SPECIAL ARTICLE

Advances in the Study of Lung Function in Infants: Forced Expiratory Maneuvers From an Increased Lung Volume

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Forced expiratory maneuvers from an increased lung volume in infants date from 1989 and consist of raising the inspiratory volume by applying a specific inflation pressure until a level close to the total lung capacity is reached. The chest and abdomen are then compressed by means of an inflatable jacket in order to obtain a forced expiratory flow–volume curve similar to that obtained for an adult. Forced expiration from an increased lung volume in infants is useful, just as the maneuver is in older patients, for studying airway function, diagnosing obstructive diseases early, and assessing response to treatment.

The objective of this review is to provide information on the physiological bases and technical aspects of a lung function test that has proven highly useful for the study of the airways of healthy infants as well as those with respiratory diseases.

Key words: *Infant lung function. Forced expiration. Raised lung volume.*

Avances en el estudio de la función pulmonar en lactantes: maniobras de espiración forzada con volumen pulmonar aumentado

En el lactante, las maniobras de espiración forzada desde un volumen pulmonar aumentado datan de 1989 y consisten en aumentar el volumen inspiratorio mediante la aplicación de una presión de inflación determinada, hasta un nivel cercano a la capacidad pulmonar total, para posteriormente proceder a una compresión toracoabdominal mediante la aplicación de una chaqueta inflable, con el fin de obtener una curva espiratoria forzada semejante a la obtenida en el adulto. La espiración forzada desde volúmenes pulmonares aumentados en el lactante, al igual que en sujetos mayores, es útil para el estudio funcional de la vía aérea, pues permite diagnosticar precozmente enfermedades obstructivas y evaluar su respuesta al tratamiento.

El objetivo de la presente revisión es dar a conocer las bases fisiológicas y los aspectos técnicos de uno de los exámenes de función pulmonar de mayor utilidad en el estudio de la vía aérea del lactante sano y patológico.

Palabras clave: *Función pulmonar en lactantes. Espiración forzada. Volúmenes pulmonares aumentados.*

Introduction

The forced vital capacity (FVC) maneuver was first used in 1947 to measure forced expiratory flow in adults.[1] Since then, spirometry has become the most commonly used method for studying lung function in older children and adults. FVC maneuvers from a volume close to total lung capacity have been possible in infants under the age of 2 years for some years thanks to the advent of the raised volume rapid thoracoabdominal compression (RVRTC) technique.

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Forced expiratory flow in infants is mainly obtained by means of such rapid compression, which consists of applying positive pressure to the thoracoabdominal region at the end of inspiration. Over the past 20 years, forced expiration has been achieved using thoracoabdominal compression in the tidal volume range, with measurement of the maximum forced expiratory flow at the level of functional residual capacity (FRC) in order to obtain a parameter known as maximal flow at FRC (V_{max}FRC).[2-4]

An important advance of recent years is the introduction of a raised lung volume in this compression technique. In RVRTC, a predetermined positive pressure is applied to the airways as inspiration commences, in order to raise the inspiratory lung volume above the tidal volume range to levels close to total lung capacity. Compression is then applied immediately to obtain a complete flow-volume

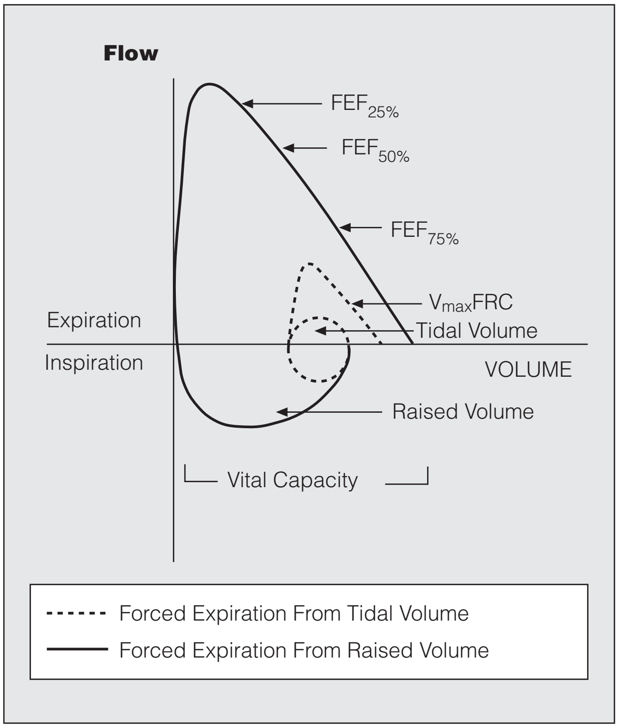

Figure 1. Parameters obtained from forced expiration curves in an infant. $FEF_{25\%}$, $FEF_{50\%}$, and $FEF_{75\%}$ indicate forced expiratory flow at 25%, 50%, and 75%, respectively, of forced vital capacity and $V_{max}FRC$, maximal flow at functional residual capacity.

curve.[5-10] In the RVRTC technique, the volumes used range from FRC to close to total lung capacity. Both give highly reproducible measurements and serve as excellent points of reference. The main parameters obtained with this technique are forced expiratory volumes in specific periods of time, measured in seconds ($FEV_{0.4}$, $FEV_{0.5}$, $FEV_{0.75}$, or FEV_1), and forced expiratory flows (FEF) as a percentage of FVC ($FEF_{25\%}$, $FEF_{50\%}$, or $FEF_{75\%}$). The values for these parameters are similar to those of spirometric curves in adults (Figure 1).

Physiological Basis

Due to the high compliance of the chest wall in infants, FRC should only be 10% of total lung capacity, a level which is incompatible with adequate stability of the peripheral airways and thus with correct gas exchange. Infants therefore require a number of breathing strategies to maintain their FRC above the passively determined level (dynamic FRC).[11-13] The result is that FRC values reach approximately 40% of total lung capacity and this means that during tidal volume the infant inspires before passive expiration has ended.[14,15]

To perform a forced expiratory maneuver without the infant inspiring before the end of expiration, a short apnea must be induced. This can be achieved by mechanical hyperventilation (a drop in $PaCO_2$) and by stimulating the pulmonary stretch receptors (Hering-Breuer reflex). This will cause a short interruption of breathing effort. This apnea, during which the respiratory system is relaxed, is long enough to perform a maximum expiratory flow-volume maneuver without the infant generating inspiratory effort during the forced expiration.[16]

Description of the RVRTC Procedure

In our lung function laboratory, the RVRTC maneuvers are performed with multiple inflations, in accordance with the standardized guidelines of the European Respiratory Society and the American Thoracic Society.[17-20] The infant is first sedated with chloral hydrate (70-100 mg/kg) and an inflatable device is then placed around the anterior part of the trunk (from the sternal manubrium to the pubic symphysis), covered by a jacket of nonexpanding material. Once the infant is asleep, the measuring equipment is connected via a mask attached to the pneumotachograph. An automatic device applies a pressure of 30 cm H_2O to the infant's lungs, in phase with spontaneous inspiration, causing an increase in inspiratory volume (V_{30}). The pressure is then released to allow passive expiration. This inflation maneuver is repeated several times (generally from 1 to 10 times) until apnea occurs and then the infant's lungs are once again inflated to V_{30}. When this inspiratory volume has been reached, the valve connecting the inflatable jacket to the pressure source is opened to inflate the jacket to a predetermined pressure and produce a forced expiration that ends when residual volume is reached. When the expiratory flow reaches zero, compression is removed and spontaneous breathing resumes. The jacket pressure is increased progressively in intervals of 5 to 10 cm H_2O until no further increase in flow is achieved at higher jacket pressures. At this point, the measurements reflecting flow limitation are considered to have been obtained and the best curve will be the technically acceptable one where the highest flow values were achieved with the lowest jacket pressure.[16]

The acceptability criteria used in our laboratory are the following: *a)* maximal flow reached during the initial portion of the curve; *b)* an appropriate, regular, and gentle flow-volume curve; *c)* expiration without inspiratory effort toward the end of the curve; and *d)* clearly identifiable apnea. Figure 2 shows the shape and reproducibility of the curve obtained using the RVRTC technique at V_{30}. The parameters are similar to those of spirometry in older children and adults: FVC, $FEV_{0.4}$, $FEV_{0.5}$, $FEF_{50\%}$, $FEF_{75\%}$, $FEF_{85\%}$, and $FEF_{25\%-75\%}$. Both the normative data and the prediction equations for lung function spirometry were recently published for this technique in infants.[21]The most useful, least variable, and most commonly described parameters are FVC, $FEV_{0.5}$, $FEF_{75\%}$, and $FEF_{25\%-75\%}$. Due to the speed with which the lungs empty in infants under 3 months, $FEV_{0.4}$ should be recorded since measurements beyond 0.5 seconds are often not obtainable.

There are several potential sources of variability in lung function maneuvers performed on infants. They include changes in neck position, the face mask support, and the way the inflatable jacket is placed.[22] A simple change in the infant's position while measuring maximal flow at FRC can increase variability from 10% to 18.2%,[23] and airway pressure can cause significant differences in absolute values of FVC, $FEV_{0.5}$, and $FEF_{75\%}$.[24]

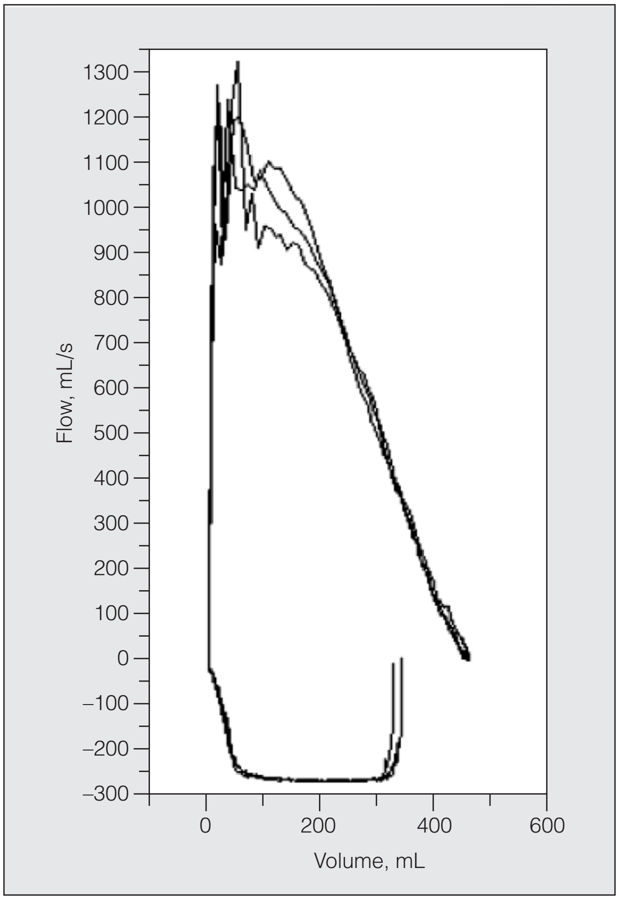

Figure 2. Shape and reproducibility of flow-volume curves (lung volume with an inflation pressure of 30 cm H_2O) in the same infant.

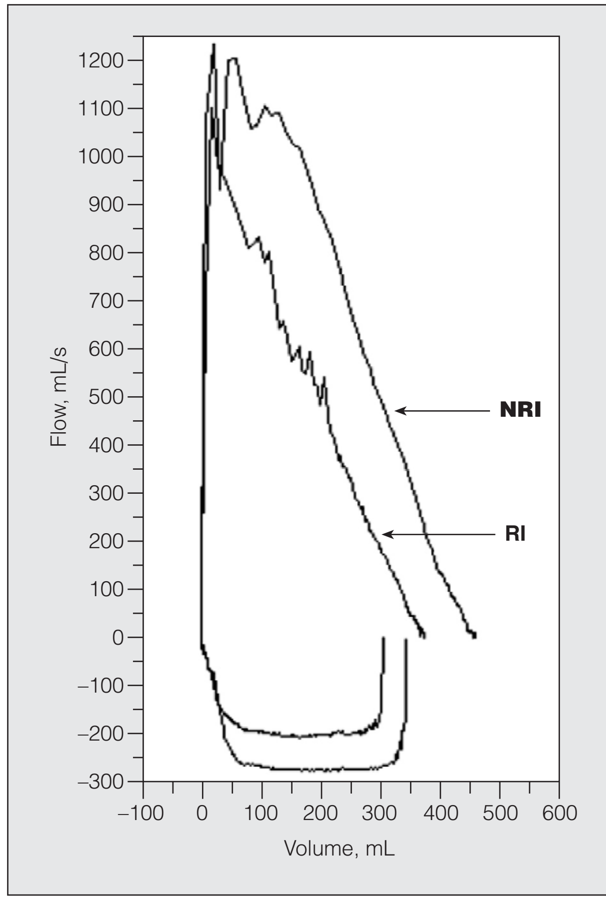

Figure 3. Curves for the same patient with a respiratory infection (RI) and no respiratory infection (NRI), with a lapse of 1 month.

Another source of variability is the level of sedation of the infant during measurement, and significant respiratory depression has been described in infants with wheezes who were recovering from bronchiolitis.[25] This has led to recommendations that the measurements be properly standardized,[26,27] that they be taken by properly trained personnel, and that minimal changes in conditions occur during the tests. Furthermore, each laboratory should provide detailed information on the technique used and its variability.[28]

Indications for Forced Expiration Measurements in Infants

Although lung function tests in children under 2 years of age have been used mainly for research purposes, they have gained increasing importance in the clinical management of patients in recent years. Wildhaber et al[29] showed that measurements taken with the RVRTC technique had an advantage over measurements taken at tidal volumes when evaluating and monitoring obstructive lung disease. A recent study by Jones et al[30] of infants with recurring wheezes that might be either symptomatic or asymptomatic upon examination showed RVRTC to be useful in identifying infants with bronchial obstruction at the time of examination and in distinguishing healthy infants from patients with wheezes. Our findings in infants with recurring wheezes are consistent with those reports. Figure 3 shows the curves of the same patient with and without acute respiratory symptoms at the time measurements were taken.

Early abnormalities in the airways of infants with cystic fibrosis,[31-34] reduced lung function in healthy infants exposed to secondhand tobacco smoke,[35,36] and airway obstruction with no bronchodilator effect in infants with wheezes who did not respond to asthma treatment[37] have all recently been described based on forced expiration measurements (at V_{30} and V_{max}FRC). RVRTC has also made it possible to objectively evaluate bronchial reactivity in healthy patients and patients with recurring wheezes[38] and the short- and long-term effects of drugs commonly used in obstructive bronchial diseases in infants, such as bronchodilators and inhaled corticosteroids.[39-41] Figures 4 and 5 show the different curve shapes of 2 patients with recurrent or permanent wheezes; one with a positive response to salbutamol and the other with nonresponsive bronchopulmonary dysplasia. Figure 6 shows the differences in the lung function of an infant with recurrent wheezes during an acute viral respiratory infection and the measurements taken a month later during an

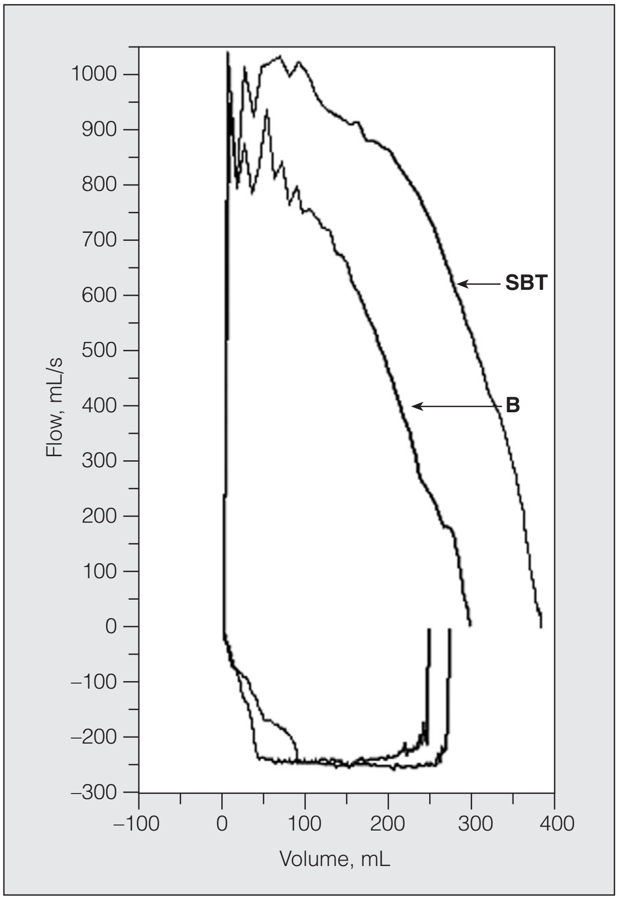

Figure 4. Bronchodilator effect in an asthmatic infant: baseline (B) and with 400 µg salbutamol (SBT).

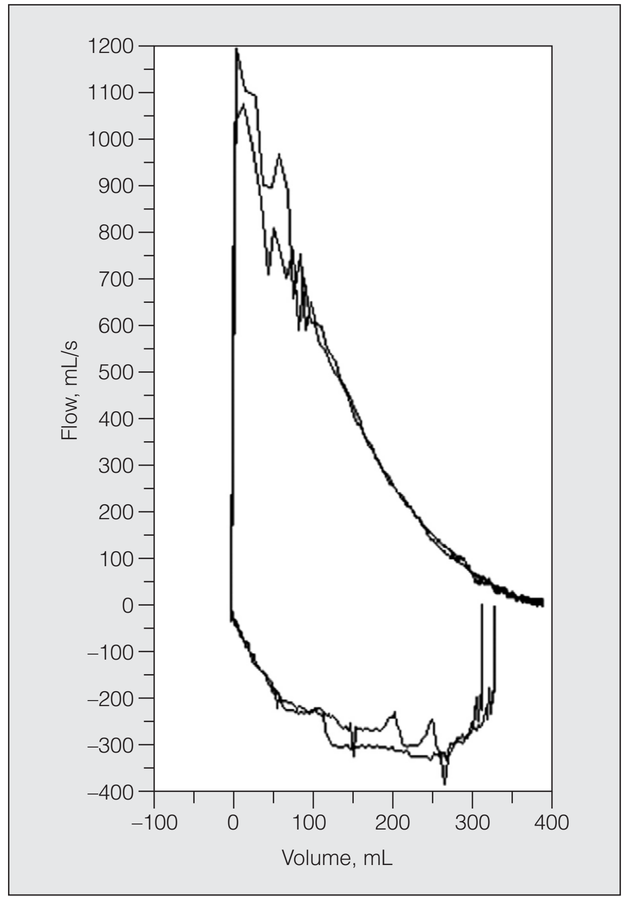

Figure 5. Absence of bronchodilator effect in an infant with bronchopulmonary dysplasia (superimposition of baseline curve and curve with salbutamol).

asymptomatic period. The figure also shows the partial bronchodilator effect of the salbutamol on the obstruction that occurred during the viral infection. Finally, this technique has allowed us to broaden our knowledge on lung development and growth in this age group and has confirmed the dissociation in the growth patterns of the airways and the lung parenchyma in the first years of life.[21,42]

The RVRTC technique will make it possible to study the effect on lung function of certain events that occur in early life (smoking during pregnancy, neonatal respiratory diseases, environmental pollution, altitude, mechanical ventilation, etc) and to evaluate factors that determine lung function (growth, age, sex, race, body size, and a family history of allergy). It will facilitate making and evaluating treatment decisions, early diagnosis of disease, identification of iatrogenic harm, determination of the type and severity of a lung disorder, and evaluation of the reactivity of the airways in different diseases. As with all new techniques, however, RVRTC has its limitations and the scope of its usefulness needs to be shown through more comparative studies to provide better knowledge of its role in the clinical management of patients under the age of 2 years with respiratory diseases.[43]

The close similarity between this technique and spirometry in older children and adults makes it one of the most promising lung function tests for infants. RVRTC is a real step forward for evaluating and following up lung function in infants under the age of 2 years, both in research and clinical practice.

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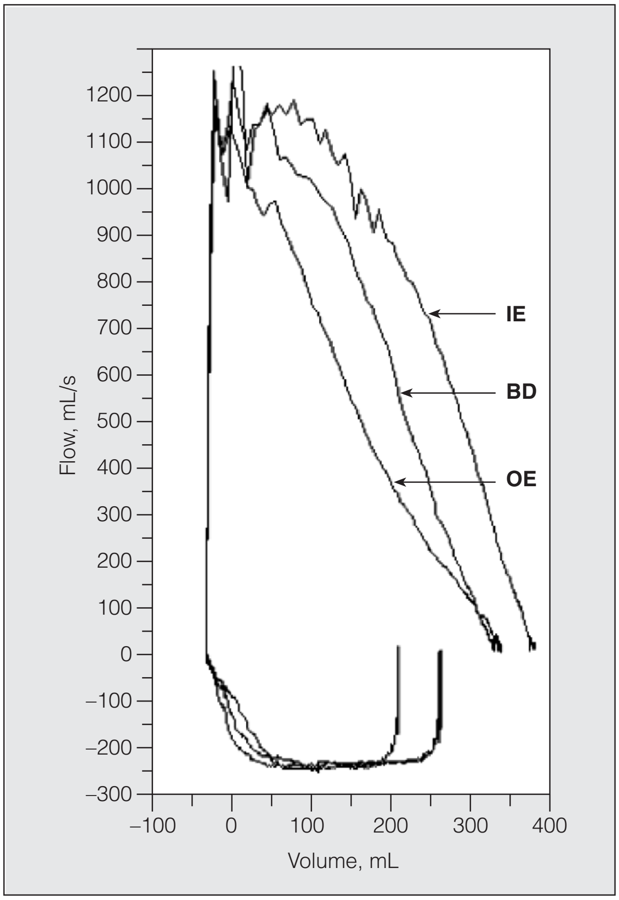

Figure 6. Infant with recurrent wheezes during an obstructive episode (OE), with bronchodilator effect during the episode (BD) and the interepisode curve (IE)

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