



Allergologia et immunopathologia

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SERIES: LUNG FUNCTION TESTING IN PAEDIATRICS: THE ESSENTIALS

Lung function in paediatrics. Lung function testing in children

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Received 24 November 2009; accepted 30 November 2009

Series editor: R. Dinwiddie

Available online 15 March 2010

Lung function testing in children is an important part of assessment, diagnosis and monitoring of children with lung disease. Regular testing can also be used to evaluate lung growth, review the effects of treatment and assess the risks and benefits of specific clinical interventions.¹ Such tests can also be useful in the pre-operative assessment of high risk patients undergoing surgical procedures.

Children aged 5 or 6 are usually able to perform standard lung function tests such as spirometry, peak expiratory flow rate (PEFR) measurements, gas dilution techniques and plethysmography. In recent years similar techniques have been successfully developed for preschool children² and infants.³ These will be discussed in later articles of this series.

Spirometry and PEFR measurements are the easiest for children to understand and to perform, both in clinic and in the respiratory function laboratory.^{4,5} Spirometry primarily measures dynamic lung volumes such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and maximal flow rates during expiration (PEFR). It also generates a diagram of flow against volume (flow-volume curve) which is particularly useful for the measurement of small airway obstruction. The spirometric forced expiratory manoeuvre begins at full inspiration—total lung capacity (TLC). At this point the airways are maintained fully open by the bony structure of the thoracic cage and the negative intrathoracic pressure generated during inspiration. During forced expiration the airways gradually close as overall chest volume decreases along with a reduction in the negative intrathoracic pressure. These changes result in closure of the small airways throughout the lung until at full

expiration airflow no longer occurs. In the healthy child this does not significantly affect airflow during normal tidal breathing. The PEFR occurs normally very early during the expiratory cycle after about 12% of the expired breath has occurred. Factors which accelerate early airway closure include airway inflammation (for example asthma or cystic fibrosis), increased airway wall thickness, as in bronchopulmonary dysplasia) and increased airway muscle tone, as in asthma. Towards the end of expiration the flow-volume curve becomes effort independent. In lungs with increased airway resistance airway closure occurs before maximal contraction of the thoracic musculature. The amount of air left in the lungs at the end of a maximal expiration is the residual lung volume (RV) which can be measured by body plethysmography.

The volume of air remaining in the lungs at the end of a normal tidal breath is the functional residual capacity (FRC). Total lung capacity (TLC) is the sum of vital capacity (VC), the volume of air in the lungs from residual volume to maximal inspiration plus RV. RV and FRC cannot be measured by spirometry. RV is calculated by measuring FRC and subtracting the expiratory reserve volume (ERV) which is the amount of air which can be expired from the end of a tidal breath down to maximal expiration. FRC is measured by various techniques including gas dilution (using helium), gas washout (using nitrogen) or plethysmography.

The helium gas dilution method requires the subject to breathe into a closed system of known helium volume and helium concentration. Rebreathing occurs until a second stable concentration of helium is reached. During measurement, carbon dioxide is absorbed from the circuit and oxygen is added. FRC can then be calculated using a simple equation involving the original system volume, the initial and final concentration of helium.⁴ The nitrogen washout

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method requires that the subject washes out the nitrogen from the lung during a series of breaths in which he or she is breathing in 100% oxygen through a one-way valve system after which all expired gas is collected. With each breath the nitrogen concentration falls until it eventually reaches zero. FRC can then be calculated knowing the initial concentration of nitrogen in air, the final nitrogen concentration and volume of the gas expired during the test.

Recently the multiple breath washout technique has been updated using other inert gases such as sulphur hexafluoride (SF₆) to measure the efficacy of distribution of ventilation in the lungs as well as the FRC.^{6,7} The methodology requires the subject to breathe through a sealed facemask or mouthpiece. Recordings of the concentration of SF₆ and respiratory flow at the airway opening are obtained. This method yields the lung clearance index (LCI) which is the cumulative expired volume required to clear the inert gas from the lungs divided by the FRC. This method has the advantage that it can be used in all age groups so that direct comparisons can be made throughout life. The LCI has been shown to be more sensitive than spirometry or measurements of airway resistance in detecting early lung disease in infants and children with cystic fibrosis.⁸ While currently a research tool, the measurement of these inert gas concentrations is likely to be simplified and the technique will become a much more widely available test for the paediatric age group.

FRC can also be measured using whole body plethysmography. This technique relies on the principle that the pressure multiplied by volume of any quantity of air is constant (Boyle's law). Any volume of air within the thorax multiplied by the pressure exerted upon it will be a constant value. If the air is expanded or compressed during tidal breathing against, for example a closed shutter, then if the pressure changes are known then a volume can be calculated. Such measurements are made within a closed body box – the whole body plethysmograph. This sealed body box can be calibrated with known volumes of air which thus generate a measured change of pressure within the box. Using this technique it is possible to measure all gas retained within the thorax at any point in time. This is known as the thoracic gas volume (TGV). If this is measured at the end of tidal breathing then it is equivalent to the FRC. Plethysmographically measured lung volumes have however one important difference from those measured using either helium or nitrogen. Since TGV measures all gas in the thorax this will include trapped gas held behind diseased and obstructed airways. This might be particularly important in chronic diseases such as for example cystic fibrosis. In this situation FRC plethysmographic (FRCpleth) will be higher than FRC_{helium} or FRC_{nitrogen}.

As already stated, spirometry utilising forced expiration from TLC is one of the earliest lung function measurement techniques that children can successfully perform. FVC and FEV₁ (forced expiratory volume in one second) are two of the most useful measurements used to assess the progress of long-term lung disease in children. FEV₁ is the most frequently used parameter to measure lung function in children with cystic fibrosis. It has been shown in several studies to be correlated to long-term outcome and is particularly useful in the assessment of life expectancy in

relation to lung transplantation for end stage CF lung disease.⁹ Large series of normal values in children have been published for various ethnic groups, including for example, white American and African-Americans¹⁰, British^{11,12} and Indian children.¹³ Data are most frequently reported as percentage predicted values for height but a more accurate system is to use standard deviation derived Z scores.^{4,5} A Z score is defined as “predicted minus measured divided by standard deviation of predicted”.⁴

Expiratory and inspiratory flow volume curves are also relatively easy for young children to perform and are particularly useful in assessing lower airway obstruction at all levels from the glottis to the small airways.¹⁴ During expiration against an obstructed airway expiratory flow becomes obstructed at gradually higher levels depending on the underlying pathology. Several patterns of major airway obstruction can be recognised on such flow volume diagrams.⁴ Major large airway obstruction such as glottic spasm or tracheal stenosis will show a curve with blunted large airway flow early on expiration. There may also be a reduction in FVC as demonstrated by a reduced volume axis on the flow volume curve. The inspiratory flow volume curve can be helpful in the diagnosis of vocal cord dysfunction. This is a condition most commonly seen in adolescent girls with or without concomitant asthma. These patients demonstrate flattening of the inspiratory loop in the presence of a normal expiratory flow volume curve unless this is also affected by co-existing asthma.¹⁵ Small airway disease is seen as a diminished peak expiratory flow early in expiration but particularly by a convex shape of the flow against volume diagram.

Peak expiratory flow rates (PEFR), particularly using portable equipment, have been widely used for the assessment and control of patients with asthma. It is now generally recognised that patient adherence to the recording of such measurements is poor. They are best reserved for short periods of outpatient or inpatient assessment and that patient held records over longer periods, unless recorded intermittently, tend to be an inaccurate record of disease severity. PEFR measurements are however very valuable in the laboratory setting, both for the assessment of response to bronchodilators and bronchial challenge including exercise challenge.

Modern lung function testing equipment shows real time flow-volume curves on screen. The performance of the child being tested and the individual manoeuvre are thus available instantaneously. This is important in determining the minimum number of tests, usually three to five, required in order to obtain reliable results while maintaining the subject's cooperation during the procedure. The physical facilities of the lung function laboratory must also be “child friendly”. Parents should be encouraged to be present to facilitate the procedure whenever possible. Normal data for children of all ages are now available for the interpretation of results from ATS/ERS resources.⁹⁻¹²

Once reliable and reproducible flow-volume curves have been obtained then analysis for airflow obstruction is possible. The most frequently used parameter is the mean forced expiratory flow (FEF) between 25% and 75% of FVC (FEF₂₅₋₇₅). This measure is particularly useful in quantifying small airway disease which most commonly occurs in conditions such as asthma, cystic fibrosis, chronic lung disease of prematurity and obliterative bronchiolitis.

As well as assessing the degree of airway obstruction it is also important to evaluate the responsiveness of the airways. This can be assessed either by the use of bronchodilators such as salbutamol, terbutaline or ipratropium bromide or by the induction of bronchoconstriction with histamine, methacholine or cold air challenge.

Bronchodilator responsiveness will be seen as improvements in FVC, FEV₁, PEFR and the expiratory flow volume curve following the administration of one of the bronchodilating agents mentioned above. Improvements in the measured parameters of one standard deviation (approximately 12–15%) are considered significant.⁵ Another measure of airway responsiveness is bronchial hyper-reactivity. The most commonly used agents to assess this response are methacholine and histamine. Those who have positive response will react with a reduction in FEV₁ of 20% or more (the provocation concentration (PC₂₀) at lower inhaled concentrations than normals.¹⁶

Carbon dioxide and oxygen levels in blood are the ultimate measures of the efficiency of minute to minute ventilation. These are best reflected by arterial blood gases but as this is a very invasive measurement in children, oxygen levels are next most accurately reflected by non-invasive oxygen saturation monitoring. Nowadays this should be a routinely reported parameter of lung function tests in children. Normal levels in healthy children and on moderate exercise should be greater than 95%.

Another useful lung function service which can be provided for infants and children is a “fitness to fly” test. In children with long-term lung disease, even those with resting oxygen saturations of >95%, but especially those whose resting oxygen saturation in air is less than 92–94% there is a risk of significant desaturation during commercial air flights. This can be tested in the whole body plethysmograph by reducing the inspired oxygen concentration to 15%. If significant desaturation is observed then the effects of oxygen supplementation at, for example, 5 l/min – readily available from most commercial airlines – can be measured.¹⁷

Another useful measurement in the lung function laboratory is the response to exercise. Sophisticated systems including treadmills and cycle ergometers are available and can be very useful in studying general fitness and also exercise-induced wheeze in the diagnosis of asthma. This equipment is however expensive to buy, maintain and to service, requiring the availability of trained technicians for its accurate and high quality daily use. They are thus generally confined to institutions with primarily research based laboratories. There are however a number of much simpler and clinically useful exercise tests which are easily applicable to children. These include the 6 minute walk test^{18,19} and the 3 min walk test.²⁰ These have been validated as useful tests of exercise tolerance in children with long-term lung diseases such as cystic fibrosis. They can easily be applied to the annual review of such patients to determine the progress of their underlying lung disease, fitness for exercise programmes and ability to air-travel or to holiday at altitude.

A further measurement of lung function in children is the diffusion of alveolar gas into the bloodstream. Although biologically this is oxygen it can be assessed by the use of carbon monoxide. The most commonly utilised measure is the single breath diffusing capacity test for carbon monoxide (DL_{CO}). This test measures the uptake of a single

breath of carbon monoxide into the bloodstream which is a reflection of gas transport across the alveolar-capillary membrane. This is impaired in conditions such as interstitial lung disease, children treated with cytotoxic therapy, post lung transplant and in systemic disease such as SLE. These are all rare conditions in clinical practice so this test is generally confined to lung function laboratories in tertiary centres.

In recent years interest has focussed on the use of fractional exhaled nitric oxide (FE_{NO}) as a marker for inflammation in the airways, especially the lungs.²¹ This is particularly useful in school children for the diagnosis and treatment of asthma. FE_{NO} levels are raised in eosinophilic driven airway inflammation and fall in response to treatment with inhaled corticosteroids. The measurements are non-invasive and guidelines for the measurement techniques have been published^{22,23} and normal reference values for children have been established.²⁴ Equipment for the accurate measurement of FE_{NO} is becoming increasingly portable and less expensive. In the future this is likely to become a further mainstream measure of airway disease activity in the paediatric age group.

Lung function testing in children is thus an increasingly useful tool in the assessment and follow-up of children with both short-term and long-term disease. Techniques of measurement are becoming ever more sophisticated but also child friendly, which continually enhances their usefulness in this age group.

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