

Assessment of Bronchodilator Responsiveness in Infants with Bronchiolitis

A Comparison of the Tidal and the Raised Volume Rapid Thoracoabdominal Compression Technique

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Whether bronchodilators should be used for the treatment of infants with bronchiolitis is subject to debate, partly because of the low sensitivity of the methods for assessing lung function changes in infants. In the present study, we compared the recently introduced raised volume (RVRTC) with the conventional end-tidal rapid thoracoabdominal compression (ETRTC) technique in infants with acute viral bronchiolitis. In 17 infants lung function was assessed by both methods, at baseline values and after salbutamol inhalation. Forced expiratory volumes ($FEV_{0.5}$, $FEV_{0.75}$, $FEV_{1.0}$) were used for the quantification of RVRTC measurement, and maximal expiratory flow at functional residual capacity ($\dot{V}_{max_{FRC}}$) for ETRTC measurements. A significant individual change was defined by a mean post-bronchodilator value that differed from baseline value by more than twice the within-subject coefficient of variation (CV). Group mean intrasubject CVs ranged from 4.7% to 5.3% for FEV parameters; it was 14.0% for $\dot{V}_{max_{FRC}}$. For the group, postbronchodilator measurements did not differ significantly from baseline measurements. For the majority of infants, however, the within-subject comparison of responses revealed substantial differences between both techniques; while no infant demonstrated a significant increase in $\dot{V}_{max_{FRC}}$, eight (47%) infants responded with significantly improved timed volumes. The RVRTC technique provides the investigator with a more sensitive diagnostic tool for documenting the effectiveness of therapeutic interventions on an individual basis. Furthermore, the findings of the present study provide a rationale for the application of bronchodilators in a subgroup of infants with acute bronchiolitis. Modl M, Eber E, Weinhandl E, Gruber W, Zach MS. Assessment of bronchodilator responsiveness in infants with bronchiolitis: a comparison of the tidal and the raised volume rapid thoracoabdominal compression technique.

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Bronchiolitis is one of the most frequent causes for hospital admission in infancy. Whether bronchodilators should be used in the treatment of this disease has remained subject to discussion (1, 2). Previous work has shown that bronchodilator responses in bronchiolitis range from marked improvement to deterioration of lung function (3-14). One reason for the persisting inconsistency of these findings is the lack of sufficiently sensitive methods for evaluation of lung function in infants (8, 13-16). Plethysmographic measurements of airway resistance and conductance, and measurements of resistance and compliance of the respiratory system by the single-breath occlusion technique, all suffer from methodological problems which potentially affect their accuracy (14-17). Presently, the end-tidal rapid thoracoabdominal compression (ETRTC) technique is the most commonly used method for the assessment of lung function in infants with airway disease. However, potential

limitations of this technique are the large intraindividual variability of measurements, the quantification of the compression-effected forced expiration in the form of a volume-dependent flow rate, and the fact that this technique operates in the tidal volume range, and, therefore, assesses expiratory flow only for a small part of the entire vital capacity (18-24).

When using the lung deflation technique, significantly improved instantaneous flow rates after bronchodilator therapy were found in most intubated infants with severe bronchiolitis (25). It has been speculated that such findings might be related to the technique used in this study, as it allows measurements from a predefined lung volume (8). However, the applicability of this method remains restricted to intubated infants. A recently introduced technique for spontaneously breathing infants, however, also allows for the assessment of lung function over an extended volume range by raising the lung volume before thoracoabdominal compression (raised volume rapid thoracoabdominal compression [RVRTC] technique). This technique has been shown to provide highly reproducible and sensitive measurements of lung function in healthy infants as well as in those with chronic airway diseases (19, 26). A recent study in infants with acute bronchiolitis documented a significantly smaller intraindividual variability for timed volume measurements from the RVRTC than for flow measurements

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from the ETRTC technique (21). This provides a promising basis for the individualized assessment of therapeutic interventions such as bronchodilator therapy. In a follow-up study, we therefore set out to assess airway responses to salbutamol comparing the conventional ETRTC and the new RVRTC technique in infants with acute viral bronchiolitis.

METHODS

Subjects

Twenty-two infants, admitted with acute respiratory syncytial virus (RSV)-positive bronchiolitis, were recruited for the study. Measurements from five infants had to be excluded as they awoke during lung function testing. The remaining 17 subjects, 10 boys and seven girls, had a mean age of 9.1 ± 4.8 mo (range 3.3 to 18.3 mo); their mean height was 71.0 ± 6.9 cm (range 61 to 82 cm) and their mean weight 8.3 ± 1.5 kg (range 5.1 to 10.3 kg); weight and height were within the normal centiles for all children. Informed consent for the study was obtained from the parents, and one or both of them were present during the investigation. The study was approved by the ethics committee of the local medical faculty.

Equipment

The equipment used has been described previously (19, 21). Briefly, the infant breathed through a sealed face mask held over mouth and nose. A special apparatus, consisting of several electronically controlled solenoid valves, a no. 1 Fleisch pneumotachograph (P.K. Morgan Ltd., Chatham, UK), a modified Vital Air nebulizer pump (Allersearch, Sydney, Australia), and a variable blow-off valve, was connected to the mask. Airway opening pressure was measured from a port in the mask by a Gould Statham P23 transducer (Gould Inc., Dayton, OH). The squeeze-jacket consisted of a rapidly inflatable and expandable inner layer within a rigid outer layer; it was wrapped around the chest and abdomen of the infant with the arms remaining outside. The inner layer was connected to a gas reservoir filled with compressed air. Care was taken that the jacket was not wrapped so tightly to restrict tidal breathing and lung inflation during RVRTC maneuvers, or so loosely to cause insufficient pressure transmission across the chest wall. Data collection and analysis were performed on a computer using a commercial data acquisition and analysis package (Labdat-Anadat 5.2; RHT-Infodat Inc., Montreal, PQ, Canada). Oxygen saturation was monitored continuously during the entire study by a pulse oximeter (Biox 3700e; Ohmeda, Louisville, CO).

ETRTC Technique

Measurements in the tidal volume range were performed by rapidly inflating the jacket at end-tidal inspiration resulting in a compression of the infant's chest and abdomen. The following forced expiration was recorded with the pneumotachograph in the form of a flow-volume plot. The partial expiratory flow-volume curves produced by this technique were evaluated by measuring maximal flow at functional residual capacity (FRC) of the preceding tidal breath ($\dot{V}_{\max_{\text{FRC}}}$) (22). The minimal jacket pressure (P_j) needed for generating $\dot{V}_{\max_{\text{FRC}}}$ was determined from a run of forced expiratory maneuvers in the tidal volume range. Initially, a P_j of 1 to 2 kPa was used; subsequently, this pressure was increased stepwise until the flow at FRC no longer increased. The P_j that produced the highest $\dot{V}_{\max_{\text{FRC}}}$ without evidence of negative effort dependence was then used to generate subsequent forced expirations (18, 27).

RVRTC Technique

Lung function measurements over an extended volume range were performed as described previously (19). Before the forced expiration, the infant's lung volume was raised above the tidal range with the pump inflating the lungs until a predetermined airway pressure, measured at the infant's mouth, was reached. Flow velocity for lung inflation was determined individually. This was done by performing repeated RVRTC maneuvers with stepwise decreasing "pumping speeds"; those flow velocities producing the best forced expiratory flow-volume curves were maintained for the following measurements. To facilitate alveolar inflation behind obstructed airways, three infla-

tion maneuvers, the first two followed by passive expirations, preceded each thoracoabdominal compression. The lung volume from which these forced expirations were initiated was defined by an airway pressure of 3 kPa. Once this pressure was reached by the last inflation procedure the pump was switched off. The main solenoid valve to the pneumotachograph closed for 200 ms; then the valve opened to initiate the forced expiration. Forced expirations with the RVRTC technique were achieved by using the same jacket pressure as for the ETRTC maneuver. Volume-time parameters, i.e., forced expiratory volume in 50, 75, and 100% of the first second of chest compression ($FEV_{0.5}$, $FEV_{0.75}$, $FEV_{1.0}$), were used for the quantification of these maneuvers.

Study Protocol

Each baby underwent lung function measurements within the first 18 h after hospital admission for acute viral bronchiolitis. Beta-mimetics were withheld for at least 6 h before lung function testing. A clinical examination was performed immediately before the measurements and the respiratory status was scored according to the system of Tal and coworkers (28). This score quantifies the clinical severity of bronchiolitis; a mild clinical stage is characterized by 4 to 6 points; 7 to 9 points stand for moderate, 10 to 12 for severe disease, respectively. In addition, a questionnaire that included information on previous episodes of wheezing, family history of asthma and allergy, as well as exposure to cigarette smoke, was completed by the parents.

For lung function measurements, infants were sedated with 80 mg/kg of orally administered chloral hydrate. Measurements were done while the infant slept in the supine position with the head supported in the midline and the neck slightly extended. After determination of jacket pressure, which was done with the ETRTC technique as described previously, baseline lung function measurements with the ETRTC and the RVRTC technique were performed in randomized order. Baseline measurements were repeated until five to 10 technically acceptable curves were obtained by each technique. P_j transmitted across the chest wall was assessed by occluding the airway opening at the end of an inspiratory maneuver. After airway opening pressure (P_{ao}) reached a plateau, the jacket was rapidly inflated while the airway remained closed; once a second plateau in P_{ao} occurred, the airway was opened and the jacket was deflated. The changes in P_{ao} , which indirectly reflect changes in intrapleural pressure, were related to P_j and expressed as percentage of driving pressure for the rapid thoracoabdominal compression (RTC) maneuver.

Salbutamol was administered by a metered dose inhaler containing 0.1 mg per actuation (Sultanol; Glaxo, Vienna, Austria) through a metal spacer device (Metallspacer; Astra, Linz, Austria) with a soft face mask. The mask was placed so as to obtain a tight seal over the infant's mouth and nose. Two puffs were delivered individually into the spacer; after each actuation the infant took at least five to six tidal breaths. The heart rate of the infant was continuously monitored throughout the study. Lung function measurements were repeated 15 min after bronchodilator inhalation; again, five to 10 technically acceptable curves were obtained by each technique. Special care was taken that the infant was not moved between the two sets of measurements (29).

Statistical Analysis

Mean values as well as intrasubject and group mean coefficients of variation (CV) for $FEV_{0.5}$, $FEV_{0.75}$, $FEV_{1.0}$, and $\dot{V}_{\max_{\text{FRC}}}$ were calculated for each infant. For each individual infant, a significant change from baseline was defined by a mean postbronchodilator value that differed from baseline measurements by more than twice the within-subject CV. Chi-square tests and regression analysis were used to relate the bronchodilator effects to gender, age, clinical severity of airway obstruction, exposure to cigarette smoke, family history of asthma or allergy, and previous episodes of wheezing. A paired *t* test was used to compare baseline to postbronchodilator heart rate. A *p* value ≤ 0.05 was taken as indicating statistical significance.

RESULTS

Infants were graded clinically as suffering from bronchiolitis of mild or moderate severity; the mean clinical score was 4.9

TABLE 1
INDIVIDUAL MEAN VALUES OF FEVs AND $\dot{V}_{max_{FRC}}$

Subject	Baseline				Postbronchodilator			
	FEV _{0.5} (ml)	FEV _{0.75} (ml)	FEV _{1.0} (ml)	$\dot{V}_{max_{FRC}}$ (ml/s)	FEV _{0.5} (ml)	FEV _{0.75} (ml)	FEV _{1.0} (ml)	$\dot{V}_{max_{FRC}}$ (ml/s)
1	202.63	236.93	—	110.96	227.2	263.35	—	101.9
2	110.9	133.06	—	40.19	131.05	150.48	—	30.48
3	107.13	121.18	130.3	22.86	125.45	140.86	151.6	21.22
4	166.69	183.97	193.72	56.93	184.73	206.38	218.24	50.16
5	114.47	—	—	33.91	122	—	—	29.16
6	136.94	151.46	159.69	80.3	155.9	174.43	189.73	88.78
7	158.64	182.07	—	124.44	150.87	175.81	—	149.43
8	204.73	237.14	—	126.55	226.36	263.44	—	121.23
9	118.14	139.04	151.91	59.46	118.55	145.23	163.1	50.62
10	185.26	208.89	220	90.36	181.47	206.01	219.53	51.27
11	164.25	193.88	205.75	50.33	155	181.44	196.97	38.26
12	95.48	110.48	121.49	42.77	87.16	101.3	110.97	34.19
13	169.49	198.13	218.3	37.6	187.26	218.09	239.66	42.79
14	232.5	292.13	327.59	127.89	251.01	310.32	347.81	121.62
15	273.36	320.63	—	182.97	260.33	314.07	—	189.68
16	218.94	257.37	282.13	62.41	216.57	255.43	281.68	58
17	241.03	284.93	—	163.11	236.73	270.13	—	85.13
Mean	168.62	203.21	201.09	83.12	177.51	211.05	211.93	74.35
SD	53.84	64.08	65.64	48.18	52.19	63.21	67.6	48.16

points (SD = 1.1; range 4 to 7 points). A previous episode of wheezing was reported for seven infants; the remaining 10 had not suffered from any prior respiratory disorder. Three infants had a positive family history of asthma or allergy, and seven were chronically exposed to cigarette smoke. After salbutamol, heart rate increased from 128 ± 12 beats/min at baseline to 139 ± 13 beats/min ($p < 0.0001$).

Table 1 shows individual and group mean data of flow and volume measurements. In baseline and postbronchodilator RVRTC measurements all 17 subjects produced an FEV_{0.5}, 16 of them an FEV_{0.75}, and only 10 an FEV_{1.0}. In the remaining children, early inspiratory efforts prevented the assessment of all three timed volumes. An assessment of FVC was not possible in the majority of investigated patients as these early inspiratory efforts tended to interfere with the completion of the compression maneuver. Measurements with the ETRTC technique were possible in all 17 subjects. Mean P_j used for the RTC maneuvers was 4.5 ± 0.7 kPa with a mean P_j transmission to the airway opening of $48 \pm 4.5\%$.

Group intrasubject CVs are shown in Table 2. CVs were much smaller for FEV parameters than for $\dot{V}_{max_{FRC}}$; this difference between the intraindividual variability of each FEV parameter and the one of $\dot{V}_{max_{FRC}}$ was highly significant ($p < 0.001$) for both baseline and postbronchodilator measurements. The baseline to postbronchodilator comparison did not reach statistical significance for the CV of any of the parameters. Assessment of baseline intraindividual variability lasted from 15 to 22 min for each technique, and this time did not correlate with the individual dimension of variability; further-

more, there was no systematic difference between values measured early and those measured late in this baseline series.

For the group, postbronchodilator measurements of flow and volume did not differ significantly from baseline measurements. Individual changes, however, were significant in roughly half of the children, and there were more significant individual changes of timed volume measurements (RVRTC technique) than of $\dot{V}_{max_{FRC}}$ (ETRTC technique). A representative set of curves is shown in Figure 1. Figure 2 shows superimposed tracings from pre- and postbronchodilator measurements to graphically illustrate reproducibility.

Both significant individual increases and decreases of measurements occurred after bronchodilator inhalation. These di-

TABLE 2

GROUP MEAN (\pm SD) CV AT BASELINE AND AFTER SALBUTAMOL ADMINISTRATION

	Baseline	Postbronchodilator
CV% FEV _{0.5}	4.74 \pm 1.85	4.27 \pm 1.75
CV% FEV _{0.75}	4.94 \pm 1.60	4.76 \pm 1.89
CV% FEV _{1.0}	5.30 \pm 1.85	5.49 \pm 1.40
CV% $\dot{V}_{max_{FRC}}$	13.99 \pm 6.91	15.94 \pm 6.93

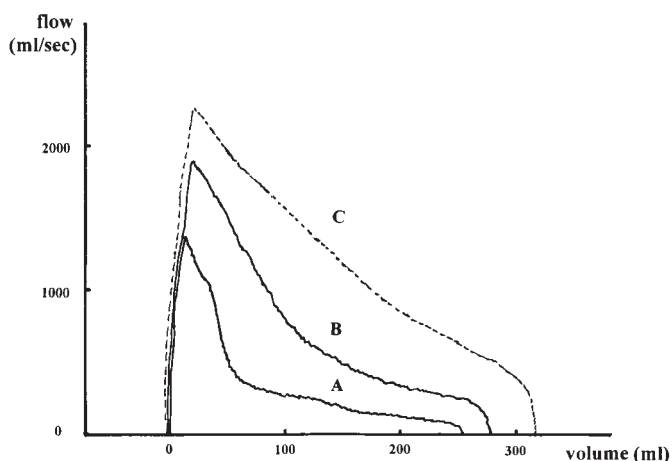


Figure 1. Superimposed forced expiratory flow-volume curves generated from a raised lung volume defined by 3 kPa inflation pressure in Subject 1 at baseline (A) and after salbutamol inhalation (B), and in a normal infant matched for weight and height (C). Concavity of curve A indicates airway obstruction. After salbutamol application a significant increase of flow rates and reduced curvilinearity is observed, but the curve's shape is not completely normalized.

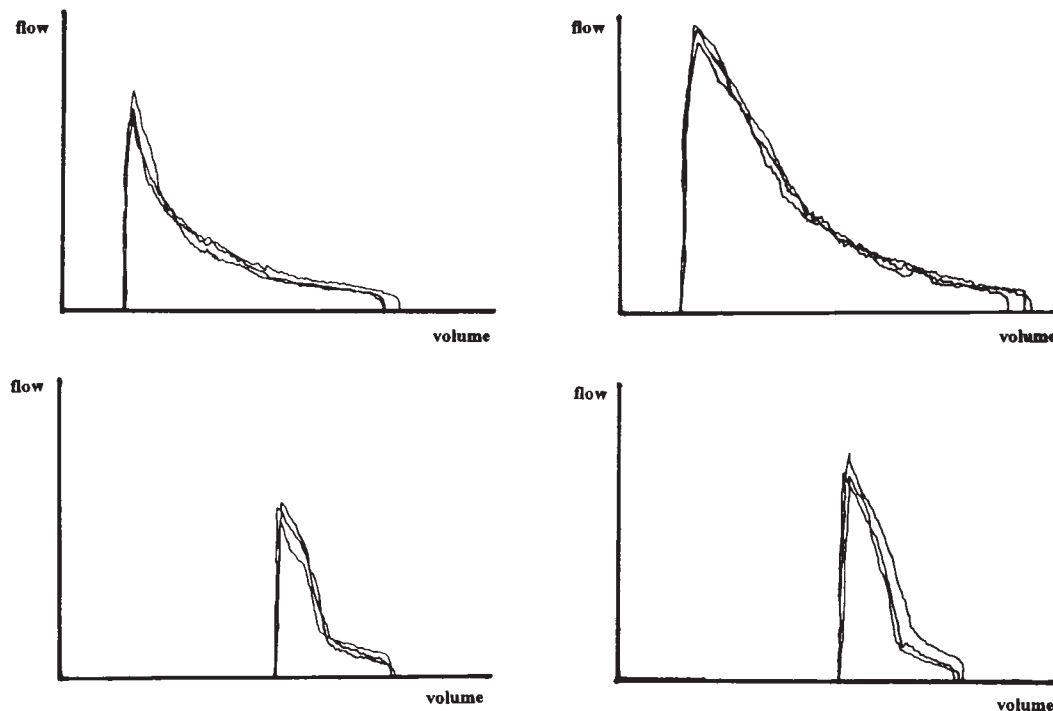


Figure 2. Reproducibility: Three pre- (left) and three postbronchodilator (right) flow-volume curves from Subject 1 are superimposed for the RVRTC (top) and for the ETRTC technique (bottom).

rectional changes of timed volumes (RVRTC technique) are compared with those of $\dot{V}_{\max_{\text{FRC}}}$ (ETRTC technique) in Table 3. As evident, the agreement between timed volumes and $\dot{V}_{\max_{\text{FRC}}}$ was relatively poor. Seven children showed a significant increase in timed volumes while $\dot{V}_{\max_{\text{FRC}}}$ changes remained insignificant. One additional child presented with the combination of significantly increased timed volumes and a significantly decreased $\dot{V}_{\max_{\text{FRC}}}$. In another three, $\dot{V}_{\max_{\text{FRC}}}$ fell significantly, but timed volumes remained unchanged. Five infants failed to show a significant change in any of the obtained measurements; finally, there was one infant who re-

sponded to the bronchodilator medication with both a significant decrease of timed volumes and $\dot{V}_{\max_{\text{FRC}}}$.

Bronchodilator responsiveness did neither correlate with age, nor with gender, clinical severity of the disease, previous history of recurrent wheezing, family history of asthma and allergy, or exposure to cigarette smoke.

DISCUSSION

In the present study airway responses to inhaled salbutamol were evaluated by the conventional ETRTC and by the RVRTC

TABLE 3
DIRECTIONAL BRONCHODILATOR-EFFECTED CHANGES:
COMPARISON OF FEV PARAMETERS AND $\dot{V}_{\max_{\text{FRC}}}$

	$\dot{V}_{\max_{\text{FRC}}}$ Significant Increase	$\dot{V}_{\max_{\text{FRC}}}$ No Significant Change	$\dot{V}_{\max_{\text{FRC}}}$ Significant Decrease
FEV_{0.5}			
Significant increase	—	7 (1, 3, 4, 6, 8, 13, 14)*	1 (2)
No significant change	—	5 (5, 7, 11, 15, 16)	3 (9, 10, 17)
Significant decrease	—	—	1 (12)
FEV_{0.75}			
Significant increase	—	7 (1, 3, 4, 6, 8, 13, 14)	1 (2)
No significant change	—	4 (7, 11, 15, 16)	3 (9, 10, 17)
Significant decrease	—	—	1 (12)
FEV_{1.0}			
Significant increase	—	5 (3, 4, 6, 13, 14)	—
No significant change	—	2 (11, 16)	2 (9, 10)
Significant decrease	—	—	1 (12)

* Numbers in parentheses are subject numbers (Table 1).

technique in infants with acute viral bronchiolitis. The within-subject comparison of responses revealed substantial differences between both techniques; whereas the ETRTC technique suggested no or negative changes, the RVRTC technique showed that approximately half of the subjects improved after bronchodilator. In combination with other methodological advantages of the RVRTC technique over the ETRTC technique (19, 21, 26), this result argues for the raised volume technique being the more sensitive method for the individualized detection of lung function changes in these patients.

In this study most of the subjects failed to show any significant change after salbutamol in $\dot{V}_{\max_{\text{FRC}}}$; a minority demonstrated significantly decreased ETRTC measurements. This result is in agreement with previous studies (8, 11, 14). Despite several basic similarities between the ETRTC and the RVRTC technique, there are three possible explanations for the discrepancies found in the present study. First, there are differences in the intraindividual reproducibility of the obtained lung function measurements; second, one method assesses lung function changes by timed volumes and the other by instantaneous flow rates; and third, lung function measurements are done over different volume ranges.

The intraindividual variability of timed volumes from RVRTC measurements was found to be 5%, and thus significantly lower than the one of $\dot{V}_{\max_{\text{FRC}}}$. These findings are in agreement with recent results obtained in infants with bronchiolitis (21); furthermore, they confirm the findings of previous work (18–24). The higher variability of $\dot{V}_{\max_{\text{FRC}}}$ is most likely a result of the lack of a reliable volume landmark for the measurement. FRC is notoriously unstable in infants; it varies depending on sleep state, degree of sedation, respiratory rate, and changes in airway caliber (30–32). Forced expiratory flow at FRC, therefore, will often be measured at different absolute lung volumes during serial assessments.

Furthermore, FRC will increase as a consequence of progressive airway narrowing. Conversely, bronchodilation will reduce hyperinflation, thereby effecting a decrease in FRC. Airflow will then be measured at a lower lung volume where elastic recoil is reduced and airway resistance is higher. As a consequence, the effect of bronchodilator medication might be disguised and the clinical value of an intervention underestimated. Such mechanisms might explain part of the findings in the present study where the RVRTC technique showed approximately half of the infants to improve after salbutamol, while they failed to show any significant increase of $\dot{V}_{\max_{\text{FRC}}}$. It follows that a significant increase in $\dot{V}_{\max_{\text{FRC}}}$ might be interpreted as indicating bronchodilation; the lack of significant changes, however, does not exclude a beneficial bronchodilator effect.

The finding that significant decreases of $\dot{V}_{\max_{\text{FRC}}}$ can occur concomitantly with unchanged or even significantly increased timed volumes suggests that the effects of bronchodilators on the volume position of FRC might occasionally prevail over a simultaneously occurring decrease in airway resistance. Two other investigations that used a lung deflation technique for evaluation of bronchodilator responsiveness in intubated infants with severe RSV bronchiolitis found significantly increased FVCs in those subjects that responded to salbutamol (25, 33). This suggests that bronchodilators may markedly reduce air trapping in these patients.

In addition, the high intraindividual variability of $\dot{V}_{\max_{\text{FRC}}}$ may also stem from lack of flow limitation when using the ETRTC technique (34). This will make measurements effort or rather compression-dependent and, therefore, more variable. Such lack of flow limitation, however, will more likely be a problem in healthy infants than in patients with airway ob-

struction. Consequently, it might have had a different influence on baseline measurements of $\dot{V}_{\max_{\text{FRC}}}$ than on post-bronchodilation ones. Thus, lack of a significant change in $\dot{V}_{\max_{\text{FRC}}}$, as observed in the majority of children, could also be the result of a flow-limited baseline assessment that was followed by an effort-limited postbronchodilator one. In contrast, the RVRTC technique starts compression maneuvers from a defined lung volume by inflating the lungs to a predetermined airway pressure. As volume history and expiratory effort (compression pressure) are controlled, intraindividual variability of obtained measurements remains relatively small (19, 21). It follows that RVRTC-derived timed volume measurements achieve a degree of quality that is comparable to lung function measurements in older children and adults.

In the present study, jacket pressures that were individually determined by trial runs with the ETRTC technique were also used with the RVRTC technique. This appeared feasible as all individual jacket pressures thus determined were in the range previously recommended for RVRTC measurements (27). Furthermore, transmission of P_j is mainly determined by absolute lung volume; it falls from tidal end inspiration toward FRC, but remains constant above tidal end inspiration (35, 36). In addition, raising P_j s above those determined by ETRTC trial runs does not further increase the resulting timed volume parameters (19).

The ETRTC technique operates in the tidal volume range, and, therefore, assesses pulmonary function only for a small part of the vital capacity. In contrast, the RVRTC technique allows for the registration of FEVs over a markedly extended volume range. These timed volumes are measured earlier in a forced expiration than $\dot{V}_{\max_{\text{FRC}}}$. The site of the maximal bronchodilator effect may vary between different infants; this again might have a different effect on early and late volume and flow measurements, thereby accounting for part of the observed discrepancies between changes in $\dot{V}_{\max_{\text{FRC}}}$ and timed volumes. In addition to a marked shift of FRC, a predominant dilation of large central airways might explain the puzzling finding of one infant responding with increased timed volumes in the presence of a decreased $\dot{V}_{\max_{\text{FRC}}}$. A similar discrepancy between changes of early and late expiratory volumes and flow rates has previously been observed in patients with cystic fibrosis (37).

From a practical perspective there is the question which of the timed volumes should ideally be used for documenting lung function changes. In the present study, $\text{FEV}_{1.0}$ could only be measured in part of the group as some infants tended to inspire before the end of the first second of chest compression. $\text{FEV}_{0.5}$, on the other side, only provides information over a relatively small initial part of the forced expiration. Therefore, $\text{FEV}_{0.75}$ appears as the parameter to be recommended for clinical application; it is characterized by a reasonable compromise between feasibility and volume.

The present study evaluated bronchodilator effects by comparing postbronchodilator lung functions with a series of baseline measurements. This allowed for assessment of individual responses; however, the assessed baseline variability over time does not include a theoretically existing component that might stem from the applied intervention, i.e., the inhalation procedure. We abstained from a placebo run for assessing this component in order not to further prolong an already time-consuming study protocol that was running the risk of premature termination by arousal of the baby.

Although this study was mainly concerned with methodological issues, it also suggests that effective bronchodilation occurred in some infants. A recent study that used the same RVRTC technique for assessing bronchodilator effects in re-

currently wheezing infants could not demonstrate such a positive effect (38). Such results might remain specific for that study population of infants who had a history of wheezing illnesses, but were asymptomatic at the time of lung function testing. With the lung deflation technique, two other investigations found significant positive responses to salbutamol in a majority of subjects with severe viral bronchiolitis (25, 33). Together with the findings of the present study, this suggests that airway smooth muscle constriction contributes to airway narrowing in some infants with viral bronchiolitis and that bronchodilators might have a therapeutic role. As illustrated by one infant, who showed a bronchodilator-effected significant decrease of all timed volumes and of \dot{V}_{maxFRC} , however, some patients might respond in the form of a further increase of airway obstruction. This suggests that such medication should only be used on an individualized basis. The RVRTC technique provides for highly reproducible measurements that distinguish infants with a beneficial bronchodilator effect from those without a significant and those with a paradoxical response. Whether an individualized bronchodilator medication that is guided by RVRTC measurements will have an impact on the clinical course of acute viral bronchiolitis in infants remains to be evaluated in future studies.

In conclusion, this study demonstrates substantial differences between the results of tidal breathing and raised volume rapid thoracoabdominal compression measurements in the assessment of airway responsiveness to salbutamol in infants with bronchiolitis. The RVRTC technique offers considerable methodological advantages over the conventional technique, and, therefore, might be of potential clinical value by providing the investigator with a more sensitive diagnostic tool for documenting the effectiveness of therapeutic interventions on an individual basis.

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