Lung function during infancy and preschool age

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Educational aims

- To analyse lung function techniques developed for preschool children and infants.
- To compare lung function techniques used in adults and children.
- To discuss the possibility of using equipment from childhood through to adulthood.

Summary

Measurements of pulmonary function are among the most important measurements in respiratory medicine, both in clinical and research work. Despite the rapid technological development during recent decades, we still struggle with a major obstacle in understanding the natural history of the lungs and airways; namely our inability to use one method and one piece of equipment from birth through childhood to adulthood.
Thus, various methods measuring, at best, approximations of similar mechanical or physical properties within the lungs and airways will have to be compared at different time-points to the best of our abilities. Recent studies have begun to report extensive work from many research groups addressing the acceptability and reproducibility of spirometry among preschool children.

The latest American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines [1] conclude that criteria for successful pulmonary function measurements in adults were inappropriate in preschool children, that two acceptable manoeuvres are sufficient and that forced expiratory volume in 0.5 s ($FEV_{0.5}$), as well as 0.75 s ($FEV_{0.75}$), should be reported rather than FEV in 1 s (FEV_1). Furthermore, the normal variation of FEV_1 has been reported to be up to 5% within a day and up to 12% from week to week in healthy adults [2]. This illustrates the problems of comparing results obtained by different methods at different time-points. There are a multitude of different techniques but most are dependent upon the co-operation of the patient. Because of this, special techniques to measure lung function have been developed for infants and preschool children, either using techniques not requiring co-operation (other than quiet breathing), or requiring a normally sleeping or sedated child or infant. The descriptions of the techniques listed below are necessarily very superficial and cannot give full justification to the different techniques described, or to the high-quality research through which these complex techniques have been developed. Instead, for further in-depth reading on this subject I refer you to two excellent books on this topic [3, 4].

In 1936, Deming and Hanner [5] described the first attempts to measure lung function by "crying vital capacity". The first report on the varying shape of the tidal breathing flow–volume loop appeared in 1957 [6]. Other lung function techniques in infants and preschool children have been developed gradually over time in accordance with developments in technology and computer science.

In infants and preschool children co-operation with the techniques is difficult to obtain. Many of the techniques used in older patients have been modified and applied in infants and preschool children. However, most techniques

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of measuring lung function in this age group may be dependent upon natural sleep (in the infant) or upon sedation. However, some types of measurement may be performed with the child breathing quietly without sedation in the awake state [7].

Tidal breathing

Tidal breathing measurements include measurements of flow, volume and time during regular tidal breathing. Quiet breathing is a condition for performing non-interventional tidal breathing measurements, but measurements may be obtained regardless of respiratory or arousal state. Measurements may be performed in both in- and outpatient settings, but are dependent upon carefully trained staff.

Various indices in the tidal breathing flow–volume loop have been demonstrated to be useful scientifically in an epidemiological setting and have been performed in a large number of newborns and young children. The parameter calculated from the tidal breathing flow–volume loop, time from start of expiration to peak expiratory flow divided by total expiratory flow, has been demonstrated to reflect airway obstruction and reversibility to bronchodilators in adults [8], as well as young children and infants [9, 10]. The shape of the tidal breathing flow–volume loop has been demonstrated to reflect various airway disorders and can give a diagnosis of the level of obstruction. Tidal breathing measurements are dependent upon a quietly breathing child and have been shown to have a greater variability in a healthy child than in a child with respiratory illness; however, the variability is usually found to be acceptable [11]. Some important findings have resulted from studies on tidal breathing. This includes the impact of parents smoking during pregnancy in the newborn child [12], including affecting lung function in premature children [13], as well as the role of lung function measured by tidal breathing parameters at birth in predicting later asthma and bronchial hyperresponsiveness at the age of 10 yrs [14].

Respiratory inductive plethysmography

Respiratory inductive plethysmography (RIP) also reflects tidal breathing and makes use of a mask and pneumotachograph superfluous. RIP consists of two sensors placed in bands around the rib cage and the abdomen which are connected to an oscillator circuit. Changes in tidal volume may be detected by changes in these two volume compartments: minute ventilation, respiratory rate and inspiratory time/expiratory time, as well as measurements of tidal flow–volume loops, may be obtained by this technique. By using computerised techniques, calibration of this technique has been simplified and the technique may be used in monitoring life-threatening events in the newborn, such as apnoeas and registration of tidal breathing flow indices. Commercial equipment is currently available for these measurements. By using Respitrace® (Non-invasive Monitoring Systems, Inc., North Bay Village, FL, USA), Stick *et al.* [15] confirmed the findings of tidal breathing measurements in relation to parents smoking during pregnancy related to lung function in the newborn child.

Passive respiratory mechanics

Passive respiratory mechanics can be determined by simultaneously measuring airflow, volume and airway pressure in the absence of respiratory muscle activity. By briefly occluding the infant's airway during expiration, the Hering Breuer inflation reflex may be induced, obtaining a short respiratory pause with a relaxed airway pressure plateau. By occlusion at end-inspiration, a passive expiratory flow–volume loop may be obtained enabling the measurement of time constant, compliance of the total respiratory system and calculating the resistance of the total respiratory system. Olinsky *et al.* [16] were the first to employ this technique. Both single-occlusion and multiple-occlusion techniques are available. Passive respiratory mechanics have been measured in healthy and sick infants in mechanistic studies to increase knowledge about basic respiratory physiology, as well as to predict outcomes in epidemiological studies [17]. In addition, passive respiratory mechanics have confirmed the findings in tidal flow–loops from birth to 10 yrs of age with respect to lung function at birth compared with asthma and bronchial hyperresponsiveness at 10 yrs of age [14]. The standards of the technique have been set by a joint ERS/ATS Task Force [18].

Infant body plethysmography

The same principle as for whole body plethysmography in adults may be used in infants for the assessment of forced residual capacity (FRC) and airway resistance. Because of the small size of the infant and the small lung volume, a small plethysmograph as well as sensitive measuring equipment is needed. This technique has been restricted to highly specialised centres as the equipment is complex and requires considerable operator training. As standards have been developed and published for this technique, it may become more commonly used [19]. For preterm babies and infants, plethysmograph sizes of 50–60 L are optimal, whereas plethysmographs of 100 L may be used in older infants and young children. Infant body plethysmography usually depends upon sedating the infant. Infant body plethysmographs are available commercially and are mainly used for research purposes. It should be maintained that the equipment is complex and that attention to detail in the technique and measurements, as well as considerable training, is required for reliable measurements [20].

Partially forced expiratory flow–volume curves: rapid thoracic compression techniques

This technique is widely used as a practical noninvasive technique for measuring airway physiology in healthy and diseased infants. An inflatable jacket is used which encircles the chest and abdomen of the infant. At end inspiration the jacket is inflated to force expiration during tidal breathing, thus enabling the registration of a partially forced expiratory flow–volume loop through a pneumotachograph. The maximal flow at FRC is then determined. The technique was developed by the pioneers of paediatric respiratory medicine, L. Taussig, L. Landau and S. Godfrey and first described in 1977 [21, 22]. The disadvantage of this technique is the possible variability of FRC and the need for sedation of the infant. The technique has been widely used to assess normal growth and development of the respiratory system [23], lung function in various disease states such as recurrent infant wheeze [24, 25], cystic fibrosis, chronic lung disease in the newborn [26], bronchial responsiveness to pharmacological substances (such as histamine, methacholine [27, 28] or to cold air) and the response to bronchodilators [29]. This technique has also been used to assess the relationship between infant lung function and lung function at the age of 22 yrs [30].

To improve the reproducibility of this technique various modifications have been made, including increased volume forced expiration, multiple inflations prior to the forced expiration and negative pressure forced deflation (in intubated heavily sedated infants) [31]. The rapid thoracic compression technique with modifications is the most commonly used technique in assessing infant lung function. The technique requires careful monitoring of the child, careful assessment of the clinical condition of the child and expertise in performance of the technique. Several commercial systems are available for this type of measurement.

Respiratory resistance by interrupter technique

This technique is used in quietly breathing, awake preschool children and is a noninvasive technique of measuring airway resistance that requires minimal patient co-operation. The interrupter resistance (R_{int}) is calculated from pressure and flow following a brief interruption of expiration during quiet breathing. The method is inexpensive and does not require sedation. The sensitivity has been demonstrated to be acceptable [32] and the method has been used to assess bronchodilator response [33] and bronchial responsiveness [34] in various respiratory disorders, particularly recurrent wheeze in preschool children. Reference values have been obtained in children aged 2–7 yrs [35]. The method is commercially available.

Forced oscillation techniques

The forced oscillation technique is noninvasive and requires little co-operation. The technique determines the impedance of the total respiratory system by applying sinusoidal pressure variations generated through a loudspeaker to the respiratory system and measuring the resulting flow. Multiple frequencies can be applied simultaneously. The impedance (the relationship between pressure variations and flow variations) is expressed through amplitude ratio and phase shift of pressure and flow signals. The calculation of impedance is performed using Fourier transformation. The results may be influenced by upper airway properties, which may be corrected by applying pressure around the head [36]. The technique can be used at all ages, and has been employed to study airway obstruction [37], bronchodilation [37] and bronchial responsiveness [34, 38]. The technique has also been used in the assessment of allergen provocation [39]. A comparison of the forced oscillation technique with the interrupter technique (R_{int}) favoured the forced oscillation technique for detecting airways obstruction and its reversibility [40]. Modifications to the technique have been applied. One of these has been called the impulse oscillation technique. In one study the impulse oscillation technique was also found to be more sensitive when compared with the R_{int} method in asthmatic and also healthy preschool children [41].

Systems for the use of the forced oscillation technique and the impulse oscillation technique are available commercially.

Spirometry

Spirometry through maximum expiratory flow volume loops or volume time curves is usually regarded as reliable from the age of 6 yrs, but some recent publications have also reported reliable values from 4 yrs old [42–44]. Reliable techniques in performing the manoeuvres are vital, and to quote P. Quanjer in a personal communication: "People cannot over perform spirometry, only under perform, and this can easily lead to erroneous interpretations." This is very important to remember when using spirometry in preschool children. One important source of error is that many preschool children are not able to perform a forced expiration over 1 s. For this reason it has been recommended to use $FEV_{0.5}$ or $FEV_{0.75}$ [44].

Recommendations for spirometry in preschool children have been provided by the ATS/ERS report on lung function measurements in preschool children [1]. It should also be noted that a lot of work has been performed in collecting spirometric values from many studies, re-assessing reference values and providing new reference values for spirometry from 4 yrs of age and upwards [45].

Multiple breath inert gas washout technique

A final technique that deserves to be mentioned is the multiple breath inert gas washout technique (MBWT). This technique can be used in infants and children of all ages requiring minimal cooperation of the child. However, the drawback of this technique is that it is only limited to highly specialised laboratories. The reason for this is that the technique is not available commercially, and the equipment is very expensive; the use of gas analysis by mass spectrometry is preferable. The technique was developed principally by P. Gustaffson and H. Ljungquist [46–48]. MBWT can employ different gases fro washout (nitrogen washout is usually used) breathing pure oxygen during washout. However, by using a combination of gases such as helium and sulfur hexafluoride enables the determination of peripheral airway involvement [47]. A detailed description of this technique is given in the ATS/ERS guidelines [1].

Conclusion

A multitude of techniques are available for measuring lung function in infants and preschool children. This is due to attempts to master the lack of cooperation with measurements in these young children. The other reason is that no method is ideal for all children and all situations. It is difficult to use techniques requiring sedation in clinical work, and also sedation cannot be used in children with respiratory distress. The most frequently used method is determination of maximal flow functional residual capacity, especially in infants, but this method requires sedation. Tidal breathing techniques have been shown useful in large epidemiological studies.

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