

Author's affiliation

M I Polkey, Department of Respiratory Medicine, Royal Brompton Hospital and National Heart & Lung Institute, London SW3 6NP, UK; m.polkey@rbh.nthames.nhs.uk

REFERENCES

- 1 **Williams TJ**, Patterson GA, McClean PA, *et al.* Maximal exercise testing in single and double lung transplant recipients. *Am Rev Respir Dis* 1992;**145**:101–5.
- 2 **Jakobsson P**, Jorfeldt L, Brundin A. Skeletal muscle metabolites and fibre types in patients with advanced chronic obstructive pulmonary disease, with and without chronic respiratory failure. *Eur Respir J* 1990;**3**:192–6.
- 3 **Maltais F**, Simard AA, Simard C, *et al.* Oxidative capacity of the skeletal muscle and lactic acid kinetics during exercise in normal subjects and in patients with COPD. *Am J Respir Crit Care Med* 1996;**153**:288–93.
- 4 **Polkey MI**, Hawkins P, Kyroussis D, *et al.* Inspiratory pressure support prolongs exercise induced lactataemia in severe COPD. *Thorax* 2000;**55**:547–9.
- 5 **Decramer M**, Gosselink R, Troosters T, *et al.* Muscle weakness is related to utilization of health care resources in COPD patients. *Eur Respir J* 1997;**10**:417–23.
- 6 **Bernard S**, LeBlanc P, Whitton F, *et al.* Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;**158**:629–34.
- 7 **Man WDC**, Soliman MGG, Nikolettou D, *et al.* Non-volitional assessment of skeletal muscle strength in patients with chronic obstructive pulmonary disease. *Thorax* 2003;**58**:665–9.
- 8 **Polkey MI**, Kyroussis D, Hamnegard C-H, *et al.* Diaphragm strength in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1996;**154**:1310–7.
- 9 **Maltais F**, LeBlanc P, Simard C, *et al.* Skeletal muscle adaptation to endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1996;**154**:442–7.
- 10 **Neder JA**, Sword D, Ward SA, *et al.* Home based neuromuscular electrical stimulation as a new rehabilitative strategy for severely disabled patients with chronic obstructive pulmonary disease (COPD). *Thorax* 2002;**57**:333–7.
- 11 **Creutzberg EC**, Schols AM, Welting-Scheepers CA, *et al.* Characterization of nonresponse to high caloric oral nutritional therapy in depleted patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;**161**:745–52.
- 12 **Eid AA**, Ionescu AA, Nixon LS, *et al.* Inflammatory response and body composition in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;**164**:1414–8.
- 13 **Spruit MA**, Gosselink R, Troosters T, *et al.* Muscle force during an acute exacerbation in hospitalised COPD patients and its relationship with CXCL8 and IGF-1. *Thorax* 2003;**58**:752–6.
- 14 **Bowyer S**, LaMothe M, Hollister J. Steroid myopathy: incidence and detection in a population with asthma. *J Allergy Clin Immunol* 1985;**76**:234–42.
- 15 **Decramer M**, de Bock V, Dom R. Functional and histologic picture of steroid-induced myopathy in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1996;**153**:1958–64.
- 16 **Decramer M**, Lacquet LM, Fagard R, *et al.* Corticosteroids contribute to muscle weakness in chronic airflow obstruction. *Am J Respir Crit Care Med* 1994;**150**:11–6.
- 17 **Harris ML**, Polkey MI, Bath PM, *et al.* Quadriceps muscle weakness following acute hemiplegic stroke. *Clin Rehabil* 2001;**15**:274–81.
- 18 **Oliviero A**, Corbo G, Tonali PA, *et al.* Functional involvement of central nervous system in acute exacerbation of chronic obstructive pulmonary disease. A preliminary transcranial magnetic stimulation study. *J Neurol* 2002;**249**:1232–6.
- 19 **Rutherford OM**, Jones DA, Round JM. Long-lasting unilateral muscle wasting and weakness following injury and immobilisation. *Scand J Rehabil Med* 1990;**22**:33–7.
- 20 **Dentener MA**, Creutzberg EC, Schols AM, *et al.* Systemic anti-inflammatory mediators in COPD: increase in soluble interleukin 1 receptor II during treatment of exacerbations. *Thorax* 2001;**56**:721–6.
- 21 **Rich MM**, Teener JWT, Raps EC, *et al.* Muscle is electrically inexcitable in acute quadriplegic myopathy. *Neurology* 1996;**46**:731–6.
- 22 **Donaldson GC**, Seemungal TA, Bhowmik A, *et al.* Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;**57**:847–52.

Interrupter technique

Measurement of lung function in preschool children using the interrupter technique

P D Sly, E Lombardi

The measurement of airway resistance using the interrupter technique shows considerable promise for assessing lung function in children of preschool age. However, proper attention must be paid to the assumptions that underlie the technique, and appropriate consideration of the effect of the measurement conditions on these assumptions is important for producing reliable data.

Measurement of lung function forms an important part of the clinical assessment and management of older children and adults with lung diseases. Our knowledge about the normal pattern of growth and development of the lungs and the effects of aging comes largely from measuring pulmonary function. While these measurements form a routine part of the life of most clinicians, there has been an age limit below which such information has not been available. Measurement of lung function in preschool children has recently generated much interest with the

publication of a number of studies reporting the use of various techniques.^{1–6} Lung function can be difficult to measure in preschool children and is prone to an increased failure rate¹ and increased variability. Two recent papers published in *Thorax*^{5,6} describing measurements of airway resistance using the interrupter technique (R_{int}) deal with the important issue of repeatability of the measurement and variability over time. These issues must be addressed before measurements of R_{int} can be recommended for routine clinical use in children of preschool age.

PRINCIPLES OF THE INTERRUPTER TECHNIQUE

The interrupter technique is not new; it was first described by Neergard and Wirz⁷ in 1927 and was used widely in the 1940s and 1950s^{8–10} before being largely discarded because it was not clear exactly what it was measuring. The advent of modern computers has allowed a thorough examination of the interrupter technique and an understanding of the physiology underlying the measurements.^{11–16} The basic assumption underlying the interrupter technique is that, following an instantaneous interruption of airflow at the airway opening (by closing a valve or shutter), there is an instantaneous equilibration of pressure between the alveoli and the airway opening (behind the occlusion). The technique further assumes that there is a single value of alveolar pressure. Following the occlusion, a rapid change in pressure is seen which is equal to the Newtonian (that is, frictional) fall in pressure between the alveoli and the airway opening. Dividing this pressure change by the flow occurring immediately before the occlusion allows the calculation of resistance (R)—that is, $R = \text{pressure/flow}$. The initial rapid pressure change is followed by a second slower change in pressure which is related to the viscoelastic properties of the respiratory tissues, together with any gas redistribution that occurs between lung units following the occlusion. The direction of these pressure changes depends on the phase of respiration,

with occlusions made during inspiration (or at end inspiration) being followed by falls in airway opening pressure, and occlusions made during expiration being followed by increases in airway opening pressure.

LIMITATIONS OF THE INTERRUPTER TECHNIQUE

There are, however, several problems with the assumptions underlying the interrupter technique that have practical consequences for its use in humans.

(1) An instantaneous occlusion is physically unrealisable and any valve or shutter takes a finite time to close. During this time some gas will continue to pass through the valve and the lung volume (and thus alveolar pressure) will continue to change. These effects have been examined in detail^{15 16} and were found to be of little clinical importance provided the valve closes within 10–20 ms.

(2) There is not instantaneous equilibration of alveolar and airway opening pressure following occlusion. The equilibration time is affected by the resistance of the airways and the time constant of pressure transmission. These effects are small in normal lungs, but become increasingly important in the presence of increased resistance and ventilation inhomogeneity. This effect can systematically bias against the use of the interrupter technique for challenge tests such as methacholine challenge.

(3) The presence of a compliant compartment between the resistive airways and the airway opening may buffer the initial rapid “resistive” pressure change, making the calculation of resistance less accurate. These effects are real and potentially clinically important in patients with markedly increased airway resistance or during challenge tests where the airway resistance is deliberately increased. The major compliant pathway in preschool children is the cheeks and upper (extrathoracic) airway, and measurements are routinely made with the subject’s cheeks supported in an attempt to minimise this problem.

(4) There is not a single value of alveolar pressure and thus not a single value of airway resistance. While this may seem like a fatal flaw, careful animal studies in which alveolar pressure was measured directly using alveolar capsules^{12 13} showed that the value of resistance calculated from the airway opening pressure represented an “average” resistance and was thus of potential clinical value.

(5) The interrupter resistance has been shown to measure more than the fall in resistive pressure across the airways, and includes all Newtonian resistance from the respiratory system including components from the pulmonary tissues and chest wall, both of

which are expected to change under various circumstances likely to be encountered during clinical measurements. Pulmonary tissue resistance increases with increasing lung volume—the opposite to the changes seen in airway resistance with changes in lung volume¹⁷—and also increases with methacholine challenge.^{18–20} Both pulmonary tissue and chest wall resistance show changes with age.^{21 22}

CLINICAL USE OF THE INTERRUPTER TECHNIQUE

Despite these reservations, measurement of Rint by the interrupter technique, if used carefully, does have a place in the measurement of lung function clinically in young children.

Commercially available equipment allows the measurement of Rint at peak tidal flow or at set flows during either inspiration or expiration. This equipment includes a rapidly closing valve that occludes the airway for 100 ms before allowing normal respiration to resume. There is no simple answer to the most correct or reliable protocol. Airway resistance is dependent on the lung volume at which it is measured, increasing with decreasing lung volume. Rint is also flow dependent, increasing with increasing flow. There are expected physiological variations between inspiration and expiration, with airway resistance being lower during inspiration due to the airway being “pulled open” by the forces of interdependence. In practice, neither flow nor volume dependence of resistance have been found to be important effects during the tidal volume range.^{23–25} What is more important is to ensure an adequate signal to noise ratio and reproducible data. For practical purposes, most investigators appear to be adopting the practice of measuring Rint during the expiratory phase of respiration at peak tidal flow, which hopefully coincides with the mid tidal volume range.^{5 6 23}

Both of the recent papers published in *Thorax*^{5 6} deal with the repeatability of Rint measurements. Repeatability is a crucial issue for the use of a lung function test. The interrupter technique has been shown to have a good short term repeatability (over a time span of minutes) in preschool children.^{23 26 27} Rint repeatability has also been shown to be age dependent, with younger children having higher variability between measurements.^{27 28} Both Chan *et al*⁵ and Beelen *et al*⁶ reported good short term repeatability. They also evaluated long term repeatability (over a time span of weeks) and found good long term repeatability, which was similar in the two papers, in children with no history of respiratory symptoms⁵ and in a sample of the general population,⁶ confirming the findings previously reported

in clinically stable preschool children with a history of either cough or wheeze.²³ However, greater long term variability between measurements was found in children with persistent cough or previous wheeze,⁵ which suggests that the lower long term repeatability in symptomatic children might be due to the variability of the disease rather than the variability of the technique.

Many other technical issues also need to be considered, including (1) what constitutes an acceptable measurement; (2) how should the post-occlusion mouth pressure be calculated; and (3) whether the mean or median of a series of measurements should be reported. Each single interruption should be considered acceptable when the trace of mouth pressure versus time has the correct shape. A trace from an occlusion made during expiration in which mouth pressure decreases or stays flat after the initial rapid change suggests air leakage around the mouthpiece or an altered ventilatory pattern^{27 29} and should be discarded. Pressure-time traces obtained when the child was breathing irregularly, had the neck hyperextended or flexed, or was speaking or moving his/her tongue should also be discarded. Several algorithms for calculating mouth pressure during airflow interruption have been proposed. Four main models have so far been used: curvilinear back extrapolation (Rint_c), two-point linear back extrapolation (Rint_t, usually from 70 and 30 ms to 15 or 0 ms after interruption), end oscillatory pressure (Rint_{eo}), and end interruption pressure (Rint_{ei}). The Rint values obtained with these algorithms have been compared with airway resistance obtained with body plethysmography (Raw) in a study by Phagoo *et al* in healthy adults.³⁰ Rint_c values were similar to Raw, while Rint values calculated with the other three algorithms were significantly higher. Another study in healthy adults showed that Rint_{ei} and Rint_t were more sensitive than Rint_c in detecting airway calibre change during methacholine challenge testing.³¹ Until more studies show which algorithm is most sensitive in detecting bronchial obstruction in clinical practice, it has been proposed that the linear back extrapolation should be used for Rint calculation.³² A recent paper has shown that mean and median Rint values are not significantly different.³³ However, since the Rint values obtained during a measurement session are not normally distributed, it was also suggested that median values should be used as they are theoretically more correct.²⁹ What is critical is for investigators to report accurately their measurement conditions—including the triggering conditions for Rint measurements—to ensure that readers are able to compare “like with like”.

CONCLUSIONS

Measurement of Rint is a technique that shows considerable promise for assessing lung function in children of pre-school age. However, proper attention must be paid to the assumptions that underlie the technique, and appropriate consideration of the effect of the measurement conditions on these assumptions is important for producing reliable data. From the studies reported to date, one has confidence that Rint can be used clinically to follow changes in lung function with growth and development, be used to manage lung disease in young children, and to measure acute response to bronchodilators. The use of Rint as the primary outcome for challenge tests such as methacholine requires further study, and whether Rint proves to be more or less useful than other measurements of lung function currently being investigated in preschool children, such as the forced oscillation technique and spirometry, remains to be seen. However, for Rint to be a useful measurement, standard procedures must be developed for performing the measurement and for reporting the results, and these standards must be adhered to.

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Authors' affiliations

P D Sly, TVW Telethon Institute for Child Health Research and Centre for Child Health Research, University of Western Australia, Perth, Australia
E Lombardi, Paediatric Allergy and Pulmonology Centre, "Anna Meyer" Children's Hospital, Department of Paediatrics, University of Florence, 50132 Florence, Italy

Correspondence to: Professor P D Sly, TVW Telethon Institute for Child Health Research and Centre for Child Health Research, University of Western Australia, Perth, Australia; peters@ichr.uwa.edu.au

REFERENCES

- 1 **Eigen H.**, Bieler H, Grant D, *et al.* Spirometric pulmonary function in healthy preschool children. *Am J Respir Crit Care Med* 2001;163:619–23.
- 2 **Beydon N**, Amsallem F, Bellet M, *et al.* Pulmonary function tests in preschool children with cystic fibrosis. *Am J Respir Crit Care Med* 2003;166:1099–104.
- 3 **Pao CS**, McKenzie SA. Randomized controlled trial of fluticasone in preschool children with intermittent wheeze. *Am J Respir Crit Care Med* 2003;166:945–9.
- 4 **Marostica PJ**, Weist AD, Eigen H, *et al.* Spirometry in 3- to 6-year-old children with cystic fibrosis. *Am J Respir Crit Care Med* 2003;166:67–71.
- 5 **Chan EY**, Bridge PD, Dundas I, *et al.* Repeatability of airway resistance measurements made using the interrupter technique. *Thorax* 2003;58:344–7.
- 6 **Beelen RMJ**, Smit HA, van Strien RT, *et al.* Short and long term variability of the interrupter technique under field and standardised conditions in 3–6 year old children. *Thorax* 2003;58:761–4.
- 7 **Neergaard KV**, Wirz K. Die messung der stromungswiderstande in den atemwegen des menschen, insbesondere bei asthma und emphysema. *Z Klin Med* 1927;105:51–82.
- 8 **Otis AB**, Proctor DF. Measurement of alveolar pressure in human subjects. *Am J Physiol* 1948;152:106–12.
- 9 **Mead J**, Whittenberger JL. Evaluation of airway interruption technique as a method of measuring pulmonary air-flow resistance. *J Appl Physiol* 1954;6:408–16.
- 10 **Marshall R**, duBois AB. The measurement of the viscous resistance of the lung tissues in normal man. *Clin Sci* 1956;15:161–70.
- 11 **Bates JHT**, Baconnier P, Milic-Emili J. A Theoretical analysis of interrupter technique for measuring respiratory mechanics. *J Appl Physiol* 1988;64:2204–14.
- 12 **Bates JHT**, Ludwig MS, Sly PD, *et al.* Interrupter resistance elucidated by alveolar pressure measurement in open-chest normal dogs. *J Appl Physiol* 1988;65:408–14.
- 13 **Ludwig MS**, Romero PV, Sly PD, *et al.* Interpretation of the interrupter resistance after histamine-induced constriction in the dog. *J Appl Physiol* 1990;68:1651–6.
- 14 **Bates JHT**, Sly PD, Kochi T, *et al.* The effect of proximal compliance on interrupter measurement of resistance. *Respir Physiol* 1987;70:301–12.
- 15 **Bates JHT**, Hunter IW, Sly PD, *et al.* Effect of the valve closure time on the determination of respiratory resistance by flow interruption. *Med Biol Eng Comput* 1987;25:136–40.
- 16 **Sly PD**, Bates JHT. Computer analysis of physical factors affecting the use of the interrupter technique in infants. *Pediatr Pulmonol* 1988;4:219–24.
- 17 **Petak F**, Hayden MJ, Hantos Z, *et al.* Volume dependence of respiratory impedance in infants. *Am J Respir Crit Care Med* 1997;156:1172–7.
- 18 **Sly PD**, Lanteri CJ. Partitioning of pulmonary responses to inhaled methacholine in puppies. *J Appl Physiol* 1991;71:886–91.
- 19 **Hayden MJ**, Petak F, Hantos Z, *et al.* Using low frequency oscillation to detect bronchodilator responsiveness in infants. *Am J Respir Crit Care Med* 1998;157:574–9.
- 20 **Hall GL**, Hantos Z, Wildhaber JH, *et al.* Methacholine responsiveness in infants assessed with low frequency forced oscillation and forced expiration techniques. *Thorax* 2001;56:42–7.
- 21 **Lanteri CJ**, Sly PD. Changes in respiratory mechanics with age. *J Appl Physiol* 1993;74:369–78.
- 22 **Hall GL**, Hantos Z, Petak F, *et al.* Airway and respiratory tissue mechanics in normal infants. *Am J Respir Crit Care Med* 2000;162:1397–402.
- 23 **Lombardi E**, Sly PD, Concutelli G, *et al.* Reference values of interrupter respiratory resistance in healthy preschool white children. *Thorax* 2001;56:691–5.
- 24 **Lanteri CJ**, Kano S, Nicolai T, *et al.* Measurement of dynamic respiratory mechanics in the neonatal and pediatric intensive care: the multiple linear regression technique. *Pediatr Pulmonol* 1995;19:29–45.
- 25 **Kano S**, Lanteri CJ, Duncan AW, *et al.* The influence of non-linearities on estimates of respiratory mechanics using multi-linear regression. *J Appl Physiol* 1994;77:1185–97.
- 26 **Oswald-Mammosser M**, Ilerena C, Speich JP, *et al.* Measurements of respiratory resistance by the interrupter technique in healthy and asthmatic children. *Pediatr Pulmonol* 1997;24:78–85.
- 27 **Bridge PD**, Ranganathan S, McKenzie SA. Measurement of airway resistance using the interrupter technique in preschool children in the ambulatory setting. *Eur Respir J* 1999;13:792–6.
- 28 **Arets HGM**, Brackel HJL, van der Ent CK. Applicability of interrupter resistance measurements using the MicroRint in daily practice. *Respir Med* 2003;97:366–74.
- 29 **Merkus PJFM**, Mijnsbergen JY, Hop WCJ, *et al.* Interrupter resistance in preschool children: measurement characteristics and reference values. *Am J Respir Crit Care Med* 2001;163:1350–5.
- 30 **Phagoo SB**, Watson RA, Pride NB, *et al.* Accuracy and sensitivity of the interrupter technique for measuring the response to bronchial challenge in normal subjects. *Eur Respir J* 1993;6:996–1003.
- 31 **Phagoo SB**, Watson RA, Silverman M, *et al.* Comparison of four methods of assessing airflow resistance before and after induced airway narrowing in normal subjects. *J Appl Physiol* 1995;79:518–25.
- 32 **Carter ER**. It is time to consider standardizing the interrupter technique. *Eur Respir J* 1997;10:1428–9.
- 33 **Bridge PD**, McKenzie SA. Airway resistance measured by the interrupter technique: expiration or inspiration, mean or median? *Eur Respir J* 2001;17:495–8.