Assessing small airways disease

To the Editors:

In their excellent study of the effect of small particle corticosteroids on small airway involvement in asthma, COHEN *et al.* [1], along with LAHZAMI and KING [2] in the accompanying lead editorial [2], decry the complexity associated with current measurements of small airways function. Those authors stress the desirability of finding simpler methods to assess small airways dysfunction.

A simple method of assessing smaller airways obstruction is easily available and could be used retrospectively. In contrast to the mean forced expiratory flow between 25 and 75% of forced vital capacity (FVC; FEF_{25–75%}), which measures the mid-portion of exhalation ending at nearly the same time as the forced expiratory volume in one second (FEV₁) in these subjects, the FEV₃/FVC% or (1-FEV₃/FVC)% are excellent measures of small airways function. They measure the fraction of volume exhaled near the end of a forced exhalation, *i.e.* from airspaces and airways with the longest time constants [3, 4]. However, because they are ratios (as are FEV₁/FVC and FEF_{25–75%}) they are not ideal measurements of airway responsiveness to bronchodilators. Rather, pre- and post-absolute volumes, such as FEV₁, FEV₃ and FEV₆, should be compared to assess bronchodilator effect. Presumably, if there is a small airways bronchodilator effect in the ciclesonide-treated group, the increase from pre- to post FEV₃ (Δ FEV₃) or FEV₆ (Δ FEV₆) should exceed that of pre- to post-FEV₁ (Δ FEV₁). For example, if the Δ FEV₁ was 150 mL and the Δ FEV₃ and Δ FEV₆ were also 150 mL, the dominant change was in the larger airways. If the Δ FEV₁ was 150 mL and the Δ FEV₃ and Δ FEV₆ were 200–250 mL, there was also an important change in the smaller airways. These simple measurements would objectively disclose whether the smaller airways were directly affected by the ciclesonide.

It would be of interest and importance if COHEN *et al.* [1] and other authors would retrospectively or prospectively measure and report these findings to see whether these simple, quick and inexpensive measures are useful in evaluating drugs that modify small airways obstruction.

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STATEMENT OF INTEREST

None declared.

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- 3 Hansen JE, Sun X-G, Wasserman K. Discriminating measures and normal values for expiratory obstruction. *Chest* 2006; 129: 369–377.

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From the authors:

J. Hansen describes an interesting method for assessing small airways dysfunction, namely *via* the bronchodilator effects on forced expiratory volume in three seconds (FEV₃) and FEV₆, as compared with the effects on FEV₁. As they are derived from flow-volume manoeuvres, these parameters are indeed simple to obtain, low-cost, show acceptable repeatability [1, 2] and may reflect relevant changes in small airways obstruction. We therefore retrospectively analysed the FEV₃ and FEV₆ values and compared the treatment effects of ciclesonide on FEV₃ and FEV₆ to FEV₁ in our study population [3]. To assess whether the changes in FEV₁, FEV₃, FEV₆ and forced vital capacity (FVC) after treatment with ciclesonide were indicative of small airway changes, we correlated them with the changes in methacholine-induced air trapping on expiratory computed tomography scans, another method of assessing small airways function.

Table 1 demonstrates the changes after treatment in FEV₁, FEV₃, FEV₆ and FVC. The ciclesonide-induced change in FEV₆

TABLE 1 Changes in forced expiratory volume in one second (FEV₁), FEV₃, FEV₆ and forced vital capacity (FVC) after treatment with ciclesonide or placebo

	Ciclesonide	Placebo	p-value
Subjects n	9	7	
ΔFEV₁			
%	18.1 (6.4–31.2)*	-0.7 (-1.9–8.6)	0.003
mL	550 (263–825)	-25 (-67.5–205)	
ΔFEV₃			
%	11.8 (7.9–14.6)*	-0.3 (-1.3–6.7)	0.002
mL	500 (360–590)	-15 (-55–205)	
ΔFEV₆			
%	8.6 (2.6–11.4)	-0.9 (-1.9–5.6)	0.038
mL	375 (150–568)	-40 (-77.5–185)	
ΔFVC			
%	6.9 (4.8–10.2)	-1.2 (-1.8–2.8)	0.002
mL	380 (210–538)	-55 (-75–92.5)	

Data are presented as median (interquartile range), unless otherwise stated. In the ciclesonide arm, three subjects failed to reach 6 s of exhalation. Between-treatment differences were tested using the Mann-Whitney U-test and within-ciclesonide differences (%) were tested using the Wilcoxon signed rank test. #: p<0.05 versus Δ FEV₃, Δ FEV₆ and Δ FVC; *: p<0.05 versus Δ FEV₆.