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Editorial

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Component-resolved diagnostics: laboratory results are not enough

Allergic diseases, such as atopic eczema, food allergy, rhinitis and wheezing disorders are among the most frequent complaints, especially in childhood. The current evidence also attests that type I allergic reactions are becoming more and more widespread, affecting up to 20% of the population. The World Health Organization (WHO) recently estimated that approximately 300 million people suffer from asthma worldwide [1], with a 10% average of European children suffering from this disorder. The global burden of asthma and – more generally – allergic diseases is impressive and well recognized, but still represents an open and unresolved challenge. The diagnosis of asthma and allergic disease is problematic, particularly in preschool children, due to onset of poorly specific symptoms and because the conventional lung function tests cannot be carried out in early ages. Traditionally, the diagnosis of allergy has been based on medical history and clinical symptoms. The identification of a new isotype of human immunoglobulin, called immunoglobulin E (IgE) [2], has however represented a milestone for improving our knowledge of the pathophysiological mechanisms underlining this very particular type of inflammation, as well as for detection of allergic diathesis, diagnosis and patient management. In particular, in vivo and in vitro tests for allergen-specific IgE (sIgE) play a key role for confirming a clinical suspicion and for choosing the most appropriate treatment. Until recently, the in vitro diagnostics of allergy was mainly based on detection of specific IgE (sIgE) against total extracts. However, allergen-extracts are heterogeneous in composition, since they contain a vast array of allergens, i.e., potent or dominant allergens, those present in modest amount or number, cross-reactive allergens of less impact and non-allergenic components [3, 4]. The immunoassays for IgE antibody have undergone significant advancements in the last decades. In particular, the capacity to more precisely measure IgE antibodies in mass units and the total automation of assay systems have generated remarkable improvements of both analytical performances and diagnostic accuracy [5]. However, further and major developments are expected with the introduction of highly purified native or recombinant allergens, which would allow a more accurate identification of individual molecules against which patients are sensitized. Assays based on recombinant and/or highly purified allergens allow a deeper examination of cross-reactions, risk molecules and prognostic significant sensitizations, thus paving the way to the so-called "molecular or component-resolved diagnostics (CRD)" [6]. CRD more suitably allows the genuine sensitization of patients toward a given allergenic source to be identified, along with cross-reactive molecules that suggest cross-sensitization to several allergen sources [7].

For routine laboratory testing, the molecular approach should be performed using two different tools, i.e., the traditional measurement of an individual specific IgE antibody, and/or multiplex multiarrays that can simultaneous screen a large number of specificities for the same allergen and for different related or significant allergens [8]. The new analytical method ImmunoCAP™ISAC microarray (ThermoFisher Immunodiagnostics, Uppsala, Sweden) has recently been introduced to the market. This system allows to test as many as 112 recombinant or purified allergen components, from 52 sources, in a single analytical step [9]. An article about the evaluation of this new microarray and the comparison of its analytical performance with that of conventional ImmunoCAP assay has been previously published in *Clinical Chemistry and Laboratory Medicine* [10]. In this issue of the journal, the article of Villalta and colleagues [11] reports and discusses an unexpected and isolated IgE reactivity to nJug r 2 (native walnut vicilin), which has been detected by ImmunoCAP ISAC™. This finding is frequently related to cross-reactive carbohydrate epitopes and lacks clinical significance. So, the value of the study relays in the authentication that technological developments do not necessarily translate in clinical improvements, and that further efforts should be placed to correctly assess and interpret test results. This is particularly true in the field of allergy testing, as confirmed by a recent survey performed in Italy which supported previous data demonstrating that general practitioners are not confident with request for and interpretation of laboratory data. The survey also emphasized that

Italian general practitioners [12] require more information and education regarding CRD and molecular diagnosis of allergic diseases, along with appropriate test request and interpretation.

The accessibility to allergists may represent an additional challenging issue. The need to provide frontline care for allergy has been widely recognized, but primary care physicians are not sufficiently trained for management of allergic diseases and, even in the past, have expressed concern about their ability to diagnose and manage children with allergic problems [13]. The take-home message is that CRD demands new knowledge and definition of a strategy for rational utilization of the different techniques before definitely entering routine care. Laboratory professionals should be proactive in cooperating with expert allergists. Not only should they provide education and valuable information to general practitioners and primary care physicians, but they should also introduce appropriate interpretative commenting in the laboratory reports to facilitate test interpretation and prevent inappropriate care [14]. Once more, this reiterates the concept that laboratory results are not self-sufficient in clinical practice: knowledge and information are still necessary.

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