

**FOOD IGE ANTIBODY DETERMINATION AS RISK
ASSESSMENT FOR SEVERE ASTHMA
REACTIONS IN CHILDHOOD**

*Dr Gideon Lack, Salton House, St Mary's Hospital -
London (United Kingdom)*



Food allergy and asthma are both atopic diseases and therefore frequently co-exist. Food allergy is common in childhood, affecting approximately 8% of infants. The diagnosis is based on a suggestive history supported by serum specific IgE, skin prick testing or food challenge. The role of diet in the aetiology of asthma and as a precipitant of exacerbations has been investigated extensively. Many people perceive diet as being an important precipitant of their asthma but objective testing suggests that it is only important in a minority. Meanwhile, there is considerable epidemiological evidence to suggest that there is a link between asthma and food allergy. Food can induce bronchospasm and food allergy has been implicated as a risk factor for life-threatening food allergy. The mechanism underlying this connection is unclear.

The relationship between food allergy and asthma is therefore complex. The following facts illustrate the close relationship between food allergy and asthma: 4-8% children with asthma have food induced wheezing; approximately 30-40% of children with food allergy have asthma; up to 40% of food allergic reactions have a respiratory component; aerosolised foods can induce allergic reactions; follow up studies of birth cohorts of children show that egg allergy in infancy predicts later respiratory allergy; anaphylaxis to food can mimic a severe exacerbation of asthma and almost always occurs in people who have asthma.

In addition to this evidence, 4 studies show the relationship between food allergy and fatal or near fatal asthma in particular.

> 4 (9%) subjects from a cohort of 46 children with peanut allergy died of asthma over a 2-14 year follow up period.

> A case controlled study of 45 subjects with near fatal asthma (age 5 to 45) showed that cases were more likely to be food allergic (OR 3.6), have had anaphylaxis (OR 5.6) and to have visited a bar/restaurant just prior to the attack.

> In a cohort of 12,000 subjects aged 5-45 prescribed > 10 prescriptions of bronchodilators, 129 had fatal or near fatal asthma. When these were matched to controls, food allergy was a significant risk factor (OR 5.1).

> A case-control study of 19 children ventilated on intensive care showed that the only independent risk factors were: 4 or more previous admissions with asthma (OR=9.85, 95%CI: 1.0-93.3, p=0.046) and food allergy (OR=5.89, 95%CI: 1.1-32.6, p=0.042).

There are three possible explanations for the link between persistent food allergy and life-threatening asthma. One explanation is that the attack is triggered by eating small amounts of allergen. The second explanation is that chronic exposure to aerosolised environmental allergens worsens bronchial inflammation. A third explanation is that persistent food allergy is a marker of an abnormal host-immune response rendering the airways more susceptible to inflammation and remodelling. ■

**INHALANT ALLERGY: CONSEQUENCES OF
MULTISENSITIZATION AND EXPOSURE**

*Prof. Adnan Custovic,
North West Lung Centre, Wythensawe Hospital -
Manchester - United Kingdom*



Sensitisation to indoor allergens is a strong risk factor for asthma in adults and older children. However, in most of the studies IgE mediated sensitisation is considered only as a dichotomous variable, i.e. individuals are assigned as either sensitised or not. There is a growing interest in the potential validity of the quantitative analysis of IgE antibody responses in predicting the presence and severity of childhood asthma. In the population-based study we have recently demonstrated that IgE mediated sensitisation is not just a yes/no phenomenon, and that the probability of persistent wheeze and early childhood asthma increases with increasing specific IgE antibody levels. In sensitized children and adults with established asthma, exposure to sensitizing allergens is implicated in exacerbation of symptoms. Increased levels of exposure in sensitized asthmatics have been related to increases in hospital admissions

and emergency room visits, increased bronchial hyper-responsiveness, increased levels of exhaled nitric oxide, lower levels of lung function, increased treatment requirements and even increased mortality. The other factor often associated with triggering asthma exacerbations are respiratory virus infections (in particular Rhinovirus infection). The mechanisms responsible for these virus-induced exacerbations remain uncertain. Proposed mechanisms include direct infection of the lower respiratory tract, the inflammatory response to viruses and increases in bronchial responsiveness and up-regulation of intercellular adhesion molecule-1 (ICAM-1) expression in bronchial epithelium.

In recent years, several experimental studies have suggested that viruses and allergens may have a synergistic effect on asthmatics, thus having a greater influence on exacerbation rate together than either factor alone. Models of experimentally induced RV infection in both allergic and non-allergic individuals using bronchoalveolar lavage and segmental allergen challenge have facilitated the investigations of the possible interaction between allergen sensitization, exposure and virus infection and their role in the induction of an asthma exacerbation.

Recent clinical studies have confirmed the experimental data that allergens and viruses may act together to exacerbate asthma, indicating that allergen exposure acts synergistically with viruses in sensitized patients, increasing the risk of hospital admission. Unfortunately, we still lack the effective strategies to control either viruses or allergen exposure. ■

NATURAL COURSE OF FOOD ALLERGY

Kirsten Beyer, M.D. -

Charité CVK - Berlin (Germany)



Allergic reactions to food affect up to 8% of children in the first years of life and then falls progressively until late childhood, after which the prevalence remains stable at 1% to 2%. Few foods, including **cow's milk, hen's egg, peanuts, tree nuts, wheat, soy, fish and shell fish**, are responsible for the vast majority of food allergic reactions, despite the enormous diversity of the human diet. Moreover, food allergy is one of the first manifestations of the "atopic march" as many of these children develop asthma and allergic rhinitis later in life.

The **natural course of food allergy** is a dynamic process that is different for each allergen. Most infants with cow's milk allergy develop symptoms in the first year of life, often before one month of age, but about 85% become clinically tolerant by the third year of life.

Hypersensitivity to hen's egg is more often recognized in the second year of life, and appear to be more persistent than cow's milk allergy, with approximately half of the patients becoming tolerant in three years and up to 66% of children in five years. As opposed to cow's milk and hen's egg allergies, peanut allergy tends to persist throughout adulthood. However, it has been reported in recent years that up to 20% of the peanut allergic children lose their allergy.

The majority of food allergic reactions are **IgE-mediated**. However, food-specific IgE is often present without clinical reactivity. Several other factors seem to influence the clinical response. Therefore, double-blind, placebo-controlled food challenges (DBPCFCs) are commonly used in sensitized children to determine the clinical relevance of measured food specific IgE antibodies. Within the last few years, food allergen-specific IgE concentrations in the serum have been correlated with the clinical reactivity in order to generate probability curves that depict the likelihood of patients with a particular food allergen-specific IgE level reacting to the food. **Diagnostic decision points** for food allergen-specific serum IgE concentration have been described for several foods including peanut, egg, milk and fish. These diagnostic decision points help to reduce the requirement for food challenges in a number of patients. In addition, it has been shown that the usage of purified or recombinant allergens instead of whole food allergen extracts, commonly used for measurement of specific serum IgE, might give additional information in food allergy diagnostic.

The natural course of food allergy is not static. Therefore, frequent re-evaluation of the patients is necessary in order to determine the actual status of clinical reactivity. Some patients will have developed tolerance; other might have developed additional food allergies. The mechanisms involved in **tolerance development** are poorly understood. However, we recently developed a model for predicting the likelihood of developing tolerance in cow's milk and hen's egg allergy based on the decrease in **food-specific IgE over time**. Using these likelihood estimates could aid clinicians in prognosis and in timing subsequent food challenges, thereby decreasing the number of premature and unnecessary DBPCFCs.

Moreover, children with persistent food allergies appear to have IgE antibodies to distinct **allergenic epitopes** that are not recognized by tolerant patients. Our studies on cow's milk proteins suggest that differences in epitope-specificity of IgE antibodies against cow's milk proteins play a role in persistence of cow's milk allergy. This might reflect differences in antigen absorption and processing, and measurement of these specific IgE antibodies could be used as an early marker of persistent cow's milk allergy. Similarly in peanut allergy determination of epitope recogni-

tion on the peanut allergens Ara h 1 and Ara h 2 provides an additional tool to diagnose symptomatic peanut allergy, especially in children with peanut-specific IgE below diagnostic decision levels.

In **summary**, food allergy is a dynamic process. Early and repeated measurement of specific serum IgE to food allergen extracts, individual proteins and/or allergenic peptides will help to determine the natural course of the disease. This will provide information for necessary therapeutic intervention. ■

EARLY DIAGNOSIS OF ALLERGY: WHY, WHO, WHEN, AND HOW?

Dr. Philippe Eigenmann - *University Children's Hospital - Geneva (Switzerland)*

The problems of allergic diseases in childhood (atopic dermatitis, asthma, allergic rhinitis and conjunctivitis) have increased considerably in developed countries in the last 20 to 30 years. Accordingly, the need of allergy testing has also increased. Based on epidemiological studies, it is estimated that the cumulative prevalence of allergic diseases in childhood is around 25 to 30%. More specifically, atopic dermatitis is diagnosed in 15 to 20% of children, asthma in 7 to 10% and allergic rhinitis and conjunctivitis in 15 to 20%. Allergy testing is a very important prerequisite for early identification of infants and young children at increa-

sed risk for later development of allergic diseases as well as for specific allergy treatment, i.e. allergen avoidance measures, pharmacotherapy or specific allergy immunotherapy. Indications for allergy testing in children should rely on objective symptoms and signs possibly indicative of an allergic disease.

Among commonly identified symptoms, atopic dermatitis should be tested when there are persisting symptoms or allergen related symptoms, particularly in case of other concurrent allergic diseases. Children with recurrent wheezing or asthma should be tested if the symptoms are severe or persisting and/or if there is a the need for daily treatment. In particular, children older than 3 to 4 years of age with asthma should always be tested for allergy. Other diseases possibly indicative of allergy are gastrointestinal symptoms, acute and chronic urticaria and angioedema, recurrent rhinitis and conjunctivitis, insect sting reactions and anaphylaxis. Specific allergens should be chosen according to the symptoms. The list of allergen suggested might be adapted according to age, and to geographical specificities. One should particularly consider the clinical relevance of the results obtained, necessitating in some cases allergen provocation tests.

Finally, allergy testing in children should be performed within a network of primary care physicians together with allergy specialists. Together, we will have the chance to successfully address the allergy epidemics, and to stop the progression of the atopic march in our patients.

