Author's response: heterogeneity of change in LCI in patients with cystic fibrosis following antibiotic treatment

I thank Yammine *et al* for their comments[1] on our paper.[2] In their interesting study, Yammine *et al*[1] have noted similar findings to those we described,[2] albeit in a less severely affected and younger population of cystic fibrosis (CF) patients. This raises important questions about what is happening in the lungs of CF patients during treatment for an exacerbation as well as the utility of lung clearance index (LCI) in this setting. It would appear that forced expiratory volume in 1 s (FEV_1) is the more sensitive marker for change in this circumstance across a wide range of disease severities. Certainly the change in FEV_1 is more impressive than that in LCI, which is at least consistently inconsistent. Some patients show impressive improvements in LCI while others show major deteriorations, and the correlation with change in spirometry is at best modest.[2]

Yammine *et al*[1] have added plethysmography to this analysis, yet the results are somewhat disappointingly unenlightening. They did not observe any significant changes in measures of trapped gas with treatment. The major positive finding was that FRC_{MBW}-RV was identified as a predictor of change in LCI in multiple regression analysis. This is a new composite measurement however, comprising variables obtained from different testing procedures, and the significance of this finding is unclear. The role of the phaseIII slope dervied parameters S_{cond} and S_{acin} in this context is also unclear. As an analysis derived originally from the study of healthy adult lungs,[3] the underlying assumptions may not hold true in children with CF.[4] Finally, the use of nitrogen as a tracer gas may complicate comparison with studies using sulphur hexaflouride, and indeed improvements in heterogeneity might even lead to worsening of LCI.[5]

This does not detract from the use of LCI in stable patients, where it has proven to be a useful and sensitive marker. The situation in exacerbations is complicated by significant heterogeneity in the severity of exacerbation and subsequent physiological impact, as well as the range of additional therapies and interventions that patients undergo. Although we may differ on the finer points of methodology, the conclusion that LCI is both complex and affected by several different competing components is entirely in accord with our own observations. As the authors note, it is likely however that the relative importance of different processes differ between patients, but so far we have not perfected the tools to accurately identify these from the washout curves. Ongoing imaging studies using hyperpolarised He^3 MRI alongside LCI offer the greatest chance of shining a light on the complex evolution and resolution of ventilation heterogeneity.[6] These will hopefully afford a functional standard against which to compare both new and old measures of gas mixing physiology that can then be applied in clinical practice.

Alex Horsley[1,2]

[1]Institute of Inflammation and Repair, University of Manchester, Manchester, UK
[2]Manchester Adult Cystic Fibrosis Centre, University Hospital of South Manchester, Manchester, UK

Correspondence to Dr Alex Horsley, Manchester Adult Cystic Fibrosis Centre, University Hospital of South Manchester, Manchester, M239LT, UK; alexander.horsley@manchester.ac.uk

Funding AH is funded by a National Institute for Health Research Clinician Scientist award. The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclaimer The views expressed are those of the author, and do not necessarily represent those of co-authors on the original study.

Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Horsley A. *Thorax* 2014;**69**:184.

Accepted 14 August 2013
Published Online First 5 September 2013

▶ http://dx.doi.org/10.1136/thoraxjnl-2013-204283

Thorax 2014;**69**:184.
doi:10.1136/thoraxjnl-2013-204359

REFERENCES

1 Yammine S, Bigler A, Casaulta C, *et al*. Reasons for heterogeneous change in LCI in children with cystic fibrosis after antibiotic treatment. *Thorax* 2014; 69:183.
2 Horsley AR, Davies JC, Gray RD, *et al*. Changes in physiological, functional and structural markers of cystic fibrosis lung disease with treatment of a pulmonary exacerbation. *Thorax* 2013;68:532–9.
3 Crawford AB, Makowska M, Paiva M, *et al*. Convection- and diffusion-dependent ventilation maldistribution in normal subjects. *J Appl Physiol* 1985;59:838–46.
4 Horsley AR, Macleod KA, Robson AG, *et al*. Effects of cystic fibrosis lung disease on gas mixing indices derived from alveolar slope analysis. *Respir Physiol Neurobiol* 2008;162:197–203.
5 Nielsen N, Nielsen J, Horsley A. Evaluation of the impact of alveolar nitrogen excretion on indices derived from multiple breath nitrogen washout. *PLOSone* 2013 (In press) doi:10.1371/journal.pone.0073335.
6 Deppe MH, Parra-Robles J, Ajraoui S, *et al*. Combined measurement of pulmonary inert gas washout and regional ventilation heterogeneity by MR of a single dose of hyperpolarized 3He. *Magn Reson Med* 2011;65:1075–83.