Infant lung function testing: What’s hot, what’s not?

Urs Frey, MD PhD
Dept of Paediatric Respiratory Medicine, University Children’s Hospital of Bern
Inselspital 3010, Bern Switzerland

After decades of research studies, infant lung function testing has gone through a phase of standardisation (1), which has potentially made it eligible for clinical application. However, the lack of reference data (and commercially available equipment) and the need for sedation for some techniques has so far impeded the wide spread use of such techniques. While in certain unclear clinical situations infant lung function may add additional information that can aid in clinical decision making, at the moment there is still international consensus that preschool and infant lung function has no clear role in the diagnosis or monitoring of wheezing disorders (2). Similarly, there is still sparse knowledge in diseases as chronic lung disease in infancy (CLDI) or cystic fibrosis, how infant lung function influences clinical management of the disease in the individual. An exception might be the measurement of inflammatory markers such as exhaled nitric oxide (FeNO), which could potentially be of diagnostic or predictive value (section 1). Nevertheless, infant lung function has an important role in research studies in order to study the influence of environmental toxins (section 2), prematurity (section 3) or atopy on lung development in this very early phase of rapid lung growth which is particularly susceptible to injury. There are some new promising techniques at the horizon which may give understanding on the interaction between control of breathing and lung mechanics in infants (Section 4). The understanding of control of breathing in infancy is particularly important since spontaneously breathing infants have a very high capacity to dynamically regulate their end-expiratory volume and airway patency. To target these mechanisms, recent work aims to link EMG of respiratory muscle activity to lung mechanics.
1) The role of nitric oxide in infancy: potential impact for clinical decision making in wheezing disorders

There are different techniques to measure exhaled nitric oxide (NO) in infants. Some techniques, like the single breath forced flow technique (3) or the on-line tidal breathing technique (4), have the ability to account for the flow dependence of exhaled NO in infants, others are simple to use with collecting expired air into a bag (5). While there are methodological differences between the techniques which require careful consideration of the limitations of the methods, there are still surprising consistencies between the techniques. In several publications there is clear evidence that environmental tobacco smoke (ETS) exposure during pregnancy and in the first year of life influences FeNO (e.g. 6,7), and that this influence is not independent of the atopic status of the mother or the infant. There is furthermore evidence that an increase in FeNO in healthy offspring of atopic mothers is predictive for later respiratory symptoms even before the onset of respiratory symptoms (7). Atopy seems to be a strong risk factor for increased FeNO in infants with wheezing disorders (e.g. 7,8,9) and decreases with anti-inflammatory drugs (steroids, LTRA) (8,10,11). This is particularly interesting since other groups of infants, e.g. premature infants with CLDI (9,12) or cystic fibrosis (e.g. 9,13), have normal or decreased levels of FeNO. Thus, in the future FeNO could potentially be used as a diagnostic marker for atopic wheezing disorders in the first year of life, provided further studies confirm these findings.

2) Detection of pollution effects in infant lung function

There is increasing evidence that air pollution may especially affect small children. Children spend more time outside, where the concentrations of pollution from traffic is higher. Furthermore, children's exposure to air pollution is of special concern because their immune system as well as their lung structure are not fully developed when exposure commences, raising the possibility of different responses than seen in adults. Now first evidence shows that long term exposure to outdoor air pollutants affects lung growth in children (14,15) (with potential impact on long term respiratory morbidity at 40-60 yrs, an effect that is already well known for early tobacco exposure and independently in utero tobacco exposure (summarised in 16).) We show for the first time that environmental air pollution in utero is related to infant lung function and inflammatory markers shortly after birth (17). Minute ventilation was higher in newborns of mothers with higher PM$_{10}$ exposure during pregnancy. Exhaled NO
was increased in infants with higher prenatal NO\textsubscript{2} exposure (17). Such alterations during early lung development have potentially profound impact upon long-term respiratory morbidity.

3) Early insult on lung function in infants born prematurely and COPD later in life

In line with these observations regarding air pollution, an interesting hypothesis has recently been raised by Silverman and co-workers (18). These authors suggested that there is more and more evidence that early insult of the lung and its function has an impact on lung growth and development and may lead to the development of COPD later in adulthood. They commented on the paper by Stern et al. (19), who observed that infants with decreased lung function at birth had a higher risk for airway obstruction at the age of 22 years of age. This tracking of lung function has also been described in a special high risk group which is prone to have an significant impairment of lung development very early in life, premature infants, particularly infants with CLDI. Baraldi and Filippine (20) pointed out that infants with CLDI have disturbed airways and lung development with a long term impact on respiratory morbidity. As a recent review series has shown, infants with CLDI tend to have lower lung volumes (summarised in 21, and related review series in the same issue) and higher degree of airflow limitation and lung ventilation inhomogeneities, particularly when they are measured in sedated sleep.

4) High capacity of spontaneously breathing infants to maintain their end-expiratory level

The question arises as to why most of these infants with CLDI are clinically doing so well, and why so few of them need persistent oxygen despite the fact that their lung volume is decreased and ventilation inhomogeneities are increased. A potential hypothesis can be derived from observation of lung function in premature infants during spontaneously unsedated sleep. Using multi-breath washout techniques, some groups (22) found no difference in end-expiratory lung volume in unsedated premature infants with CLDI when appropriately adjusting for body weight. Our own so far unpublished data in a larger cohort of 150 premature infants show similar results. We speculate that during normal breathing conditions, infants have a very high capacity to dynamically elevate their end-expiratory lung volume level. Furthermore, recent studies looking at EMG of respiratory muscle activity showed that infants are capable of breath by breath modulation of their respiratory muscle activity, but resulting flow and volume are weakly correlated to muscle activity (23). Simply
speaking, we can therefore speculate that the main objective of spontaneous infant breathing is to maintain not only adequate homogeneous ventilation but also a constant lung volume, similar to the cardiovascular system, where a series of adaptive mechanisms work together in order to maintain a constant blood pressure. It is possible that the disease states of the infant lung may be better identified by observing these compensation mechanisms (breathing pattern, EMG activity) instead of the lung volume alone. Such consideration may also help us to better understand the reaction of the infant respiratory system to environmental pollutants (14) or infections.

References


