

Correspondence

Reply

To the Editor:

We thank Bourdin et al¹ for their comments on our article.² We concur with their view that asthma, and in particular severe disease, is a heterogeneous condition comprised of multidimensional phenotypes.³ *Airway remodeling* is a term that encompasses several different structural changes in the airway, such as thickening of the reticular lamina and reticular basement membrane (RBM), increased vascularity, and airway smooth muscle mass. The pattern and degree of remodeling is also heterogeneous and adds further complexity to the disease. In contrast to the work by Bourdin et al,⁴ we found that measurement of the RBM did not distinguish between different severities of asthmatic and nonasthmatic eosinophilic bronchitis. However, we found that the RBM was associated with the intensity of eosinophilic inflammation. This is in keeping with earlier work by Wenzel et al⁵ in patients with severe asthma. It is therefore perhaps not surprising that RBM thickening can discriminate patients with asthma from patients with chronic obstructive pulmonary disease and healthy control subjects because eosinophilic inflammation is less prominent, and we would predict that in a population of patients with eosinophil-predominant severe asthma, RBM thickness would indeed be increased.

We have now demonstrated in 3 separate studies using biopsies and computed tomographic imaging that thickening of the airway wall and structural remodeling are present in both asthmatic and nonasthmatic bronchitis.^{2,6,7} The key differentiators between these 2 polar conditions were the relative airway narrowing⁶ and the increased number of mast cells in the airway smooth muscle bundle in patients with asthma,² which were both related to airway hyperresponsiveness. Therefore the consequences of remodeling on airway geometry rather than the changes in the structural components per se, in combination with the location of mast cells to the airway smooth muscle bundle and their consequent effect on airway smooth

muscle function,⁸ are likely to be critical determinants of airway hyperresponsiveness.

Further large longitudinal studies with multimodality approaches are required to fully address the interplay between the different domains of severe asthma.

Salman Siddiqui, BM, MRCP
Christopher Brightling, PhD, FRCP

From the Institute of Lung Health, Leicester, United Kingdom. E-mail: ceb17@le.ac.uk. Supported by Asthma UK and a DOH Clinician Scientist award, Wellcome Senior Clinical Fellowship (C.E.B.).

Disclosure of potential conflict of interest: C. Brightling has received research support from AstraZeneca, MedImmune, and GlaxoSmithKline. S. Siddiqui has declared that he has no conflict of interest.

REFERENCES

1. Bourdin A, Vachier I, Godard P, Chanez P. Airway wall structural remodeling from endobronchial biopsies: what does it really mean? *J Allergy Clin Immunol* ■■■:■■■.
2. Siddiqui S, Mistry V, Doe C, Roach K, Morgan A, Wardlaw A, et al. Airway hyperresponsiveness is dissociated from airway wall structural remodelling. *J Allergy Clin Immunol* 2008;122:335-41.
3. Haldar P, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, et al. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 2008;178:218-24.
4. Bourdin A, Neveu D, Vachier I, Paganin F, Godard P, Chanez P. Specificity of basement membrane thickening in severe asthma. *J Allergy Clin Immunol* 2007;119:1367-74.
5. Wenzel SE, Schwartz LB, Langmack EL, Halliday JL, Trudeau JB, Gibbs RL, et al. Evidence that severe asthma can be divided pathologically into two inflammatory subtypes with distinct physiologic and clinical characteristics. *Am J Respir Crit Care Med* 1999;160:1001-8.
6. Siddiqui S, Gupta S, Cruse G, Haldar P, Entwisle J, McDonald S, et al. Airway wall geometry in asthma and non-asthmatic eosinophilic bronchitis. *Allergy* 2009. In press.
7. Siddiqui S, Sutcliffe A, Shikotra A, Woodman L, Doe C, McKenna S, et al. Vascular remodelling is a feature of asthma and non-asthmatic eosinophilic bronchitis. *J Allergy Clin Immunol* 2007;120:813-9.
8. Woodman L, Siddiqui S, Cruse G, Sutcliffe A, Saunders R, Kaur D, et al. Mast cells promote airway smooth muscle cell differentiation via autocrine up-regulation of TGF-beta1. *J Immunol* 2008;181:5001-7.

Available online ■■■.
doi:10.1016/j.jaci.2008.10.061