

Correspondence

The multimorbid polysensitized phenotype is associated with the severity of allergic diseases

To the Editor:

We read with great interest 3 consecutive articles recently published in the *Journal*.¹⁻³

Allergic diseases are complex and represent multiple phenotypes that have not been well characterized until recently. Mechanisms of the Development of Allergy (MeDALL) has pooled 14 European birth cohorts with omics and IgE measurements using a refined microarray technique.⁴ An important message from MeDALL was the identification of the multimorbid polysensitized phenotype of allergic diseases.⁵ Although polysensitization and multimorbidity were known, they had never been associated in a single phenotype. In MeDALL, using hypothesis and data-driven methods, this novel phenotype was shown to be associated with some important features of allergic diseases including longitudinal trajectories with a low probability of remission of IgE sensitization and clinical allergy, elevated levels of total and specific IgE, high levels of blood eosinophils, and a high rate of family history.

However, the links between this phenotype and the severity of allergic diseases were not fully understood. The 3 recent studies published in the journal bring new knowledge to the understanding of severe asthma in a well-defined population. The studies were based on the same population and were analyzed using 3 different methodologies including a cluster analysis.¹⁻³ Interestingly, they all found that rhinitis and polysensitization were associated with severe or uncontrolled asthma. In addition, the cluster approach showed that the severe asthma phenotype was associated with both severe rhinitis and polysensitization.¹ As in MeDALL, it was found that phenotype characterization is complex⁶ and that more than a single phenotype is associated with severe disease in sensitized and nonsensitized individuals.

We think that the authors have confirmed the previously described multimorbid polysensitized phenotype⁵ that is now associated with the severity of asthma and rhinitis¹⁻³ or peanut allergy.⁷ The results of the short follow-up of the studies¹⁻³ and those generated by MeDALL⁴ provide novel insight and generate hypotheses in the implication of this severe phenotype on the prediction of the severity of allergic disease.

The additional impact of polysensitization in asthma and rhinitis multimorbidity suggests the importance to better characterize subjects with allergic diseases and sensitization to specific allergens both for clinical practice and for mechanistic studies.

Clinical and population studies, as well as those on genotypic associations or mechanisms, should consider the multimorbid polysensitized phenotype to improve interpretation of the results and better understand allergic diseases.

Jean Bousquet, MD^a

Josep M. Anto, MD^b

Jocelyne Just, MD^c

Thomas Keil, MD^d

Valérie Siroux, PhD^e

Magnus Wickman, MD^f

From ^aMACVIA-France, Contre les Maladies Chroniques pour un Vieillessement Actif en France, European Innovation Partnership on Active and Healthy Ageing Reference Site, Montpellier, France; ^bISGLoBAL, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; ^cthe Allergology Department, Centre de l'Asthme et des Allergies, Hôpital d'Enfants Armand-Trousseau (APHP), Paris, France; ^dthe Institute of Social Medicine, Epidemiology and Health Economics, Charité - Universitätsmedizin Berlin, Berlin, Germany; ^eINSERM, Université Grenoble Alpes, Montpellier, France; and ^fSachs' Children and Youth Hospital, Södersjukhuset, Stockholm, Sweden. E-mail: jean.bousquet@orange.fr.

Disclosure of potential conflict of interest: J. Bousquet reports personal fees from Almirall, Meda, Merck, MSD, Novartis, Sanofi-Aventis, Takeda, Teva, and Uriach. J. Just reports grants and personal fees from Novartis, ALK Abello, Stallergenes-Green, AstraZeneca, and Thermofischer. T. Keil reports personal fees from the European Union for FP7-project MeDALL. V. Siroux reports personal fees from TEVA, AstraZeneca, and Novartis. The rest of the authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Zoratti EM, Krouse RZ, Babineau DC, Pongracic JA, O'Connor GT, Wood RA, et al. Asthma phenotypes in inner-city children. *J Allergy Clin Immunol* 2016; 138:1016-29.
2. Liu AH, Babineau DC, Krouse RZ, Zoratti EM, Pongracic JA, O'Connor GT, et al. Pathways through which asthma risk factors contribute to asthma severity in inner-city children. *J Allergy Clin Immunol* 2016;138:1042-50.
3. Pongracic JA, Krouse RZ, Babineau DC, Zoratti EM, Cohen RT, Wood RA, et al. Distinguishing characteristics of difficult-to-control asthma in inner-city children and adolescents. *J Allergy Clin Immunol* 2016;138:1030-41.
4. Bousquet J, Anto JM, Akdis M, Auffray C, Keil T, Momas I, et al. Paving the way of systems biology and precision medicine in allergic diseases: the MeDALL success story. *Allergy* 2016;71:1513-25.
5. Bousquet J, Anto JM, Wickman M, Keil T, Valenta R, Haahtela T, et al. Are allergic multimorbidities and IgE polysensitization associated with the persistence or re-occurrence of foetal type 2 signalling? The MeDALL hypothesis. *Allergy* 2015;70:1062-78.
6. Pinart M, Benet M, Annesi-Maesano I, von Berg A, Berdel D, Carlsen KC, et al. Comorbidity of eczema, rhinitis, and asthma in IgE-sensitized and non-IgE-sensitized children in MeDALL: a population-based cohort study. *Lancet Respir Med* 2014;2:131-40.
7. Just J, Elegbede CF, Deschildre A, Bousquet J, Moneret-Vautrin DA, Crepet A; Mirabel study group. Three peanut allergic/sensitized phenotypes with gender difference. *Clin Exp Allergy* 2016;46:1596-604.

<http://dx.doi.org/10.1016/j.jaci.2016.12.961>