Airway Resistance, Airway Conductance, Specific Airway Resistance, and Specific Airway Conductance in Children

M. LEBEN⁽³¹⁾ AND H. VON DER HARDT

Children's Hospital of the Medical School of Hannover, Division of Pediatric Pneumology [H. von der Hardt], D-3000 Hannover, Federal Republic of Germany

Summary

In 82 healthy children and in asthmatic children before and during positive allergen provocation test, airway resistance (R_{aw}), airway conductance (G_{aw}), specific airway resistance (SR_{aw}), and specific airway conductance (SG_{aw}) were measured by body plethysmography during quiet breathing. R_{aw} over total flow range ($R_{aw\ t}$) and R_{aw} at a flow rate of 0.5 liter/sec ($R_{aw\ 0.5}$) are compared: $R_{aw\ 0.5}$ is 10.3% smaller and shows a smaller coefficient of variation in healthy children. This is interpreted as a less important influence of variations of glottis opening. $SR_{aw\ t}$ mean value is 7.08 hPa·sec; $SG_{aw\ t}$ mean value is 0.141 hPa⁻¹·sec⁻¹. In asthmatic children, $R_{aw\ 0.5}$ proves to be a more sensitive parameter for the evaluation of inhalation provocation tests than $R_{aw\ t}$. The most sensitive indices of obstruction in the central and more peripheral bronchi are $SR_{aw\ 0.5}$ and $SG_{aw\ 0.5}$.

Abbreviations

BTPS, body temperature and ambient pressure saturated with water vapor
 FRC_{box}, functional residual capacity measured by body plethysmography
 G_{aw} , airway conductance
 hPa, hecto Pascal
 ΔP_M , pressure at the mouth
 R_{aw} , airway resistance
 $R_{aw\ t}$, terminal airway resistance
 SG_{aw} , specific airway resistance
 $SR_{aw\ t}$, specific airway resistance over total flow range
 $\text{tg}\alpha$, $\Delta V_b/\Delta P_M$
 $\dot{V}$, airflow
 ΔV_b , volume displacement
 ΔV_M , tidal volume

The development of body plethysmography has furnished a noninvasive method of assessing R_{aw} . R_{aw} is defined as the ratio of alveolar pressure to air flow. Usually, the pressure or volume changes of the plethysmograph corresponding to alveolar pressure are plotted *versus* air flow. R_{aw} is then calculated from the slope of the resulting S-shaped curve. DuBois and co-workers (8) measured R_{aw} at a certain flow rate on the linear part of the curve during panting. After the problem of maintaining BTPS conditions in the breathing air was solved, many investigators turned to measuring R_{aw} during quiet breathing instead of panting. It was then proposed to measure R_{aw} over the total range of alveolar pressure ("total R_{aw} ", 26) or over the points of maximum inspiratory and expiratory air flow (23, 20). For the latter way of interpretation, Haluszka (13) suggested the term "terminal R_{aw} " ($R_{aw\ t}$) because the terminal points of the curve are used. At present, there seem to be mainly two groups of investigators: those

who measure R_{aw} at fixed flow rates during panting and those who measure R_{aw} at maximum flow during quiet breathing.

It is the aim of the present study to compare the fixed flow and the "terminal" R_{aw} interpretation applied to the same measurements during quiet breathing in healthy and in asthmatic children.

MATERIALS AND METHODS

Measurements of FRC_{box} and of R_{aw} were performed in an air conditioned pressure-corrected volume displacement whole-body plethysmograph (29). The technical details have been described previously (15). The electronic signals for volume displacement (integrated and pressure-corrected flow signal) of the body plethysmograph (ΔV_b), ΔP_M , $\dot{V}$, and its integral, ΔV_M , were stored simultaneously on a magnetic tape and played back at a lower speed on an X/Y recorder (30). The breathing air was kept at body temperature and water vapour saturated in a 60 l-Douglas bag. For inhalation challenges, the additional equipment described by von der Hardt and co-workers (15) was used.

The investigation was performed in 82 school children (47 boys and 35 girls with comparable distribution of standing height), age 6–15 years, with the consent of their parents. Medical history and physical examination did not reveal any respiratory disease. In addition, inhalation provocation tests taken for clinical purpose from six asthmatic children (four boys and two girls, age 9–14 years, standing height 136–162 cm) were analysed. Measurements were taken in the sitting position, the nose closed by a nose clip. The following measurements and calculations were performed.

(1) In 76 of the 82 children (43 boys and 33 girls) FRC_{box} was calculated from $\text{tg}\alpha$ of the $\Delta V_b/\Delta P_M$ diagram obtained by the Pflüger maneuver (20). Final values were corrected for the dead-space volume of the mouthpiece and the shutter (0.11 l) and for deviation from the end-expiratory level detected by the spirogram recorded simultaneously. In the remaining six children, the latter correction was not exactly possible because the spirogram did not show a sufficient number of respiratory cycles preceding the close of the shutter. $\text{tg}\alpha$ was used only to calculate R_{aw} if the shutter was closed within the lower third of the tidal volume.

(2) In 82 children, resistance curves ($\Delta V_b/\dot{V}$ diagrams) were recorded during quiet breathing. BTPS conditions were checked by the $\Delta V_b/\Delta V_M$ loops (20). R_{aw} was calculated in two different ways. (A) In all children, $R_{aw\ t}$ was calculated from the slope of the line connecting the points of maximum inspiratory and expiratory flow in the $\Delta V_b/\dot{V}$ diagram (Fig. 1). (B) In 46 of the 82 children (28 boys and 18 girls), R_{aw} was also calculated from the slope of the line connecting the points at an inspiratory and expiratory flow of 0.5 liter/sec ($R_{aw\ 0.5}$). If there was a difference in ΔV_b at the level of 0.5 liter/sec, the bisecting points of the ΔV_b difference at this level were used (Fig. 1).

R_{aw} was determined as the mean of three to five successive and nonselected respiratory cycles according to the formula by Mat-

thys (20). The airflow resistance of the apparatus (0.5 hPa/liter/sec) was subtracted.

In three of the taller boys, it was not possible to determine $R_{aw\ 0.5}$ for technical reasons (the zero line for $\dot{V}$ was not registered). The remaining 33 of the 82 children (34% of the boys and 49% of the girls) did not reach a sufficient air flow for this calculation during quiet breathing. This did not only pertain to smaller children, but also to taller ones; however, the % of children not reaching sufficient flow rates decreased with increasing standing height. Most of the lacking flow rates were around or slightly below 0.5 liter/sec. The distributions of standing height in the two groups of different R_{aw} calculation compare well (Fig. 2).

(3) G_{aw} was calculated as the reciprocal of the $R_{aw\ t}$ and $R_{aw\ 0.5}$ values. In this study, G_{aw} values were not calculated as the mean of the reciprocals of R_{aw} of different respiratory cycles, but as the reciprocal of the mean, in order to avoid overestimation of G_{aw} (4).

(4) SR_{aw} was calculated as the product of R_{aw} and FRC_{box} ; SG_{aw} was derived as the reciprocal from SR_{aw} , both for $R_{aw\ t}$ and $R_{aw\ 0.5}$.

(5) In six asthmatic children, the changes of FRC_{box} and of resistance and conductance values were analysed in 22 inhalation tests with provoked bronchial obstruction. A test was called positive if there was a rise of $R_{aw\ t}$ of at least 50% of the initial value or if a rise of $R_{aw\ t}$ of at least 25% was combined with an increase of FRC_{box} of at least 25%. This definition takes into consideration the spontaneous intra-individual variation of R_{aw} values—the

Fig. 1. Determination of $\tan \beta = \Delta V_b / \dot{V}$ for calculation of R_{aw} . $\dot{V}$, respiratory flow; ΔV_b , volume changes of the plethysmographic box. For $R_{aw\ t}$, the line connecting the points of maximum flow is used (A). For $R_{aw\ 0.5}$, the line is drawn through the points at an inspiratory and expiratory flow of 0.5 liter/sec. If there is a loop, the bisecting points of the ΔV_b difference at 0.5 liter/sec are used (B).

Fig. 2. Distribution of standing height of 82 healthy boys and girls in whom $R_{aw\ t}$ was measured. The dotted area represents the 46 children in whom also calculation of $R_{aw\ 0.5}$ was possible.

breath-to-breath coefficient of variation of 6 to 10 breathing cycles in asthmatic children before provocation was 19.5%—and the observation that an increase of FRC_{box} suggests peripheral bronchial obstruction (15).

RESULTS

The results of the measurements and calculations are as follows.

(1) Double logarithmic (or power) regression equations for FRC_{box} , $R_{aw\ t}$, and $R_{aw\ 0.5}$ versus standing height are given in Table 1. FRC_{box} shows a significant difference between boys and girls regarding the distance of the regression lines ($P < 0.001$), but not regarding the slope. FRC_{box} increases with standing height at a high correlation.

For $R_{aw\ t}$, data has been published previously (14). There is no significant difference between boys and girls ($P > 0.2$); $R_{aw\ t}$ decreases with increasing standing height, the residual standard deviation is considerable.

In healthy children, $R_{aw\ 0.5}$ is significantly smaller than $R_{aw\ t}$. Comparing the individual $R_{aw\ 0.5}$ and $R_{aw\ t}$ values ($n = 46$), there is a mean difference of $10.3 \pm 10.1\%$ of $R_{aw\ t}$ ($P < 0.001$).

For further interpretation, $R_{aw\ t}$ values of 82 children were compared to $R_{aw\ 0.5}$ values of the 46 children selected from the 82. This procedure seems to be justified because there is no significant difference between the $R_{aw\ t}$ regression lines of 82 and of 46 children concerning the slope or the distance. But, the correlation coefficient is higher and residual standard deviation is smaller in the group of 46 children (about the same as in $R_{aw\ 0.5}$ regression) as a consequence of selection.

The mean intra-individual standard deviations (coefficients of variation) of three to five successive and nonselected respiratory cycles of $R_{aw\ 0.5}$ and $R_{aw\ t}$ in the same group of 46 children are given in Table 2. In healthy children, variation of $R_{aw\ 0.5}$ is smaller than of $R_{aw\ t}$.

(2) Double logarithmic regression equations for $G_{aw\ t}$ and $G_{aw\ 0.5}$ versus standing height are given in Table 1. Because in double logarithmic regression the equation for reciprocal values is the same as for the original values except for the signs, G_{aw} from the G_{aw} regression is the same as G_{aw} calculated on R_{aw} from the R_{aw} regression equation, which is not true in linear regression. G_{aw} increases with standing height. There is a significant difference between the $G_{aw\ t}$ and $G_{aw\ 0.5}$ regression lines regarding the slope ($P < 0.001$) and the distance ($P < 0.01$). $G_{aw\ 0.5}$ values are higher than $G_{aw\ t}$ values, the difference being more distinct in taller children (5.8% of $G_{aw\ t}$ at 120 cm standing height, 14.3% at 160 cm).

(3) Because there is a significant difference between boys and girls for FRC_{box} , regression equations and mean values of SR_{aw} and SG_{aw} were considered for boys and girls separately and together. There is no significant correlation to standing height: SR_{aw} and SG_{aw} can be considered to be constant in children.

The geometric mean of $SR_{aw\ t}$ is 7.08 hPa·sec for boys and girls together, the upper 95% confidence limit is 13.5 hPa·sec. In boys alone, the mean value is 7.57 hPa·sec (95% limit 14.19 hPa·sec), in girls 6.48 hPa·sec (95% limit 12.24 hPa·sec). $SR_{aw\ t}$ is significantly smaller in girls than in boys ($P < 0.05$). For $SR_{aw\ 0.5}$, boys and girls together, the geometric mean value is 6.46 hPa·sec and is not significantly smaller than that of $SR_{aw\ t}$ ($P > 0.05$).

The geometric mean value of $SG_{aw\ t}$ for boys and girls together is $0.141\text{ hPa}^{-1}\cdot\text{sec}^{-1}$ (lower 95% limit $0.074\text{ hPa}^{-1}\cdot\text{sec}^{-1}$), for boys alone it is $0.132\text{ hPa}^{-1}\cdot\text{sec}^{-1}$ (95% limit $0.070\text{ hPa}^{-1}\cdot\text{sec}^{-1}$), and for girls $0.154\text{ hPa}^{-1}\cdot\text{sec}^{-1}$ (95% limit $0.082\text{ hPa}^{-1}\cdot\text{sec}^{-1}$), the difference between the mean values of boys and girls being significant ($P < 0.05$). For $SG_{aw\ 0.5}$, boys and girls together, the geometric mean value is $0.155\text{ hPa}^{-1}\cdot\text{sec}^{-1}$ and is not significantly higher than that of $SG_{aw\ t}$ ($P > 0.05$).

(4) Except for one test, all the provocation tests are positive according to the definition from the rise in $R_{aw\ t}$ alone. The difference between $R_{aw\ 0.5}$ and $R_{aw\ t}$ is more distinct before provocation (at a mean of $33.2 \pm 10.0\%$ of $R_{aw\ t}$) than during

Table 1. Regression equations for FRC_{box} , $R_{aw\ t}$, $R_{aw\ 0.5}$, $G_{aw\ t}$, and $G_{aw\ 0.5}$ versus standing height¹

Regression equation ²	n	lg s	r	Mean values		(unit)
				120 cm	160 cm	
lg FRC_{box} (boys) = $2.4579 \cdot \lg H - 5.1309$ FRC_{box} (boys) = $7.4 \cdot 10^{-6} \cdot H^{2.458}$	43	0.0914	0.79	0.955	1.936	(l)
lg FRC_{box} (girls) = $2.5655 \cdot \lg H - 5.4014$ FRC_{box} (girls) = $3.97 \cdot 10^{-6} \cdot H^{2.566}$	33	0.0837	0.74	0.859	1.797	(l)
lg $R_{aw\ t}$ = $-1.9789 \cdot \lg H + 4.9735$ $R_{aw\ t}$ = $9.41 \cdot 10^4 \cdot H^{-1.979}$	82	0.1225	-0.57	7.23	4.09	(hPa/liter/sec)
lg $R_{aw\ 0.5}$ = $-2.2492 \cdot \lg H + 5.5117$ $R_{aw\ 0.5}$ = $3.25 \cdot 10^5 \cdot H^{-2.249}$	46	0.1097	-0.65	6.85	3.59	(hPa/liter/sec)
lg $G_{aw\ t}$ = $1.9789 \cdot \lg H - 4.9735$ $G_{aw\ t}$ = $1.06 \cdot 10^{-5} \cdot H^{1.98}$	82	0.1225	0.57	0.139	0.245	(liter/sec/hPa)
lg $G_{aw\ 0.5}$ = $2.2492 \cdot \lg H - 5.5117$ $G_{aw\ 0.5}$ = $3.08 \cdot 10^{-6} \cdot H^{2.25}$	46	0.1097	0.65	0.147	0.280	(liter/sec/hPa)

¹ Abbreviation: n, number of children investigated; s, residual standard deviation; r, coefficient of correlation; and H, standing height in cm.

² Except for FRC_{box} , regression equations are for boys and girls together.

Table 2. Coefficients of variation (mean intra-individual standard deviation of three to five successive and non-selected respiratory cycles) of $R_{aw\ t}$ and $R_{aw\ 0.5}$ in healthy and in asthmatic children before provocation and during provoked bronchial obstruction

	Coefficient of variation	
	$R_{aw\ t}$	$R_{aw\ 0.5}$
Healthy children	$13.6 \pm 8.6\%$ (2.4–42.7%)	$9.3 \pm 6.1\%$ (0.1–20.8%)
Asthmatic children before provocation	$5.3 \pm 2.8\%$ (2.0–13.9%)	$11.5 \pm 7.3\%$ (4.3–32.7%)
Asthmatic children during provoked bronchial obstruction	$3.4 \pm 1.9\%$ (1.4–8.3%)	$6.6 \pm 3.1\%$ (1.8–12.2%)

positive reaction ($23.1 \pm 7.4\%$). The mean rise of $R_{aw\ t}$ is 113%, for $R_{aw\ 0.5}$ it is 154%, the % being only in 4 tests slightly higher in $R_{aw\ t}$ than in $R_{aw\ 0.5}$. The mean changes of the different parameters in % of the initial value are summarized in Table 3. Standard deviations in % of the mean changes (coefficients of variation) do not differ for the terminal and the fixed-flow type of interpretation. Individual changes in $SR_{aw\ t}$ are shown in Figure 3.

The mean intra-individual standard deviation of $R_{aw\ t}$ and $R_{aw\ 0.5}$ (coefficient of variation) of three to five successive and nonselected respiratory cycles in this group of asthmatic children before and during positive provocation is given in Table 2.

DISCUSSION

(1) *Comparison to literature.* There are some publications compiling predicted values of plethysmographic data including FRC_{box} and R_{aw} from different authors (1, 13, 21, 25). But even the comprehensive review by Michaelson and co-workers (21) omits some important publications and quotes only two authors who measured R_{aw} during spontaneous breathing. In order to compare our results for R_{aw} , SR_{aw} , G_{aw} , and SG_{aw} to those reported in the literature, we compiled the data available (Table 4). Only investigations with larger numbers were included. FRC_{box} is added in order to supplement information on resistance. Our data on FRC_{box} is in line with that of other authors except for Haluszka (13) whose values are substantially higher.

The methods of determination of R_{aw} differ concerning the type of breathing, the graphical interpretation of the resistance curve, the formula for calculating R_{aw} , and the statistical approach. Moreover, some authors did not state their method exactly. Because there is no standardization of plethysmography, comparability of predicted values is limited.

The problem of differences in R_{aw} measured during panting

Table 3. Mean change of different parameters in 22 positive provocation tests¹

	$\bar{\Delta}$ (%)	SD	VC (%)	range (%)	t test ²
FRC_{box}	+17	± 12	71	-13 to +39	
$R_{aw\ t}$	+113	± 73	64	+28 to +332	} $P < 0.001$
$R_{aw\ 0.5}$	+154	± 95	62	+18 to +414	
$G_{aw\ t}$	-49	± 13	25	-22 to -77	} $P < 0.01$
$G_{aw\ 0.5}$	-56	± 14	26	-16 to -81	
$SR_{aw\ t}$	+149	± 82	55	+46 to +280	} $P < 0.001$
$SR_{aw\ 0.5}$	+193	± 111	58	+52 to +312	
$SG_{aw\ t}$	-56	± 12	21	-31 to -80	} $P < 0.01$
$SG_{aw\ 0.5}$	-62	± 13	21	-34 to -85	

¹ $\bar{\Delta}$, mean change in % of initial value; S.D., standard deviation; and CV, coefficient of variation (S.D. in % of $\bar{\Delta}$).

² Paired t test shows significantly higher changes for $R_{aw\ 0.5}$ and its derivatives.

and during quiet breathing is very complex (2). R_{aw} during panting may be smaller or higher than R_{aw} during quiet breathing depending on frequency, flow rate, and normal or abnormal status of the lungs. Therefore, if the equipment of the plethysmograph allows, R_{aw} should be measured during quiet breathing.

R_{aw} at fixed flow rates is definitely smaller than R_{aw} over total flow range, in the present results at a mean of 10.3%. If only the inspiratory resistance is measured, the difference is even more pronounced (9, 22).

Differences due to different opinions on correction for dead-space volume and resistance of the apparatus are especially important in smaller children because of higher R_{aw} values and larger dead-space volume in relation to lung volumes. Because there is no correction of $tg\alpha$ for dead-space in Matthys' (20) formula for the calculation of R_{aw} , R_{aw} was measured smaller than it would have been with a correction: the difference is about 5–11%, depending on height.

We prefer R_{aw} to G_{aw} for reasons discussed by other authors (4, 7). For comparison G_{aw} values are given, too.

Some authors agree on R_{aw} with values around 5 hPa/liter/sec at 120 cm standing height and around 2.5 hPa/liter/sec at 160 cm. Weng and Levison (27) and Kamel and co-workers (19) found higher values in smaller children. The values of Godfrey and co-workers (11) are generally not accepted because they are far below the values observed by all the other investigators, probably due to some systematic error (13). Dab and Alexander (6) reported values much higher than all the others. Düggelin and Bühlmann (9) calculated R_{aw} at a high flow rate separately for inspiration and expiration. Inspiratory R_{aw} is in line with the above-mentioned authors, combined values for a whole breathing cycle would

Fig. 3. Changes of $SR_{aw\ t}$ in 22 positive inhalation tests. The tests were considered positive from the change in $R_{aw\ t}$ and FRC_{box} (see text). The illustration shows the rise in $SR_{aw\ t}$ from initial value (lower limit) to the value during positive reaction (upper limit). The broken line represents the upper 95% confidence limit of $SR_{aw\ t}$ for boys and girls together. R.E. (1 and 2), T.B. (3 and 4), F.B. (5–9), and S.B. (10), are boys; M.B. (11–16) and C.A. (17–22) are girls.

probably be similar to our values. Dab and Alexander, Düggelin and Bühlmann, and ourselves are using a body plethysmograph of the same design (29). Dab and Alexander (6), whose R_{aw} values are the highest in literature, even went so far as to postulate that every laboratory should establish its own predicted values, which seems quite reasonable in face of the lack of standardization.

As with R_{aw} , there is good agreement among many authors on SR_{aw} and SG_{aw} results, too, with mean values around 5 hPa·sec and 0.2 hPa⁻¹·sec⁻¹, respectively. Values of Cogswell and co-workers (5) and Haluszka (13) are higher (probably because of higher FRC_{box} values) with mean values around 7 hPa·sec. They agree with our results. Dab and Alexander (6) reported an even higher SR_{aw} mean value of 10 hPa·sec.

Because of log-normal distribution of SR_{aw} values (24), the geometric mean should be used, which is smaller than the arithmetic mean (in our study 5%), whereas the geometric upper 95% confidence limit is higher (in our study 11%). Calculation of SR_{aw} mean value and upper 95% limit as the reciprocal of SG_{aw} is correct only if the geometric mean is used, otherwise SR_{aw} mean value and upper 95% limit will be underestimated. Geometric mean values are given only by Pelzer and Thomson (24), who reported values in adults, by Dab and Alexander (6), and by ourselves. Upper 95% limits differ considerably among the investigations.

(2) *Comparison of $R_{aw\ t}$ and $R_{aw\ 0.5}$.* According to Ferris and co-workers (10), in the range of flow of ± 2 liter/sec (in adults) the non-linearity of R_{aw} is mainly contributed by the upper airways, whereas the resistance of the intrathoracic airways is linear. The highest R_{aw} values during a breathing cycle are measured at the points of maximum inspiratory and expiratory flow rates where turbulent flow in the upper airways can be suspected. The variation of upper airway resistance has been related to changes in glottis opening (17). $R_{aw\ 0.5}$ is calculated at a flow rate on the linear part of the resistance curve; it can therefore be expected that $R_{aw\ 0.5}$ represents better than $R_{aw\ t}$ the resistance of the intrathoracic airways. Our observation that the intra-individual coefficient of variation in healthy children is smaller for $R_{aw\ 0.5}$ than for $R_{aw\ t}$ seems to confirm this conclusion.

In the provocation tests, the difference between $R_{aw\ 0.5}$ and

$R_{aw\ t}$ is more evident before provocation than during positive reaction, and thus the rise in $R_{aw\ 0.5}$ is higher than in $R_{aw\ t}$ (Table 3), suggesting $R_{aw\ 0.5}$ to be a more sensitive parameter for detecting bronchial obstruction. This, too, can be interpreted as a better representation of the intra-thoracic resistance.

From these data, $R_{aw\ 0.5}$ seems to be preferable to $R_{aw\ t}$. The applicability of $R_{aw\ 0.5}$ is limited because some children do not reach a sufficient flow rate in inspiration and expiration during quiet breathing. Children would have to be stimulated to breathe at a slightly higher frequency. This was done by Haluszka (13) even for measurement of $R_{aw\ t}$. It can be assumed that little stimulation of breathing will not alter $R_{aw\ 0.5}$ as much as it would $R_{aw\ t}$; moreover, in clinical investigation we are observing sufficient flow rates during quiet breathing without stimulation in almost all children.

In contrast to healthy children, the variation coefficient of $R_{aw\ t}$ in the few asthmatic children investigated is smaller than that of $R_{aw\ 0.5}$ (Table 2). First, this might be caused partly by reading errors occurring in the $R_{aw\ 0.5}$ determination. Because in asthmatic children the resistance curves are somewhat looped, the auxiliary line has to be drawn through the bisecting points at a flow of 0.5 liter/sec (Fig. 1). These points cannot be determined as exactly as the points of terminal flow; moreover, with a certain graphical error at the level of 0.5 liter/sec, the slope of that line is more influenced than with the same error at terminal flow level. Second, the variation of the glottis opening seems to be less important in asthmatic children well trained in the laboratory methods than in healthy children. Although our group of asthmatic children is not comparable to that of healthy children because of the small number and lack of normal distribution, the discrepancy in the variation coefficients is not fully intelligible and deserves further investigation.

(3) *Evaluation of inhalation provocation tests.* According to the above stated definition, a provocation test would be positive if there is an increase in $R_{aw\ t}$ or $R_{aw\ 0.5}$ of at least 50% or if an increase of $R_{aw\ t}$ or $R_{aw\ 0.5}$ of at least 25% occurs together with an increase in FRC_{box} of 25% or more. Using G_{aw} , there must be a fall of at least 33% or of at least 20% if combined with an increase in FRC_{box} of 25% or more. With these definitions, one of the tests

Table 4. Values from literature for FRC_{box} , R_{aw} , SR_{aw} , G_{aw} , and SG_{aw} in healthy children

References	Subjects		Method of R_{aw} determination ¹	FRC _{box} (l) values		R_{aw} (hPa/liter/sec) values ³		SR_{aw} (hPa·sec)		G_{aw} (liter/sec/hPa) values ²		SG_{aw} (hPa ⁻¹ ·sec ⁻¹)	
	n	age range (yr)		120 cm	160 cm	120 cm	160 cm	Mean value ⁴	Upper 95% limit	120 cm	160 cm	Mean value	Lower 95% limit
Pelzer and Thomson (24)	82	16–82 (adults)	p 0.6 in	2				4.65 ⁵	8.8 ⁵			0.215	0.114
Nolte (22)	80	5–11	qt w corrected for tidal volume according to (23)			5.93	1.60						
Zapletal <i>et al.</i> (28)	25	6–18	p	♂ 1.058 ♀ 0.890	2.140 1.912	5.4 ⁵	2.7 ⁵			0.185	0.373		
				(n = 61)									
Zapletal <i>et al.</i> (1968) as quoted by (27)								5.5 ⁵	2.7 ⁵			0.182	0.086 ⁵
Weng and Levison (27)	83	4–18	p 0.5 in			6.23	2.70	5.0 ⁵	9.5 ⁵			0.199	0.105 ⁵
Kamel <i>et al.</i> (19)	39	7–23	p 0.5 in			7.05	2.60						
Godfrey <i>et al.</i> (11)	382	5–18	p 0.5 in			♂ 1.33 ♀ 1.36	0.97 1.08	2.2 ⁵ 2.1 ⁵		0.77 0.81	1.09 1.05	0.446 0.469	
Baran and Englert (1)	60	6–18	q			4.44 ⁵	2.53 ⁵	5.2 ⁵	14.3 ⁵	0.225	0.369	0.194	0.070 ⁵
Doershuk <i>et al.</i> (7)	103	5–18						4.3 ♂ 4.6 ♀ 3.9	7.1 ⁵ 7.2 ⁵ 6.7 ⁵				
Cogswell <i>et al.</i> (5)	233	5–15	p 0.25 in	1.16	2.16	5.5	3.2	6.9 ⁵					
Haluszka (13)	625	7–15	q t w	♂ 1.360 ♀ 1.327	2.815 2.666	4.41	2.78	7.055 7.184 6.928	12.31 ⁵ 13.03 ⁵ 11.51 ⁵	0.239	0.307		
von der Hardt and Leben (14)	40	6–15	q t w corrected for tidal volume according to (23)			5.78	3.63						
Berger and Nolte (3)	116	3–16	q t w	1.0	1.9	5.3	2.5	5 ⁵					
Michaelson <i>et al.</i> (21)	376	7–17	p	0.926	2.061	4.25	2.43	5.1 ⁵	10.9 ⁵	0.28	0.52	0.196	0.092 ⁵
Dab and Alexander (6)	474	3–16	q t w	1.018	2.100	8.98	4.98	10	16				
Hötter (16)	796	3–18	q	♂ 1.100 ♀ 1.159	2.301 2.317	4.67 4.72	2.21 2.27	5.1 ⁵ 5.4 ⁵					
Düggelin and Bühlmann (9)	89	8–12	q 1.0 in ex			4.71 7.80	2.10 3.77						
Present study	82	6–15	qt w	♂ 0.955 ♀ 0.859	1.936 1.797	7.23	4.09	7.08 7.57 6.48	13.50 14.19 12.24	0.139	0.245	0.141 0.132 0.154	0.074 0.070 0.082
	46	6–15	q 0.5 w			6.85	3.59	6.46		0.147	0.280	0.155	

¹ Concerning the method of R_{aw} determination, only breathing pattern (p, panting and q, quiet breathing), flow rate at which R_{aw} is calculated (liter/sec; t, terminal R_{aw}), and respiratory phase (in, only inspiratory R_{aw} ; ex, only expiratory R_{aw} ; and w, whole breathing cycle) are stated; for further details see the original literature.

² Blank spaces indicate that information is not available. If not stated otherwise, values are for boys and girls together. Pressure units cmH₂O and hPa (1 cmH₂O = 0.98 hPa) were considered to be equal.

³ For R_{aw} and G_{aw} , predicted values at 120 cm and 160 cm standing height were calculated from regression equations or read from illustrations to indicate the degree of change with height. Both heights are within the height range of most of the investigations.

⁴ If the authors did not provide information on SR_{aw} , SR_{aw} mean values were calculated or estimated from given data where possible; of course, estimation of SR_{aw} from FRC_{box} and R_{aw} predicted values is only a rough approximation. Upper 95% confidence limits were estimated as mean value plus 2 S.D.

⁵ All data not originally provided by the authors.

would not have been considered to be positive if $R_{aw 0.5}$ or $G_{aw 0.5}$ were used (the rise in $R_{aw 0.5}$ was only 18%, whereas in $R_{aw t}$ it was 28%).

If only R_{aw} (or G_{aw}) is looked at, only obstruction in the more central airways becomes apparent, whereas changes in FRC_{box} also suggest obstruction of the more peripheral airways (15). Because FRC_{box} is included in SR_{aw} and SG_{aw} , a positive reaction can be recognized by the change in SR_{aw} or SG_{aw} alone. These parameters are more sensitive in detecting bronchial obstruction than R_{aw} or G_{aw} alone (Table 3) with the additional advantage of being independent of standing height. They are especially helpful in determining whether the respiratory system is in condition to be challenged or not. We suggest not to perform a provocation test if the initial SR_{aw} or SG_{aw} value is beyond the 95% confidence

limit, which would indicate bronchial obstruction. For considering a test positive, the SR_{aw} value during provocation must rise above (or SG_{aw} fall below) the 95% limit (12). But the rise in SR_{aw} must be at least 50% of the initial value in order to avoid falsely positive tests due to spontaneous intra-individual changes; if G_{aw} is used, there has to be a fall of at least 33%.

In Figure 3, for the 22 positive provocation tests, only the change in $SR_{aw t}$ is shown. For practical reasons, the upper 95% confidence limit for boys and girls together is used, although there was a significant difference between the mean values of boys and girls separately. According to our suggestion, one of the tests would not have been continued because the initial SR_{aw} value was above the 95% limit in a child with otherwise smaller SR_{aw} values (number 13 in Fig. 3). In three tests (number 3, 17, and 18 in Fig.

3), the result would not have been positive because the 95% limit was not reached, although there was a sufficient rise in % of the initial SR_{aw} value (except for $SR_{aw\ t}$ in one test: number 18 in Fig. 3, there was a decrease in FRC_{box}). Continuing the challenge with higher concentrations of the allergen, a positive result would have been to be expected.

In the small group of asthmatic children investigated, calculation of $R_{aw\ 0.5}$ improves the sensitivity in detecting bronchial obstruction. The mean rise (in %) of $R_{aw\ 0.5}$ during positive reaction equals that of $SR_{aw\ t}$, the mean fall of $G_{aw\ 0.5}$ that of $SG_{aw\ t}$, $SR_{aw\ 0.5}$ and $SG_{aw\ 0.5}$ are even more sensitive (Table 3). Judging from the change in % of the initial value, the most sensitive parameter for detecting bronchial obstruction is $SR_{aw\ 0.5}$. For positive reaction, the range of interest is in the borderline area of the definition, not far above it. Therefore, even though the change of G_{aw} or SG_{aw} in % is not as impressive as of R_{aw} or SR_{aw} (e.g., an R_{aw} increase of 300% instead of 100% results in a G_{aw} decrease of only 75% instead of 50%), $SG_{aw\ 0.5}$ equals $SR_{aw\ 0.5}$ regarding the sensitivity.

Comparing asthmatic children before and during positive provocation reaction, the coefficients of variation for both $R_{aw\ 0.5}$ and $R_{aw\ t}$ become distinctly smaller under positive reaction (Table 2). This can be explained by a smaller influence of upper airway resistance during hyperventilation (17, 18). A similar observation was reported and discussed by von der Hardt and co-workers (15) who found a coefficient of variation in R_{aw} of 19.5% before provocation and of 10.1% during bronchial obstruction. The present data show distinctly smaller coefficients of variation.

REFERENCES AND NOTES

- Baran, D. and Englert, M.: La conductance des voies aériennes chez l'enfant et l'adolescent normaux. *Bull. Physio-Path. Resp.*, 7: 125 (1971).
- Barter, C. E. and Campbell, A. H.: Comparison of airways resistance measurements during panting and quiet breathing. *Respiration*, 30: 1 (1973).
- Berger, D. and Nolte, D.: Bodyplethysmographische Sollwerte für Kinder. *Prax. Pneumol.* 31: 600 (1977).
- Clement, J. and van de Woestijne, K. P.: Resistance or conductance? Compliance or elastance? *J. Appl. Physiol.*, 30: 437 (1971).
- Cogswell, J. J., Hull, D., Milner, A. D., Norman, A. P., and Taylor, B.: Lung function in childhood. 2. Thoracic gas volumes and helium functional residual capacity measurements in healthy children. *Brit. J. Dis. Chest*, 69: 118 (1975). 3. Measurement of airflow resistance in healthy children. *Brit. J. Dis. Chest*, 69: 177 (1975).
- Dab, I. and Alexander, F.: Lung function measured with a whole body plethysmograph. Standard values for children and young adults. *Acta Paediatr. Belg.*, 32: 259 (1979).
- Doershuk, C. F., Fisher, B. J., and Matthews, L. W.: Specific airway resistance from the perinatal period into adulthood. *Amer. Rev. Resp. Dis.*, 109: 452 (1974).
- DuBois, A. B., Botelho, S. Y., and Comroe, J. H., Jr.: A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *J. Clin. Invest.*, 35: 327 (1956).
- Düggelin, S. and Bühlmann, A. A.: Lungenvolumina und Atemwegwiderstände bei gesunden Zürcher Schulkindern-Normalwerte. *Helv. Paediatr. Acta*, 35: 21 (1980).
- Ferris, B. G., Jr., Mead, J., and Opie, L. H.: Partitioning of respiratory flow resistance in man. *J. Appl. Physiol.*, 19: 653 (1964).
- Godfrey, S., Kamburoff, P. L., and Nairn, J. R.: Spirometry, lung volumes and airway resistance in normal children aged 5 to 18 years. *Brit. J. Dis. Chest*, 64: 15 (1970).
- Gonsior, E., Meier-Sydow, J., and Thiel, C.: Routine application of body plethysmography in bronchial allergen challenge. *Bull. Physio-path. Resp.*, 8: 519 (1972).
- Haluszka, J.: Application of the whole body plethysmography in examination of respiratory system in children. Predicted values, interrelations, methodical suggestions. National Institute for Mother and Child, Branch in Rabka, Poland (translated from Polish by Maria Teutsch M.A.). Rabka (1976).
- von der Hardt, H. and Leben, M.: Bodyplethysmography in healthy children. Measurement of intrathoracic gas volume and airway resistance. *Europ. J. Pediatr.*, 124: 13 (1976).
- von der Hardt, H., Miels, M., and Geubelle, F.: Bronchial inhalation challenge by plethysmography in asthmatic children. *Respiration*, 34: 9 (1977).
- Hötter, G. J.: Spirographische, bodyplethysmographische und gasanalytische Sollwerte bei Kindern und Jugendlichen. *Prax. Pneumol.*, 33: 1178 (1979).
- Hyatt, R. E. and Wilcox, R. E.: Extrathoracic airway resistance in man. *J. Appl. Physiol.*, 16: 326 (1961).
- Jaeger, M. J. and Matthys, H.: The pattern of flow in the upper human airways. *Respiration Physiol.*, 6: 113 (1968).
- Kamel, M., Weng, T. R., Featherby, E. A., Jackman, W. S., and Levison, H.: Relationship of mechanics of ventilation to lung volumes in children and young adults. *Scand. J. Resp. Dis.*, 50: 125 (1969).
- Matthys, H.: Lungenfunktionsdiagnostik mittels Ganzkörperplethysmographie. Chpt. 2. (Stuttgart—New York, F. K. Schattauer 1972).
- Michaelson, E. D., Watson, H., Silva, G., Zapata, A., Serafini-Michaelson, S. M., and Sackner, M. A.: Pulmonary function in normal children. *Bull. Europ. Physio-path. Resp.*, 14: 525 (1978).
- Nolte, D.: Der bronchiale Strömungswiderstand im Kindesalter. *Klin. Wochenschr.*, 46: 783 (1968).
- Nolte, D., Reif, E., and Ulmer, W. T.: Die Ganzkörperplethysmographie. Methodische Probleme und Praxis der Bestimmung des intrathorakalen Gasvolumens und der Resistance-Messung bei Spontanatmung. *Respiration*, 25: 14 (1968).
- Pelzer, A. M. and Thomson, M. L.: Effect of age, sex, stature, and smoking habits on human airway conductance. *J. Appl. Physiol.*, 21: 469 (1966).
- Polgar, G. and Promadhat, V.: Pulmonary function testing in children: techniques and standards. Chpt. 5. (Philadelphia—London—Toronto, W. B. Saunders 1971).
- Ulmer, W. T. and Reif, E.: Die obstruktiven Erkrankungen der Atemwege. Klinische Bedeutung und objektiver Nachweis mit der Ganzkörperplethysmographie. *Dtsch. Med. Wochenschr.*, 90: 1803 (1965).
- Weng, T. R. and Levison, H.: Standards of pulmonary function in children. *Amer. Rev. Resp. Dis.*, 99: 879 (1969).
- Zapletal, A., Motoyama, E. K., van de Woestijne, K. P., Hunt, V. R., and Bouhuys, A.: Maximum expiratory flow-volume curves and airway conductance in children and adolescents. *J. Appl. Physiol.*, 26: 308 (1969).
- Pulmorex, Dr. Fenyves & Gut, Basel, Switzerland.
- Houston Instruments, Texas, USA.
- Requests for reprints should be addressed to: M. Leben, Kinderklinik der Medizinischen Hochschule Hannover, K.-Gutschow-Straße 8, D-3000 Hannover 61.
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