Lung function testing in infancy

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After a relatively static period, a number of new and relatively simple techniques have become available for assessing lung function in infancy. This has led to a proliferation of studies into lung growth and the effects of treatment in a wide range of pulmonary disorders. These are obviously to be welcomed but it is perhaps an appropriate time to look critically at the reproducibility of the techniques and the quality of the information they are providing.

A problem associated with all these techniques is that few infants outside the immediate neonatal period will tolerate masks so that sedation is usually required. Most investigators use chloral hydrate in doses of up to 120 mg/kg body weight.

The two techniques which have stood the test of time most successfully are measurements derived from oesophageal pressure and mouth flow measurements and plethysmography.

(1) Oesophageal pressure and mouth flow measurements

Although flow and volume changes at the mouth can be recorded using a suitably designed spirometer, flow is usually measured using a pneumotachograph and volume obtained by then electronically integrating this signal against time. These devices ensure that laminar flow occurs across a small resistance, conditions under which the flow will be directly proportional to the pressure drop across the resistance. These measurements are affected by temperature, the constituent gases, and the water vapour pressure. During tidal breathing the errors introduced tend to cancel out. Unfortunately tidal breathing patterns are very variable and provide little information on any breathing problem the infant may have. It is, however, possible to learn a considerable amount about the mechanical characteristics of the lungs by simultaneously measuring the pressure changes within the thorax. This is achieved by placing the tip of a water filled catheter, a soft rubber balloon mounted on a feeding tube, or even a micropressure transducer in, the lower third of the oesophagus. A measure of the stiffness of the lungs is provided by dividing the tidal volume by the intrathoracic pressure difference between the beginning and end of inspiration (fig 1A). This measure, the dynamic compliance, provides reasonably accurate information on the stiffness of the lung, providing the oesophageal measuring device has been correctly positioned, the baby’s lungs are relatively healthy, and the respiratory rate less than 60/minute.

If the pressure recording device is inappropriately positioned it will tend to under-record, leading to inappropriately high values. On the other hand, in the presence of lung disease and rapid respiratory rates there will be insufficient time for air to enter all the alveoli equally and in these circumstances the dynamic compliance will be reduced—that is, the lungs will appear to be stiffer than they actually are. If respiration is associated with striking chest wall distortions, the displaced pressure often does not provide a true measure of the mean intrathoracic pressure changes. It is possible to check that the oesophageal recording device is responding appropriately by temporarily occluding the output from the pneumotachograph for two or three breaths and simultaneously measuring the pressure changes within the face mask. Under these circumstances, the oesophageal and mouth pressure changes should be within 10% of each other.

Although measurements of lung stiffness are of interest when assessing the progress of babies with the idiopathic respiratory distress syndrome, this measurement is rarely of value later in infancy when the problem is usually that of airways obstruction. This (total pulmonary resistance) can be measured by selecting the mid-inspiratory and mid-expiratory points on the volume trace and dividing the oesophageal pressure by the flow gradients between these two points (fig 1B). Although this measurement is not sensitive to the child’s respiratory rate, it is obviously essential to know that the oesophageal pressure is being recorded accurately, preferably by comparing the mouth and oesophageal pressure during occlusion as described.
from measurements of mouth pressure and box pressure at times when the shutter is closed. Airways resistance is calculated by, in addition, measuring tidal flow and box pressure as the baby breathes in and out of the rebreathing bag.

(2) Total body plethysmography
The other traditional method for assessing lung function in infancy is total body plethysmography. This is a relatively expensive technique and involves nursing the child in an air tight chamber similar to an incubator while ensuring that a face mask—pneumotachograph-shutter system maintains a seal around the child’s mouth and nose (fig 2). The resting lung volume (functional residual capacity) can be measured by closing the shutter system for three to four breaths. The baby will continue to make respiratory efforts, producing pressure changes within the lungs and the face mask which can be measured by a suitable pressure transducer. The small changes in lung volume associated with these pressure changes can be calculated by calibrating the pressure changes within the chamber produced by the child’s respiratory efforts against a syringe. It is then relatively easy to calculate the volume, using Boyle’s law from these two measurements. This measurement, the thoracic gas volume, will be raised in the presence of airways obstruction and reduced if the baby has pulmonary hypoplasia or restrictive lung defect. Unfortunately, in severe airways obstruction, the pressure measured at the mouth will tend to underestimate the mean alveolar pressure changes, due to airway closure. This will produce spuriously high results. Occluding the shutter at the top rather than the bottom of the breath and subsequently subtracting the tidal volume can reduce this problem. It has been suggested that it is also possible to get spuriously low results in airways obstruction, although this has not been reported by other investigators.

The main advantage of plethysmography is that airways resistance can also be measured, as tidal breathing is inevitably associated with changes in alveolar pressure. Thus although the volume of air in the chamber and the infant’s airways and lungs remain constant, there will be small swings in chamber pressure during quiet breathing. It is crucial to ensure that the baby’s inspired air is both fully humidified and at 37°C, as otherwise these pressure changes will be swamped by oscillations due to expansion of the tidal volume on inspiration. Under these circumstances it is possible to measure the airway resistance by relating the chamber pressures to tidal flow. There are, however, two other problems associated with this technique.

First, the thoracic gas volume has to be measured accurately as part of the calculation of the airways resistance. As already stated, this can be a problem when airways resistance is high. Secondly, air flow may be turbulent rather than laminar during parts of the respiratory cycle. Measurements taken under these conditions will then be dependent on the simultaneous flow rate in addition to the mechanical characteristics of the child’s airways. This is complicated by the fact that when the baby is breathing out actively there will be dynamic compression of the airways, which will also raise airways resistance. These problems are largely overcome by restricting the measurements to the initial part of inspiration while flow is predominantly laminar. Despite these problems, total body plethysmography is still generally recognised as the gold standard.

(3) Weighted spirometer system
The weighted spirometer technique can provide useful information on the stiffness of the lung. This is a simple technique. All that is required is to connect the child to a circuit that contains a water filled spirometer (fig 3). Once a stable tidal breathing trace has been established, a weight is added to the spirometer which effectively produces continuous positive airway pressure. There will then be a measurable increase in the end tidal baseline. The compliance of the respiratory system can then be calculated by dividing the change in end tidal baseline by the pressure generated in the circuit by the weight. It will obviously be necessary to subtract the compliance of the circuit. This produces reproducible results in healthy babies but will tend to underestimate the lung compliance if there is a significant degree of airways obstruction, as the lung will already be hyperinflated and the pressure will only be distending those alveoli that are connected to open airways. This error can be reduced by adding more than one
weight and deriving a slope from the volume changes at the different levels of continuous positive airway pressure.

(4) Closed circuit lung volume measurements
The infant's lung volume can also be measured by incorporating a helium meter into the circuit (fig 4). Helium is added to this circuit and the circulating pump turned on until the meter reading is stable, indicating complete mixing. The infant then rebreathes from the circuit via a face mask until the helium reading is once again stable, indicating that the helium is now distributed equally throughout the child's lung as well as the circuit. It is then possible to calculate the baby's functional residual capacity by knowing the initial volume of the spirometer circuit and the relative fall in helium concentration. As the baby will need to rebreathe for at least 1.5-2 minutes it is necessary to incorporate a carbon dioxide absorber and to add oxygen to the circuit to match the baby's oxygen consumption. Although this technique provides reproducible information on babies with restrictive lung disease, the lung volume will tend to be underestimated in the presence of airways obstruction, due to slow penetration of the helium into areas of trapped gas.

(5) Single breath lung mechanics
This is an ingenious and simple method for obtaining information on the infant's lung mechanics. It makes use of the fact that there is a pronounced Hering-Breuer reflex throughout infancy. Thus respiratory efforts can temporarily be terminated by occluding the outlet from a face mask pneumotachograph system at the end of inspiration. The total respiratory compliance can then be calculated by dividing the expiratory volume on release of the obstruction by the pressure within the face mask during the occlusion. In healthy babies the expiratory volume will then tend to follow an exponential curve. The time taken for 63% of the expiratory volume to be released is the time constant of the system.
volume change to occur is defined as the time constant. It is then easy to calculate the total respiratory resistance using the following formula: time constant = resistance × compliance. Unfortunately, as with all techniques used to measure lung function in infancy, there are a number of problems.

Infants with lung disease have increased respiratory drive, so that it is not always possible to induce a Hering-Breuer response purely by occlusion at the end of inspiration. The baby will then make respiratory efforts during the period of occlusion. This will cause the mouth pressure to rise so that the stiffness of the lung will be overestimated. There is also good evidence that, even after a brief occlusion, babies tend to commence their next inspiratory effort before reaching their true functional residual capacity—that is, that volume which is determined purely by the elastic recoil characteristics of the lung and the chest wall. Thus the expiratory volume will be reduced, again tending to lead to an underestimation of the lung compliance. This problem can be overcome by carrying out multiple occlusions throughout the expiratory cycle, plotting the volume against the pressure measurements and using the slope of the regression line. This will also provide information on the extent to which the functional residual capacity is being dynamically raised.

A further problem is that, even after the period of occlusion, babies with lung disease tend to breathe out actively. This will inevitably shorten the time constant and introduce a further source of error. This can to some extent be overcome by plotting expiratory flow against expiratory volume. At any time that expiration is occurring passively there will be a linear relationship between flow and volume. The time constant can then be calculated from the slope of this linear portion. In practice, however, it can be extremely difficult to identify any portion of the expiratory flow-volume curve that is linear in babies who have extensive lung disease, limiting the application of this technique.

(6) Forced partial expiratory flow volume curves
This technique, which was first modified for use in infancy in 1982, has been set up in many respiratory units throughout the world. It is now used more than any other to define response to treatment in infants with airways obstruction. The technique itself is relatively simple. Tidal flow and volume are measured using a face mask and pneumotachograph system during quiet breathing. The baby’s chest and abdomen, and usually arms as well, are encompassed by an inflatable jacket which has a relatively small internal volume and a rigid outer cover. This is connected to a reservoir which contains air at a pressure of up to 60 cm H₂O (fig 5). The aim is to rapidly inflate the jacket at the end of inspiration so that the chest is then exposed to a compressing pressure of approximately 30–40 cm H₂O and air thus forced out of the child’s lungs (fig 6). In the past the maximum expiratory flow rate (equivalent to the peak expiratory flow rate) has been measured but this tends to be poorly reproducible. More reliance has been placed on the measurement of flow at functional residual capacity, as defined by the end expiratory point on the previous breaths before the manoeuvre was commenced. It has been claimed that the flow rate at this point is largely independent of the compressing pressure once a critical value has been exceeded. Additional information is provided by the shape of the expiratory flow volume curve, as this tends to be curvilinear when airways obstruction is present.

Since this technique was introduced there have been a number of attempts to refine it further. It is now generally recommended that a wide range of compressing pressures should be used, ranging from 20–50 cm H₂O, selecting only the pressure that is associated with the maximum expiratory flow at functional residual capacity. There is evidence that once this critical pressure is exceeded some babies with lung disease will actually show a reduction in flow, possibly as a result of dynamic airway compression. Used in this way, the technique appears to be satisfactorily reproducible. One study, however, has shown that, as has previously been documented, the baby responds reflexly to external compression by making rapid inspiratory efforts, so that the
intrathoracic pressure as measured by an oesophageal balloon is actually falling during the manoeuvre. Thus in some situations the flow at functional residual capacity may be determined by the balance between the external compression pressure and the baby’s own inspiratory efforts, rather than the mechanical characteristics of the child’s own lungs.

Further problems arise if, as a result of treatment, the baby’s lung volume alters, as an increase in lung volume will tend to produce higher flows at the new functional residual capacity while a reduction in lung volume may disguise what is, in fact, a useful clinical improvement.17 To overcome this problem some authors routinely measure lung volume, either by plethysmography or with a helium closed circuit system.

What then represents the best buy? Those with a major interest in pulmonary physiology and a generous budget are likely to wish to buy a total body plethysmograph, as this also provides the facility for most of the other methods described for measuring lung mechanics. If the aim is just to investigate the baby’s airway obstruction and assess response to treatment, the forced partial expiratory flow volume system is currently the most popular technique.