

EDITORIAL

Standards for infant respiratory function testing: what(ever) next?

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This month sees the first two of a series of articles that have been produced by the European Respiratory Society (ERS)/American Thoracic Society (ATS) Task Force on standards for infant respiratory function testing (RFT) [1, 2]. The aim of this task force was to summarize what is currently seen to be good laboratory practice, and to provide recommendations for both users and manufacturers of infant lung function equipment and software. These recommendations have been developed after widespread international consultation and are directed towards future developments in this field, including the use of more automated and standardized equipment than has been available in the past. Despite the very heavy existing commitments of all concerned, the output of this task force during the past 3 yrs has been prodigious. The core set of seven documents provide recommendations regarding equipment [1], software [3] and measurement protocols for the most commonly used tests of infant respiratory function, including: the rapid thoracoabdominal compression technique for measuring partial forced expiratory manoeuvres [2]; tidal breathing analyses [4]; the occlusion techniques for assessing passive respiratory mechanics [5]; plethysmographic measurements of lung volume and airway resistance [6] and the nitrogen washout technique for measuring functional residual capacity [7]. In addition, this international collaborative effort has resulted in the production of several ancillary articles that share the common aim of improving the quality of infant lung function testing [8–17].

Inevitably, in the time available it has not been possible to tackle all current tests, nor the specialized circumstances in which they may be applied. Thus considerable further work is still required to produce similar standards for oesophageal manometry [18], forced expiratory manoeuvres from raised lung volumes [19–25], oscillation mechanics [26–33] and ventilation inhomogeneity [30, 34]. Similarly, guidelines still need to be produced with respect to the use of these measurements in clinical trials, on the intensive care unit and when assessing bronchial res-

ponsiveness in infants and young children. Nevertheless a start has been made.

Attempts to standardize measurements of respiratory function in infants are by no means new and, have in fact, been ongoing for at least the last 20 yrs [35–47]. So why has it taken so long? During recent years, the gradual miniaturization of equipment, availability of disposable sensors and increasing automation meant that infant respiratory function tests were no longer limited to specialized research establishments. Despite the obvious advantages of such increased availability, these advances were accompanied by an increased risk of misuse of such tests by those without specialized training, especially if inappropriate or poorly validated equipment had been purchased. By contrast, because of the general lack of commercially available, well validated systems, most research establishments had already established their own home made equipment and software, which made any meaningful comparison of results between different centres very difficult. Both these factors, together with an increasing appreciation of the potential benefits of performing collaborative multicentre studies when using infant lung function results as outcome measures in clinical or epidemiological studies [48, 49] or when constructing reference values [50, 51] have led to a renewed commitment to establishing more standardized measurements of respiratory function during infancy. Publication of a textbook specifically describing such tests in young infants [47] went some way to providing much of the essential background information, but the need for more specific details regarding the necessary equipment and software for such tests led to the present initiatives.

During the development of the current standards, a vital role has been played by various manufacturers, who have been invited to attend workshops and comment on draft versions of the documents. Indeed during the last 18 months, there has been an encouraging trend towards a new generation of commercially available infant lung function systems, which no longer resemble the "black boxes" that were previously all that was available commercially. The latter were generally shunned by clinical scientists and physiologists, who preferred to use their own trusted home made systems, thus driving a divide between them and clinicians, who generally had neither the time, nor expertise, to develop their own systems. Bridging this gap by producing equipment and software that adheres to sufficiently high standards and is detailed and flexible enough to satisfy scientific research needs, while remaining simple enough for "routine" clinical use is no mean feat. Understandably, this equipment will take some time to produce.

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Nevertheless, a start has been made, much of which can be attributed to the activities of this task force over the past few years and the remarkable international collaboration between scientists, clinicians and members of the industry that it facilitated.

Future directions

In addition to developing standards for additional infant lung function tests and providing guidance for their use in special circumstances, much further work remains to be undertaken in this field. For example, there is a need to develop improved methods of sedating infants for such tests, and to provide firm guidelines regarding data confidentiality, particularly when undertaking multicentre studies. Greater collaboration with those experienced in developing physiological standards for use in older children and adults would be of great benefit. Such an initiative has commenced recently with the formation of a new ERS Task Force that will be developing clinical guidelines for respiratory impedance measurements.

Since it is impossible to check infant lung function equipment in the factory using infant "test subjects", most equipment for this age range is released without undergoing any *in vivo* validation. The lack of an appropriate lung model to assess complex parameters such as plethysmographic lung volumes, resistance and forced flows has meant that even *in vitro* assessments have been minimal, these being largely left to the initiative of individual investigators after release of the equipment. This lack of properly standardized devices and protocols for assessing infant lung function equipment has made it difficult to develop quality control protocols for use in infant pulmonary function laboratories. It has also impeded the development and validation of new equipment and software, and made it virtually impossible to compare results obtained with different systems or from different centres. Recent development of a mechanical model that is capable of assessing many aspects of the equipment used for infant RFTs will hopefully overcome some of these problems [8]. Establishment of standardized physiological signals for use when testing equipment and algorithms, based on those actually recorded in infants, rather than reliance on some idealized and generally inappropriate sinusoidal signal, would also represent a huge step forward.

It should be remembered that no matter how much equipment and software are improved, automated and standardized, the results obtained are still likely to be unreliable unless those performing the tests have had sufficient training and experience of infant lung function testing. Assessments of lung function are far more complex in infants and young children than in older cooperative subjects, and sedation is often required before undertaking these tests. This means that RFTs will never be applied as routinely in infants as in later life. In contrast to the training opportunities available to respiratory therapists and technicians who assess lung function in adults, those specializing in infant measurements cannot practise on their colleagues or test subjects, nor can the various sources of variability within and between operators and laboratories be assessed by performing repeat measures on the same subjects at regular intervals. The importance of adequate training in this field cannot be overemphasized, since it takes 6

months of intensive training for most individuals to become reasonably competent and several years before responsibility for running an infant respiratory function laboratory should be assumed. A major initiative required in the near future is therefore the establishment of recognized training centres and programmes for those wishing to undertake these measurements.

The other major difficulty that still needs to be addressed is that of reference data and predicted values. Both manufacturers and users need to be aware that, despite the numbers regularly displayed on commercially available equipment, valid reference values for any parameter of infant lung function that are applicable outside the centre that developed them, are not currently available. While many research groups have reported so called "normative data", these are generally based on relatively few observations and are only applicable to a specific population (according to sex, ethnic, socioeconomic and age-related factors), specific equipment and software and the type of respiratory function test used. Even when based on appropriate data, expression of results as a percentage of the predicted value, may be particularly misleading since for some parameters such as maximum flow at functional residual capacity ($V_{\max, \text{FRC}}$) the "normal" range may span 20–200% "pred" in the first few months of life. Thus, as soon as equipment and methodology have been standardized sufficiently, to allow collation of results from different departments, there is an urgent need to develop more reliable reference standards which will allow results to be expressed as standard deviation (Z) scores.

Conclusions

It is important to emphasize that the recommendations presented in the accompanying documents do not invalidate previously published data collected with less automated systems or without all the quality control now available, but do provide guidance for current and future applications. It is recognized that the documents will need to be updated regularly in response to advances in both technology and understanding. In the meantime, every attempt has been made to avoid being too prescriptive so as not to stifle future developments, while at the same time offering guidance as to minimum standards for those developing equipment and performing tests. It is anticipated that acceptance and application of these recommendations will be of particular value when attempting to compare data between centres, develop or use reference data, or participate in multicentre trials, which use parameters of infant respiratory function as outcome measures.

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