Interrupter Resistance in Preschool Children

Measurement Characteristics and Reference Values

PETER J. F. M. MERKUS, JACQUELINE Y. MIJNSBERGEN, WIM C. J. HOP, and JOHAN C. de JONGSTE

Department of Paediatrics, Subdivision of Respiratory Medicine, Sophia Children's Hospital, and Department of Epidemiology and Biostatistics, Erasmus University and University Hospital, Rotterdam, The Netherlands

There is a need for quick, reliable, and noninvasive lung function tests to assess airway obstruction in preschool children both for pediatric pulmonary care as well as for research purposes. We studied feasibility, reproducibility, and validity of measurements of the respiratory system using the interrupter technique (interrupter resistance [Rint]) and obtained reference values in children from a general population, 2 to 7 yr of age. Accuracy was studied by comparisons of Rint with plethysmographic airway resistance (Raw) in 20 patients (7 to 14 yr) with mild to severe chronic airways obstruction and was satisfactory in patients with $FEV_1 > 60\%$ predicted. The technique proved sensitive enough to detect changes in airway caliber within a small group of 12 children who developed mild respiratory tract infections. Among children from a general population, subgroups with mild respiratory symptoms or mild respiratory disease had higher mean Rint values. Airway obstruction was better detected using expiratory rather than inspiratory interruptions, both programmed at peak tidal ventilatory flow. Reproducibility within subjects was satisfactory (intraclass correlation 0.82 and 0.79). The same applied to interobserver agreement (intraclass correlation 0.98). The interrupter technique proves to be a reliable and practical test of airway function, suitable for clinical and epidemiologic studies in preschool children.

Reliable lung function testing in preschool children is difficult because little cooperation and coordination can be expected at this age. Spirometric reference values for children have been obtained in children as young as 5 yr of age (1, 2) but reliable measurements are often not feasible. Several passive techniques have been developed (3–5), but have their limitations with respect to reliability, sensitivity, or interpretation (6). In the group between 2 and 7 yr there is a need for lung function techniques that require minimal cooperation and yet are reliable and sensitive enough to be valuable as a diagnostic tool (7, 8). The interrupter technique (9) requires only quiet breathing and is based on measurements of tidal airflow and mouth pressure before and directly after closure of a fast shutter near a pneumotachograph. The ratio between pressure difference and airflow equals the interrupter resistance (Rint). Thus, Rint reflects the resistance of the respiratory system. Only after equilibration of pressure within the airways, when mouth pressure equals alveolar pressure, Rint reflects airway resistance (Raw). Validation studies against Raw measured plethysmographically came up with satisfactory results (10–12). However, the within-subject variability may be higher than that of other techniques (6, 10, 13, 14), which has been attributed to factors such as the natural variability of inflation level and flow during quiet breathing, upper airway compliance, and position of the neck, glottis, and vocal cords (7, 13, 15). Large variability, and the lack of standardization and reference values (16) explain why the technique has not been widely used in clinical or epidemiologic lung function studies in the past. During the last decade, however, reference values have been published (17), modern applications of the technique have been evaluated (6, 10), and it has been demonstrated that within-subject variability of Rint measurements is sufficiently small to study the response to bronchoconstricting (6, 8, 10) and bronchodilating agents (6–8, 14) in young children. Together with the quick and noninvasive nature of the method, these data suggest that the technique is a potential diagnostic tool in pediatric pulmonology (6–8, 10, 11, 13, 14, 16, 18). More widespread acceptance and application of Rint measurements can only be expected when it is demonstrated that this technique is feasible, that its within-subject variability can be reduced further, and that the method can be used to identify groups of preschool children with minor respiratory symptoms or disease.

The aim of the present study was to investigate the feasibility and measurements characteristics of the interrupter method in preschool children. We explored ways to improve its precision, assessed within-subject and within-observer variability, characterized normal Rint values in healthy children, and investigated the biologic validity of the technique using a portable device.

METHODS

Subjects

Feasibility of the technique, reference values, and short-term reproducibility were investigated in children 2 to 4 yr of age from a daycare center and in children 4 to 7 yr of age from a kindergarten. Both institutions were located in suburban parts of the Rotterdam area, inhabited by middle-class income Dutch families. In this group we studied: (*1*) children with mild respiratory symptoms or mild respiratory disease to assess the sensitivity of the technique; (*2*) children without a history of any cardiorespiratory disease (such as prematurity with respiratory distress) and without current respiratory symptoms, to obtain reference values. We intended to obtain reference values from a normal population rather than from an ideal population (19). Therefore, respiratory infections in the past was not an exclusion criterion for this subgroup. Furthermore, children exposed to parental smoking but with a negative history of respiratory symptoms or disease were not analyzed separately but included in the normal population, unless it would appear that their mean Rint values would be significantly different from that of the reference group. Exclusion criteria were: anatomic abnormalities of the upper or lower airways, vocal cord disorders, chronic cardiopulmonary or other illnesses. In children attending the outpatient clinic of the Sophia Children's Hospital because of asthma or cystic fibrosis, we investigated within-observer reproducibility of the technique and its validity by comparisons with Raw measured plethysmographically. The study was approved by the medical ethics committee of Erasmus University and University Hospital, and by the principals of the institutions involved. Written informed consent was given by the parents of the participating children. Measurements were carried out on a strictly voluntary basis.

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Correspondence and requests for reprints should be addressed to Peter J. F. M. Merkus, M.D., Ph.D., Department of Paediatrics, Subdivision of Respiratory Medicine, Sophia Children's Hospital, Erasmus University and University Hospital, Dr Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands. E-mail: merkus@alkg.azr.nl

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Equipment Specifications

Measurements were carried out using the MicroRint (Micro Medical Ltd, Rochester, UK), a portable device including a shutter and pneumotachograph, connected to a palmtop computer with an online display showing mouth pressure, time of shutter closure, Rint values, and the median value of all Rint data recorded during one session. Its software calculates Rint using the back extrapolation technique to t = 15 ms after shutter closure during 100 ms (6). A maximum of 10 tracings can be gathered for each measurement. Daily calibrations of pressure and flow (volume) were carried out using a manometer and a 2-L precision pump. All measurements were carried out with a filter (Micro Medical Ltd) in place for reasons of hygiene, and to prevent dysfunction of the pneumotachograph due to any saliva, as recommended (20). The mean (± SEM) filter resistance was assessed in 10 healthy members of the laboratory personnel and estimated at 0.03 (± 0.007) kPa/L/s. This equals the value incorporated in the software of the device.

Procedures

Reference values, learning effect, and short-term reproducibility of the measurement were assessed in children from the daycare center and kindergarten. Information on respiratory symptoms, eczema, allergy, parental smoking, doctor's diagnosis of asthma, and asthma medication was obtained using a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (21). These children were then classified according to their respiratory history. Before the measurement sessions the teacher of each group of children explained the purpose of the measurements. The technique was then demonstrated on the teacher.

Validity of the technique and interobserver variance were studied in schoolchildren with asthma or cystic fibrosis attending the outpatient clinic of Sophia Children's Hospital who were not familiar with the technique. The method was briefly explained to them and demonstrated once by the observer before the measurement. The validity of the technique was compared with Raw measurements using the whole-body plethysmograph as the gold standard for Raw. Interrater reliability was studied in two observers who investigated 20 outpatients in a random order with an interval between 1 and 3 h.

Biologic validity in preschool children was assessed prospectively within children from the general population who were asymptomatic first, and developed mild respiratory symptoms 2 wk later. These symptoms consisted of a productive cough with or without rhinitis; wheezing, dyspnea, or fever were not observed. Biologic validity was also assessed from comparisons between subgroups of children with and without respiratory disease or symptoms.

Measurement Protocol

Measurements were carried out in a familiar and quiet room. Standing height and weight were assessed in triplicate and averaged: subjects were measured without shoes, wearing light summer clothing. They were seated and watched a peaceful child's video for 10 min; no physical exercise was allowed during that period. During measurements, children were instructed to sit upright, while breathing quietly. The position of the Micro Rint was adjusted on a support arm to facilitate unobstructed breathing. The functioning of the shutter was demonstrated once to make children familiar with the sound. A minimal number of 5 correct tracings (maximal 10) was then obtained for both the inspiratory [Rint(i)] and expiratory [Rint(e)] maneuver. During this period the cheeks and chin were supported from behind by the observer, the head was positioned in slight extension, and a nose clip was used. Shutter closure was programmed at maximal inspiratory or expiratory tidal flow. Thus, Rint values are obtained at or near midinspiration or midexpiration, minimizing the breath-to-breath variation in inflation level and hence on Raw (15). Timing of the shutter closure (at the peak of flow) can be checked on the display. Tracings were inspected immediately after the measurement in the presence of the child. Rejection criteria were: tachypnea, usage of the vocal cords, extreme neck flexion or extension, leakage of the mouthpiece. Tracings not showing the timing of the shutter closure were discarded; tracings with a horizontal or declining pressure signal after shutter closure were considered artifacts owing to air leakage or altered ventilation pattern and were discarded as well (7). We attempted to obtain 10 reliable tracings on each measurement session.

Feasibility

When children refused to cooperate before the measurement, the attempt was classified as a refusal; when they began the measurement but stopped halfway, or if too few (< 5) reliable tracings were obtained, an attempt was classified as a failure. A measurement session was discontinued after 20 min or 10 attempts, whichever came first. The feasibility of the technique was rated on the basis of the proportion of failures and refusals relative to the total number of attempts. The success rate was defined as the percentage of approved tracings relative to the number of occlusions.

Data Analysis

Rint(i) and Rint(e) were expressed as median or mean values, depending on the individual data distribution of up to 10 measurements. The coefficient of variation was used to compare reproducibility with conventional lung function measurements. The minimal number of individual measurements needed to obtain a reliable estimate of Rint was assessed based on the improvement of the standard error of the estimate relative to the mean (SEM/mean) with increasing number of attempts. Reference values were described using linear regression, including standard independent variables such as standing height, weight, and age. When no effects of passive parental smoking or sex could be demonstrated, these subgroups were not analyzed separately. Z-scores [(measured Rint − predicted Rint)/(RSD of the reference population)] were computed for each individual, to compare children or groups of children.

Biologic variability was studied in a group of 22 stable schoolchildren who were measured twice 10 to 21 d apart, while there was no change of respiratory symptoms. Within-observer variability was studied on Rint(e) in 20 outpatients by two investigators. Reproducibilities were studied according to Bland and Altman (22), and expressed as intraclass correlation (23) The existence of a learning effect was investigated in the reference population in whom Rint(e) and Rint(i) were studied in random order, using unpaired *t* tests of the Rint(e)−Rint(i) differences, according to measurement order. Validity of Rint measurements using plethysmographic Raw as the gold standard was studied in 20 young patients with asthma or cystic fibrosis according to Bland and Altman as well (22) The biologic validity of the technique in the preschool children was studied in two ways: First, in a group of 12 children who were asymptomatic during the first measurement and developed respiratory symptoms 10 to 21 d later, mean differences were analyzed using paired *t* tests. Second, we studied Z-scores for various subgroups classified according to respiratory symptoms or disease, and compared them with the reference population (unpaired *t* tests).

RESULTS

Participants

Invitations to participate, including questionnaires, were sent to the parents of 298 children of the kindergarten and daycare center. Informed consent and answered questionnaires were returned for 169 (57%) children. Measurements were refused by 21 children, and failed in eight (Figure 1). Rint measurements were conducted in 139 (46%) children. In 128 of 139 children, disposable 22-mm-diameter cardbox mouthpieces were used. In 11 toddlers younger than 2 yr of age, a Laerdal face mask size 2 was used, whereas in three infants younger than 6 mo of age a Laerdal size 0 mask was used.

Feasibility

The feasibility of Rint(e) measurements was 12% in children 0 to 1 yr of age, 55% at age 1 to 2 yr, and 100% in children older than 6 yr of age. Feasibilities of the inspiratory maneuver were similar, being only slightly better in the youngest children (Figure 1). In 88% of children older than 2 yr of age feasible Rint measurements were obtained. The mean number of interruptions for Rint(e) varied from 9.2 for the 2- to 3-yr-olds to 9.8 for the 6- to 7-yr-olds; for Rint(i) these numbers were similar (9.7 to 9.9, respectively). Mean (± SD) success rates (percentage of acceptable tracings) in children with 9 to 10 in-

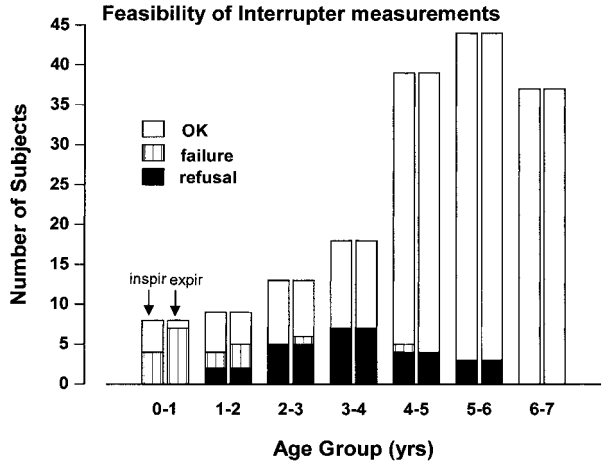

Figure 1. Bar diagram showing feasibility of the interrupter technique in different age groups, for inspiratory (*left columns*) and expiratory (*right columns*) Rint measurements. Failure and refusals as defined in METHODS.

terruptions were 73 ± 17% and 74 ± 17% for Rint(e) and Rint(i), respectively, and not related to age or respiratory symptoms. Two 4-yr-olds with mental retardation (developmental age approximately 2 yr) successfully completed the measurements. The whole procedure of measuring height, weight, Rint(i), and Rint(e) in a child took between 20 min in some of the 2-yr-olds, and 7 min in children age 6 yr.

Measurement Characteristics

The mean (95% CI) difference between individual mean and median values of Rint(e) was 0.007 (0.002, 0.012) kPa/L/s. Rint(i) measurements showed a similar trend ($p = 0.16$). Because of this skewed distribution for individual measurements, all further analyses were based on the median value of up to 10 individual measurements.

The mean (± SD) coefficients of variation for Rint(e) and Rint(i) were 11.6 ± 5.6% and 10.6 ± 5.4%, respectively. Average individual SEM relative to the mean (SEM/mean) for 5 and 10 Rint(e) measurements were 5.1% and 3.7%, respectively; for Rint(i) these values were 4.7% and 3.5%. This implies that for 95% of subjects the precision of the single measurement (based on 10 interruptions) of Rint(e) or Rint(i) is better than 7.4% or 7.0%, respectively.

Reference Values

Reference equations were based on children 2 yr of age and older because below that age, measurements could only be conducted using a face mask with unknown (compliance) characteristics, unlikely to be comparable with a cardboard mouthpiece. Reference values were obtained from those children with a negative history of asthma, recurrent rhinitis, or eczema, without cardiorespiratory or other chronic disease, and with no respiratory symptoms in the past month. Significant differences of Rint values owing to sex or parental smoking could not be demonstrated in asymptomatic nor in symptomatic children ($p > 0.37$). Therefore, 54 children of either sex, and with different passive smoking history were pooled in the reference equations. The number of children age 2–3, 3–4, 4–5, 5–6, and 6–7 yr of age were 3, 5, 12, 18, and 16, respectively. The best predictor for Rint was standing height in a linear model. The addition of other variables (age, weight, or sex) did not contribute significantly to the model ($p > 0.07$). Least squares regression equations related to height (expressed in cm) were:

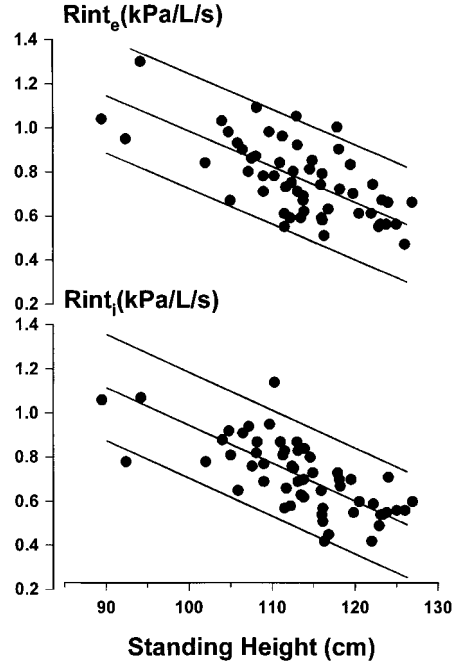

Figure 2. Individual Rint data points of healthy children 2 to 7 yr of age, with regression line and reference interval according to standing height. *Upper panel*: Rint(e); *lower panel*: Rint(i).

$$\text{Rint(e) (kPa/L/s)} = 2.61 - 0.016 \cdot \text{height (RSD: 0.13)}$$
$$r = -0.64 \ (p < 0.001)$$
$$\text{Rint(i) (kPa/L/s)} = 2.59 - 0.017 \cdot \text{height (RSD: 0.12)}$$
$$r = -0.69 \ (p < 0.001)$$

Reference curves are shown in Figure 2. Rint(e) was systematically higher than Rint(i) in all children and the difference between the two did not correlate with sex or age: mean (95% CI) difference was 0.051 (0.17, 0.85) kPa/L/s. No learning effect could be demonstrated ($p = 0.17$).

Biologic Validity

In 12 healthy children who developed mild respiratory tract infections 10 to 21 d after their first measurement, Rint was increased the second time. Mean (95% CI) difference between two consecutive measurements for Rint(e) was 0.08 (0.03, 0.13) kPa/Ls, $p = 0.002$ (Figure 3). For Rint(i) this difference was 0.04 (0.002, 0.07) kPa/L/s), $p = 0.04$.

The 128 children were classified according to their history of respiratory symptoms or disease (Table 1). Mean Z-scores of Rint values of subgroups of children are listed in Table 2. Asymptomatic children with asthma or eczema or both ($n = 32$) had significantly elevated Z-scores for Rint(e) ($p < 0.02$) as well as for Rint (i) ($p = 0.005$). In 20 children with asthma or eczema or both, with current respiratory symptoms, Rint(e) Z-scores were increased ($p = 0.006$) and Rint(i) showed a similar trend. In a subgroup of nine children with eczema without asthma who had no current respiratory symptoms, Rint(e) was elevated ($p = 0.002$), and Rint(i) tended to be higher too ($p = 0.06$). In children with recurrent rhinitis, Rint(e) and Rint(i) were of similar magnitude as the reference group.

Validity, Interobserver Variability, and Reproducibility

The validity of Rint measurements was assessed by comparisons with plethysmographic Raw in 20 outpatients (13 boys) with asthma or cystic fibrosis [mean (± SD) age 12.9 ± 2.7 yr,

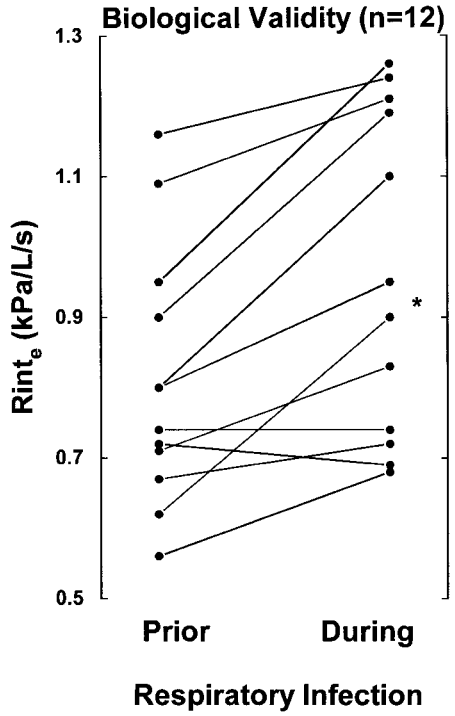

Figure 3. Paired observations of Rint(e) in 12 children with no chronic respiratory disease who developed (mild) respiratory tract infections 2 wk after the first measurement.

and mean (range) FEV_1 87 (37 to 113%) predicted]. The mean (95% CI) differences between Raw − Rint(e), and Raw − Rint(i) were 0.05 (−0.1, 0.2) kPa/L/s and 0.09 (−0.08, 0.28) kPa/L/s, respectively. The difference became greater with decreasing FEV_1 (percent predicted): $r = -0.55$ ($p = 0.05$). This was mainly affected by measurements in three cystic fibrosis patients with severe airways obstruction ($FEV_1 < 60\%$ predicted): When these were excluded, no significant correlation was found ($r = 0.31$, $p = 0.39$) and the mean (95% CI) differences between Raw − Rint(e) and Raw − Rint(i) were −0.05 (−0.16, 0.11) and −0.02 (−0.48, 0.088) kPa/L/s, respectively.

Interrater reliability was assessed from Rint(e) measurements in 20 patients with asthma or cystic fibrosis, by two investigators. One observer had conducted several hundreds of tests (J.M.); the other was new to the procedure. Intraclass correlation coefficient was 0.98. Within-subject variability was studied in 22 stable children from the reference population with an interval of 2 wk. Mean (95% CI) differences between duplicate measurements of Rint(e) and Rint(i) were −0.05 (−0.10, 0.15) kPa/L/s and 0.03 (−0.08, 0.16) kPa/L/s, respectively. Short-term variability intraclass correlation coefficients were 0.82 for Rint(e) and 0.79 for Rint(i).

TABLE 1. MEAN (SD) CHARACTERISTICS OF SUBGROUPS ACCORDING TO QUESTIONNAIRES

Category (*n*)	Age (*yr*)	Weight (*kg*)	Height (*cm*)	Sex (*M/F*)	Passive Smoking (*n*)	Asthma Drugs (*n*)
Normals (54)	5.4 (1.0)	20.4 (3.1)	114 (7)	23/31	13	0
Normals, symptoms (10)	5.4 (0.8)	21.0 (3.7)	113 (7)	7/3	2	0
Recurrent rhinitis (7)	5.6 (0.5)	21.4 (2.6)	115 (6)	4/3	5	0
Recurrent rhinitis, symptoms (5)	5.5 (1.0)	21.3 (1.8)	114 (5)	4/1	1	0
Asthma and/or eczema (32)	5.1 (1.2)	20.7 (3.0)	114 (9)	19/13	11	6
Asthma and/or eczema, symptoms (20)	5.1 (1.0)	20.5 (2.9)	113 (7)	11/9	8	7

TABLE 2. MEAN (95% CI) DIFFERENCES BETWEEN Z-SCORES OF DIFFERENT SUBGROUPS AND THE REFERENCE POPULATION

Category (*n*)	Rint(e)	Rint(i)
Normals, symptoms (10)	0.87 (0.09, 1.65)*	0.43 (−0.28, 1.14)
Recurrent rhinitis (7)	−0.19 (−1.07, 0.69)	−0.36 (−1.18, 0.46)
Recurrent rhinitis, symptoms (5)	0.15 (−0.77, 1.06)	−0.09 (−2.11, 1.94)
Asthma and/or eczema (32)	0.73 (0.12, 1.33)*	1.0 (0.32, 1.69)†
Asthma and/or eczema, symptoms (20)	0.72 (0.22, 1.23)†	0.4 (−0.1, 0.9)

* $p \leq 0.03$; † $p \leq 0.006$, unpaired *t* tests.

DISCUSSION

Searching for a quick, noninvasive, reliable and yet sensitive tool to assess airway function in preschool children, we investigated the interrupter technique with a portable device. We explored ways to improve its precision, compared the sensitivity of Rint during expiratory and inspiratory interruptions, and obtained reference values. We confirmed that it is feasible to obtain reliable measurements of Rint in the majority of children older than 2 to 3 yr of age (7, 8). Once the mouthpiece was accepted, 9 or more successful interruptions could be carried out in almost all children. Because of factors such as upper airway compliance and lack of standardization of inflation level, we expected the natural variability of the method to be considerable. Mean coefficients of variation were approximately 11%, which was close to values reported by others (6, 8), and similar as found for measurements of plethysmographic Raw in this age category (17). SEM/mean was used as a measure to study the yield in precision with increasing number of interruptions. Precision was considerably improved by conducting 10 interruptions instead of 5 during each measurement session. We also found that data were not normally distributed, justifying the use of the median rather than the mean. Rint values showed acceptable agreement with plethysmographic Raw in patients with $FEV_1 > 60\%$ predicted. The biologic validity was demonstrated to be satisfactory. The reproducibility within subjects was fair, the interobserver reproducibility excellent.

Biologic Validity

We observed that mean Rint values were elevated in children with minor respiratory symptoms or disease compared with the reference population. We consider this remarkable as these differences only reflected minor disease. Both Rint(e) and Rint(i) were elevated in 32 children who had asthma or eczema, or both, and no current respiratory symptoms according to the questionnaires. The latter may indicate that these children had respiratory symptoms that were not recognized by their parents nor perceived by the children themselves.

Rint(e) seemed slightly more sensitive in detecting (subclinical) differences in airway caliber within and between subjects than Rint(i) because: (*1*) in healthy children with current mild respiratory tract infections, Rint(e) was elevated compared with control subjects, unlike Rint(i); (*2*) Rint(e) increased somewhat more than Rint(i) within subjects who developed respiratory symptoms (productive cough without dyspnea or wheeze); (*3*) in the subgroup of nine children with eczema only

(and no asthma or current respiratory symptoms), Rint(e) was elevated whereas Rint(i) only showed a trend to be higher; (*4*) in 20 symptomatic children with asthma or eczema, or both, mean Rint(e), but not Rint(i) was increased compared with the reference group. From the present study it cannot be inferred why mean Rint(i) in 32 asymptomatic children with asthma or allergy was elevated compared with control subjects, whereas mean Rint(i) in 20 symptomatic children with asthma or allergy showed more overlap with the reference group. There may be differences between the groups accounting for this: sample size, asthma severity, treatment, biologic variability, and misclassification based on the questionnaires may all affect mean Rint(i) values of these two subgroups.

The greater sensitivity of Rint(e) in detecting abnormal airway patency compared with Rint(i) remains to be explained. Factors such as dynamic airway compression, and airway hysteresis patterns may partly explain this phenomenon. It is conceivable that peripheral airway obstruction, resulting in a larger pressure drop in the airways during tidal expiration, leads to more dynamic airway compression and larger Rint values than in unobstructed children. Likewise, if airway hysteresis occurs during tidal breathing, and results in different airway behavior in asthmatic children compared with normals as occurs in adults (24, 25), then this may add to less airway patency during expiration and not during inspiration in the asthmatic group. To our knowledge, such studies on airway hysteresis in children are lacking, and both hypothesized mechanisms need further studies to be verified. Obviously, we were not able to standardize level of inflation, as volume is not registered during Rint procedures (and difficult to assess with conventional technique in preschool children). However, airway obstruction would normally be compensated for by increased levels of inflation. This would rather lower Rint values than increase them (15), resulting in an underestimation of the differences between subgroups or within children. However, in spite of all this, the technique still appeared sensitive enough to detect the differences caused by mild respiratory symptoms within subjects and between subgroups. The increase of Rint within subjects who developed mild respiratory infections cannot be explained by rhinitis because of the nose clip, but oropharyngeal inflammation may have contributed to increased Rint values, in addition to lower airway obstruction.

Reference Values

The reference equations in the present study showed an inverse relationship between standing height and Rint with low biologic variability. This contrast with reference equations of Rint in preschool children as published by Klug and Bisgaard (17) may be due to a difference in measurement procedure rather than to differences in the equipment or population size. We assessed Rint using interruptions at the peak tidal inspiratory and expiratory flow, whereas Klug and Bisgaard standardized interruptions to occur during inspiration, at 50 ml above FRC (17). The latter implies that with increasing age, interruptions occurred at relatively lower inflation levels, which may explain less decline of Rint with increasing standing height. Interruptions in our study were programmed at peaks of expiratory or inspiratory flow (7, 10, 13) with no standardization of inflation level. However, when the two studies are compared, the explained variance of our equations (40%) and standard deviation (0.12 kPa/L/s) compare favorably with 21% explained variance and standard deviation of 0.16 kPa/L/s (17). This suggests that because of a different measurement procedure, a volume correction was introduced which has improved the sensitivity of the technique. The inverse relationship between Rint values and standing height can very well be explained by increasing airway dimensions during growth and is consistent with the reported reference equations for Raw (26).

This study demonstrates that within a group of preschool children from a general population, the interrupter technique is sensitive enough to detect alterations in Raw within children, and differences between subgroups of children. It shows that short-term changes in Raw within children resulting from minor respiratory infections could be documented, and that Rint(e) seems more sensitive than Rint(i). Furthermore, it was possible to discriminate between subgroups with respiratory symptoms or disease. As is the case for more conventional lung function parameters, there was a considerable overlap of Rint with normals, but mild symptoms did not go undetected, and children with reported eczema or asthma had significantly higher Rint values than the reference population. It should be stressed that this was a group of children with only mild asthma, that used little or no medication (only 13 of 52 used medication on a regular basis). We did not observe a negative relationship between parental smoking and Rint values. From this it can not be concluded that airway function is not affected by passive smoking. It may also reflect a bias of selective smoking, or may indicate that the effects of smoke exposure are too small to detect with Rint in a population of this size. The validity of the technique using plethysmographic Raw as the gold standard seems acceptable as long as airways obstruction is not severe, as was published previously (12). This is partly explained by the fact that body plethysmography measures Raw only, whereas the interrupter technique determines resistance of the respiratory system. In the presence of significant airway obstruction, however, measurements of both techniques will be affected by time constants of the upper airways and incomplete equilibration of airway pressures. Moreover, tracings of Raw measurements become more difficult to interpret (open loops) and there is no consensus on how to approach this issue (26). The excellent interobserver reliability is a reflection of both the simplicity of handling the equipment and interpreting the tracings and the relatively large natural variability of the signal.

In conclusion, this study supports the statement that the interrupter technique is one of the few valuable and feasible diagnostic tools to assess airway function in preschool children (6–8, 10, 11, 13, 14, 16, 18). Furthermore, it also addresses several issues that have not received much attention so far in the literature. Other investigators have studied the use of Rint in a laboratory setting in patients but did not study ways to improve precision, and did not compare the clinical usefulness of Rint(e) versus Rint(i). We found that the natural variability of the data can be reduced using median values and 10 interruptions during each measurement and that Rint(e) measurements were more sensitive than Rint(i) measurements in detecting increased Raw. The biologic validity of the interrupter technique has not been assessed before. This study indicates that the technique is sensitive enough to detect small changes in airway function within children from a general population, and to distinguish groups of children with minor respiratory symptoms or mild respiratory disease from normals. Reference values of Rint(e) and Rint(i) related to standing height, based on interruptions at peak expiratory and inspiratory tidal flow, improved the explained variance considerably. These aspects make strong arguments to use this technique for assessment of airway function in preschool children. This holds for pediatric pulmonary care, pediatric clinical research, but also for epidemiologic studies, because measurements can be carried out quickly, and with a portable device. For these applications, the interrupter technique is a welcome diagnostic tool

for a category of children in whom respiratory function testing was often needed, but not feasible.

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References

1. Dickman ML, Schmidt CD, Gardner RM. Spirometric standards for normal children and adolescents (ages 5 years through 18 years). *Am Rev Respir Dis* 1971;104:680–687.
2. Wang X, Dockery DW, Wypij D, Fay ME, Ferris BG Jr. Pulmonary function between 6 and 18 years of age. *Pediatr Pulmonol* 1993;15:75–88.
3. Duiverman EJ, Neijens HJ, van Strik R, Van Der Snee-Van Smaalen M, Kerrebijn KF. Bronchial responsiveness in asthmatic children aged 3 to 8 years measured by forced pseudorandom noise oscillometry. *Bull Eur Physiopathol Respir* 1986;22:27–34.
4. Wilson NM, Phagoo SB, Silverman M. The use of transcutaneous oxygen tension, arterial oxygen saturation and respiratory resistance to assess the response to inhaled methacholine in asthmatic children and normal adults. *Thorax* 1991;46:433–437.
5. Cutrera R, Filtchev S, Merolla R, William G, Haluszka J, Ronchetti R. Analysis of expiratory pattern for monitoring bronchial obstruction in school-age children. *Pediatr Pulmonol* 1991;10:6–10.
6. Phagoo SB, Wilson NM, Silverman M. Evaluation of a new interrupter device for measuring bronchial responsiveness and the response to bronchodilator in 3 year old children. *Eur Respir J* 1996;9:1374–1380.
7. Bridge PD, Rangantathan S, McKenzie SA. Measurement of airway resistance using the interrupter technique in preschool children in the ambulatory setting. *Eur Respir J* 1999;13:792–796.
8. Bisgaard H, Klug B. Lung function measurement in awake young children. *Eur Respir J* 1995;8:2067–2075.
9. Von Neergaard K, Wirz K. Die Messing Des Stromungswiderstandes in den Atem-Wegen des Menschen, ins besondere bei asthma und emphysema. *Z Klin Med* 1927;105:51–82.
10. Phagoo SB, Watson RA, Pride NB, Silverman M. Accuracy and sensitivity of the interrupter technique for measuring the response to bronchial challenge in normal subjects. *Eur Respir J* 1993;6:996–1003.
11. Chowienczyk PJ, Lawson CP, Lane S, Johnson R, Wilson N, Silverman M, Cochrane GM. A flow interruption device for measurement of airway resistance. *Eur Respir J* 1991;4:623–628.
12. Oswald-Mammosser M, Charloux A, Donato L, Albrech C, Speich JP, Lampert E, Lonsdorfer J. Interrupter technique versus plethysmography for measurement of respiratory resistance in children with asthma or cystic fibrosis. *Pediatr Pulmonol* 2000;29:213–220.
13. Phagoo SB, Wilson NM, Silverman M. Evaluation of the interrupter technique for measuring change in airway resistance in 5-year-old children. *Pediatr Pulmonol* 1995;20:387–395.
14. Bridge PD, Lee H, Silverman M. A portable device based on the interrupter technique to measure bronchodilator response in schoolchildren. *Eur Respir J* 1996;9:1368–1373.
15. Oswald-Mammosser M, Llerena C, Speich JP, Donato L, Lonsdorfer J. Measurements of respiratory system resistance by the interrupter technique in healthy and asthmatic children. *Pediatr Pulmonol* 1997; 24:78–85.
16. Carter ER. It is time to consider standardizing the interrupter technique. *Eur Respir J* 1997;10:1428–1429.
17. Klug B, Bisgaard H. Specific airway resistance, Interrupter resistance, and respiratory Impedance in healthy children aged 2–7 years. *Pediatr Pulmonol* 1998;25:322–331.
18. Carter ER, Stecenko A, Pollock B, Jaeger M. Evaluation of the interrupter technique for the use of assessing airway obstruction in children. *Pediatr Pulmonol* 1994;17:211–217.
19. Dezateux C, Wade A, Schmalisch G, Landau L. Maximizing effective research in infant respiratory function. In: Stocks J, Sly PD, Tepper RS, Morgan WJ. Infant Respiratory Function Testing. New York: Wiley Liss; 1996. p. 521–550.
20. Frey U, Stocks J, Coates A, Sly P, Bates J. Standards for infant respiratory function testing: specifications for equipment used for infant pulmonary function testing. ERS/ATS Task Force. *Eur Respir J* 2000; 16:731–740.
21. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483–491.
22. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.
23. Chinn S. Repeatability and method comparison. *Thorax* 1991;46:454–456.
24. Katz I, Zamel N, Slutsky AS, Rebuck AS, Hoffstein V. Relative hysteresis of the airway and lung parenchyma in normal subjects. *J Appl Physiol* 1998;65:2390–2394.
25. Braddock Burns C, Taylor WR, Ingram RH. Effects of deep inhalation in asthma: relative airway and parenchymal hysteresis. *J Appl Physiol* 1985;59:1590–1596.
26. Quanjer PhH, Stocks J, Polgar G, Wise M, Karlberg J, Borsboom G. Compilation of reference values for lung function measurements in children. *Eur Respir J* 1989;2:184s–262s.