Commentary

Can the Pattern of Early Sensitization to Allergen Molecules Drive a New Approach for Prevention of Allergy?

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Identifying the causative agent is a major aim of diagnostic work-up for allergy. However, a positive result from skin tests or *in vitro* specific IgE measurement indicates sensitization but not necessarily clinical allergy. In fact, it is quite common to see a patient with positive tests to pollens with no respiratory symptoms during the specific flowering seasons of such pollens. Using as example the most recent study, 53.5% of 501 unselected subjects aged 12–21 years from Austria showed IgE reactivity to at least one allergen, with the highest rate for grass pollen, dust mites, birch pollen and cat, but only 21.9% had a diagnosed allergy (Stemeseder et al., 2017). Among the different hypotheses on the immunological mechanisms underlying asymptomatic sensitization, some issues, as reviewed by Bodtger in 2004, were apparent to characterize asymptomatic sensitization (Bodtger, 2004). They included the lack of a late-phase reaction and of eosinophil stimulation and migration in response to allergen challenge, and low levels of interleukin (IL)-5, that is the major cytokine responsible for activation, proliferation and survival of eosinophils. A role for allergen avoidance was suggested to be successful in reducing development of allergy (Bodtger, 2004). Actually, in a study assessing during 5 years the longitudinal sensitization to 6 aeroallergens in 828 children aged 6–11 years living in the semi-arid US southwest, new allergen sensitizations were detected in 30.2%. Also remittance from positive to negative tests was observed, mostly concerning seasonal allergens (Stern et al., 2004). In recent years, the introduction of molecular diagnostics, by which specific IgE (sIgE) to single allergen molecules are measured, was a significant advance not only for diagnosis of allergy but also for investigating epidemiologic and natural history aspects (Matricardi et al., 2016). In the present issue of the Journal, Wickman et al. report the results of a study on IgE reactivity to 132 allergen molecules in a population based birth cohort of children from Sweden and in birth cohort of children from U.K. (Wickman et al., n.d.) The Swedish cohort included a random sample of 786 children (from the original number of 4089). At the age of 4, 8 and 16 years IgE reactivity was analyzed, along with the collection of any allergic symptom of rhinitis, asthma or eczema by questionnaires. In the British cohort 248 children underwent the same assessment at the age of 3, 5, 8 and 11 years. Risk allergen molecules were defined by the detection of sIgE at all time points. In the Swedish cohort, 4 risk molecules were identified, namely Bet v 1 from birch, Phl p 1 from grass, Fel d 1 from cat, and Ara h 1 from peanut. IgE reactivity to >3 of these molecules at 4 years predicted incidence and persistence of asthma and rhinitis at 16 years in 87% and 95% of cases, respectively. In the British cohort, 5 risk molecules were identified: Der p 1 and Der f 2 from dust mites, Phl 1 and Phl p 5 from grass and Fel d 1 from cat. IgE reactivity to >3 of these molecules resulted in 100% of incidence and persistence of asthma and rhinitis. The authors concluded that this outcome may help in developing individualized risk prediction charts for allergic respiratory diseases. We agree with such expectation. In fact, other recent researches used similar models, as in the study by Posa et al., who found that in a birth cohort from Germany including 722 subjects parental hay fever and early exposure to mite allergens were associated with IgE polysensitization to several *Dermatophagoides pteronyssinus* molecules and resulted in later mite related rhinitis and asthma (Posa et al., 2017). The strength of the study by Wickman et al. is the demonstration that the allergen molecules linked to the risk of respiratory allergy are variable according to different geographic areas. In particular, sIgE to *Dermatophagoides* molecules were predictive of allergy in all cases in the British cohort but were not comprised in the 4 risk molecules in the Swedish cohort. In fact, due to different climatic environments, mites are a dominant cause of allergy in UK but not in Sweden (Rönmark et al., 2003). This should stimulate further studies comparing the pattern of sensitization to allergen molecules in different countries. As suggested by Wickman et al., expanding the knowledge on the mechanisms of sensitization and allergy is likely to result in preventive strategies for rhinitis and asthma. Avoidance measures to reduce the concentration of indoor allergens have partial evidence of success (di Mauro et al, 2016), while allergen immunotherapy (AIT), that is the only treatment able to modify the natural history of allergy, is more feasible. In particular, based on the current advance in understanding the evolution from sensitization to allergy, the use of AIT for primary prevention of respiratory allergy could be reappraised. In fact, the available studies, performed by administration to children at risk of mixtures of the most common allergens,

were unsuccessful (Martignago et al., 2017), but new studies founded on the risk allergen molecules identified in different regions could achieve a positive outcome.

Disclosure

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