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Scientific news, opinions and reports

CAPture - study on new hazelnut components and more

Two hazelnut storage protein components - Cor a 9 and Cor a 14 - were recently launched by Thermo Fisher Scientific, and the utility of these as risk markers for severe hazelnut allergy is demonstrated in one of the articles presented in this issue. Thirteen other recent publications in the field of allergy, demonstrating the utility of allergen components and the quantification of specific IgE are presented in brief.

Thermo SCIENTIFIC

CAPture - Hazelnut storage proteins

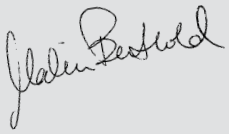
For almost 40 years, Thermo Fisher Scientific ImmunoDiagnostics, previously known as Phadia, have maintained global leadership in allergy testing and become one of the world's leading autoimmune disease test providers. Through clinical excellence, laboratory efficiency and our dedication, we strive to deliver the highest quality and clinical value in our diagnostic tests, as well as providing clinical expertise and scientific information.

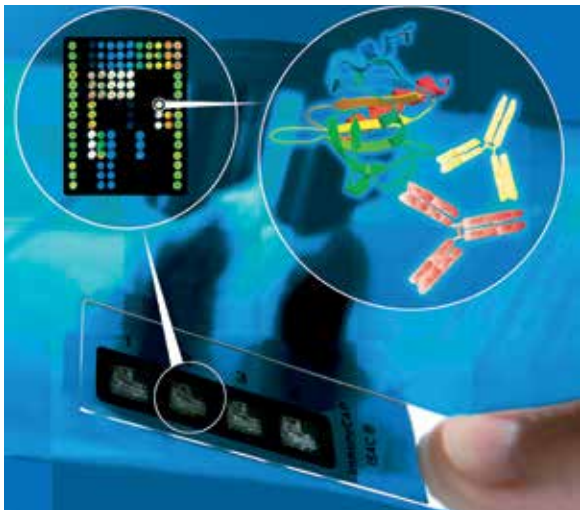
Pioneering the field of allergen components, we have recently launched new hazelnut components – Cor a 9 and Cor a 14 - which both are storage proteins of high stability that are present in high amounts in the hazelnut. We highly recommend the use of these components in the daily clinical practice as they most certainly will help to improve the diagnosis and risk assessment of hazelnut allergic patients.

The entire sixth issue of ImmunoDiagnostics Journal is dedicated to CAPture where recently published articles in the field of allergy showing the utility of quantitative IgE measurements using allergen components are summarized. The use of allergen extracts for detecting IgE have benefits in terms of not only specificity but also sensitivity over skin prick testing as demonstrated in the LEAP study on peanut allergy prevention. You will also find articles where ImmunoCAP® ISAC has been used in studies, and sensitization could be detected before on-set of clinical symptoms, implying a possibility for intervention.

We hope you will find that the selection gives a good overview of the latest publications regarding allergy diagnostics, and that among the fourteen referred articles you will find some that are of special interest to you.

Wishing you all a relaxing summer,





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Editor

Malin Berthold

Contributor(s)

Jan Hed, Anita Kober

Overview

In this issue we present selected publications from allergy journals that demonstrate the utility of the ImmunoCAP® tests in clinical diagnostic routine. The majority of the selected articles show the benefit of allergen components to identify different sensitization phenotypes in patients that correlate with different clinical expressions of allergy.

Hazelnut/Peanut

New tests for hazelnut storage proteins (Cor a 9 and Cor a 14) are now available. *Masthoff et al*. show that sensitization to these are associated with systemic reactions. In this study, sensitization to the hazelnut 11S globulin (Cor a 9) has a slightly better diagnostic capacity in children than IgE to 2S albumin (Cor a 14) and the reverse is indicated in adults. However, both Cor a 9 and Cor a 14 improve the diagnosis and risk assessment of hazelnut allergy.

Using an atopic infant population, *Du Toit et al*. studied the association between egg allergy and/or atopic dermatitis and peanut sensitization. They show that about 30% of infants with severe atopic dermatitis and/or egg allergy are sensitized to peanut (cut off at 0.1 kU_A/l) despite a negative skin prick test. Peanut sensitized infants show a broad co/cross-sensitization to tree nuts and sesame seed.

Birch pollen-sensitized children sensitized to only to Ara h 8 in peanut have a low risk for peanut-related reactions which is demonstrated by *Asarnoj et al*. Less than 10% of the children reacted in challenge and the majority only with oral symptoms in the provocation test when performed outside the pollen season.

Clinical utility of ISAC

ImmunoCAP ISAC is a valuable tool to identify sensitizations as markers for subclinical inflammations before onset of clinical symptoms. *Patelis et al*. show that pollen-sensitized patients with related food allergen sensitization have ongoing inflammation as measured by FENO but no increase in bronchial hyper-reactivity. *Onell et al*. demonstrate sensitization to fish, peanut/soy, nuts, wheat and mites before expression of any clinical symptoms in Swedish children. A similar observation was done in roughly half of the children finally developing symptoms to animal dander and pollen. Both of these studies show the clinical utility of mapping the full sensitization profile.

Using ImmunoCAP ISAC for profiling latex sensitized patients, *Schuler et al*. show that in cases with positive IgE to the latex extract but unclear symptoms, component resolved diagnostics should be used and that Hev b 8 mono-sensitized patients are unlikely to react upon contact with latex.

Egg/Milk

Caubet et al. demonstrate that serum IgE against casein has significantly greater accuracy to predict baked milk reactivity than IgE to cow's milk extract or ß-lactoglobulin. No patient who tolerated to baked milk was sensitized to casein, indicating 100% sensitivity for identifying baked milk reactive children in this study.

In *Wood et al*. the likelihood of tolerance development by age five in milk allergic infants is investigated. The severity of atopic dermatitis and IgE levels against milk extract are used in a suggested index that is intended to be further evaluated in clinical routine.

A probability curve for IgE titers to egg ovomucoid vs. egg white extract in atopic patients allergic or tolerant to boiled egg white is presented by *Haneda et al.* IgE to ovomucoid is shown to better identify patients with a true allergy to boiled egg, which can help to reduce the number of necessary challenge tests.

Food dependent exercise induced anaphylaxis (FDEIA)

Wheat omega-5 gliadin is a major allergen component in wheat-dependent exercise induced anaphylaxis (WDEIA). In the study of *Takahashi et al.* 81% of the WDEIA patients are sensitized to omega-5 gliadin, and 17% to HMW-glutenin. By combined testing to both omega-5 gliadin and HMW glutenin, the sensitivity for identifying WDEIA patients is increased although the specificity is slightly decreased.

The importance of co-factors to trigger clinical symptoms is discussed in three publications. *Cardona et al.* present a retrospective study of suspected co-factor-enhanced food allergic reactions in adult Spanish patients. The most common co-factor was NSAIDs, and sensitization to peach LTP, wheat omega-5 gliadin, and kiwi thaumatin (Act c 2) were the dominating food allergens.

In Italy *Romano et al.* analyzed the sensitization profiles of FDEIA patients by ImmunoCAP ISAC. They show that multiple food sensitizations are a hallmark in FDEIA and that the sensitization to LTP might be the causative factor for allergic FDEIA in the area. *Pascal et al.* studied the sensitization profiles of food-allergic patients sensitized only to LTPs in plants/plant foods in Spain. They found that one third of these patients only reacted when a co-factor was involved, and most commonly they were sensitized to peach LTP. They also speculate that plane tree pollen might be a source for LTP-sensitization.

Venoms

Vos et al. verified that spiking ImmunoCAP wasp venom extract with wasp venom Antigen 5 (Ves v 5) increased the sensitivity from 83.4% to 96.8% without affecting the specificity. Thus, the new spiked test allows a more reliable detection of wasp venom sensitization.

CAPture – Hazelnut/Peanut allergy

SYNOPSIS

- Hazelnut-sensitized children (n=81) and adults (n=80) where roughly half passed and half failed DBPCFC in each age group were recruited.
- Serum IgE to hazelnut and birch extracts, hazelnut and birch components (Cor a 1, Cor a 8, Cor a 9 , Cor a 14, Bet v 1, Bet v 2) and CCD were measured with ImmunoCAP® applying a cut off of 0.35 kU_A/l. (Phadia Laboratory System, Thermo Fisher Scientific, Uppsala, Sweden).
- Children with symptoms were significantly younger than those without symptoms (median 7 *vs.* 9 years).
- Birch pollen sensitization was significantly lower in children with symptom (73% *vs.* 95%).
- Mono-sensitization to Cor a 1 in symptomatic patients was more common in adults than in children (49% *vs.* 13%).
- The majority of children and almost half of the adults with hazelnut allergy were sensitized to Cor a 9 and Cor a 14.

Citation: Masthoff LJ et al. Sensitization to Cor a 9 and Cor a 14 is highly specific for a hazelnut allergy with objective symptoms in Dutch children and adults. J Allergy Clin Immunol. 2013 Apr 10. [Epub ahead of print].

Hazelnut storage proteins (Cor a 9, Cor a 14) are risk markers for severe hazelnut allergy in both children and adults

The clinical expression of hazelnut allergy varies in severity and differs between children and adults. The aim of this study was to correlate the sensitization profile in hazelnut sensitized children and adults in a birch-endemic area with the clinical expression of hazelnut allergy. Sensitizations to the storage proteins Cor a 9 and Cor a 14, Cor a 1 (PR-10 protein) and Cor a 8 (LTP) were measured and double blind placebo controlled hazelnut challenges were performed.

The prevalence of IgE to the tested storage proteins was significantly higher in symptomatic than non-symptomatic hazelnut-sensitized patients (70-83% *vs.* 20-24%), while no such difference was seen for IgE to Cor a 1or Cor a 8. ROC analysis showed that IgE to Cor a 9 (11 S globulin) had a slightly better capacity than IgE to Cor a 14 (2S albumin) to identify symptomatic children.

In children, cut offs at 1 kU_A/l for Cor a 9 and 5 kU_A/l for Cor a 14 gave specificity and sensitivity of 93% and 83%, respectively. In adults, a cut off at 1 kU_A/l for both Cor a 9 and Cor a 14 gave a specificity of 98% and a sensitivity of 44%. This low sensitivity might be due to a high prevalence of birch-pollen related hazelnut allergy in the adult population below this cut off level.

In conclusion the study shows that Cor a 9 and Cor a 14 are markers for a severe hazelnut allergy phenotype.

SYNOPSIS

- Infants with atopic dermatitis, egg allergy or both (n=834, 4-10 months) were recruited from a screening study investigating prevention of peanut allergy.
- Infants with severe atopic dermatitis were divided into sub-groups according to skin prick test reactivity to peanut.
- Serum IgE to peanut, egg white, cow's milk, sesame seed, Brazil nut, hazelnut, cashew, almond, and walnut were tested by ImmunoCAP.
- Peanut sensitization (> 0.1 kU_A/l) was seen in 91% of the subgroup with highest skin reactivity (> 4 mm).
- The prevalence of peanut sensitization increased significantly (< 0.001) with the prevalence of egg allergy in patients with severe dermatitis.
- High odd ratios were shown for predicting peanut sensitization by using severe atopic dermatitis or egg sensitization (> 0.35 kU_A/l).

Citation: Du Toit et al. Identifying infants at high risk of peanut allergy: the Learning Early About Peanut Allergy (LEAP) screening study. J Allergy Clin Immunol. 2013;131-5.

About 30% of infants with severe atopic dermatitis and negative skin tests to peanut show serum IgE to peanut above 0.1 kU_A/l

Peanut sensitization may start during the first year of life and then often with serum IgE against storage proteins. This kind of sensitization is associated with a high risk for systemic reactions during early childhood. In this study the association between peanut sensitization and egg allergy and/or atopic dermatitis was studied.

In infants with severe atopic dermatitis but negative skin test to peanut, 16.8% and 30% of the children were positive for peanut IgE above the levels of 0.35 and 0.1 kU_A/l respectively and among the peanut sensitized infants 64.5% were also sensitized to tree nuts and sesame seed. More than a fourth (26.8%) of all infants were sensitized to tree nuts or sesame seed, Sensitization to sesame seed, Brazil nut, hazelnut and cashew were most common. Peanut serum IgE could be detected in 91% of the children who had a skin prick wheal diameter of 4 mm or above. Infants with mild atopic dermatitis and no egg allergy were not sensitized to peanut.

The important finding of this study was that about 30% of infants with severe atopic dermatitis and/or egg allergy were sensitized to peanut (cut off 0.1 kU_A/l) despite a negative skin prick test. Furthermore, peanut sensitized infants are shown to display a broad co/cross-sensitization to tree nuts and sesame seed.

SYNOPSIS

- Children with peanut sensitization related to birch pollen (Ara h 8) without previously detected sensitization to storage proteins Ara h 1, Ara h 2, or Ara h 3 were recruited (n=144).
- Just over half (57%) of the children could eat peanut without problem.
- Twelve patients reported symptoms to peanut of which four indicated systemic symptoms.
- At challenge new blood samples were taken and serum IgE to storage proteins Ara h 1, Ara h 2, Ara h 3 and Ara h 6, PR-10 Protein (Ara h 8), and LTP (Ara h 9) were tested by ImmunoCAP.

Citation: Asarnoj A et al. Peanut component Ara h 8 sensitization and tolerance to peanut. J Allergy Clin Immunol. 2012;130:468-72.

Less than 10% of children with only birch pollen related peanut sensitization react in oral peanut challenge, and most of these react with oral symptoms only

The authors have previously shown that only 17% of children with a birch pollen dependent sensitization to peanut display clinical symptoms. The aim of this study was to investigate the risk of systemic reactions to peanut in patients sensitized only to the peanut component Ara h 8 (PR-10 Protein) and not to storage proteins Ara h 1, Ara h 2 and Ara h 3 (n=144).
Only 9.7% reacted with oral symptoms at challenge, indicating that 90% of the sensitized children were not allergic to peanut. One patient had a systemic reaction (grade I) when challenged during pollen season but not when challenged outside season. Furthermore, five children had reported previous mild systemic reaction but only one had been documented. Another patient with systemic reaction (grade I) to peanut challenge but negative to Ara h 1, Ara h 2 or Ara h 3 was after further investigation shown to be sensitized to the storage protein Ara h 6. This is a rare case of a positive Ara h 6 but negative Ara h 2 which otherwise usually is positive if Ara h 6 is positive.
The authors conclude that most patients with only birch pollen related peanut sensitization (*i.e.* mono-sensitized to Ara h 8) are tolerant to peanut at doses used in this study and may be subject to supervised reintroduction of peanut. However some might experience symptoms during pollen season and in rare cases patients may also be sensitized to peanut storage proteins other than Ara h 1, Ara h 2 or Ara h 3.

CAPture – FDEIA

SYNOPSIS

- Patients reporting at least one episode of exercise induced anaphylaxis within 4 hours after a meal were recruited (n=82, mean age 22.8 years).
- Thirty-one subjects (37.8%) had only had one episode of FDEIA.
- The most common symptoms were flushing (98%), angioedema (93.9%), urticaria (91.5%), dyspnea (79.2%) and hypotension (34.1%).
- Roughly 80% of patients could report a suspected causative food.
- Twenty-eight percent reported co-factors for the reactions such as NSAID and symptoms of allergic pollen rhinitis.
- Serum IgE was measured by ImmunoCAP and ImmunoCAP® ISAC.

Citation: Romano A et al. Lipid transfer proteins: the most frequent sensitizer in Italian subjects with food-dependent exercise-induced anaphylaxis. Clin Exp Allergy. 2012;42:1643-53.

Multiple plant food sensitizations are hallmarks of FDEIA and sensitization to LTP is likely a causative factor in southern Europe

The pathological background of food-depended exercise-induced anaphylaxis (FDEIA) is not known but it is frequently associated with sensitization to and intake of plant-derived foods. The aim of this study was to identify the most frequent culprit allergen components in patients with FDEIA (n=82) using ImmunoCAP ISAC containing 89 different allergen components.

The most commonly reported allergen associated with FDEIA was tomato (30.4%). All other suspected foods were reported in less than 10% of the cases. Almost all (96.3%) patients were sensitized to at least one food and 62% of those were sensitized to more than 20 distinct food sources, primarily plant food allergens. Only a few patients were sensitized to food allergens of animal origin. Sensitization to LTP (Pru p 3) dominated with a frequency of 78%, and corresponding figures were 15.5 % to profilin, 4.8% to PR-10 proteins and 1.2 % to both tropomyosin and gliadin. Sensitization to LTP was more common in the patient population with FDEIA compared to in the control group of allergic patients without FDEIA.

The authors conclude that multiple food sensitizations is a hallmark in FDEIA patients and suggest that LTP-sensitization is the causative factor in FDEIA.

SYNOPSIS

- Consecutive patients sensitized to peach and/or hazelnut LTP and at least two non-related plant food allergens but not to other plant pan-allergens were recruited (n=45, age 14-47 years).
- Involvement of cofactors was determined by reviewing the clinical history.
- The most common cofactor was NSAIDs (88.9%) while exercise was identified in just one patient.
- Serum IgE to plant allergens were analyzed by using ImmunoCAP ISAC 103.
- No sensitizations to other defined plant allergens such as profilins, PR-10 proteins or storage proteins were detected.

Citation: Pascal M et al. Lipid transfer protein syndrome: clinical pattern, cofactor effect and profile of molecular sensitization to plant-foods and pollens. Clin Exp Allergy. 2012;42:1529-39.

The LTP-syndrome is characterized by heterogeneous clinical expression including OAS and association to co-factors and plane pollen sensitization

The LTP syndrome has been suggested to be due to peach LTP as a driving cause. The clinical expression of the syndrome shows a great variability from oral allergy syndrome (OAS) to anaphylactic shock even within the same patient. The aim of the present study was to describe the clinical expression and the sensitization profile of plant-food allergic patients sensitized to LTP but not to PR-10 proteins or profilins.

OAS was frequent (75%) but no patient expressed only OAS. Most patients (78%) had experienced anaphylactic reactions and one third of these only if in combination with a co-factor. Seven more patients reported involvement of co-factors for reactions other than anaphylaxis. About 75% of the patients had pollen rhinitis, in one third associated with asthma. Almost all patients were sensitized to peach LTP (98%) but none to pollen related proteins such as profilin or PR-10 protein. Most patients (89%) were sensitized (> 0.1 kU_A/l) to plane tree pollen and 75% of those were sensitized to the major pollen allergens Pla a 1 and/or Pla a 2 indicating a primary sensitization to plane tree. All these plane tree positive patients were sensitized to hazelnut LTP (Cor a 8).

The authors conclude that the LTP-related food allergy in the region is not only characterized by a strong relation to peach but also to plane tree pollen pollinosis and co-factors.

SYNOPSIS

- Patients with positive wheat challenge test after exercise (WDEIA) were recruited (n=48).
- Wheat sensitized but asymptomatic atopic dermatitis patients (n=16) were studied and healthy subjects (n=12) were used as controls.
- Specific IgE to wheat extract, gluten, omega-5 gliadin, a HMW-glutenin peptide and HMW-glutenin were tested by ImmunoCAP technology.
- IgE levels equal to or above 0.7 kU_A/l were defined as positive.

Citation: Takahashi H et al. Recombinant high molecular weight-glutenin subunit-specific IgE detection is useful in identifying wheat-dependent exercise-induced anaphylaxis complementary to recombinant omega-5 gliadin-specific IgE test. Clin Exp Allergy. 2012;42:1293-8.

IgE to HMW-glutenin in combination with omega-5 gliadin increase the test sensitivity from 81.3% to 93.8% in the diagnosis of WDEIA

Omega-5 gliadin has been shown to be a major allergen component in wheat-dependent exercise induced anaphylaxis (WDEIA). Previously, high molecular-weight glutenin (HMW-glutenin) has also been suggested as a major allergen in WDEIA. In the present study the value of including HMW-glutenin as an ImmunoCAP based test, together with omega-5 gliadin is evaluated. Sera from patients with WDEIA were compared to sera from wheat-sensitized patients with atopic dermatitis (AD) without wheat-related symptoms and healthy controls.

More than 80% of the WDEIA patients but none of the wheat sensitized AD patients or healthy controls were sensitized to omega-5 gliadin, which gives 100% specificity for this test. Seventeen percent of the WDEIA and 12.5% of the AD patients were sensitized to HMW-glutenin. Including test results for HMW-glutenin (positivity to both or either) in the diagnostic workup of WDEIA patients, increases the sensitivity to 93.8% while decreasing the specificity to 88% if AD patients are the controls.

The authors conclude that the ImmunoCAP test based on recombinant HMW-glutenin verifies their earlier results based on native HMW-glutenin and epitopes of this protein.

CAPture – FDEIA/Milk allergy

SYNOPSIS

- Adult patients with co-factor enhanced food allergy were recruited in a retrospective study (n=74, median age 34.5 years).
- More than one third had experienced recurrent reactions.
- Co-factors described were NSAID, exercise and alcohol in 58%, 53% and 12% of the cases, respectively.
- Culprit plant foods, mainly vegetables and cereals (99%), were reported in all cases.
- The sensitization profile was analyzed by using ImmunoCAP ISAC.

Citation: Cardona V et al. Co-factor-enhanced food allergy. Allergy. 2012;67:1316-8.

Analysis of the sensitization profile to plant food allergens are important in anaphylactic reactions where co-factors are likely to be involved

The triggering of a severe food allergic reaction may depend both on the serum concentration of allergen specific IgE but also on the dose of the culprit food allergen and how the food allergen withstand the environment in the gastrointestinal tract. During recent years the awareness that other factors may contribute to make the difference between "reaction" and "no reaction" to food allergens in an individual has increased. Certain food allergen sensitization profiles may be related to an increased risk for co-factor dependent allergic reactions, which is the focus of this study.

The presented report is a retrospective descriptive study of suspected co-factor-enhanced food allergic (CEFA) reactions in adult patients and with focus on co-factors such as exercise, alcohol and NSAID intake. Most patients (85%) had had anaphylactic reactions and the rest urticaria or angioedema. Many patients (39.2%) had experienced several CEFA reactions. When the allergens were avoided there were no reactions to NSAID alone. Sensitization to peach LTP (Pru p 3) (91.7%), wheat omega-5 gliadin (20%) and kiwi thaumatin (Act c 2) (8.3%) were most frequent.

The conclusion of these results is that analysis of the sensitization profile to plant food allergens are important in patients with systemic reaction where co-factors such as NSAID, exercise or alcohol could be involved.

SYNOPSIS

- Children with present or recent milk allergy were recruited to the study (n=225, age 2.1-17.3 years).
- Tolerance to baked milk was tested by oral food challenge.
- Serum IgE and IgG4 to cow's milk, casein and ß-lactoglobulin were tested by ImmunoCAP.
- Changes in the ratio IgE/IgG4 was believed to be due to changes in IgE and not IgG4.
- The clinical relevance of IgE to casein was suggested to be due to its high heat stability.
- Levels of casein specific IgE below 1 kU_A/l were calculated to be highly predictive of tolerance to extensively heated milk.
- No children who tolerated baked milk in this study had detectable casein-specific IgE levels.

Citation: Caubet JC et al. Utility of casein-specific IgE levels in predicting reactivity to baked milk. J Allergy Clin Immunol. 2013;131:222-4.

Quantitative measurements of casein-specific IgE using ImmunoCAP are useful in the management of cow's milk allergic children and low/absent levels are good indicators of tolerance to extensively heated milk products

The authors have previously shown that children allergic to baked milk products have a higher risk of anaphylactic reactions and slower development of tolerance than children allergic to only fresh but not baked milk. Here, the diagnostic value of serum IgE to the milk components casein and ß-lactoglobulin (Bos d 5) to identify this milk allergy phenotype was analyzed.

Serum IgE to cow's milk, casein and ß-lactoglobulin were significantly higher in the baked milk reactive population than in those tolerating baked milk. Using ROC analysis, serum IgE against casein was shown to have a significantly greater accuracy to predict baked milk reactivity than IgE to cow's milk or ß-lactoglobulin. None of the patients who tolerated baked milk were sensitized to casein, indicating 100% sensitivity to identify baked milk reactive children and 100% negative predictive value to exclude reactivity by measuring serum IgE to casein. A positive decision point to prove the reactivity (95% specificity) was defined at 20.2 kU_A/l casein-specific serum IgE and a negative decision point to exclude reactivity (95% sensitivity) at 0.94 kU_A/l.

The authors conclude that serum IgE to casein is the best diagnostic marker for identifying patients who react to all forms of milk, and casein levels below approximately 1 kU_A/l is highly predictive of tolerance to extensively heated milk.

SYNOPSIS

- Infants (n=239, 3-15 months of age) with milk allergy were recruited, 89% of which had atopic dermatitis (87% moderate/severe).
- Median age at the last follow-up was 66 months and all but 6 were followed for more than 4 years.
- Serum IgE to cow's milk was measured by using ImmunoCAP.
- Milk allergic infants with no or mild atopic dermatitis were more likely to grow out of their milk allergy than those with moderate/severe dermatitis.
- Infants with milk-specific serum IgE < 2 kU_A/l showed a 5.74-fold increased hazard (probability) ratio to resolve the allergy compared to those with milk-specific serum IgE above 10 kU_A/l.
- The resolution of milk allergy was not associated with other food allergies.

Citation: Wood RA et al. The natural history of milk allergy in an observational cohort. J Allergy Clin Immunol. 2013;131:805-12.

A combined index based on IgE-sensitization to milk and severity of atopic dermatitis at baseline predicts resolution of milk allergy at five years of age

There is conflicting data about the rate of resolution of milk allergy, and the authors speculate that this partly depend on different study design and patient selection. The aim of this study was to evaluate predicting factors such as serum IgE to milk for the resolution of milk allergy at 5 years of age in milk allergic subjects (n=293) from a large well-characterized infant cohort.

In roughly 50% of the milk allergic infants the milk allergy had resolved at years of age. The serum level of IgE to milk and the severity of atopic dermatitis at baseline were shown to be predicting markers for milk allergy resolution. Most (70%) infants with a serum IgE to milk below 2 kU_A/l at baseline became tolerant to milk at 5 years of age, compared to 23% of infants with levels above 10 kU_A/l. It was also shown that the most recently assessed levels of milk IgE were highly significant predictors of resolution.

Based on the observation that the level of IgE-sensitization and severity of atopic dermatitis at baseline could be used to predict milk allergy resolution, the authors designed a combined index to predict this likelihood in clinical routine in children.

CAPture – Egg allergy/Utility of ISAC

SYNOPSIS

- The infants (n=100, age range 12-23 months) recruited to the study had atopic dermatitis, other food allergies or a family history of atopy but unknown previous exposure to egg.
- Oral food challenge was performed by using boiled egg white.
- Serum IgE to egg white (f1) and ovomucoid (Gal d 1, f233) was tested by ImmunoCAP using a cut off of > 0.35 kU_A/l.
- Logistic regression showed a PPV of 54% for ovomucoid and 30% for egg white at 10 kU_A/l.
- IgE to ovomucoid was (< 0,35 kU_A/l) IgE was highly predictive of tolerance to extensively heated egg (21 of 24 patients, 88% likelihood).

Citation: Haneda Y et al. Ovomucoids IgE is a better marker than egg white-specific IgE to diagnose boiled egg allergy. J Allergy Clin Immunol. 2012;129:1681-2.

IgE to Ovomucoid is a more specific marker for tolerance to boiled egg than IgE to whole Egg white

The serum levels of food allergen specific IgE are often used to calculate the predictive values to fail or pass a food challenge test. The aim of the present study was to evaluate the utility of specific IgE to egg white and ovomucoid (Gal d 1) to predict the outcome of oral food challenge with boiled egg white in an infant population. The infants recruited to the study had atopic dermatitis, other food allergies or a family history of atopy but had not previously been exposed to egg.

One third of the infants reacted in challenge tests to boiled egg white. The level of serums IgE to egg white (15.6 kU_A/l *vs.* 4.3 kU_A/l) and ovomucoid (8.1 kU_A/l *vs.* 1.0 kU_A/l) were significantly higher in challenge-positive than challenge-negative infants.

From the plots presented, the specificity of ovomucoid-IgE is shown to be higher than for IgE to egg white. This gives that the positive predictive value for ovomucoid specific IgE is higher than for egg white. An optimal cut off is estimated to be around 3 kU_A/l for ovomucoid which gives a specificity of 77% and a sensitivity of 81%.

Most importantly, these results showed that a negative (<0.35 kU_A/l) IgE value to ovomucoid was highly predictive (88% likelihood) of tolerance to extensively heated egg, irrespective of the IgE level to complete egg white (f1).

SYNOPSIS

- A retrospective analysis of a birth cohort, followed from 3 months to 18 years of age (n=67).
- The allergen sensitization profiles to 103 allergen components from 47 different allergen sources were assayed by ImmunoCAP ISAC.
- Each child displayed a unique IgE profile.
- Out of 82 triggering allergens causing symptoms as defined by doctors diagnosis, 76 (93%) were identified by the microarray results.
- In most cases, IgE antibodies were detected before symptom on-set.
- The IgE antibody development over time generally started with a low-level sensitization to one component and continued to spread to several components of the same allergen source as well as higher IgE levels to each component.

Citation: Onell A et al. Exploring the temporal development of childhood IgE profiles to allergen components. Clin Transl Allergy. 2012 Dec 19;2(1):24.

Microarray analysis of sensitization profiles reveals early sensitization before onset of clinical allergy

In the present retrospective study the sensitization profiles to 103 allergen components of a Swedish birth cohort were followed from 3 months to 18 years of age.

Doctor's diagnosis made at each time-point was compared to the microarray sensitization profile, and in 93% of the cases the suspected triggering allergens were verified by the test results. Based on the sensitization profiles, two subgroups were identified; those with sensitization before 18 months of age, and those with later sensitization development. In the early sensitization subgroup (19%), the dominating sensitizations were to egg (14%), milk (11%), and peanut (6%, storage proteins). In older children (6-18 years) sensitization to timothy (42%), birch (28%) and cat (22%) were most common.

An important observation was that sensitizations to fish, peanut/soy, nuts, wheat and mites were always detected before the onset of clinical symptoms. A similar observation was done in roughly half of the children eventually developing symptoms to animal dander and pollen. No history of food sensitization at early age could be seen in the late sensitization subgroup (38%, > 6 years). The authors conclude that early sensitization profiling by microarray technology is a promising tool especially in multi-sensitized children for potential benefits of early intervention.

SYNOPSIS

- Adult patients with self-reported asthma (n=96) and healthy controls (n=371) were recruited to the study.
- Serum IgE to 103 different allergen components were measured with ImmunoCAP ISAC.
- 70% of the asthma patients were sensitized compared to 40% of the non-asthmatics.
- The risk of asthma, FENO and bronchial responsiveness increased with multiple sensitizations to the tree allergen groups.
- Sensitization to pollen-related food allergens was independently associated with increased FENO and increases the risk of asthma in subjects with simultaneous sensitization to pollen allergens.

Citation: Patelis A et al. Population-based study of multiplexed IgE sensitization in relation to asthma, exhaled nitric oxide, and bronchial responsiveness. J Allergy Clin Immunol. 2012;130:397-402.

Multiple sensitizations to different allergens groups as well as sensitization to plant food allergens in pollen-sensitized patients increase the risk for asthma

Polysensitization is known to be associated with increased asthma prevalence and severity. The aim of the present study was to investigate the relationship between a detailed sensitization profile and asthma prevalence, bronchial inflammation (exhaled NO) and bronchial hyperreactivity (metacholine challenge) in adults.

Asthma patients had higher sensitization frequency to animal dander, pollen and pollen-related food allergens than controls. The sensitization to mite and animal food allergens was below 5% and did not differ from the controls.

Simultaneous sensitization to perennial allergens (*e. g.* cat and dog), pollen, and food allergens gave the highest risk for asthma (odds ratio 18.3), bronchial inflammation and responsiveness. Asthma and bronchial hyper-reactivity/ inflammation was more prevalent in subjects sensitized to both pollen and food allergens, than in those only sensitized to inhalants.

In conclusion the results indicate that sensitization to plant food allergens in pollen-sensitized patients might be markers of a bronchial subclinical inflammation. The study also shows that patients sensitized to several different groups of allergens have an increased risk for asthma and that these multi-sensitization profiles can be identified using ImmunoCAP ISAC.

CAPture – Utility of ISAC/Venom allergy

SYNOPSIS

- Latex sensitized adults were recruited and analyzed retrospectively (n=41, mean age = 38 years).
- The sensitization profiles to latex were analyzed by ImmunoCAP ISAC (containing latex components Hev b 1, Hev b 3, Hev b 5, Hev b 6, Hev b 7, Hev b 8, Hev b 9, Hev b 10 and Hev b 11 and CCD (Bromelain).
- Four patients (of which two had latex-related symptoms) were negative to the tested latex components but positive to latex extract.
- Only two of 24 Hev b 8 (profilin) sensitized patients were sensitized to other latex components.
- No sensitization was shown to Hev b 3, Hev b 7 or Hev b 9.
- Hev b 8 mono-sensitized patients did not show symptoms upon contact with latex.

Citation: Schuler S et al. Microarray-based component-resolved diagnosis of latex allergy: isolated IgE-mediated sensitization to latex profilin Hev b 8 may act as confounder.
Clin Transl Allergy. 2013;3:11.

Hev b 8 mono-sensitized patients are unlikely to react upon contact with latex

It is important to before surgery assess whether a patient with serum IgE to latex is suffering from latex allergy or not. The use of microarray technology can be used to evaluate latex sensitization on the molecular level in patients.

The aim of the present study was to analyze the sensitization profiles of latex sensitized patients and relate these to clinical symptoms.

Approximately a third of the patients in the studied population reported clinical symptoms to latex. Most patients with clinical symptoms were mono-sensitized to Hev b 6 and to a lesser extent to Hev b 5.

Half of the patients were mono-sensitized to latex profilin (Hev b 8) but only one reported mild latex related symptoms. Another two of the patients sensitized only to profilin, were sensitized to CCDs and these reported clinical symptoms to latex, however this reactivity may be due to IgE to latex proteins not included in the present study such as Hev b 12 and Hev b 13.

The authors conclude that in cases with positive IgE to the latex extract ImmunoCAP but unclear symptoms, component resolved diagnostics should be used and that Hev b 8 mono-sensitized patients are unlikely to react upon contact with latex.

SYNOPSIS

- Patients with systemic reaction to wasp venom were recruited (n=308).
- Determination of the culprit insect was based on interview or testing with serum IgE, skin prick test or basophil activation test.
- Serum IgE to wasp venom extract and component tests were measured with ImmunoCAP (Ves v 5- spiked wasp extract, Ves v 1 and Ves v 5).
- Cut off levels at > 0.35 kU_A/l were used.
- Serum IgE levels to Ves v 5 were higher than to non-spiked wasp venom.
- Serum IgE levels to Ves v 1 were lower than to wasp extract in most patients.
- Updating the ImmunoCAP i3 by spiking the wasp venom extract with Ves v 5 increased the test sensitivity to 96.8% without affecting the specificity.

Citation: Vos B et al. Spiking venom with rVes v 5 improves the sensitivity of IgE detection in patients with allergy to Vespula venom.
J Allergy Clin Immunol. 2013;131:1225-7.

Testing with ImmunoCAP wasp venom extract spiked with Ves v 5 increases the sensitivity from 83.4 % to 96.8% without affecting the specificity

Tests for wasp venom "Antigen 5" (Ves v 5) frequently has given higher reactivity than test for wasp venom extracts. A new wasp venom extract test (ImmunoCAP i3) spiked with Ves v 5 has therefore been developed, and the validation of the new wasp extract test is presented in this study.

In patients with a history of anaphylactic reactions to wasp sting, sensitization (defined as 0.35 kU_A/l or above) to non-spiked wasp extract was 83.4% compared to 96.1% sensitization to Ves v 5 and/or Ves v 1 (Phospholipase A1) components.

Only one of the patients negative to wasp extract was sensitized to Ves v 1 whereas 84.4% were sensitized to Ves v 5. Spiking the wasp extract with Ves v 5 increased the sensitivity to 96.8% without any change in specificity. No difference in reactivity between spiked and non-spiked wasp venom extract was shown in Ves v 5 negative sera.

The authors conclude that the new ImmunoCAP wasp venom extract spiked with Ves v 5 has an increased sensitivity and thus allows for a more reliable detection of wasp venom sensitization in patients with hymenoptera allergy.

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Manufacturer; Phadia AB, Uppsala Sweden.

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