Food allergy
– From molecular biology to daily patient care
The EAACI-WAO 2013 joint congress in Milan, organized by the European Academy of Allergy and Clinical Immunology and the World Allergy Organization, with the theme Allergy, A Global Health Challenge attracted around 7,700 clinicians and scientists from all parts of the world. The scientific program covered most aspects of allergy and clinical immunology and many new findings in the field were presented during the lectures as well as in the poster presentations and through the over 2,100 abstracts that were submitted to the congress.

Thermo Fisher Scientific sponsored symposium
This year’s Thermo Fisher Scientific sponsored symposium had the title Food allergy – From molecular biology to daily patient care and took place Sunday, 23 June, at 13:30-15:00. The great interest in Molecular Allergology among clinicians and scientists was reflected by over 900 delegates participating in the symposium. The aim of the symposium was to invite leading scientists presenting new front line research combined with education and advice for how specific IgE to food and food allergen components can be used in daily clinical practice.

The chair Ulrich Wahn was accompanied by three prominent speakers who contributed with their extensive clinical experience in food allergy with focus on the use of allergen components in specific IgE testing. The speakers were Barbara Ballmer-Weber, Philippe Eigenmann and Hugh Sampson. Take home messages from their talks are summarized below.

Introduction
Ulrich Wahn, Germany
- A EuroPrevall birth cohort study including 12,000 newborns and their families from nine European countries has described a lifetime prevalence of self-reported food allergy among the mothers ranging from 5–8 % to 30 % (McBride et al. PAI 2012). But it is well known among clinicians that not all adverse reactions to food reported by patients are allergies.
- The degree of sensitization is associated with clinical reactivity in food allergy (Johannsen et al. CEA 2011) and has a prognostic value for persistent or outgrowing allergy (Wood et al. JACI 2013).
- Molecular diagnostics may help us understand and make clinical decisions. For example, specific IgE to Ara h 2 has been shown to be highly associated with peanut allergy and may reduce the need of food challenge testing (Nicolaou et al. JACI 2011).
- ImmunoCAP ISAC is a new allergen microarray test where specific IgE to more than 100 components can be measured in semi-quantitative manner using only 30 µl serum.
- Ongoing health economy studies will show if molecular allergology is cost-effective.
- A proper allergy diagnosis may reduce the costs for emergency room visits and hospitalization related to severe allergic diseases. However, a German study has shown that allergy diagnostics only stands for 1 % of the total healthcare costs for children’s asthma (Weinmann et al. PAI 2003).

Differentiation of severe vs. mild reactions to food using allergen components
Barbara Ballmer-Weber, Switzerland
- Up to 35 % of the population have a self-perceived food allergy while less than 22 % are sensitized and just 1–10 % have a true food allergy.
- Allergenicity of plant food proteins is associated with certain protein families. Important food allergens such as storage proteins in seeds and nuts are generally stable to food processing and digestion and are often highly abundant in the food.
- Lipid transfer proteins are highly stable allergens associated with severe allergic reactions to Rosaceae fruits in the Mediterranean area (i.e. Mal d 3 in apple), while pollen-related allergens like the Bet v 1 homologous allergens (i.e. Mal d 1) and profilins (i.e. Mal d 4) generally induce only mild reactions such as oral allergy syndrome (OAS) in sensitized subjects (Fernandez-Rivas et al. JACI 2006).
- IgE antibodies to the storage proteins Cor a 9 and Cor a 14 are associated with objective symptoms in hazelnut-sensitized individuals (Masthoff et al. JACI 2013).
- New unpublished data from the EuroPrevall project shows that IgE antibodies to Cor a 9 and Cor a 14 are associated with severe symptoms to hazelnut (Datema et al. Manuscript in preparation).
- Act d 1 belongs to the actidin family. It is a stable protein, highly abundant in kiwi fruit, and associated with severe food allergic reactions according to a recently published EuroPrevall study (Le et al, JACI 2012).
Molecular Allergology – Clinical reactivity vs. tolerance in children
Philippe Eigenmann, Switzerland

• Specific IgE levels to cow’s milk, egg white and wheat are associated with risk of allergic reactions in sensitized children (Sampson, JACI 2001).
• One third of children with moderate-to-severe atopic dermatitis may suffer from food allergy and should be tested for sensitization to common food allergens according to the recently published European guideline on allergy diagnosis in children (Eigenmann et al, PAI 2013).
• High specific IgE levels to ovomucoid (Gal d 1) are associated with allergy to cooked egg in egg white-sensitized children (Ando et al. JACI 2008).
• The level of IgE antibodies to casein (Bos d 8) has been shown to predict clinical reactivity to various forms of cow’s milk including baked milk (Boyano-Martínez et al. JACI 2009, Ito et al. CMA 2012, Caubet et al. JACI 2013,) and a high level of specific IgE against several casein epitopes may predict persistent milk allergy (Järvinen et al. JACI 2002).
• A combination of specific IgE to wheat and omega-5 gliadin (Tri a 19) and other wheat components provides an aid in diagnosis and risk assessment of severe allergic reactions to wheat in children (Palosuo et al. JACI 2001, Takahashi et al. CEA 2012).
• Follow-up of wheat allergy should include measurement of IgE antibodies to wheat. Measuring specific IgE to wheat and wheat allergen components might be helpful in regard to long-term prognosis (Keet et al. AAAI 2009, Shibata et al. AAAI 2011).

Diagnosing food allergy in daily practice – The emerging role of component testing
Hugh Sampson, USA

• The NIH Guidelines on the Diagnosis and Management of Food Allergy in the USA states that allergen-specific IgE tests and/or skin prick tests (SPT) are helpful in the identification of foods that may be provoking IgE-mediated food allergic reactions. However, the test results alone cannot be considered diagnostic of food allergy and should be used in connection with case history and physical examination (Boyce et al. JACI 2010).
• Fluorescence-labeled IgE antibody assays (like ImmunoCAP Specific IgE) have comparable sensitivity to that of SPT, and the absolute levels of specific IgE may directly correlate with the likelihood of clinical reactivity to food allergens.
• Different brands of specific IgE assays give divergent test results and are not interchangeable when using established clinical cut off levels for specific IgE (Wood et al. AAAI 2007, Wang et al. JACI 2008, Hamilton et al. AAAI 2011).
• Specific IgE to Ara h 2, a 2S albumin in peanut, is highly associated with clinical reactivity to peanut (Eller and Bind- slev-Jensen Allergy 2013, Lieberman et al. JACI-IP 2013).
• An unpublished American study by Kattan and Sampson et al. shows that specific IgE to the storage proteins Cor a 9 and Cor a 14 is highly predictive of clinical reactivity to hazelnut.
• Unpublished data using ImmunoCAP ISAC shows that IgE antibodies to Jug r 1 and Ses i 1 are highly specific for clinical reactivity to walnut and sesame, respectively (Kattan and Sampson et al.).
• For some foods in particular, including peanut, hazelnut and sesame, component-specific IgE testing provides further confirmatory evidence of clinical allergy.

Summary and conclusion
Ulrich Wahn, Germany

• Although molecular IgE antibody testing has improved food allergy diagnostics, the patient’s history and classical food allergy evaluation are still necessary parts of a proper diagnosis.
• The future will require testing that combines the quantitative assessment of IgE antibodies and molecular resolution using allergen components.
• In infancy and childhood, repeated specific IgE testing may be relevant every 2–3 years due to the natural history of food allergy, i.e. to predict the outgrowth or persistence of allergy.
• Allergen component-specific IgE testing may predict clinical reactivity (anaphylactic reactions to food) and help to reduce the number of food challenge tests.
Journal title abbreviations

AAAI, Annals of Allergy, Asthma and Immunology
CMA, Clinical and Molecular Allergy
CEA, Clinical and Experimental Allergy
JACI, Journal of Allergy and Clinical Immunology
JACI-IP, Journal of Allergy and Clinical Immunology – In Practice
PAI, Pediatric Allergy and Immunology

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