Intensive Care Med (2003) 29:2004–2008
DOI 10.1007/s00134-003-1895-8

Jürg Hammer
Neal Patel
Christopher J. L. Newth

Effect of forced deflation maneuvers upon measurements of respiratory mechanics in ventilated infants

Received: 27 September 2002
Accepted: 3 June 2003
Published online: 25 July 2003

J. Hammer (✉)
Division of Pediatric Intensive Care
and Pulmonology,
University Children's Hospital,
Römergasse 8, 4005 Basel, Switzerland
e-mail: juerg.hammer@unibas.ch
Tel.: +41-61-6856565
Fax: +41-61-6855059

N. Patel · C. J. L. Newth
Division of Critical Care,
Children's Hospital Los Angeles,
University of Southern California,
Los Angeles, Calif., USA

Abstract *Objective:* To determine the effect of forced deflation maneuvers on respiratory mechanics and to assess the reproducibility of such measurements in intubated infants with lung disease. *Design and setting:* Prospective study in the pediatric intensive care unit of a university children's hospital. *Patients:* Ten clinically stable infants requiring mechanically assisted ventilation for acute pulmonary disease, mean age 5.9 months (1–18), mean weight 5.8 kg (3.2–13). *Interventions:* Two sets of measurements of compliance (Crs) and resistance (Rrs) were obtained at 20-min intervals both before and after +40/–40 cmH_2O forced deflation maneuvers. Forced deflation measurements were repeated at the end of the study. *Results:* Forced deflation caused a significant increase in Crs from 0.53±0.09 and 0.58±0.11 $ml/cmH_2O/kg$ to 0.71±0.11 and 0.68±0.11 $ml/cmH_2O/kg$. Rrs measurements did not differ. The low coefficients of variation for repeated measures of the baseline measurements (Crs 4.2±0.5%, Rrs 7.1±0.8%, for forced vital capacity 8.6±2.5%, maximum expiratory flows at 25% vital capacity 16.0%±3.3%) confirmed the good reproducibility during stable conditions. *Conclusions:* Inflation and deflation maneuvers affect subsequent measurements of respiratory system compliance but not measurements of maximum expiratory flow-volume relationships in intubated infants, probably through recruitment of lung volume. Careful interpretation and planning of the sequence of infant pulmonary function testing is necessary to reassure that changes are not related to short-term alterations in volume history.

Keywords Forced expiration · Infant pulmonary function testing · Volume recruitment · Reproducibility · Maximum expiratory flow volume curves

Introduction

Measurements of pulmonary function in intubated and critically ill infants are used to describe and understand the pathophysiology of respiratory failure and to document the beneficial effects of therapeutic interventions. The analysis of maximum expiratory flow-volume relationships is one of the most valuable clinical tests in lung function in general. The forced deflation (FD) technique is regarded as the gold standard in examining maximal flow characteristics in intubated and critically ill infants since it has been demonstrated to produce flow limitation consistently for flows at and below 25% forced vital capacity in intubated infants with normal lungs [1, 2, 3, 4]. The diagnostic value of FD measurements for recognizing flow limitation is particularly useful in assessing therapeutic interventions in severe obstructive airway diseases. The technique has been used in several studies to describe pathophysiological changes and to assess therapeutic interventions such as bronchodilator responsiveness [5, 6, 7, 8, 9, 10, 11]. In this technique the lungs are inflated to total lung capacity (defined as +40 cmH_2O inspiratory pressure), and then the intubated airway is suddenly exposed to negative pressure resulting in rapid lung deflation to residual volume.

Serial measurements of pulmonary function in intubated infants are used to determine the efficacy of therapeutic interventions in the treatment of respiratory disorders or the progression or resolution of respiratory failure. Measurements of respiratory mechanics are generally included in a series of testing maneuvers which may include FD techniques. The need for studies investigating the impact of testing sequences or altered volume history on airway and parenchymal characteristics in ventilated infants has been reported previously [12]. The present study examined whether the FD maneuvers themselves lead to alterations in respiratory mechanics and assessed the variability in results obtained by repeated FD maneuvers upon the individual patient.

Methods

Ten clinically stable infants (mean age 5.9±1.8 months, mean weight 5.8±1.0 kg) requiring mechanically assisted ventilation for acute pulmonary disease were studied at the pediatric intensive care unit at Children's Hospital Los Angeles. All infants were managed using pressure-controlled ventilation. The underlying diagnoses included pneumonia (n=2), bronchopulmonary dysplasia (n=3), bronchiolitis (n=3), acute respiratory distress syndrome (n=1), and absent pulmonary valve syndrome (n=1). All infants were intubated with cuffed endotracheal tubes of 3.5 mm or 4.0 mm internal diameter (Mallinckrodt, Glens Falls, N.Y., USA) [5]. The cuff was inflated to prevent any air leak detectable by auscultation when the lungs were inflated to +40 cmH_2O pressure. The infants were placed supine and the stomach contents were drained via a pediatric nasogastric tube. Sedation was provided by intravenous diazepam (0.1 mg/kg) and/or morphine (0.1 mg/kg). All infants received vecuronium (0.1 mg/kg) for neuromuscular blockade during the testing procedure. Each infant was suctioned for secretions at the beginning of testing and subsequently as necessary. Ventilator settings remained unchanged throughout the study. This study was approved by the Committee on Clinical Investigations of our institution, and informed consent was obtained on behalf of the patients in this study.

Studies consisted of two sets of measurements of respiratory mechanics separated by a 20 min before and two sets of measurements of respiratory mechanics separated by a 20 min after the measurement of four FD maneuvers. A second set of FD measurements was then obtained at the end of the study. The two sets of FD measurements were separated by about 30 min. The period between the different sets was chosen to reflect the timing used in studies to test the effect of inhaled medications such as bronchodilators. All measurements were performed by the same investigator.

Respiratory mechanics were determined using the single-breath occlusion, passive deflation flow-volume technique to document normal total respiratory system resistance (Rrs) and compliance (Crs) [13]. Testing was performed by interrupting a breath close to end-inspiration during mechanical ventilation (SensorMedics 2600 Pediatric Pulmonary System, Yorba Linda, Calif., USA) with the infants under neuromuscular blockade. The resulting passive exhalation to barometric pressure was analyzed for flow, relaxation airway pressure and volume to calculate Crs and Rrs. At least eight curves free of artifact were analyzed per patient and study period; the values were averaged and the data recorded.

Maximum expiratory flow-volume curves were generated by the FD technique [1, 3]. Before and between the deflation the patient was manually ventilated via the side port of a three-way directional sliding valve (Series 8540, Hans Rudolph, Kansas City, Mo., USA) placed at the proximal end of the endotracheal tube by squeezing a 0.5 l Jackson-Rees anesthesia bag filled from a continuous wall oxygen supply. Manual ventilation was controlled by a wall manometer and delivered at approximately the same inspiratory pressures as on mechanical ventilation. FD was initiated by activation of a sliding valve after lung inflation was generated to +40 cmH_2O inspiratory pressure and held static for at least 3 s. Within 50 ms the inflow of gas was occluded, and the infant's airways were opened to a 100-l negative pressure reservoir by a pneumotachograph (Model 4700, Hans Rudolph) linear between 0.01 and 1.7 l/s. The lungs were deflated until expiratory flow ceased or no longer than 3 s. The resulting maximum expiratory flow-volume curves were recorded with a sampling frequency of 256 samples/s utilizing a personal computer-based data acquisition system (Model 2600 Pediatric Pulmonary Cart, SensorMedics, Anaheim, Calif., USA). Four forced deflation maneuvers were analyzed per patient and study period. The values of forced vital capacity (FVC) and maximum flow at 25% vital capacity (MEF_{25}) were averaged and the data recorded. After completion of the FD maneuvers the infants were connected to the ventilator avoiding further recruitment maneuvers by manual ventilation.

The mean, standard error of the mean, and 95% confidence interval were calculated for each patient's measurements of Crs, Rrs, FVC, and MEF_{25}. The between-test coefficient of variation for repeated measurements was calculated for Crs, Rrs, FVC, and MEF_{25} determined in each individual at baseline. The two-sided absolute and relative percentage change in the difference between the initial and the repeated-measurement set were calculated in each patient. The means of this percentage change for all patients with their respective 95% confidence intervals and SE were calculated for each measurement to describe intrapatient variability. To examine the effect of time on repeated measurements of Crs and Rrs and to determine whether there was a significant difference between measurements before and after FD a repeated measures analysis of variance was performed, with a significance level of $p<0.05$. The Bonferroni adjustment was used. The two sets of FD measurements were compared by using the Wilcoxon signed-rank test.

Results

The mean coefficients of variation for repeated measures of the baseline measurements were for 4.2±0.5% Crs, 7.1±0.8% for Rrs, for 8.6±2.5% FVC, and 16.0±3.3% for MEF_{25}. Individual data of measurements of respiratory mechanics and forced expiration at the various time points of the study are presented in Tables 1 and 2, respectively. Figure 1 presents the changes in repeated measurement sets of Crs, Rrs, FVC, and MEF_{25} expressed as the absolute mean ±SE percentage change.

Crs measurements did not differ significantly between the two measurement sets separated by 20 min before and after FD. The FD maneuvers, however, caused a significant increase in mean Crs before FD of 0.53±0.09 and 0.58±0.11 ml/cmH_2O/kg at 0 and 20 min before per-

Table 1 Measurements of respiratory mechanics obtained at different intervals before and after performing inflation and deflation maneuvers to measure maximum expiratory flow-volume curves in intubated children. Crs units: ml cmH_2O^{-1} kg^{-1}; Rrs units: cmH_2O ml^{-1} s^{-1}. Measurements at t_O and t_{20} are separated by 20 min

Patient no.	Before forced deflation*				After forced deflation			
	Crs		Rrs		Crs		Rrs	
	t_0	t_{20}	t_0	t_{20}	t_0	t_{20}	t_0	t_{20}
1	1.19	1.21	0.08	0.08	1.26	1.29	0.09	0.08
2	0.32	0.39	0.18	0.14	0.45	0.43	0.15	0.14
3	0.74	1.04	0.35	0.29	1.25	1.08	0.26	0.33
4	0.23	0.16	0.31	0.51	0.51	0.25	0.36	0.54
5	0.46	0.53	0.09	0.07	0.56	0.59	0.07	0.06
6	0.61	0.59	0.32	0.33	0.88	0.93	0.31	0.29
7	0.74	0.78	0.14	0.14	0.86	0.88	0.12	0.12
8	0.44	0.43	0.21	0.21	0.47	0.42	0.21	0.22
9	0.29	0.31	0.28	0.29	0.40	0.48	0.27	0.22
10	0.29	0.37	0.40	0.37	0.43	0.45	0.53	0.59
Mean	0.53	0.58	0.23	0.24	0.71*	0.68*	0.24	0.26
SE	0.09	0.11	0.04	0.04	0.11	0.11	0.05	0.06

*p<0.05 vs. measurements before forced deflation

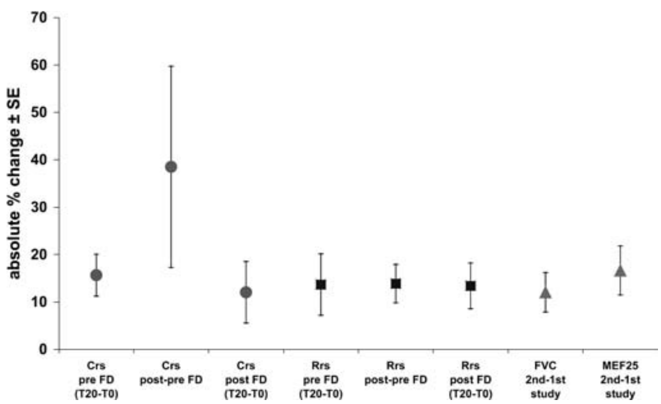

Fig. 1 Changes in respiratory mechanics (Crs, Rrs) and maximum expiratory flow-volume relationships (FVC, MEF_{25}) between measurements separated by 20 min (*T20-T0*) or forced deflation maneuvers (*post-/pre FD*). Data are means ±SE of absolute changes between two consecutive measurements. The mean percentage change of Crs measured in ventilated infants before and after forced deflation was significantly higher than that observed during a 20- to 30-min interval. *FD* Forced deflation technique

Table 2 Measurements of maximum expiratory flow-volume relationships by forced deflation separated by 30 min in intubated infants with lung disease. MEF_{25} units: ml kg^{-1} s^{-1}, FVC units ml kg^{-1}

Patient no.	FVC		MEF_{25}	
	1st study	2nd study	1st study	2nd study
1	59.5	61.9	35.72	53.57
2	17.4	19.5	17.86	21.43
3	49.4	47.5	14.29	14.29
4	25.4	33.5	10.72	7.14
5	20.5	19.0	51.79	57.14
6	41.3	38.3	42.90	42.90
7	30.0	29.5	44.70	50.00
8	22.8	20.7	19.65	21.43
9	8.5	11.9	12.95	12.50
10	12.2	12.6	12.50	8.93
Mean	28.70	29.44	26.31	28.93
SE	5.2	5.1	5.0	6.3

forming FD compared to the mean Crs after FD 0.71±0.11 and 0.68±0.11 ml/cmH_2O/kg at 0 and 20 min (p<0.01, analysis of variance). The relative change in the three Crs measurements sets was 8.3% for Crs_{t20-t0} before FD (95% CI 20.6% to −3.9%), −3.7% for Crs_{t20-t0} after FD (95% CI 8.1% to −15.5%), and much higher for Crs before and after FD by 38.5% (95% CI 80.1% to −3.1%).

Measurements of Rrs did not differ significantly in any of the four sets of measurements and were not affected by the FD maneuvers (p=0.71, analysis of variance). The relative change in the three Rrs measurements sets was low, with 1.3% for Rrs_{t20-t0} before FD (95% CI 16.8% to −14.2%), 5.3% for Rrs_{t20-t0} after FD (95% CI 17.7% to −7.1%), and −1.0% for Rrs before and after FD (95% CI 11.0% to −13.0%).

FVC and MEF_{25} were also not significantly different between the two sets of FD measurements. The relative mean change in FD measurements between the two sets of measurements separated by 30 min was 12.6% for FVC (95% CI 16.8% to −4.4%) and +3.6% for MEF_{25} (95% CI 18.3% to −11.1%).

Discussion

The FD technique for measuring maximum expiratory flow-volume relationships in intubated infants utilizes combined inflation and deflation maneuvers of the lungs. In this study we found that the FD maneuvers cause a significant increase in Crs for as long as 20 min after the testing procedure in intubated and ventilated infants with lung disease. In contrast, serial measurements of Rrs were not altered by the inflation and deflation maneuvers.

The clinical value of physiological measurements as diagnostic tools depends on their reproducibility. We demonstrated that the reproducibility of FD measurements with an absolute mean change of 12% for FVC and 16.6% for MEF_{25} over a 20–30-min period was in a range that should allow detection of clinically relevant changes in flow limitation. No value changed by more than 2 CV of repeated baseline measurements, and all lay either within or marginally outside the 95% CI of the preceding measurements. This finding adds further evidence for the ability of the FD technique to characterize and monitor the pulmonary pathophysiology in pediatric respiratory failure and to assess the benefit of therapeutic interventions. As with recruitment maneuvers there are uncertainties regarding whether forced deflation maneuvers using inflation pressures up to 40 cmH_2O cause stretch injury themselves. Nevertheless, forced deflation maneuvers have been repeatedly and safely used in term infants and children with lung diseases [1, 10, 11]. Likewise, recruitment maneuvers applying sustained pressures of up to 50 cmH_2O at the airway for 30–60 s have been proposed and studied as an adjunct of mechanical ventilation in adult patients with acute respiratory distress syndrome [14, 15]. The technique has never been used, however, in premature neonates, where inflation pressures up to +40 cmH_2O might be more hazardous.

Measurements of respiratory mechanics showed a similar intrapatient variability with a mean relative change in the range of 15% for Crs and Rrs over 20–30 min with stable conditions and without interventions. There are patient-related factors contributing to the variability in pulmonary function measurements in intubated infants: position of the infant, depth of sedation and neuromuscular blockade, tube position, and the presence of secretions. In the present study efforts were made to control these variables. Other factors may be related to the equipment itself, such as the frequency response of the transducers, a potential phase shift between the flow and pressure signals, a drift in calibration values, and the rate of digitization. We are unable to comment on the potential impact of technical factors related to the equipment. Gonzales et al. [16] have previously demonstrated that the reproducibility of respiratory mechanics measurements is better in mechanically ventilated infants (in the range of our results) than in spontaneously breathing infants. Similarly, we have previously suggested defining a clinically significant change in respiratory mechanics in ventilated infants as a change of more than 4 CV rather than 2 CV from repeated baseline measurements [17]. This was based on our findings that the range of measurements of respiratory mechanics under conditions of neuromuscular blockade with controlled mechanical ventilation, sedation, and intubation with a cuffed endotracheal tube is about one-half that reported in spontaneously breathing infants [18].

In contrast, the mean relative change in Crs was significantly higher (in the range of 40%) when FD maneuvers were performed between the measurements. Our study was designed to exclude that possibility that improvement in Crs is due to improvement over time rather than to the FD maneuver itself. The observed increase in Crs may be due to a change in lung volume secondary to recruitment of atelectatic lung units, reopening of collapsing small airways, or changes in bronchomotor tone induced by inflating the lungs to total lung capacity prior to deflation [19]. In newborn infants Ratjen and colleagues [20] found that Crs measured at volumes above the tidal volume was consistently greater than Crs measured during tidal breathing. They related this finding to recruitment of lung units that are closed or atelectatic in the tidal volume range. It has also been demonstrated that sighs up to 40 cmH_20 inspiratory pressure cause an increase in Crs in adult patients with acute respiratory distress syndrome [21]. The deflation maneuver alone is expected to affect respiratory mechanics in the opposite manner, analogously to the effect of endotracheal suctioning, and cause bronchoconstriction, an increase in lung tissue resistance, and atelectasis. Such effects, however, are easily reversed by performing a recruitment maneuver after suctioning, as previously demonstrated by others [22, 23]. Our data suggest that inflating the lungs to total lung capacity before the FD maneuvers not only prevents or offsets possible adverse effects on respiratory mechanics caused by applying negative pressure to the airways but also recruits previously collapsed lung units in anesthetized and intubated children with lung disease. This effect may be less pronounced in intubated children with healthy lungs.

Platzker et al. [24] have recently demonstrated that the rapid thoracoabdominal compression technique, another method used to produce a forced expiratory maneuver in uncooperative infants, causes a temporary decrease in Crs that is more pronounced in children with abnormal lung function. They hypothesized that the decrease in Crs measured in infants who were asleep and breathing spontaneously was a result of atelectasis induced by forceful deformation of the chest and abdominal wall by the squeeze jacket. They emphasized that the sequence of performing the infant lung function testing has important implications on the measured parameters. Although our study is limited by the small number of subjects studied and the heterogeneity of their lung disease, our data support the notion that the testing sequence should be the same each time that the testing is repeated, with the forced expiratory maneuver being the last test of the sequence. All our study patients demonstrated mixed restrictive and obstructive alterations in respiratory mechanics adequately described by a linear one-compartment model as commonly found in children requiring assisted ventilation for respiratory failure. Nevertheless, forced deflation maneuvers might have a different effect in children with purely obstructive pulmonary disease (e.g., a decrease in Crs due to reflex bronchoconstriction) or with normal lungs. We doubt, however, that studying a larger cohort of patients would have changed our conclusions.

In conclusion, our study demonstrates that the inflation and deflation maneuvers used to study maximum expiratory flow-volume relationships in intubated infants are very reproducible over time but affect subsequent measurements of respiratory system compliance. The results of this study suggest that careful interpretation and planning of the sequence of infant pulmonary function testing is necessary to assure that changes in lung function are not related to short-term alterations in volume history but reflect changes related to therapeutic interventions or alterations in the disease process.

References

1. Motoyama EK (1977) Pulmonary mechanics during early postnatal years. Pediatr Res 11:220–223
2. Hammer J, Newth CJL (1996) Effort and volume dependence of forced deflation flow-volume relationships in intubated infants. J Appl Physiol 80:345–350
3. Hammer J (1997) Forced expiratory flow analysis in infants and preschool children. In: Carlsen CH, Sennhauser F, Warner JO, Zach MS (eds) New diagnostic techniques in paediatric respiratory medicine. Eur Respir Monit 5:1–26
4. Hammer J, Newth CJL (1997) Influence of endotracheal tube diameter on forced deflation flow-volume curves in rhesus monkeys. Eur Respir J 10:1870–1873
5. Hammer J, Numa A, Newth CJL (1997) Acute respiratory distress syndrome induced by respiratory syncytial virus. Pediatr Pulmonol 23:176–183
6. Newth CJL, Stretton M, Deakers TW, Hammer J (1997) Assessment of pulmonary function in the early phase of ARDS in pediatric patients. Pediatr Pulmonol 23:169–175
7. Hammer J, Numa A, Newth CJL (1995) Albuterol responsiveness in infants with respiratory failure due to RSV infection. J Pediatr 127:485–490
8. Mallory GB, Motoyama AK, Koumbourlis AC, Mutich RL, Nakayama DK (1989) Bronchial reactivity in infants in acute respiratory failure with viral bronchiolitis. Pediatr Pulmonol 6:253–259
9. Motoyama EK, Fort MD, Klesh KW, Mutich RL, Guthrie RD (1987) Early onset of airway reactivity in premature infants with bronchopulmonary dysplasia. Am Rev Respir Dis 136:50–57
10. Koumbourlis AC, Mutich RL, Motoyama EK (1995) Contribution of airway hyperresponsiveness to lower airway obstruction after extracorporeal membrane oxygenation for meconium aspiration syndrome. Crit Care Med 23:749–754
11. Mallory GB, Chaney H, Mutich RL, Motoyama EK (1991) Longitudinal changes in lung function during the first three years of premature infants with moderate to severe bronchopulmonary dysplasia. Pediatr Pulmonol 11:8–14
12. American Thoracic Society/European Respiratory Society (1993) Respiratory mechanics in infants: physiologic evaluation in health and disease. Am Rev Respir Dis 147:474–496
13. LeSouëf PN, England SJ, Bryan AC (1984) Passive respiratory mechanics in newborns and children. Am Rev Respir Dis 129:727–729
14. Villagra A, Ochagavia A, Vatua S, Murias G, Del Mar Fernandez M, Lopez Aguilar J, Fernandez R, Blanch L (2002) Recruitment manoeuvres during lung protective ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 165:165–170
15. Grasso S, Mascia L, Del Turco M, Malacarne P, Giunta F, Brochard L, Slutsky A, Ranieri V (2002) Effects of recruiting maneuvers in patients with acute respiratory distress syndrome ventilated with protective ventilatory strategy. Anesthesiology 96:795–802
16. Gonzales A, Tortorolo L, Gerhardt T, Rojas M, Everett R, Bancalari E (1996) Intrasubject variability of repeated pulmonary function measurements in preterm ventilated infants. Pediatr Pulmonol 21:35–41
17. Patel NR, Hammer J, Nichani S, Numa A, Newth CJL (1999) Effect of inhaled nitric oxide on respiratory mechanics in ventilated infants with RSV bronchiolitis. Intensive Care Med 25:81–87
18. Sly PD, Lanteri CJ, Raven JM (1991) Do wheezy infants recovering from bronchiolitis respond to salbutamol? Pediatr Pulmonol 10:36–39
19. Markstrom A, Hedlund A, Sjostrand U, Nordgren A, Lichtwarck-Aschoff M (2001) Effects of sustained pressure application on compliance and blood gases in healthy porcine lungs. Acta Anaesthesiol Scand 45:1235–1240
20. Ratjen F, Zinman R, Stark AR, Leszczynski LE, Wohl ME (1989) Effect of changes in lung volume on respiratory system compliance in newborn infants. J Appl Physiol 67:1192–1197
21. Lim CM, Koh Y, Park W, Chin JY, Shim TS, Lee SD, Kim WS, Kim DS, Kim WD (2001) Mechanistic scheme and effect of "extended sigh" as a recruitment maneuver in patients with acute respiratory distress syndrome: a preliminary study. Crit Care Med 29:1255–1260
22. Lu Q, Capderou A, Cluzel P, Mourgeon E, Abdennour L, Law-Koune JD, Straus C, Grenier P, Zelter M, Rouby JJ (2000) A computed tomographic scan assessment of endotracheal suctioning-induced bronchoconstriction in ventilated sheep. Am J Respir Crit Care Med 162:1898–1904
23. Sigurdsson S, Svantesson C, Larsson A, Jonson B (2000) Elastic pressure-volume curves indicate derecruitment after a single deep expiration in anaesthetised and muscle-relaxed healthy man. Acta Anaesthesiol Scand 44:980–984
24. Platzker AC, Colin AA, Chen XC, Hiatt P, Hunter J, Koumbourlis AC, Schluchter MD, Ting A, Wohl ME (2000) Thoracoabdominal compression and respiratory system compliance in HIV-infected infants. Am J Respir Crit Care Med 161:1567–1571