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Issue 2

# CAPture

A Selection of Recent Allergy Papers

## SYNOPSIS

- Hazelnut IgE antibody positive children (n=26, mean age =7 years) who had underwent hazelnut provocation (DBPCFC) were recruited.
- Eight children demonstrated objective symptoms (angioedema, generalized urticaria, vomiting, diarrhea, rhinoconjunctivitis and/or dyspnea).
- Sera from the patients with objective symptoms were compared with sera from children with only oral allergy syndrome, OAS (n=4) and children without symptoms (n=14).
- Serum IgE antibodies to purified hazelnut nsLTP (nCor a 8) and recombinant peach nsLTP (rPru p 3) were tested by binding the allergens to Sepharose beads.
- Hazelnut-specific IgE antibodies were measured by ImmunoCAP® (Phadia AB, Uppsala, Sweden).
- IgE antibody levels to hazelnut were significantly higher ($p<0.001$) in patients with objective symptoms (median 32.5 *v.s.* 1.5 $kU_A/l$).
- An IgE antibody level ≥ 0.65 $kU_A/l$ to rCor a 8 showed 87.5% probability for having an objective reaction during DBPCFC.

*Citation: Flinterman AE et al. Lipid transfer protein-linked hazelnut allergy in children from non-Mediterranean birch-endemic area. J Allergy Clin Immunol 2008;121:423-8.*

### IgE antibodies to hazelnut nsLTP (Cor a 8) are common and associated with more severe symptoms in children from birch-endemic region of northern Europe

Recently, sensitization to Lipid Transfer Protein (nsLTP) has been shown to be a risk factor for anaphylactic reaction to hazelnut in the Mediterranean region. The aim of this study was to investigate if this is the case also in birch-endemic regions of northern Europe. The component specificity of IgE antibodies from hazelnut sensitized children with objective symptoms were compared to the IgE component profile from patients without symptom or only OAS. All eight children with objective symptoms to hazelnut were sensitized to hazelnut nsLTP (Cor a 8), but only two of them to peach LTP (Pru p 3) as well. Only one child of the 18 children in the group without objective symptoms was sensitized to hazelnut nsLTP.

It was shown, using multivariate analysis in a logistic regression model, that sensitization to hazelnut nsLTP was the only factor independently associated to provocation-verified objective symptoms. Sera from children with objective symptoms recognized significantly ($p = 0.001$) more protein bands in immunoblots and were also sensitized to more other nuts. In birch sensitized children from the same outpatient clinic of pediatric allergology, 30.9% were sensitized to hazelnut nsLTP and the prevalence increased up to 3 years of age.

The authors conclude that sensitization to hazelnut nsLTP is a risk factor for severe symptoms to hazelnut and that nsLTP from hazelnut and peach LTP show poor cross-reactivity.

## SYNOPSIS

- Infants (n=2184, mean age 17.6 months, range 11.8-25.4) were recruited from the Early Prevention of Asthma in the Atopic Child (EPAAC) study.
- The infants had atopic eczema and family history of atopy and were clinical assessed with Scoring Atopic Dermatitis (SCORAD).
- Serum IgE antibodies were measured to inhalant allergens (grass, tree, mite, cat and *Alternaria*) and food allergens (egg, milk and peanut) by ImmunoCAP®.
- Infants defined as "high-risk immunoglobulin E food sensitization" (HR-IgE-FS) were based on earlier published IgE decision point levels for egg, milk and peanut with probability of clinical relevant sensitization > 90% (PPV).
- The decision point for milk was ≥ 2.5 $kU_A/l$ in children < 1 year.
- The decision point for egg was 0.35 $kU_A/l$ in children < 2 years.
- The decision point for peanut was ≥14 $kU_A/l$ in older children, mean age 3.8 years.
- The earlier the age of onset, and the greater the severity of eczema, the greater the frequency of associated high levels of IgE food sensitization.

*Citation: Hill DJ et al. Confirmation of the association between high levels of immunoglobulin E food sensitization and eczema in infancy: an international study. Clin Exp Allergy 2008;38:161-8.*

### Every second infant with moderate/severe atopic eczema with onset before six months of age has a high risk for clinical relevant food sensitization

The aim was to study the relationship between IgE-mediated food allergy and atopic eczema in infants. The authors have recruited infants with active atopic eczema from a big international, multi-center study. The disease severity was assessed by SCORAD and IgE sensitization to common food and inhalant allergens. The proportion of infants in the moderate/severe eczema SCORAD category was 68%.

In an adjusted regression analysis HR-IgE-FS infants had the most severe eczema and the youngest age of onset ($p<0.001$). The frequency of HR-IgE-FS was greatest in those with eczema onset in the first 3 months of life (50.3%) and gradually decreased with increased age at onset up to after 12 months (21.8%) of age. There was also an association between eczema severity and the frequency of HR-IgE-FS in infants with eczema onset before but not after 12 months. In moderate/severe eczema the frequency of HR-IgE-FS varied between 46-64% in infants with onset before 6 months depending on onset age.

The authors conclude that early onset of severe atopic eczema is associated with high levels of IgE antibodies to food allergens and high risk for clinical food allergy. They claim that food allergies should be routinely assessed in infants with moderate to severe atopic eczema.

## SYNOPSIS

- Patients (n=13 391, age range 27.8-40 years) were recruited from the European Community Respiratory Health Survey (ECHRS I).
- IgE sensitization to house dust mite, timothy grass pollen, cat and *Cladosporium* was tested by skin prick test and ImmunoCAP®
- A positive serum test ≥ 0.35 $kU_A/l$ was considered as the gold standard.
- Sensitivity for SPT (grass, mite, and cat) increased from 53.9-66.5 to 63.4-73.4% when cut-off decreased from 3 mm to > 0 mm.
- Specificity for SPT (grass, mite, cat) decreased from 96.1-97.4 to 93.1-95.6% when cut-off decreased from 3 mm to > 0 mm.
- Analysis of *Cladosporium* was excluded due to weak relation between *in vivo* and *in vitro* diagnostics
- Using Youden index (> 0.81) a SPT > 0 mm was suggested to detect IgE sensitization (> 0.35 $kU_A/l$).
- Although data from the ECHRS I are from1990's the authors find the results useful to validate the suggestion to use a cut-off at > 0 mm in SPT to show sensitization.

*Citation: Bousquet P-J et al. Assessing skin prick test reliability in ECRHS-I. Allergy 2008;63:341-6.*

### Skin prick testing, using a cut-off at > 0 mm, only detect 63.4-73.4% of subjects with a serum IgE > 0.35 $kU_A/l$ to grass, mite and cat in a general population

It is a rather common believe that the skin prick test (SPT) is a more sensitive test than *in vitro* diagnostic tests to detect an IgE-mediated allergen sensitization. The aim of this study was to identify the best cut-off level in skin prick testing to identify an allergen sensitization when 0.35 $kU_A/l$ allergen-specific serum IgE was used as the gold standard. The study was a multi-center international cross-sectional survey of the general population. Four allergen extracts (mite, grass pollen, cat and *Cladosporium*) from the same manufacturer were tested with both the skin prick test and for allergen-specific serum IgE antibodies.

When a cut-off of 3 mm was used in the SPT the sensitivity to detect an allergen sensitization was only 53.9-66.5% for the three allergens grass, cat, and mite. A decrease in SPT cut-off to > 0 mm resulted in only a small increase in sensitivity to 63.4-73.4% for the allergens. Since this was a survey from a general population the authors calculated the positive predictive value for a positive SPT to show an allergen sensitization to be 58-79.3% when using a cut-off at > 0 mm.

By using the Youden index, the authors suggest a cut-off at > 0 mm for SPT in epidemiology studies to be most discriminative for allergen sensitization. However, they finally point out, based on the low sensitivity, that there are subjects with allergic sensitization proved by serum tests who are negative in the SPT.

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