

## Correspondence

## Reply

To the Editor:

We acknowledge the suggestion made by Rondón et al<sup>1</sup> that some of the patients with nonallergic rhinitis investigated in our study might have “entopy”<sup>2</sup> (local mucosal allergy), and for clarity, this will be defined. Entopy is the presence of local mucosal allergy in the absence of systemic markers of atopy, and although it is commonly interpreted that this is IgE mediated, our original report does not implicitly specify this. Accordingly, although patients with allergic rhinitis undoubtedly have a local nasal mucosal IgE production component that might or might not contribute to the expression of atopy, they do not satisfy the definition of entopy because they are atopic.

The emphasis of our present study is to provide a possible mechanism to explain nasal hypersensitivity in nonatopic subjects showing signs of local mast cell activation, as demonstrated by increased tryptase concentrations in nasal lavage specimens. We have shown that in these patients increased local concentrations of free light chains (FLCs) are present, and based on our previous work, we suggest that these FLCs might be involved in antigen-specific mast cell activation.<sup>3</sup> Indeed, Rondón et al<sup>4</sup> have shown that nonatopic patients might present with normal or low levels of total IgE but, importantly, have increased specific IgE levels in nasal secretions, and as the authors state, measurement of total IgE might not be sufficient to discriminate the existence of nasal IgE-mediated hypersensitivity. In our study we have analyzed nasal secretions from patients with nonatopic rhinitis with eosinophilic syndrome for the presence of specific IgE but no specific IgE to seasonal or perennial allergens was found (as stated in Table I of the article by Powe et al<sup>5</sup>). However, when we analyze concentrations of nasal total IgE on an individual basis (Fig 1), it is evident that a small percentage of the patients with nonatopic rhinitis with eosinophilic syndrome have increases in local total IgE concentrations (with undetermined specificity), which could point to an IgE-driven hypersensitivity in these subjects.

We agree that further studies are needed to investigate the possible function of FLCs in local hypersensitivity to aeroallergens. A good starting point would be to more closely define the nonallergic rhinitis cohort by performing nasal allergen provocation tests with common allergens to positively select a more homogenous responsive study group. Analysis of nasal fluids for FLCs and IgE after nasal allergen provocation tests would categorize subjects into (1) IgE producers, (2) IgE and FLC producers, (3) FLC producers, and (4) mediator-negative subjects. By using our definition, groups 1 to 3 are entopic, whereas group 4 (if they exist) has idiopathic rhinitis.

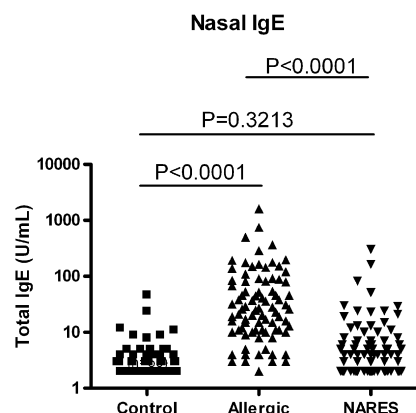


**FIG 1.** A small proportion of nonatopic patients with nonatopic rhinitis with eosinophilic syndrome (NARES) show increased local mucosal total IgE levels (with undetermined specificity) in nasal secretions, which could point to an IgE-driven hypersensitivity in these subjects.

Desmond G. Powe, PhD<sup>a</sup>  
Tom Groot Kormelink, MSc<sup>b</sup>  
Melanie Sisson, BSc<sup>a</sup>  
Bart J. Blokhuis<sup>b</sup>  
Matthias F. Kramer, MD<sup>c</sup>  
Nicholas S. Jones, MD<sup>a</sup>  
Frank A. Redegeld, PhD<sup>b</sup>

From <sup>a</sup>Molecular Medical Sciences and Surgical & Medical Sciences, Queen's Medical Centre, Nottingham University Hospitals Trust, Nottingham, United Kingdom; <sup>b</sup>the Division of Pharmacology and Pathophysiology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands; and <sup>c</sup>the Department of Oto-Rhino-Laryngology, Head and Neck Surgery, Campus Grosshadern, Ludwig-Maximilians-Universität, Munich, Germany. E-mail: [des.powe@nottingham.ac.uk](mailto:des.powe@nottingham.ac.uk).

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

## REFERENCES

1. Rondón C, Canto G, Fernández J, Blanca M. Are free light chain immunoglobulins related to nasal local allergic rhinitis? *J Allergy Clin Immunol* ■■■;■■■:■■■.
2. Powe D, Mason M, Jagger C, Jenkins D, Jones N. “Entopy”: localised mucosal allergic disease in the absence of systemic responses for atopy. *Clin Exp Allergy* 2003;33:1374-9.
3. Redegeld FA, van der Heijden MW, Kool M, Heijdra BM, Garssen J, Kraneveld AD, et al. Immunoglobulin-free light chains elicit immediate hypersensitivity-like responses. *Nat Med* 2002;8:694-701.
4. Rondón C, Romero JJ, Lopez S, Antunez C, Martin-Casanez E, Torres MJ, et al. Local IgE production and positive nasal provocation test in patients with persistent nonallergic rhinitis. *J Allergy Clin Immunol* 2007;119:899-905.
5. Powe DG, Groot Kormelink T, Sisson M, Blokhuis BJ, Kramer MF, Jones NS, et al. Evidence for the involvement of free light chain immunoglobulins in allergic and nonallergic rhinitis. *J Allergy Clin Immunol* 2010;125:139-45, e1-3.

doi:10.1016/j.jaci.2010.06.046