Clinician's Commentary on Morgan et al.¹

Airway-clearance treatments (ACTs) are an integral part of the physiotherapy treatment regimen for people with cystic fibrosis, along with inhalation therapy and exercise. Autogenic drainage (AD) is an ACT that can be performed without either assistance or equipment, which makes it an attractive option for airway clearance for many people. In clinical practice, AD is often the treatment of choice for people with CF who have collapsible airways and have not been successful in clearing their mucous with other techniques. Morgan and colleagues point out that many people with CF prefer AD and that it is the third most used technique by Canadians with CF, although to date no systematic review examining the effects of AD has been completed.¹ A thorough review of this technique is warranted, as ACTs have a large treatment burden for people with CF. Studies showing the effectiveness of a treatment can help both caregivers and people with CF believe that their time commitment is worthwhile.

Although Jean Chevallier developed AD in 1967, Morgan and colleagues' extensive search found only four studies, just two of them long-term, that were deemed appropriate for inclusion in their systematic review, and the only outcome measure common to all four studies was forced expiratory volume in 1 second (FEV₁), which was underpowered to detect change. The number of participants using AD in each study was low ($n = 10\text{--}17$).¹ Clearly, studies with more participants and/or using different outcome measures are needed, as this technique—though introduced in Canada only in the early 1990s—has been practised for almost 50 years.

Investigators who have difficulty in recruiting enough participants from their own sites for a properly powered airway-clearance study should consider a multi-centre trial design. This design is often used in clinical trials to increase the pool of eligible candidates; further, if the aim is to achieve a heterogeneous sample population, a multi-centre design could help achieve that goal.² Standardizing how interventions are taught and how outcome measures are administered and measured is also important for proper interpretation of results, not only within a study but across different studies. Morgan and colleagues were unable to do a meta-analysis in their review because of the low numbers of participants and the different methodologies used in the various studies.¹ The two short-term studies both used sputum yield as an outcome measure, but did not use a standardized collection method.

The International Physiotherapy Group for Cystic Fibrosis publishes a booklet, now in its fourth edition, that can be a useful reference for standardizing airway-clearance techniques.³ Having a core teaching site or sites for training research personnel could also facilitate standardization.^{4,5}

Morgan and colleagues note that FEV₁, once considered the gold standard for measuring CF disease progression, may not be the appropriate outcome measure for physiotherapy studies in a population who are living much longer without a large, steady annual rate of decline in their FEV₁.¹ The number of participants and the duration needed would make conducting a study prohibitive, in many cases. An example is Sontag and colleagues' multi-centre study of airway clearance, which had to be halted before the end of the planned 3-year study period because of the large number of drop-outs, especially in one arm of the study (postural drainage and percussion), and the smaller than expected decline in FEV₁.⁶

More recent clinical studies have used the number of pulmonary exacerbations (PE),^{2,5} time to first (PE)^{2,5} and lung clearance index (LCI)^{7–9} as outcome measures in an effort to find a more sensitive marker for detecting change. An analysis by Waters and colleagues¹⁰ suggested that 50% of lung function decline is explained by PEs, meaning that quantification of the number of PEs could serve as a surrogate for this outcome measure. Waters and colleagues also found that PEs <6 months apart were associated with a greater overall decline in lung function.

LCI, measured by multiple breath washout, is a noninvasive measure of ventilation inhomogeneity.⁸ LCI has been shown to better predict later lung-function abnormalities than FEV₁ and to detect treatment responses to interventions in children with CF between the ages of 6 and 18 with baseline spirometry in the normal range;⁷ therefore, it may be a more appropriate outcome measure for airway-clearance studies, especially in this well population.

As we learn more about CF mucus properties and airway mechanisms, and as physiotherapists continue to search for evidence for our practice, airway-clearance treatments must continue to evolve to meet the needs of our clients at all stages of their lives and throughout the progression of their disease.

*Jennifer L. Agnew, BHK, BScPT
Physiotherapist, Respiratory Medicine, The Hospital
for Sick Children; Lecturer, University of Toronto;
SickKids Research Institute*

REFERENCES

1. Morgan K, Osterling K, Gilbert R, et al. Effects of autogenic drainage on sputum recovery and pulmonary function in people with cystic fibrosis: a systematic review. *Physiother Can.* 2015;67(4):319–26. <http://dx.doi.org/10.3138/PTC.2014-64>
2. Treggiari MM, Retsch-Bogart G, Mayer-Hamblett N, et al. Early anti-pseudomonal acquisition in young patients with cystic fibrosis: Rationale and design of the EPIC clinical trial and observational study. *Contemp Clin Trials.* 2009;30(3):256–68. <http://dx.doi.org/10.1016/j.cct.2009.01.003>. Medline:19470318
3. International Physiotherapy Group for Cystic Fibrosis. *Physiotherapy for people with cystic fibrosis: from infant to adult* [Internet]. 4th ed. The Group; 2009 [cited 2015 Jul 15]. Available from: <http://www.cfww.org/docs/ipg-cf/bluebook/bluebooklet2009websiteversion.pdf>.
4. Saunders C, Bayfield J, Davies K, et al. Lung Clearance Index as a clinical trial outcome measure: Establishing the CTN LCI core facility. *J Cyst Fibros.* 2015;14(Suppl 1):S41. [http://dx.doi.org/10.1016/S1569-1993\(15\)30129-6](http://dx.doi.org/10.1016/S1569-1993(15)30129-6).
5. McIlwaine MP, Alarie N, Davidson GF, et al. Long-term multicentre randomised controlled study of high frequency chest wall oscillation versus positive expiratory pressure mask in cystic fibrosis. *Thorax.* 2013;68(8):746–51. <http://dx.doi.org/10.1136/thoraxjnl-2012-202915>. Medline:23407019
6. Sontag MK, Quittner AL, Modi AC, et al, and the Investigators and Coordinators of the Airway Secretion Clearance Trial. Lessons learned from a randomized trial of airway secretion clearance techniques in cystic fibrosis. *Pediatr Pulmonol.* 2010;45(3):291–300. <http://dx.doi.org/10.1002/ppul.21179>. Medline:20146387

7. Amin R, Subbarao P, Jabar A, et al. Hypertonic saline improves the LCI in paediatric patients with CF with normal lung function. *Thorax*. 2010;65(5):379–83. <http://dx.doi.org/10.1136/thx.2009.125831>. Medline:20435858
8. Subbarao P, Stanojevic S, Brown M, et al. Lung clearance index as an outcome measure for clinical trials in young children with cystic fibrosis. A pilot study using inhaled hypertonic saline. *Am J Respir Crit Care Med*. 2013;188(4):456–60. <http://dx.doi.org/10.1164/rccm.201302-0219OC>. Medline:23742699
9. Lin B, Yabsley P, Middleton A, et al. Acute changes in the lung clearance index after physiotherapy in children with cystic fibrosis. *J Cyst Fibros*. 2015;14(Suppl 1):S39. [http://dx.doi.org/10.1016/S1569-1993\(15\)30123-5](http://dx.doi.org/10.1016/S1569-1993(15)30123-5).
10. Waters V, Stanojevic S, Atenafu EG, et al. Effect of pulmonary exacerbations on long-term lung function decline in cystic fibrosis. *Eur Respir J*. 2012;40(1):61–6. <http://dx.doi.org/10.1183/09031936.00159111>. Medline:22135280

DOI:10.3138/ptc.2014-64-CC