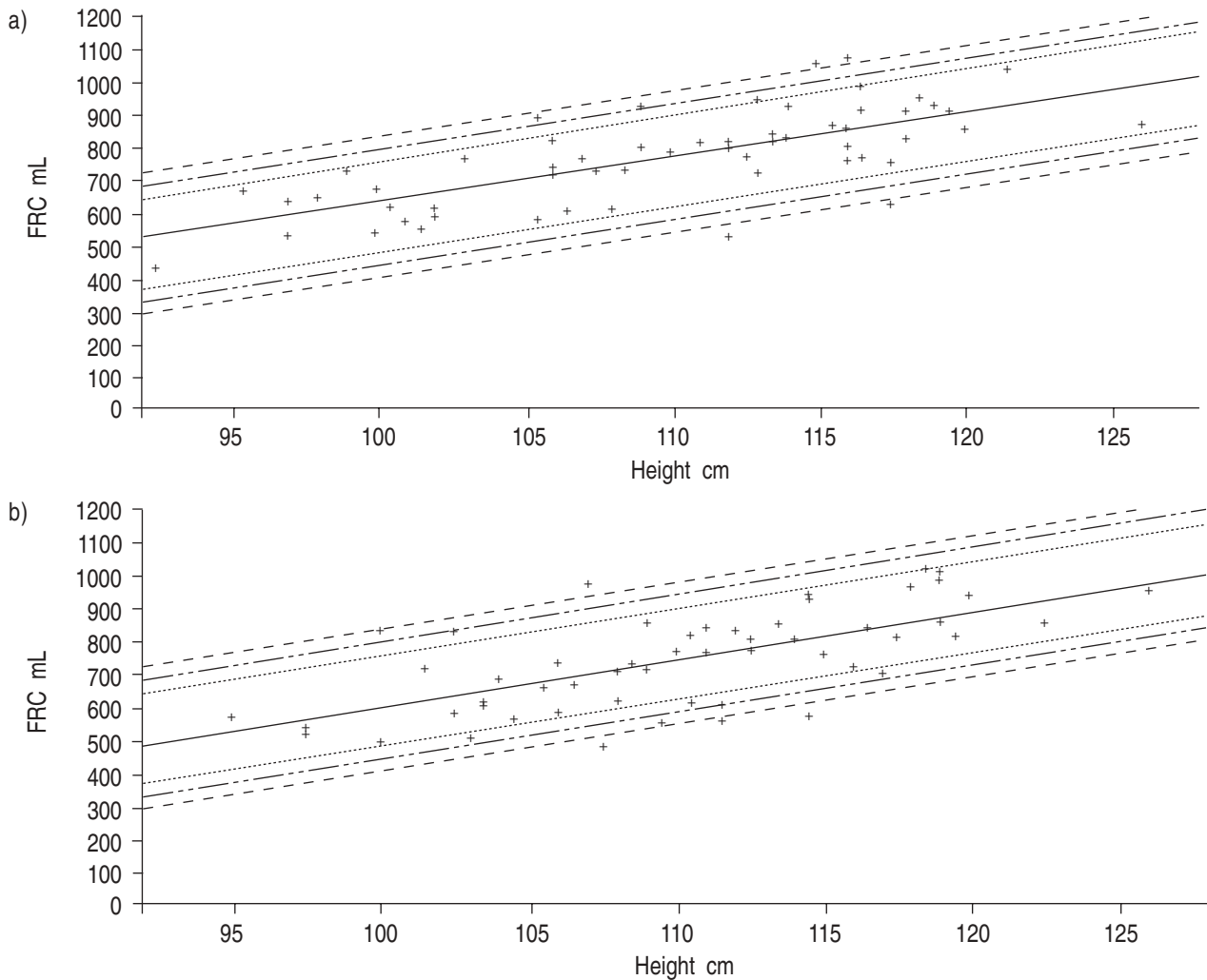


Fig. 2. – Regression of functional residual capacity (FRC) on height for a) boys and b) girls. The 95% confidence limits are indicated by the broken lines. - - - - : 3% and 97% prediction limits; - - - - : 95% prediction limits; : 90% prediction limits.

Table 3. – FRC values, measured with the helium dilution technique for preschool children and older infants, in sitting, supine or unspecified position, normalized for a height of 120 cm and 95 cm obtained in different studies

First author	[Ref.]	Height range cm	Ss n	Position	FRC boys mL		FRC girls mL	
					120 cm	95 cm	120 cm	95 cm
Present study		92–126	113	SI	912	568	877	523
COTES	[21]	119–179	254	US	889	-	889	-
COOK	[22]	110–203	171	US	902	-	948	-
DEMUTH	[23]	110–180	294	US	895	-	905	-
ENGSTROM	[24]	110–169	93	SI	813	-	813	-
GAULTIER	[19]	48–93	70	SU*	-	483	-	449
GEUBELLE	[20]	110–170	128	SI	807	-	835	-
GREENOUGH	[8]	92–129	42	SI	775	448	778	415
GREENOUGH	[9]	109–127	53	SI	871	-	871	-
GEURINI	[26]	103–177	116	SI	746	-	-	-
HELLIESEN	[27]	106–184	82	SI	988	-	988	-
PISTELLI	[28]	110–162	78	SI	-	-	886	-
STOCKS	[10]	50–125	191	US	912	502	912	502
SOLYMAR	[29]	120–192	75	SI	870	-	-	-
TAUSSIG	[7]	87–125	51	SI	778	462	725	445
THIEMANN	[30]	110–180	490	US	919	-	884	-
VON DER HARDT	[31]	115–160	134	SI	1039	-	921	-
WENG	[32]	111–182	83	US	833	-	833	-

FRC: functional residual capacity; Ss: subjects; SI: sitting; SU: supine; US: unspecified. *: FRC value corrected for supine position [20].

90th, 95th and 97th percentile were 117.1, 126.7 and 128.1% of the predicted values, respectively; whereas the 3rd, 5th and 10th percentile were 71.8, 73.8 and 83.0%, respectively. As at least 100 subjects per gender group would be required for precise calculation of percentiles, we did not subdivide the percentiles according to gender. For comparison with other studies, a power function and an exponential function of FRC versus height and the standard errors of the estimated values were calculated:

$$\text{FRC (mL)} = -766.2 \text{ (SE 37.8)} + 13.8 \times \text{H (cm)} \text{ (SE 0.4)}$$

$$\text{FRC (L)} = 0.620 \text{ (SE 0.016)} \times \text{H (m)}^{2.03} \text{ (SE 0.020)}$$

$$\text{FRC (mL)} = 99.5 \text{ (SE 19.8)} \times e^{0.018 \text{ H (cm)}} \text{ (SE 0.002)}$$

The linear as well as the power and the exponential function fit well with the present data ($r=0.69$, $r=0.69$ and $r=0.69$, respectively).

Discussion

The aim of the present study was to evaluate the feasibility and reproducibility of routine FRC measurement in preschool children using a mass-produced He dilution device and, if the method appeared to be suitable, to provide reference values for this age group.

The results show that, with the present equipment and provided certain precautions are taken, FRC can be routinely measured in children aged 3–6 yrs. Full co-operation was obtained in 96% of the children, provided the procedure was well explained. If we consider the 45 subjects in whom three attempts were made, the overall success rate, defined as two technically acceptable measurements within 10% of each other in the same child, was 73%. A major problem was leakage at the mouth: this problem was solved in older children by

using the Vacumed mouthpiece, which is flatter and broader. The success rate in the 3 year olds could have been improved if a better fitting mouthpiece had been available. Another problem was irregular breathing pattern, which resulted in a difference of more than 10% between two measurements. GREENOUGH *et al.* [8], who investigated an identical age group, report a comparable success rate of 67%.

We were able to perform 95% of the measurements within 127 s, which makes He absorption during the test negligible [12]. This time lapse is very close to the 2 min proposed by the ERS guidelines [12] and the figure mentioned by GREENOUGH *et al.* [8], but is longer than the 20–60 s reported by TAUSSIG *et al.* [7]. In the latter study, however, He stabilization criteria were based on more than three measurements over 30 s, whereas the ERS standard criteria require He sampling every 15 s over a time interval of 30 s [12, 15].

The mean difference of 40 mL between two consecutive FRC measurements, which we found, is higher than the 20 mL found by TAUSSIG *et al.* [7]. The mean tidal volume was equal during two consecutive measurements as was the respiratory rate. The mean tidal volume of 17.1 mL·kg⁻¹ is higher than the 12.0 and 8.8 mL·kg⁻¹ observed by TAUSSIG *et al.* [7] and by DOERSHUK *et al.* [16], respectively. In the study by DOERSHUK *et al.* [16], the children were sedated, which may reduce the tidal volume [5]. Respiratory frequency was within the expected range and comparable to the value of 26.5 breath·min⁻¹ observed by TAUSSIG *et al.* [7] and ILIFF and LEE [17].

Both the intra- and the intersubject variability in the present study were satisfactory. The intrasubject variability, as estimated by a repeatability coefficient of 95.3 mL, resulted in more than 95% of differences lying within 2 SD of the mean. Because BLAND and ALTMAN [14] pointed out that a coefficient of variation, as used in most previous studies is obsolete, comparison with other

data is impossible. Biological variability for measurements with an interval of 24 h was still acceptable, but with an interval of 1 week the variability was higher.

The linear regression equation of FRC on height shows an identical correlation to the exponential or the power function. Most probably due to the narrow range in height, power function or exponential function had no significant advantage over linear function. The value of 2.03 for the power function is close to the 2.24 found by DOERSHUK *et al.* [16], but remains lower than the theoretically expected figure of 3 that is often found experimentally [15]. The value of 0.018 for the exponential function is close to 0.020, which is most frequently found [15].

Since gender appears to be important, the use of separate regression curves for boys and girls seems appropriate. That no significant influence of gender has been observed by others in the same age group may be due to the smaller number of children studied [7–9]. As can be seen in table 3, the regression values in the present study are comparable to those in adults and children of 120 cm or more. The wide variation in normal values observed in the literature may, besides the technical difference in equipment, be explained by a different definition of normal controls: in some studies, controls are even included that have mild asthma [10, 18]. Ethnic differences also play an important role [9, 10]. A detailed description of the normal controls is therefore mandatory [10, 12, 15].

The present data are comparable to the predicted values in the second study by GREENOUGH and co-workers [9], in which the first regression equations were corrected for ethnic origin, and with those of the study by DOERSHUK *et al.* [16] in children 1 month to 5 yrs of age using the plethysmographic method. Furthermore, our values are very close to the published tentative equation from STOCKS and QUANJER [10] based on individual data of three different laboratories: $FRC_{He} \text{ (mL)} = 0.0031 \cdot H^{2.56} \cdot k$, when k (representing a constant to indicate significant differences between laboratories) has a value of 1.4, as is the case in the second study of GREENOUGH and co-workers [9].

The linear equation in our children has the same slope in function of height as observed by GREENOUGH and co-workers [8] in their first study in 2–7 year olds, and by TAUSSIG *et al.* [7] in 3–6 year olds within the same height range, but the values in the present study are 17% higher. In the first case, this difference is due to the pooling of FRC values of children of different ethnic origin; if the regression equation is corrected solely for Caucasian children, the values are much higher (close to the present results) [9]. In the second case, the discrepancy might be due to the fact that He stabilization in the present study was based on a breath-by-breath analysis, resulting in a much stricter He stabilization, especially in children with a high respiratory frequency. The present FRC values are close to those found in older children and can also be predicted by extrapolation of most regression equations for adults [15]. The present values are higher than those observed by GAULTIER *et al.* [19] in the 0–3 yrs age group (tallest child only 93 cm) even after correction for supine position, which might be due to the early growth spurt, which was not taken into consideration in the study by GAULTIER *et al.* [19] because of the limited number of children measured [20].

In conclusion, using the present mass-produced device, functional residual capacity can be measured routinely in preschool children. Cooperation by the children is very satisfactory. As shown by the intra- and inter-subject variation, reliable measurements are obtained. In contrast to other studies, a sex difference in functional residual capacity measurements was found, as is also the case in older children and adults. Separate curves with normal values for different heights were constructed for boys and girls. These curves matched appropriately with a recent study by GREENOUGH and co-workers [9] and with the tentative equation of STOCKS and QUANJER [10], and agree very well with most values found in older children and adults. Discrepancies with normal values from other studies in preschool children can probably be ascribed to a larger sample size and stricter criteria of health and ethnic origin, as well as technical improvements resulting in stricter criteria for helium stabilization.

Acknowledgements: The authors thank the boards of the kindergartens for their permission to investigate their schools and all the children and parents for their co-operation during this study.

Appendix

The prediction limit is more precise than the overall use of $1.65 \times SD$, because it takes into account the larger errors at the ends of the regression curve [33]. It also compensates for the greater interindividual variability in the youngest subjects. After calculating the prediction limits for all experimental points, a least square fit was performed.

Prediction limit = $1.65 \times S_Y$

$$S_Y = S_{YX} (1/n + 1 + (\bar{x} - x)^2 / \sum (x_i - \bar{x})^2)^{0.5}$$

Confidence limit =

$$Y \pm t_{0.05} (S_{yx}^2 (1/n + (x - \bar{x})^2 / \sum (x_i - \bar{x})^2)^{0.5})$$

(with t following a Student's t distribution with $n-2$ degrees of freedom).

Prediction limits (PL) for boys

$$Pl_{97}: y = -547.384 + 13.789 \times H \text{ (cm)}$$

$$Pl_{95}: y = -585.767 + 13.798 \times H \text{ (cm)}$$

$$Pl_{90}: y = -624.021 + 13.806 \times H \text{ (cm)}$$

$$Pl_3: y = -985.010 + 13.884 \times H \text{ (cm)}$$

$$Pl_5: y = -946.794 + 13.877 \times H \text{ (cm)}$$

$$Pl_{10}: y = -908.450 + 13.868 \times H \text{ (cm)}$$

Prediction limits for girls

$$Pl_{97}: y = -552.058 + 13.831 \times H \text{ (cm)}$$

$$Pl_{95}: y = -589.455 + 13.831 \times H \text{ (cm)}$$

$$Pl_{90}: y = -627.017 + 13.833 \times H \text{ (cm)}$$

$$Pl_3: y = -980.563 + 13.845 \times H \text{ (cm)}$$

$$Pl_5: y = -943.036 + 13.843 \times H \text{ (cm)}$$

$$Pl_{10}: y = -905.582 + 13.842 \times H \text{ (cm)}$$

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