

## Standardised lung function testing

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In 1983 a supplement entitled "Standardised Lung Function Testing" was published by one of our parent journals, the Bulletin Européen de Physiopathologie Respiratoire [1]. This seminal and widely quoted work reported the recommendations of a Working Party established originally under the auspices of the European Community for Coal and Steel and reflecting the long-standing interest of that body in the respiratory health of industrial workers. The Working Party Report discussed the physiological basis for most of the commonly used tests of lung function and proposed standard methods for their performance.

In addition the Working Party reviewed all the available series of normal or reference values and developed a series of "summary equations" based on the pooled data from several reports. These equations were derived by calculation from the various published regression equations of a series of average values for different combinations of height and age. The authors hoped that these equations would be widely applied and might provide standard reference values for use in all laboratories in Europe. Despite some reservations over the statistical validity of this exercise [2], the aims of the Working Party have generally been achieved and the equations proposed are widely used.

The current supplement of the journal [3] contains updated versions of two of the most important sections of the original Working Party Report dealing with: (i) lung volumes and forced ventilatory flows and (ii) CO transfer factor (diffusing capacity). A third article reviews tests of airway responsiveness and in effect updates a report produced by the SEPCR, also in 1983 [4].

The sections on respiratory mechanics and CO transfer factor include useful discussions of pathophysiology and interpretation as well as important practical points and recommendations. Most of the recommendations can be supported wholeheartedly, *e.g.* the definition of a 'restrictive' ventilatory defect in terms of a reduction in total lung capacity; the emphasis on measurement of relaxed rather than forced vital capacity; the recommendation, in the plethysmographic technique for measurement of total lung capacity (TLC), for the subject to perform an inspiratory capacity manoeuvre immediately after estimation of thoracic gas volume; clarification of the confusing distinction between forced expiratory flow (FEF) and maximal expiratory flow (MEF) with a recommendation to report the latter, *i.e.* flow related to the lung

volume remaining to be expired rather than volume already expired. In some cases, however, the recommendations are less clear: *e.g.* the point is made that increasing expiratory effort in individuals with marked hyperinflation leads to progressive reduction in the forced expiratory volume in one second (FEV<sub>1</sub>) because of compression of intrapulmonary gas, but there is no clear statement on which value should be reported. Other recommendations are counsels of perfection which are unlikely to be followed in all laboratories: examples include the use of inspiratory vital capacity rather than the relaxed expiratory vital capacity (VC) (impracticable with the commonly used bellows spirometers); the use of standardised residuals to report results (desirable, but likely to be adopted only slowly as understanding increases); the use, in calculation of the transfer factor for carbon monoxide (TLCO), of the alveolar volume (VA) measured by a multibreath or plethysmographic technique (as originally proposed, but cumbersome and not employed by most automated equipment). A few (generally minor) statements and recommendations are questionable, *e.g.* nocturnal hypoxaemia may be predictable in patients with sleep apnoea from the postural fall in functional residual capacity (FRC) but with the ready availability of oximeters such prediction is unnecessary; the suggestion that measurements during (forced inspiration forced inspiratory volume in one second and maximal inspiratory flow (FIV<sub>1</sub>, MIF)) are useful in separating emphysema from other causes of airway obstruction is not generally accepted; the implication that the subdivisions of TLCO (diffusing capacity of the alveolar capillary membrane (D<sub>m</sub>) and the volume of blood in alveolar capillaries (Q<sub>c</sub>)) are of any clinical (as opposed to research) value does not accord with majority experience.

Important differences from the earlier recommendations are few, although there are some minor changes in the recommended procedures, *e.g.* in the inert gas technique for measuring lung volumes the Working Party no longer recommends the back extrapolation of the concentration time curve of helium. It is also instructive to note certain differences from the recommendations of the American Thoracic Society (ATS) [5, 6, 7]: the emphasis on VC rather than forced vital capacity (FVC) in the European document was mentioned above, as was the recommendation to use a multibreath estimate of (VA) in calculation of TLCO rather than the single breath estimate favoured by the ATS; the method of recording the most appropriate maximal expiratory flow volume (MEFV) curve also differs, with a preference for the 'envelope' method

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rather than the 'best curve' method obtained with the highest sum of  $FEV_1$  and FVC (as proposed by the ATS).

Of most practical importance to those responsible for lung function laboratories, the summary equations are, with one exception, restated unchanged. Many workers when using the equations for transfer coefficient ( $KCO = TLCO/VA$ ) found that the values obtained were generally larger than those measured in healthy subjects. LOVE and SEATON [8] pointed out that the recommended equations for calculating TLCO and KCO gave reference values which were internally inconsistent. Such discrepancies are to some extent inevitable when different populations are used to derive equations for related variables. As an alternative, Love and Seaton proposed that the reference value for KCO should be obtained by dividing the predicted value of TLCO by the predicted TLC. This produced lower values for KCO which were in general accord with those measured in their own normal subjects. The Working Party have taken note of this discrepancy and the previous summary equations for predicting KCO have been withdrawn. The method suggested by Love and Seaton is now recommended *i.e.* use of the equations to calculate predicted values for TLCO and TLC with the reference value for KCO expressed simply as the ratio of the two.

The Working Party reviewed several series of normal values published since the original report and, as agreement with the original summary equations was generally good, they saw no reason to change them. The equations may, however, require revision in due course, especially as they are based on data collected 20–30 yrs ago which may be influenced by cohort efforts within the healthy population. Recent experience in the EUROSCOP study [9] suggests that such an effect may already be becoming evident as the average  $FEV_1$  of healthy individuals screened for that study is larger than that predicted by the original ECCS equations.

The Working Party have reconsidered the vexed question of the appropriate reference range, with a preference now expressed for using the mean reference value  $\pm 1.64$  SD. This range would be expected to encompass 90% of the values of the 'normal' population. Alternatively, if the data are expressed as standardised residuals, values  $< -1.64$  or  $> +1.64$  would be outside this range.

Tests of airway responsiveness have had a major influence on research related to epidemiology and mechanisms of airway narrowing both in asthma and COPD. They are, however, much less relevant to investigation of the individual patient than the standard tests of ventilatory and gas exchange function. Inevitably, therefore, the section of the Working Party report on airway responsiveness has a rather different emphasis. No single preference for a specific test is given, nor would one be appropriate in the current state of knowledge. The report does give an exhaustive account of the variety of challenge agents and methods which can be used, together with practical

suggestions for the application of each. The authors distinguish challenges using pharmacological agents, physical stimuli and sensitising agents. They point out that the bronchoconstrictor response varies from one stimulus to another (even between histamine and methacholine) and recommend, therefore, that the term 'nonspecific' airway responsiveness should be abandoned. They support the widely held view that the main clinical applications of such investigations are in aiding the diagnosis of asthma in subjects without documented variable airway obstruction and in demonstration of the aetiological role of specific occupational agents.

A preference is expressed for assessing the results in terms of dose-response curves, modelled on *in vitro* methods. Such an approach allows identification of sensitivity (the threshold response) and reactivity (the slope of the response). It is, however, admitted that this approach is not always practicable and some stimuli cannot be applied in such a way as to measure a dose-response relationship. Moreover, a complete sigmoid dose-response curve is often not obtainable *in vivo*, so that an interpolated provocative dose or concentration resulting in a given change in lung function has to be used. Although this may be taken as an index of sensitivity, it may also depend on reactivity. Recent interest in the presence or absence of a 'maximal' response is emphasised. This phenomenon may have important pathophysiological implications but essentially its assessment remains a research tool, to be used only under carefully controlled conditions because of the danger of provoking dangerous airway narrowing. The role of 'baseline' airway calibre and airway function has been a contentious subject for many years. The literature relating to this topic is usefully reviewed and it is pointed out that the 'baseline effect' is much better established in patients with COPD than in asthma, the latter being characterised by increased bronchial responsiveness with little relation to the pre-existing level of function.

The Working Party is to be congratulated on producing a series of comprehensive and definitive reports which are likely to gain wide acceptance. With increasing automation and computerisation of lung function, there is a danger that those responsible for operating and overseeing the equipment will become more out of touch with the precise details of the measurements made. The manufacturers of lung function testing equipment and computer software should be encouraged to adopt the principles and methods recommended in these reports. Perhaps they should also be asked to submit details of their products to the Working Party to ensure that the criteria are met. It would be helpful to users of such systems to know that these standards are achieved.

In future, attempts might be made to harmonise the recommendations of the European Working Party and ERS with those of the ATS. This has now been achieved in the field of infant lung function testing [10] and further dialogue between those involved with adult testing would clearly be useful. There is,

however, a fundamental difference of philosophy over the application of reference equations. The European ideal is for a set of standardised equations which would be applicable in all laboratories, while the North American view [7] is that each laboratory should choose equations from the literature which best suit a group of 20–40 healthy subjects studied in that laboratory.

The attention of the Working Party might now turn to other tests: the earlier report [1] included sections on measurements of lung elasticity and airway resistance: it is unlikely that the section on lung elasticity requires material alteration but much more widespread application of the forced oscillation technique means that the section on measurements of airway resistance should be ripe for updating. Other areas which warrant standardisation include arterial blood gas measurements (particularly related to the newer, noninvasive methods of measuring  $\text{SaO}_2$  and transcutaneous gas tensions), tests of respiratory muscle function and measurements made during sleep.

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