## CORRESPONDENCE

# Reasons for heterogeneous change in LCI in children with cystic fibrosis after antibiotic treatment

With great interest we read the paper of Horsley *et al.*<sup>1</sup> In their prospective observational study they showed significant improvement in indices of ventilation capacity (spirometry) and ventilation heterogeneity (multiple-breath washout (MBW)) after a course of intravenous antibiotics in subjects with cystic fibrosis (CF). There was considerable heterogeneity of lung clearance index (LCI) response as observed previously.<sup>2</sup> Here we aim to disentangle underlying physiological mechanisms of this heterogeneous response.

We assessed changes of lung function parameters before and after 23 courses of intravenous antibiotics in 19 children with CF aged 5–18 years. Children performed arterial blood oxygen measurement, nitrogen MBW,<sup>3 4</sup> body plethysmography and spirometry.

We observed a very heterogeneous change in LCI, with a mean decrease from 13.2 to 12.9, (p=0.41), and clear improvement in 7 of 23 subjects (>1 lung turnovers, see online supplementary figure S1). Spirometric indices improved significantly (see online supplementary table S1).

We found that change in LCI and moment ratio is best explained by change in functional residual capacity from MBW ( $FRC_{MBW}$ ) minus residual volume (RV) (figure 1, see online supplementary figure S2). To our knowledge there is currently no established expression for this parameter.

In multivariable regression analysis, change of FRC<sub>MBW</sub>-RV and ventilation homogeneity of conductive airways (Scond) explained 58% variability of delta LCI (R<sup>2</sup>, see online supplementary table S2). These results suggest that improvement of LCI after antibiotic treatment in this patient group can be explained by: less secretion and obstruction (better ventilation of conductive airways=lower Scond), better ventilated lung units (net increase of expired tracer gas=FRC<sub>MBW</sub>) and less hyperinflation (lower RV). Depending on the dominating effect and the resulting time constant of overall ventilated lung units,2 LCI will change accordingly in the individual, explaining heterogeneous results.

The picture for moment ratio change is comparable, but understandably more influenced by peripheral ventilation



**Figure 1** Association of lung clearance index (LCI) improvement and change in FRC<sub>MBW</sub>—RV. Improvement of LCI ( $\Delta$  LCI before minus after treatment) and change of functional residual capacity from nitrogen multiple-breath washout (FRC<sub>MBW</sub>) minus residual volume (RV) from body plethysmography after 19 antibiotic courses in children with cystic fibrosis.

(Sacin) (see online supplementary table S3 and figure S2).

Change in abnormal LCI remains complex and is determined by several components contributing to overall ventilation heterogeneity, generated at different levels of the lung. We speculate that in severe CF lung disease airway collapse might hamper decrease of RV and consequently improvement of LCI. Thus, depending on the magnitude of reversibility of the single components, LCI seems to be a marker suited to monitor changes better <sup>5</sup> or less good in the course of CF lung disease.

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**Contributors** Conceived and designed the experiments: SY, CC, FS, PL. Performed the experiments: SY. Analysed the data: SY, AB, PL. Wrote the paper: SY, PL. Qualified as the guarantor of the paper, took responsibility for the integrity of the work as a whole, from inception to published article: PL.

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#### Patient consent Obtained.

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### REFERENCES

- 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.
- 2 Robinson PD, Cooper P, Van AP, et al. Using index of ventilation to assess response to treatment for acute pulmonary exacerbation in children with cystic fibrosis. *Pediatr Pulmonol* 2009;44:733–42.
- 3 Singer F, Houltz B, Latzin P, et al. A realistic validation study of a new nitrogen multiple-breath washout system. PLoS ONE 2012;7:e36083.
- 4 Singer F, Kieninger E, Abbas C, et al. Practicability of nitrogen multiple-breath washout measurements in a pediatric cystic fibrosis outpatient setting. *Pediatr Pulmonol* 2013;48:739–46.
- 5 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;188:456–60.