

Journal

ImmunoDiagnostics

The role of IgE in Respiratory Allergies

IgE plays a major role in respiratory allergic diseases. Recently published data adds further evidence that atopy is not simply a matter of being sensitized or not, but that poly-sensitizations and quantitative levels of IgE have significant influence on the prognosis and development of these diseases. Resolving sensitizations down to the allergen component level has further added to our understanding of disease development and supports improved patient management.

Three articles on the importance of IgE in respiratory allergies and on how component resolved analysis affects the prescription of specific immunotherapy for patients with pollen related allergies are presented in CAPture.



3 CAPture

4 The importance of IgE in asthma/rhinitis

IgE - a key factor in respiratory allergies

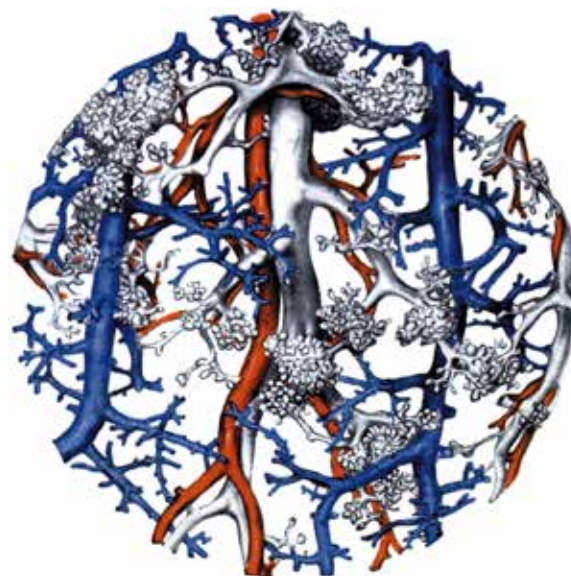


In this issue of the Immunodiagnosics Journal we present a review on the major role that specific IgE antibodies have in the development and expression of respiratory allergic diseases. Allergic asthma is the most common form of asthma,

where the disease progression and severity is related to IgE sensitizations. An increasing number of publications shows that detailed analyses of the levels of specific IgE antibodies, the number and nature of the allergens to which a patient is sensitized and the persistency of sensitizations all influence the disease manifestations. Optimal avoidance advice and patient management aiming at slowing down the disease progression, as well as appropriate prescription of specific immunotherapy treatment both are reliant on a detailed sensitization profile. The use of molecular allergology, where sensitizations are resolved at the component level, have now been used to follow the disease progression and for improving the diagnosis of pollen allergic patients.

Adequate testing of IgE sensitizations in the diagnostic work up of patients can help to improve the patient's quality of life in addition to lessening the economic burden of allergic respiratory diseases on society.

I hope you will find useful information and references for further reading in this issue of ImmunoDiagnostics Journal.



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CAPture – A selection of recent allergy papers

SYNOPSIS

- A birth cohort of allergy high-risk children was followed up to 9 years of age (n=289).
- Serum IgE to perennial allergens (mites, cat, dog, *Alternaria*) were measured at the 1, 3, 6, and 9 year follow ups (ImmunoCAP[®], Phadia Laboratory System, Thermo Fisher Scientific, Uppsala, Sweden).
- Serum IgE to pollen allergens (ragweed, birch, timothy) were measured at the 6 and 9 year follow up (ImmunoCAP).
- Current asthma was diagnosed at 6 and 8 years of age.
- At 6 years of age 28% had asthma, 46% rhinitis, and 16% both asthma and rhinitis.
- The prevalence of sensitization to tested allergens increased to 53% at the age of 9 years.
- Poly-sensitization increased from 4.4% to 16% between one and three years of age.

Citation: Stoltz DJ et al. Specific patterns of allergic sensitization in early childhood and asthma & rhinitis risk. Clin Exp Allergy. 2013;43:233-41.

Early childhood sensitizations to perennial allergens are risk markers for asthma at school age whereas sensitizations to seasonal pollens are strongly associated with rhinitis

Poly-sensitization to aeroallergens is associated with the risk for respiratory allergy. The aim of the present study was to characterize the relationship between sensitization profile, current disease and with the risk to develop allergic asthma or rhinitis. The sensitization profile during the first three years was focused on perennial indoor allergens. At 6 years of age measurements of IgE to pollen allergens were also included.

The sensitization frequency to indoor allergens was doubled (13.5% vs. 27.7%) from year 1 to year 3 and continued to increase up to 9 years of age. At one year of age only IgE to cat (OR 5.9) and dog (OR 7.6) were significantly associated with an increased risk of asthma at age 6. Sensitization to any of the indoor allergens at 3 and 6 years of age were significantly associated with current asthma at 6 years of age. The only pollen allergen associated with asthma at that age was ragweed (OR 2.2) whereas all pollen allergens were strongly associated with current rhinitis (OR 5.1-7.0).

The level of allergen-specific IgE provided additional prognostic information; whereas any detectable levels of IgE to pollen allergens were associated with current rhinitis, higher levels of serum IgE to indoor allergens were positively associated with both concurrent rhinitis and asthma.

The data suggest that the levels of specific IgE to perennial allergens during early life are important for the prognosis of disease development. Examination of specific patterns of sensitizations could have potential impact in clinical practice, as opposed to merely defining the patient as atopic or not.

SYNOPSIS

- Patients (n=175, age range 6-62 years) with diagnosed respiratory pollen allergy and immunotherapy prescription based on skin allergy testing were recruited from the daily routine.
- Skin testing was performed with timothy grass extract, olive tree extract, native profilin from palm pollen and native LTP from peach.
- Specific IgE to species specific allergens (Phl p 1-p 5b, Ole e 1) and cross-reactive allergens (Phl p 12, Phl p 7/profilin, Pru p 3/LTP) were measured by ImmunoCAP. All but Ole e 1 were recombinant.
- In 27 patients the immunotherapy prescription changed from a mix of grass and olive pollen to only olive pollen.

Citation: Letrán A et al. Measurement of IgE to pollen allergen components is helpful in selecting patients for immunotherapy. Ann Allergy Asthma Immunol. 2013 in press.

Prescription of immunotherapy was changed in 50% of pollen allergic patients when component resolved diagnostics were used

Prescription of allergens for immunotherapy in pollen allergic patients is often based on serum IgE to allergen extracts. Using extract tests it is difficult to judge whether the detected IgE antibodies in patients with positive tests to both grass and tree pollen depends on cross-reactions or true co-sensitization. The availability in recent years of *in vitro* tests for IgE to species-specific allergen components as well as broadly cross-reactive allergen components (pan-allergens) has made it possible to address this.

The purpose of this study was to evaluate if the use of tests based on allergen components (mostly recombinant) affect the prescription for immunotherapy focusing on grass and tree pollen (olive).

In the studied population 76% had serum IgE to both grass and olive tree extracts. These apparent double-positive patient sera decreased with 17% when allergen components were used in the test design (ImmunoCAP). Based on the results from component resolved diagnostics the clinicians changed the prescriptions of immunotherapy in 50% of the patients.

The authors point out the importance of using tests based on species-specific as well as cross-reacting allergen components to obtain a correct allergen prescription in immunotherapy in pollen allergy.

SYNOPSIS

- A prospective study recruiting patients (n=318, mean age = 37 years) with respiratory allergy and at least two positive skin tests to allergen extracts.
- Patients were classified in five groups based on sensitizations of clinical relevance, suspected cross-reactivity and reported food allergy.
- The doctor's diagnosis of poly-sensitizations was followed up *in vitro* by ImmunoCAP[®] ISAC.
- 66.3% of the patients had IgE to cross-reacting components; Bet v 1 (42.1%), LTP (23.9%), profilin (16.3%).
- Immunotherapy was prescribed in 32 patients before ISAC and after ISAC the prescription was altered in 3 patients and additionally prescribed in 85 patients.

Citation: Passalacqua G et al. The additional values of microarray allergen assay in the management of polysensitized patients with respiratory allergy. Allergy. 2013;68:1029-3.

Clinical reclassification of the majority of poly-sensitized patients when using ImmunoCAP ISAC as compared to a diagnostic routine based on allergen extracts

Microarray technology in allergy diagnostics may become a valuable tool in respiratory allergy as shown in earlier studies. Poly-sensitizations as well as the cumulative allergen specific IgE levels are related to the risk of respiratory allergy and the disease severity. The aim of the present study was to investigate how often the results of component resolved diagnosing altered the doctor's decision using today's clinical routine primarily based on skin testing using allergen extracts. Poly-sensitized patients were recruited and classified into five groups according to the current clinical routine. Using results from ImmunoCAP ISAC, more than half of them (58%) had to be reclassified and all patients not possible to classify (2.5%) could now be classified.

The prevalence of patients classified as poly-sensitized due to cross-reactivity and patients also reporting symptoms to foods were both doubled due to additionally detected sensitizations with the microarray. Sixty-three percent of patients with serum IgE to grass and birch pollen extracts were specifically sensitized to only one of them, as shown by component based results. Prescription of environmental control measurements or prophylaxis (mainly indoor allergens) needed to be changed in 60% of the patients.

The authors conclude that the use of ImmunoCAP ISAC gives additional clinical value in poly-sensitized patients with respiratory allergy compared to current routine.

The importance of specific IgE in asthma/rhinitis

Ninety percent of children with asthma are allergic and among adult asthmatics about sixty percent are atopic. Despite this studies show that there is a care gap in determining whether a patient's asthma is allergic or not. This review briefly describes allergic respiratory diseases and demonstrates the role allergies have in these, summarizing evidence for the importance of an early, complete and quantitative analysis of IgE antibodies for an accurate diagnosis and optimal patient management.

The United Airway Disease

Historically, many diseases were named and described based on pure clinical observation of the symptoms they elicited long before any understandings of their pathophysiological mechanisms were known. During the past decades, considerably more has been learnt about the disease mechanisms, not least in inflammatory diseases such as asthma and rhinitis. This has led to a paradigm shift in how to treat patients, where instead of only treating the symptoms the aim is to stop or at least slow down the disease progress.

Asthma was originally described in patients with reversible bronchial obstruction and bronchial hyper-reactivity, and asthma and rhinitis were considered two separate diseases. However, new understanding about the pathophysiology, epidemiology, and the disease characteristics reveal that there are common links between upper (rhinitis) and lower airways (asthma) allergic diseases. Today, these diseases are described as clinical manifestations of a "united airway disease" involving common tissue factors, not least IgE (1-3). The link between allergic rhinitis and asthma is recognized in the evidence-based document ARIA (Allergic Rhinitis and its Impact on Asthma) (1), which has continuously been revised and validated since then.

Asthma phenotypes

Asthma and rhinitis are complex polygenic diseases (4) and their progression is due to a combination of genetic, environmental and lifestyle factors. A number of disease variants thus exist which have different causes, prognoses and therapeutic needs although their clinical expressions are similar. The main challenge for the management of allergic airway diseases in the 21st century is to properly describe the disease subtypes to enable the development of medicine specific for the different disease phenotypes, as stated by the ARIA group (1).

Allergic asthma is characterized by the presence of T helper 2 cells (T_H2), and has been further divided into different phenotypes; early-onset, late-onset and exercise induced (5).

- *Early-onset allergic asthma* is associated with increased levels of total and specific IgE antibodies, eosinophils, mast cells and T_H2 cytokines.
- *Late-onset allergic asthma* is an adult-onset, less prevalent form of asthma compared to childhood asthma. It is associated with higher levels of eosinophils, and often a severe phenotype of asthma.
- *Exercise-induced asthma* is a milder form which is more common in atopic athletes and pathologically associated with higher percentage of eosinophils.

Early-onset allergic asthma is an important asthma phenotype as most persistent adult asthma originates in early childhood (6). This phenotype of asthma is also associated with other atopic diseases; for example 40% of people with early-onset asthma have a history of atopic dermatitis, whereas only 4% of those with late-onset asthma do (5). Given how prominent this phenotype is, the transition of disease from mild to persistent, and coexistence with other allergic diseases, it is necessary to diagnose and manage this phenotype appropriately to avoid further exacerbation of the disease.

Disease development

It is well established that an underlying eosinophilic inflammation in the respiratory mucosa is the most important pathogenic mechanism for triggering the acute respiratory symptoms seen in rhinitis/asthma. While the degree of inflammation influences both the disease progression and the severity, allergen exposure and sensitizations are the key factors for driving the inflammation. This disease development may be depicted as an iceberg where an atopic predisposition together with tissue factors, inflammation markers and IgE antibodies contribute to finally eliciting symptoms (see figure 1).

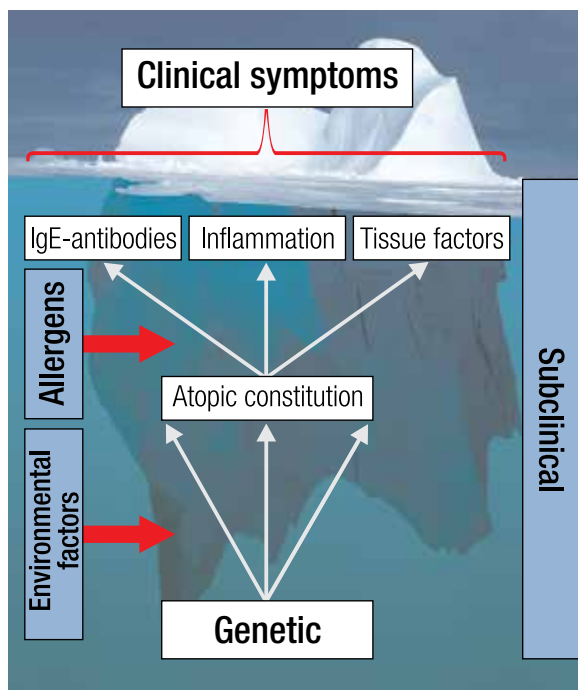


Figure 1. Allergic respiratory diseases can be depicted as an iceberg with a huge subclinical phase before clinical symptoms appear.

In addition to sensitizations, viral infections play an important role in asthma (7). Interestingly, recent evidence suggests that allergic sensitizations precede rhinovirus induced wheezing. This sequential relationship and the plausible mechanisms by which allergic sensitization can lead to more severe rhinovirus-induced lower respiratory illnesses support a causal role for allergic sensitization in this developmental pathway. Therefore, therapeutics aimed at preventing allergic sensitization may modify virus-induced wheezing and the development of asthma (8).

Subclinical inflammations are on-going already early in the sensitization process and both the inflammation and sensitization precede the on-set of clinical symptoms (9). As there may be a failure to identify or measure these early signs of disease before symptoms are elicited, there is often a delay in reaching a correct diagnosis and in introducing appropriate therapeutic interventions (10-13). If on the other hand patients at risk of disease development are identified the disease progression can be slowed down by allergen avoidance measures. This has been shown in birth cohort studies to be effective (14-17)

Progression from rhinitis to asthma symptoms

In the adolescent and adult populations allergic rhinitis often precedes the onset of asthma. Indeed, 80% of asthmatic patients have been shown to have rhinitis (1) while considerably fewer - 10-40% - of rhinitis patients suffer from asthma (3). Even in allergic rhinitis patients that do not display any asthma symptoms, asthma-related changes such as basement membrane remodeling, atopic inflammation and bronchial hyper reactivity can be detected (18-24), and identifying sensitization to inhalation allergens is important for the prediction of disease development. This shows that allergic rhinitis is a very important clinical risk marker for the future development of asthma, and the ARIA guidelines recommend that allergic rhinitis patients, especially those with severe and/or persistent rhinitis, should be checked for asthma (25). In spite of this, rhinitis is often regarded as a banal disease and not always recognized as an early sign of a progressing respiratory allergy. The under-treatment of respiratory allergy revealed by several studies (26-28) reflects that focus often is put on patients with moderate to severe symptoms and that a "wait and see" mentality is prevalent for those with milder symptoms. Also, patients with symptoms of rhinitis often do not even visit a doctor but use OTC drugs or other self-treatments (12, 29). These aspects were the focus of a debate in the EU Parliament in 2012 with the aim to develop a strategy for how to reduce the asthma and allergy burden (30).

Prediction markers of Respiratory Allergy

Asthma development in children

Early onset wheezing is considered one of the major risk factors of asthma morbidity, with a greater risk of relapse with earlier onset (31-33). Wheeze is however rather common during infancy – particularly in association with respiratory infections – and is often transient and resolves spontaneously by the age of three. In a subset of children however, wheeze becomes persistent, indicative of early onset asthma. This wheezing phenotype is strongly associated with early sensitization to aeroallergens (7, 13, 31).

Early signs of allergic rhinitis is another risk factor for the development of asthma in children (34). Allergic sensitization and allergen exposure, together with viral upper respiratory infections have been demonstrated to synergistically increase the risk of emergency care with asthma (35).

Generally, the risk for developing respiratory symptoms is higher in a child that is atopic as compared to non-atopic.

In recent studies on two birth cohorts that had been followed up to the age of 8 years, the children could be best classified into five different subclasses depending on the onset and persistence of their wheeze. Those who had intermediate onset and persistent wheeze also had the strongest association with atopy (36, 37).

A history of severe atopic dermatitis and food sensitizations – especially to egg white and cow's milk (13) are other well-established risk factors for allergic diseases. The risk is also related to how early the sensitization appears and if it is persistent in nature. Kulig *et al.* (38) have shown that this risk of respiratory allergy increased dramatically if the children were sensitized to food at two years of age and if the sensitization persisted for more than a year. The risk of developing allergic rhinitis and allergic asthma at five years of age increased 3.4-fold and 5.5-fold, respectively, in this group of children compared to if only transiently sensitized during infancy.

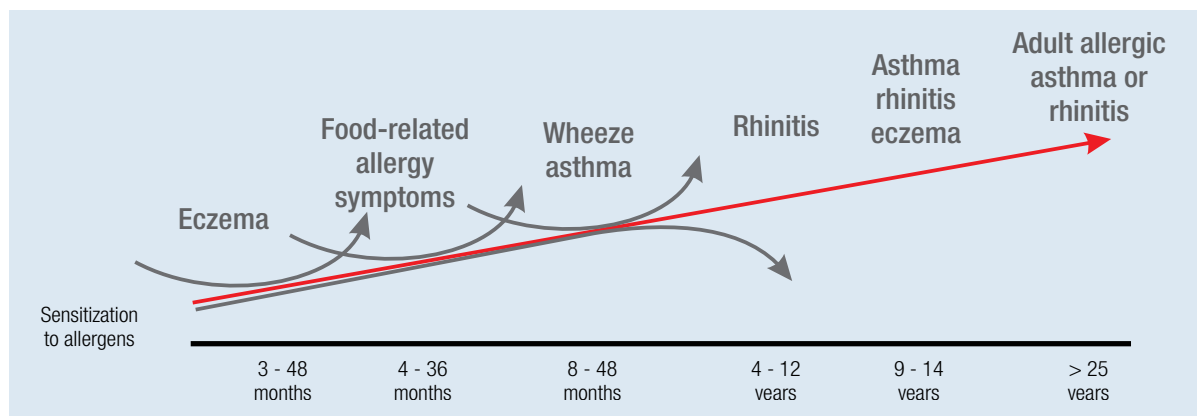


Figure 2. The Allergy March describes the progression of atopic disorders from atopic dermatitis in infants to allergic rhinitis and asthma in children (re-drawn from (39)). This starts with sensitizations to food allergens through the gastrointestinal tract in early childhood, followed by sensitization via the respiratory tract to inhalant allergens (33, 39, 40). Sensitizations to indoor allergens such as mites and animal dander have been shown to precede that to pollen allergens (41).

Early sensitization

By measuring specific IgE antibodies, children at risk may be identified early which can provide opportunities to prevent the disease on-set as stated in the recent update on allergy testing in children by the pediatric section of EAACI (42). Several studies have shown the relation between early sensitization and later disease development and severity (41, 43, 44).

At least two years before the onset of respiratory symptoms, pollen-specific IgE antibodies were detected

in children (9). Eysink *et al.* (45) showed that allergen-specific serum IgE to inhalation allergens before the age of 4 increased the probability of asthma at 6 years of age from 75% to 95%. In a Swedish birth cohort, two year old sensitized but symptom free children were shown to have an increased risk of developing allergic symptoms by the age of five (46). The same group could also demonstrate that low levels of IgE, defined as below 0.7 kU_A/l, were associated with later symptom development (47).

In an attempt to improve the way in which atopic asthma phenotypes are defined, Simpson and co-workers used a machine learning strategy on a birth cohort. The children could be grouped into several different atopic phenotypes, where the one comprising children with multiple and early sensitizations (approximately 25% of the atopic children), was predictive not only of the presence of asthma but also of its persistency and severity (48).

Quantitative IgE levels and disease probability

Atopy is not a simple yes or no phenomenon, but the absolute levels of IgE antibodies are shown to correlate with diseases probability (49, 50). That quantitative levels of specific IgE antibodies offers more information to the clinicians than simple presence or absence of atopy is recognized in the latest EAACI position paper on pediatric rhinitis (35). Below, a few studies supporting this are briefly summarized.

In a prospective birth cohort, asthma at 10 years was shown to best be predicted by a combination of the severity of obstructive airway symptoms with the sum of IgE antibodies to inhalant allergens, both at the age of two (51).

The sum of IgE to three indoor allergens (mite, cat & dog) at the age of three was shown to correlate with the risk of persistent wheeze in five year old children. The risk increased 2.15 times per logarithmic unit increase in the specific IgE levels (52). The probability of current rhinitis is shown to increase with increasing pollen-specific IgE levels, and the absolute levels of sIgE were shown also to correlate with disease severity (53).

In American children, Stoltz *et al.* demonstrated that the sensitization profile gives additional information regarding relevant disease associations as compared to only classifying a patient as atopic or not. Increased levels of specific IgE to perennial allergens were associated with increased risk for asthma, whereas any detectable levels of IgE to seasonal allergens were associated with increased rhinitis risk (54). As they conclude; poly-sensitization and increased levels of IgE are associated with increased risk for allergic diseases.

These and many other studies, show the importance of quantifying specific IgE and following the allergen sensitization development in children to enable early identification of respiratory allergies allowing relevant interventions to slow down the disease progression.

Adults

The disease development in adult patients differs to some extent from that seen in children, but also here, sensitizations play an important role. Schoefer *et al.* (55) showed that the OR for development of allergic rhinitis in adults within the coming 10 years was 2.16 for individuals sensitized to grass pollen and 7.84 in those sensitized to

birch pollen. In an adjusted logistic regression model the OR for asthma development was 1.64 in mite sensitized patients and 2.63 in cat dander sensitized patients. The incidence of allergic rhinitis decreased continuously after 25 years of age whereas asthma increased up to the age of 50 years.

Poly-sensitizations

As shown above, the clinical severity in allergic asthma and rhinitis is related to the quantitative levels of specific IgE. Poly-sensitizations as well as high levels to individual allergens add up to the total sum of specific IgE antibodies. Also the total allergen exposure over time influences the IgE levels, and hence perennial allergens are important contributing factors to disease severity. While the quantification of IgE antibodies is straight forward, exposure levels are often difficult to measure. These may however be followed indirectly by measuring the IgE levels (56, 57).

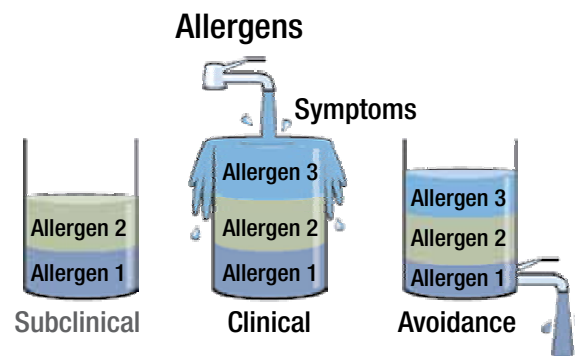


Figure 3. Patients with poly-sensitizations may not display symptoms until their combined exposure to several individual allergens pushes them over the symptom threshold. The allergen that triggers acute symptoms may be apparent; however other sensitizations that contribute to building up the inflammation often go un-identified, but are important for understanding how avoidance measures best are taken.

Several studies have shown that poly-sensitization to inhalation allergens is related to the severity of allergic asthma as well as allergic rhinitis (54). In a convincing study Simpson *et al.* (58) present results from multivariate regression analyses of a large population of adult asthma patient in the UK. This study shows that sensitization to house dust mite, cat, dog and grass are all independently associated with current asthma. The odds ratios for current asthma is increased 2.4 times (from OR 4.3 to OR 10.4) when the numbers of allergens to which patients are sensitized increases from 2 to 4 four. Pollen sensitization was more strongly associated with allergic rhinitis as compared to sensitization to the indoor allergens studied (OR 13.6 vs. OR 0.68-1.5).

This differential association of pollen allergens to rhinitis but indoor allergens to asthma has been shown in several studies (34- 36). Jaakkola and coworkers (59) showed that sensitization to mite is associated with increased risk for asthma onset in adults. A likely explanation for the difference in symptoms elicited by pollen allergens on the one hand, and indoor allergens on the other, might be the difference in size of the pollen grains. Pollen grains have a size between 10 and 100 μm and are therefore primarily trapped in the nasal mucosa. (Unless the allergen components are released as smaller particles in which case they may reach further down in the respiratory tract.) Indoor allergens on the other hand are often much smaller than pollen and will be trapped in the lower respiratory tract (1).

In a population of asthmatic children Sarpong *et al.* (60) studied indoor allergen sensitization and the relation to disease severity. They could show that sensitization to cat increased the likelihood for having more severe asthma; while sensitization to dog, cockroach and mite allergens did not correlate with the asthma severity. However, polysensitization to all four allergens increased the risk for having a more severe asthma, giving further support of the importance of mapping the total sensitization profile in respiratory allergy.

Multi-allergen tests

The use of multi-allergen test can be helpful in identifying atopy if there is a suspicion of allergen involvement (61). Several common allergens can be tested for in a single test, thus helping to confirm whether the patient is sensitized or not. The tests display high negative predictive values for atopic diseases, and thus a negative test helps to rule out atopy as an underlying cause with a high probability (61, 62). Two such tests, Phadiatop and Food mix fx5, were recently recommended by the National Health Institute in the US as core outcome biomarkers for atopic status in clinical asthma studies (63).

Wickman *et al.* (64) used the above mentioned multi-allergen tests relevant for quantitative measurements of inhalant and food allergen sensitization (Phadiatop[®], Food mix fx5, respectively) to obtain a measurement for predicting clinical allergy. A 97% positive predictive value for an atopic clinical disease in 4 years old children was obtained if both of the multi-allergen tests were positive (above 3.5 kU_A/l). This suggested cut off was also associated with the severity of asthma and with increased numbers of clinical manifestations of atopic diseases. In a follow up study (65) they compared the multi-allergen tests

with test for individual allergens on the same cohort. They found that the number of sensitizations and the total level of sensitization to individual allergen predict allergic rhinitis and asthma. In a similar way Simpson *et al.* (52) summed up the specific IgE levels to mite, cat and dog in a birth cohort and obtained odds ratio for current wheeze at 5 years of age of OR 3.1 at 10 kU_A/l and OR 4.24 at 30 kU_A/l . Arshad *et al.* (66) came to a rather similar conclusion in children who were followed up to the age of four.

ImmunoCAP[®] ISAC

Component based multiplex microarrays are important tools to describe the full sensitization profile in patients. With ImmunoCAP ISAC it is possible to in one go get a profile of the sensitization pattern to over a hundred allergen components representing more than 50 allergen sources. The test allows discrimination between species-specific sensitizations and cross-reactivity but also identification of sensitization to minor allergens (67, 68). There are now a number of publications demonstrating its usefulness for improving diagnosis and patient management in allergic respiratory diseases (69, 70), but it has also been used to analyze the allergy march (71), sensitization in preclinical stages and molecular spreading (72, 73).



Patelis and colleagues (74) showed that asthma prevalence and bronchial hyper-reactivity/inflammation were not increased in subjects sensitized to pollen who were not concomitantly sensitized to related food allergens. However, in patients sensitized to pollen as well as pollen-related food allergens, an increase in asthma prevalence

and bronchial inflammation (but not hyper-reactivity) was seen. Sensitization to perennial allergens, however, showed a correlation with all three readout measurements irrespective of other sensitizations. In a study on children with severe un-controlled asthma a detailed analysis of their IgE profiles with ImmunoCAP ISAC showed that the children poly-sensitized to certain pet allergen components were those who had the severest form of asthma (75).

Sastre *et al.* propose using component-based tests before selecting allergen extract for immunotherapy treatment in clinical routine. They showed that in 54 % of patients with asthma/rhinitis microarray-based test results changed the indication of specific immunotherapy treatment as compared to when relying only on data from extract-based tests (skin prick test) (69). In a study on Italian asthma/rhinitis patients, a conventional diagnostic work up employing skin prick testing and *in vitro* IgE measurements was compared to when in addition using ImmunoCAP ISAC. In terms of doctor's diagnosis and treatment of patients the authors report that in 90-95 % of the cases, the doctor had gained new information on the patients' disease and was more confident in how to manage the disease (76).

Conclusion

There is sound evidence of the major role that IgE plays in the disease progression of respiratory allergies, and ample evidence show that sensitizations start long before any symptoms are displayed. Acknowledging the importance of sensitizations in the diagnostic workup is vital for the asthmatic patient. To test early in infancy/childhood for sensitization, to understand the patient's overall sensitization pattern and to follow the sensitization over time in a quantitative fashion gives support for adequate advice of avoidance and treatment. Disease progression can then ideally be slowed down, increasing the quality of life of the patient in addition to lessening the burden of respiratory allergic diseases on the health economy. Recently, resolving the sensitizations down to the allergen component level has shown to further improve the patient management in allergic respiratory diseases.

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