Eur Respir J 1997; 10: 891–895
Printed in UK - all rights reserved

Copyright ©ERS Journals Ltd 1997
European Respiratory Journal
ISSN 0903 - 1936

Respiratory resistance by the forced oscillation technique in asthmatic children and cystic fibrosis patients

P. Lebecque*, D. Stănescu**

Respiratory resistance by the forced oscillation technique in asthmatic children and cystic fibrosis patients. P. Lebecque, D. Stănescu. ©ERS Journals Ltd 1997.

ABSTRACT: Measurement of the total resistance of the respiratory system (R_{rs}) is an attractive alternative to measurement of forced expiratory volume in one second (FEV_1) in young children because it requires minimal co-operation. The purpose of this study was to assess the ability of the forced oscillation technique (FOT) to detect airway obstruction in asthmatic children and in patients with cystic fibrosis (CF).

Spirometry and R_{rs} were recorded in 45 asthmatic children (32 males and 13 females) and in 45 patients with CF (28 males and 17 females). R_{rs} was measured at 10 Hz with the Siregnost FD5 (Siemens, Germany).

The asthmatic children were slightly younger than the patients with CF (10±3 *vs* 14±7 yrs), and had milder airway obstruction (FEV_1 80±19 *vs* 66±27% of predicted). R_{rs} was significantly higher in the asthmatic children (6.6±1.7 $cmH_2O \cdot L^{-1} \cdot s$) than in the patients with CF (4.8±1.4 $cmH_2O \cdot L^{-1} \cdot s$). A normal FEV_1 (≥mean -2SD) was associated with a normal R_{rs} (≤mean +2SD) in 17 of the 45 asthmatic children and in 13 of the 45 CF patients. By contrast, a low FEV_1 (<mean -2SD) was associated with an increased R_{rs} (>mean +2SD) in 21 of the 45 asthmatic children, but in only 3 of the 45 CF patients. Thus, FEV_1 and R_{rs} yielded concordant information in asthmatic children much more often (38 out of 45) than in CF patients (16 out of 45) ($p<0.001$). In CF, R_{rs} failed to detect even severe airways obstruction. These findings might be accounted for by the inability of R_{rs} to reflect peripheral obstruction.

We conclude that total respiratory resistance is suitable to assess airways obstruction in asthmatic children but not in cystic fibrosis patients.

Eur Respir J 1997; 10: 891–895.

*Pediatric Pulmonology Division, and Pulmonary Laboratory, **Pulmonary Division, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

Correspondence: D. Stănescu
Cliniques Universitaires Saint-Luc
Avenue Hippocrate 10
1200 Bruxelles
Belgium

Keywords: Airway obstruction
bronchial asthma
cystic fibrosis
forced expiratory volume in one second
forced oscillations
respiratory resistance

Received: January 23 1996
Accepted after revision November 29 1996

Presented in part at the European Respiratory Society Meeting, Barcelona, 1995.

Measurement of forced expiratory volume in one second (FEV_1) is considered to be the basic test for the assessment of airway obstruction. However, it requires comprehension and co-operation from the subject. Usually, it cannot be performed by young children, less than 6 yrs of age. Measurement of total resistance of the respiratory system (R_{rs}) with the forced oscillation technique (FOT) is a particularly attractive tool, especially in young children, since it requires minimal co-operation [1].

In two previously published studies, R_{rs} has been found to have a large interindividual variability and wider normal limits than FEV_1 [2, 3]. More recently, predicted values with a much lower dispersion [4] have been described using a simple system, which provides a continuous display of R_{rs} and allows immediate detection of artefacts, such as swallowing or leaks at the mouth. This suggests that the clinical value of this technique could be substantially improved.

In the present study, we therefore aimed to assess the ability of the R_{rs}, using a simple technique, to detect airway obstruction in patients with cystic fibrosis (CF) and bronchial asthma, the most frequent chronic pulmonary diseases of childhood.

Materials and methods

Forty five asthmatic children (32 males and 13 females) and 45 CF patients (28 males and 17 females), without associated bronchial asthma or allergic bronchopulmonary aspergillosis, were studied.

R_{rs} was measured with the FOT at 10 Hz, using the Siregnost FD5 (Siemens, Erlangen, Germany). Details of the procedure have been reported previously [5]. Briefly, respiratory resistance can be computed from measurements both of impedance and phase angle, referred to as R_{ez}, or a simplified approach measuring impedance and an approximation of phase angle, called R_{os}. Both indices were computed in this study.

The child was seated, breathing quietly, with the cheeks and chin supported. Resistance was measured over the entire respiratory cycle, and the R_{rs} reported is the mean of three consecutive R_{rs} values, each recorded over 2.5 s. R_{rs} was always recorded before forced expiration to preclude any effect of the latter manoeuvre on resistance measurements. Forced vital capacity (FVC) and FEV_1 were determined with an automated 8 L water-sealed spirometer (Eagle 1; W.E. Collins, Boston, MA, USA) [6], using standard techniques [7]. Predicted values for

R_{rs} and spirographic indices were obtained in our laboratory, using the same technique and apparatus as in the present study [4]. In 10 CF patients more than 18 yrs of age, reference values for spirometry were from DICKMAN *et al*. [8]. Both R_{rs} and FEV_1 were expressed as absolute values and as SD scores, *e.g.* multiples of the standard deviation away from the mean. R_{rs} and FEV_1 were considered within normal limits when both values were within mean±2SD, and outside normal limits when these limits were exceeded.

In 20 of the 45 asthmatic children, with reversible airways obstruction (FEV_1 increase of ≥20%), R_{rs} and FEV_1 were also measured before and 20 min after inhaled salbutamol (two puffs of 100 µg each). To assess the reversibility of airflow obstruction, we considered, like most authors, that a 20% improvement in FEV_1 is beyond the variability of this index, and reflects a significant change. For R_{rs}, we considered as significant those changes exceeding twice the average intraindividual coefficient of variability (CV) of these 20 asthmatic children.

A Fisher's exact test was used to compare the concordance of the R_{rs} and FEV_1 in asthmatic and CF patients. Physical data and FEV_1 and R_{rs} values were compared with the Mann-Whitney test. A paired t-test assessed changes in FEV_1 and R_{rs} after bronchodilation. A p-value of less than 0.05 was considered significant.

Results

Physical data and average values of FEV_1 and R_{rs} are presented in table 1. Height, which is the single most important determinant both of R_{rs} and FEV_1, was comparable in the two groups, but asthmatic children were slightly younger than CF patients ($p<0.05$). If we discard 10 patients with CF older than 18 yrs, then age in the two groups (asthmatics: n=45, age 10±3 yrs; CF patients: n=35, age 11±4 yrs; p:>0.05) as well as height (asthmatics: 139±15 cm; CF patients: 137±19 cm) become comparable.

R_{os} was 4.8±1.4 $cmH_2O{\cdot}L^{-1}{\cdot}s$ and R_{ez} 4.9±1.9 $cmH_2O{\cdot}L^{-1}{\cdot}s$ ($r=0.97$; $p<0.001$) in CF patients. Corresponding values in children with bronchial asthma were 6.6±1.7 and 7.0±2.2 $cmH_2O{\cdot}L^{-1}{\cdot}s$ ($r=0.91$; $p<0.001$). Since comparable results were obtained for R_{os} and R_{ez}, only the results of the former index were presented, and referred to as R_{rs}.

Table 1. – Physical data, FEV_1 and R_{rs} values in asthmatic and cystic fibrosis patients

	Bronchial asthma (n=45)	Cystic fibrosis (n=45)
Age yrs	10±3	14±7*
Height cm	139±15	144±22
FEV_1 L	1.69±0.67	1.46±0.62
% pred	80±19	66±27**
R_{rs} $cmH_2O{\cdot}L^{-1}{\cdot}s$	6.6±1.7	4.8±1.4
% pred	131±32	101±18***

Values are presented as mean±SD. FEV_1: forced expiratory volume in one second; R_{rs}: total resistance of the respiratory system. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$, compared to asthmatic children.

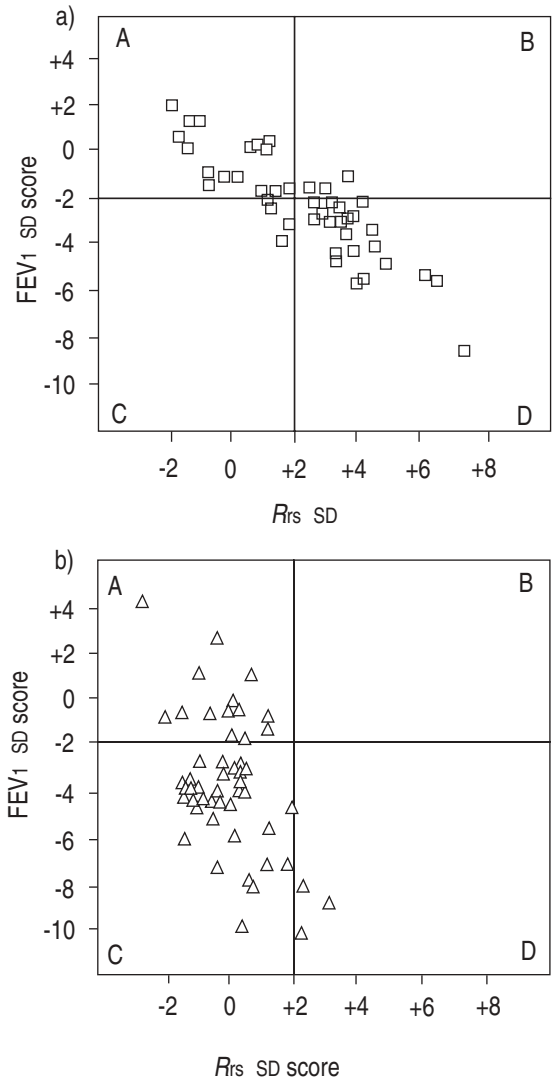

Fig. 1. – Relationship between forced expiratory volume in one second (FEV_1) and total resistance of the respiratory system (R_{rs}) in patients with: a) bronchial asthma; and b) cystic fibrosis. Values of both indices were expressed as SD scores (see Materials and methods). They were considered to provide concordant information (quadrants A and D) when both FEV_1 and R_{rs} were either within (R_{rs} ≤mean +2SD and FEV_1 ≥mean -2SD) or outside normal limits (R_{rs} >mean +2SD and FEV_1 <mean -2SD). When FEV_1 and R_{rs} provided discordant information their values were located in quadrants B and C.

R_{rs} was significantly higher ($p<0.001$) in the children with bronchial asthma (6.6±1.7 $cmH_2O{\cdot}L^{-1}{\cdot}s$) than in the patients with CF (4.8±1.4 $cmH_2O{\cdot}L^{-1}{\cdot}s$). The latter had a lower FEV_1 (66±27 *vs* 80±19% predicted, respectively; $p<0.01$).

Both FEV_1 and R_{rs} were within normal limits in 17 of the 45 asthmatic children and in 13 of the 45 CF patients. A low FEV_1 was associated with an increased R_{rs}, in 21 of the 45 asthmatic children, but in only 3 of the 45 CF patients (fig. 1). Thus, FEV_1 and R_{rs} yielded concordant information (fig. 1, quadrants A and D) much more often in asthmatic children (38 out of 45) than in CF patients (16 out of 45), and this difference was highly significant ($p<0.001$). If the 10 CF patients more than 18 yrs of age are omitted, a similar conclusion is reached. Concordant information was observed in 38 of the 45 asthmatic children but in only 14 of the

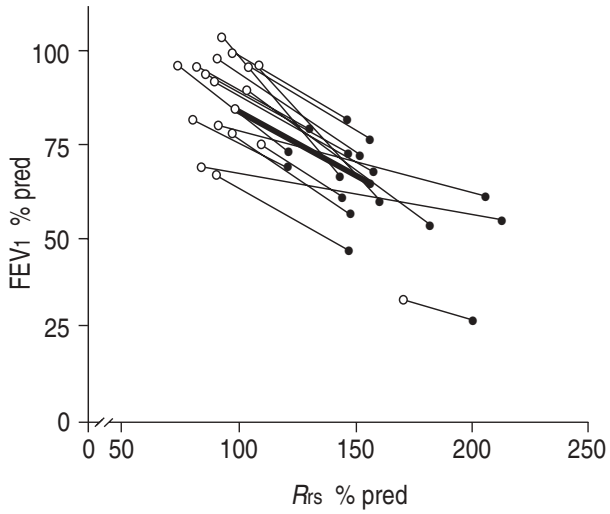

Fig. 2. – Individual and average (thick line) relationship between forced expiratory volume in one second (FEV1) and total resistance of the respiratory system (R_{rs}) (expressed as percentage of predicted) in 20 asthmatic children before (•) and after (○) bronchodilation.

35 CF patients ($p<0.001$). In CF patients, R_{rs} failed to detect even severe airway obstruction, as assessed by FEV1.

Inhalation of salbutamol by 20 asthmatic children (15 males and 5 females; (mean±SD) age 10±3 yrs; height 138±13 cm) increased FEV1 from 65 to 85% pred ($p<0.001$) and decreased R_{rs} from 155 to 99% pred ($p<0.001$) (fig. 2). The average intraindividual CV of R_{rs} for the group of asthmatic children as a whole was 6.9%. Significant changes in R_{rs}, *i.e.* two times the CV, were recorded in each patient after bronchodilatation. In fact, in all but one child, these changes exceeded five times the intraindividual CV.

Discussion

In the present study, it was found that in bronchial asthma measurement of FEV1 and R_{rs} provided concordant information, *i.e.* either of these tests could be used to demonstrate the functional abnormality. However, in CF R_{rs} values failed to identify most of the patients with an abnormal FEV1.

In order to define the comparative merits of two or more tests, the appropriateness of the reference values is of utmost importance. Since some of the CF patients studied were older than the children from whom we derived reference values [4], their FEV1 values were compared with those of DICKMAN *et al.* [8] for adults. The reason for this choice is that at 18 yrs of age our reference values in children [4] and the reference values of DICKMAN *et al.* [8] are very similar. However, the latter values are somewhat higher than those of CRAPO *et al.* [9] used in the USA [10], or QUANJER *et al.* [11] in Europe. When using these latter two equations, there was, however, little change in the SD scores of the present patients. In CF patients more than 18 yrs of age, our own reference values for R_{rs} [4] were used. With the same apparatus as used in the present study, GIMENO *et al.* [12] found that in adults R_{rs} is related only to height and does not change with age.

When compared to more sophisticated systems providing access to additional parameters of respiratory mechanics, the simple technique used in the present study has a practical advantage probably derived from the lower dispersion of normal values: most asthmatic children with a low FEV1 also had an increased R_{rs} (fig. 1a). This is in contrast to results of KÖNIG *et al.* [13], who found that only 2 out of 13 R_{rs} values fell outside the normal range in asthmatic children with an abnormal FEV1. COGSWELL [14] reported that asthmatic children "may have values of R_{rs} several times greater than the expected mean". However, almost half of these values were within their normal limits in a group of asthmatic children, most of whom had grossly abnormal spirometry [13]. More recently, in agreement with our data, BUHR *et al.* [15] found, in children (5–8 yrs of age) with asthma, that the diagnostic values of forced oscillations, spirometry and plethysmography (for measuring airway resistance) were similar.

In bronchial asthma, it is considered that there is an involvement both of large and small airways [16]. Our results are in keeping with this view; both FEV1 and R_{rs} provided concordant information (fig. 1). Furthermore, inhalation of a sympathicomimetic bronchodilator induced a change both in FEV1 and R_{rs} (fig. 3), suggesting a decrease in the obstruction both of large and small airways. The decrease of R_{rs} was larger than that of FEV1 emphasizing the sensitivity of this index to changes in the large airways. Following salbutamol, all children decreased their R_{rs} beyond the average intraindividual CV, suggesting that R_{rs} may be used to assess reversibility of airway obstruction not only in a group of patients [17–20], but also in a given individual [13].

Due to the diversity of techniques of measurement and sometimes to a lack of detailed spirometric data, results on R_{rs} measurements in CF are rather difficult to compare. Among 44 children with CF, 24 of whom were too young to perform spirometry, COGSWELL [14] observed an increase in R_{rs} (measured at 5 Hz) in only five patients. In 46 children, LANDAU and PHELAN [21] concluded that the FOT (at 4 Hz) was without significant relationship to the clinical score and was poorly correlated with other functional tests. In 13 patients with abnormal FEV1 and/or maximal flow at 50% forced vital capacity ($V'_{max,50}$), SOLYMAR *et al.* [22] found a low discriminatory power of R_{rs} (measured at 2, 4 and 12 Hz). In a recent abstract, HELLINCKS *et al.* [23] reported that with the FOT (between 4 and 24 Hz) both R_{rs} and airways resistance (R_{aw}) were within normal limits in 20 children (mean age 12 yrs) with a moderate decrease in FEV1. In keeping with the present data, previous studies suggest that R_{rs} is of limited value in this disease.

The discrepancy between R_{rs} and FEV1 in CF is not actually surprising. Indeed, peripheral airway obstruction is an early and prominent feature of this disease [24–26]. Therefore, R_{rs}, reflecting essentially the calibre of large airways, would not be affected by a distal, peripheral airway obstruction. The latter would instead be reflected by a decrease in FEV1.

Some authors [27, 28] using a forcing function containing multiple frequencies have claimed, from the behaviour of the frequency dependence of resistance, the possibility of partitioning resistance into a central and peripheral component. These attempts, as emphasized by PESLIN

et al. [29] are based on a model proposed by MEAD [30]. However, if the model proposed by MEAD [30] is not an accurate reflection of the behaviour of the lung, partitioning of resistance into its two components is not warranted. Furthermore, upper airway wall motion is responsible for large errors in the estimation of frequency dependence of resistance, especially so in patients, and PESLIN *et al*. [29] have suggested the use of a head plethysmograph to correct for these errors. The method, thus, becomes cumbersome and expensive. On the basis of electrical models of the lung, it might be predicted that peripheral obstruction would be poorly explored by the use of a single and relatively high frequency (10 Hz). R_{rs} measurements at lower frequencies (2 Hz) could prove to be more sensitive but are often inaccurate in children, as harmonics of a high respiratory rate will interfere with the R_{rs} measurements.

An increase in upper airway compliance in CF was proposed by some authors [31–33]. If this was the case, it would magnify the frequency dependence of R_{rs}. However, in a recent investigation, we found no difference in upper airway distensibility between patients with CF and healthy controls [34].

From the practical point of view, our results and data from other recent studies suggest that, in asthmatic children, either total respiratory resistance or forced expiratory volume in one second can assess airway obstruction and its reversibility. However, this is not true in cystic fibrosis. Indeed, in this latter disease forced expiratory volume in one second, but not total resistance of the respiratory system, should be used to demonstrate airway obstruction.

Acknowledgements: The authors thank K.P. Van de Woestijne for critical reading of the manuscript and Cl. Veriter for technical assistance.

References

1. Stanescu D, Moavero NE, Veriter Cl, Brasseur L. Frequency dependence of respiratory resistance in healthy children. *J Appl Physiol: Respirat Environ Exercise Physiol* 1979; 47: 268–272.
2. Duiverman EJ, Clement J, Van de Woestijne KP, Neijens J, van den Bergh AC, Kerrebijn KF. Forced oscillation technique: reference values for resistance and reactance over a frequency spectrum of 2–26 Hz in healthy children aged 2.3–12.5 years. *Bull Eur Physiopathol Respir* 1985; 21: 171–178.
3. Hordvik NL, Konig P, Morris DA, Kreutz C, Pimmel RL. Normal values for forced oscillatory respiratory resistance in children. *Pediatr Pulmonol* 1985; 1: 145–148.
4. Lebecque P, Desmond K, Swartebroeckx Y, Dubois P, Lulling J, Coates A. Measurement of respiratory system resistance by forced oscillation in normal children: a comparison with spirometric values. *Pediatr Pulmonol* 1991; 10: 117–122.
5. Franetzki M, Prestele K, Korn V. A direct-display oscillation method for measurement of respiratory impedance. *J Appl Physiol: Respirat Environ Exercise Physiol* 1979; 46: 956–965.
6. Black KH, Petusevsky ML, Gaensler EA. A general purpose microprocessor for spirometry. *Chest* 1980; 78: 605–612.
7. American Thoracic Society. Standardization of spirometry: 1994 update. *Am J Respir Crit Care Med* 1995; 152: 1107–1136.
8. Dickman ML, Schmidt CD, Gardner RM, Marshall HW, Day CW, Warner HR. On-line computerized spirometry in 738 normal adults. *Am Rev Respir Dis* 1969; 100: 780–790.
9. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. *Am Rev Respir Dis* 1981; 123: 659–664.
10. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. *Am Rev Respir Dis* 1991; 144: 1202–1218.
11. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Official statement of the European Respiratory Society. *Eur Respir J* 1993; 6 (Suppl. 16): 5–40.
12. Gimeno F, van der Weele LT, Koeter GH, de Monchy JG, van Altena R. Variability of forced oscillation (Siemens Siregnost FD 5) measurements of total respiratory resistance in patients and healthy subjects. *Ann Allergy* 1993; 71: 56–60.
13. König P, Hordvik NL, Pimmel RL. Forced random noise resistance determination in childhood asthma. *Chest* 1984; 86: 884–890.
14. Cogswell JJ. Forced oscillation technique for determination of resistance to breathing in children. *Arch Dis Child* 1973; 48: 259–266.
15. Buhr W, Jorres R, Berdel D, Landser FJ. Correspondence between forced oscillation and body plethysmography during bronchoprovocation with carbachol in children. *Pediatr Pulmonol* 1990; 8: 280–288.
16. Pride NB, Macklem PT. Lung mechanics in disease. *In*: Fishman AP, section editor. Handbook of Physiology. The respiratory system. Volume III. Mechanics of breathing. Part 2. Bethesda, Maryland, American Physiological Society, 1988; pp. 659–692.
17. Menon P, Hilman BC, Menon V, Bairnsfather L. Assessment of response to oral metaproterenol sulfate by forced oscillation in young children. *Ann Allergy* 1988; 60: 547–551.
18. Berdel D, Kellersman U. The bronchodilator effect of a fixed-combination metered aerosol (fenoterol and ipratropium bromide). *Pediatr Pulmonol* 1985; 1: 297–302.
19. Nussbaum E, Eyzaguirre M, Galant SP. Dose-response relationship of inhaled metaproterenol sulfate in preschool children with mild asthma. *Pediatrics* 1990; 85: 1072–1075.
20. König P, Gayer D, Kantak A, Dreutz C, Douglass B, Hordvik NL. A trial of metaproterenol by metered-dose inhaler and two spacers in preschool asthmatics. *Pediatr Pulmonol* 1988; 5: 247–251.
21. Landau LI, Phelan PD. The spectrum of cystic fibrosis: a study of pulmonary mechanics in 46 patients. *Am Rev Respir Dis* 1973; 108: 593–602.
22. Solymar L, Aronsson PH, Sixt R. The forced oscillation technique in children with respiratory disease. *Pediatr Pulmonol* 1985; 1: 256–261.
23. Hellincks J, De Boeck K, Demedts M. Comparison of forced oscillation technique and standard pulmonary functional tests in patients with cystic fibrosis. (Abstract) *Eur Resp J* 1995; 8 (Suppl. 19): 575.
24. Lamarre A, Reilly BJ, Bryan C, Levison H. Early detection of pulmonary function abnormalities in cystic fibrosis. *Pediatrics* 1972; 50: 291–298.
25. Esterly JR, Oppenheimer EH. Cystic fibrosis of the

pancreas: structural changes in peripheral airways. *Thorax* 1968; 23: 670–675.
26. Mellins RB. The site of airway obstruction in cystic fibrosis. *Pediatrics* 1969; 44: 315–318.
27. Pimmel RL, Tsai MJ, Winter DC, Bromberg PA. Estimating central and peripheral respiratory resistance. *J Appl Physiol: Respirat Environ Exercise Physiol* 1978; 45: 375–380.
28. Slutsky AS, Drazen JM. Estimating central and peripheral respiratory resistance: an alternative analysis. *J Appl Physiol: Respirat Environ Physiol* 1979; 47: 1325–1331.
29. Peslin R, Duvivier C, Gallina C, Cervantes P. Upper airway artifact in respiratory impedance measurements. *Am Rev Respir Dis* 1984; 132: 712–714.
30. Mead J. Contribution of compliance of airways to frequency-dependent behavior of lungs. *J Appl Physiol* 1969; 26: 670–673.
31. Brooks LJ. Tracheal size and distensibility in patients with cystic fibrosis. *Am Rev Respir Dis* 1990; 141: 513–516.
32. Zach MS, Oberwaldner B, Forche G, Polgar G. Bronchodilators increase airway instability in cystic fibrosis. *Am Rev Respir Dis* 1985; 131: 537–543.
33. Griscom NT, Vawter GF, Stigol LC. Radiologic and pathologic abnormalities of the trachea in older patients with cystic fibrosis. *Am J Roentgenol* 1987; 148: 691–693.
34. Lebecque P, Liistro G, Veriter C, Stanescu D. Tracheal distensibility in cystic fibrosis. *Eur Resp J* 1996; 9: 770–772.