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Equipment for multiple breath washout

To the Editors:

We read with interest the article “Paediatrics in Berlin” [1] in a recent issue of the *European Respiratory Journal*, which summarised the paediatric topics of the European Respiratory Society’s Annual Congress in Berlin.

In this article, inert gas multiple breath washout (MBW) technique was highlighted as a promising tool for assessing parameters of ventilation inhomogeneity, such as the lung clearance index (LCI) for detecting early peripheral airway disease, *e.g.* in cystic fibrosis. However, equipment using mass spectrometry, the current “gold standard” for MBW, has no prospect to become commercially available. Alternatively, an ultrasonic flow sensor or an infrared analyser has been introduced for indirectly measuring gas concentrations during a washout procedure. Our recent study reporting within-test repeatability and between-test reproducibility of the LCI in healthy children and adolescents using a side-stream ultrasonic flow sensor [2] was cited in this article [1].

As there has already been a lot of confusion regarding equipment for MBW, we feel it is important to emphasise that we did not use equipment sold by Eco Medics (Dürnten, Switzerland) for any of our studies in preschool children through to adults.

Rather, we have developed equipment based on a similar flow sensor but with the sensor in a side-stream position, utilising a sophisticated valve system controlled by the appropriate software. This equipment is not yet commercially available but was developed as EasyOne Pro, MBW module, in collaboration with ndd Medical Technologies (Zurich, Switzerland). This prototype equipment has been validated in a stepwise approach including comparison with the gold standard mass spectrometry [3], proof of hygienic safety [4], demonstration of feasibility in patients with cystic fibrosis and healthy controls [5], data on short-term and long-term variability in healthy subjects [6] and will now be used in a multicentre trial.

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From the authors:

We thank S.I. Fuchs and M. Gappa for their interest in our review [1]. The points they make are of general importance. As with all lung function measurements, lung clearance index (LCI) must be measured with equipment that has adequate frequency responses, precision and stability, and has been suitably calibrated. Their work with an ultrasonic flow meter is welcome, because it has been compared with a gold standard, and may make measurement of LCI more accessible. The use of equipment which has not been so carefully validated must be firmly discouraged.

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Distinct clinical phenotypes of airways disease: a primary-care clinician perspective

To the Editors:

As a clinician involved in the diagnosis, treatment and aetiological research of obstructive airways disease in primary care practice-based networks, I read with interest the description by WEATHERALL *et al.* [1] of four or five distinct clinical types of airways disease. Their results appear to confirm and extend observations from an earlier population-based study that distinguished asthma and chronic airway obstruction, which was termed AS-CAO (analogous to their Cluster 1), from smoking-associated emphysematous chronic obstructive pulmonary disease (COPD) (Cluster 2) [2].

I would like to offer a personal perspective on the potential value to airway disease diagnosis, treatment and research, of this new taxonomy in the primary-care setting. In my experience AS-CAO and smoking-associated COPD represent two distinct clinical patterns of airways disease that can be easily recognised by an experienced clinician armed only with spirometry and home peak flow monitoring. The distinction is potentially important since AS-CAO and smoking-associated COPD may have different aetiologies and response to treatment [3]. Distinguishing Cluster 3 (classic atopic, eosinophilic asthma) from Cluster 4 (mild, nondescript disease) required further laboratory testing (serum immunoglobulin E and exhaled nitric oxide) not currently routinely used in primary care. Pending the results of further research, the importance of making this distinction in the primary-care setting is unclear to me. An important topic for future investigation is to describe the natural history of Cluster 4. Can WEATHERALL *et al.* [1] comment on the possibility that Cluster 4 subjects had had episodes of self-limited “acute asthmatic bronchitis” [4] that did not evolve into more severe forms of airways disease?

I agree with WEATHERALL *et al.* [1] that AS-CAO (Cluster 1) patients are a very ill group yet are excluded from both asthma and COPD studies. An ongoing clinical trial [5] was rejected for funding by the National Institute of Health because it aimed to enrol all eligible primary-care patients with reversible airways disease regardless of smoking status or other lung comorbidities (especially COPD). Until this dogma is overcome it is unlikely that progress will be made towards conducting long-term “real world” effectiveness trials in reversible airways obstructive disease(s) [6]. For these reasons I support adoption of this or a similar new taxonomy that: 1) is

more congruent with the realities of airways disease than the current taxonomy; and 2) will enable successful implementation of effectiveness trials.

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From the authors:

We thank D. Hahn for his interest in our paper [1]. We agree that following the natural history of individuals defined by these clusters may help define whether they represent distinct phenotypes, and we plan to do this in a follow-up cohort study of the Wellington Respiratory Survey. We agree that the fourth cluster identified by the “Diana” method may represent a phenotype of airway inflammation characterised by sputum production without marked elevation of exhaled nitric oxide and without marked airflow variability, as has been previously described [2, 3]. However, we are cautious in extrapolating the results of the cluster analysis too far. The analysis was of a