



SPEAKER ABSTRACTS

FOOD ALLERGY AND SAFETY ASSESSMENT WORKSHOP

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Nairobi Central Business District
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HESI Protein Allergenicity Technical Committee



SPEAKER ABSTRACTS

FOOD ALLERGY *Sessions 1-4*



Session 1. Food Allergy: Mechanisms, Diagnosis and Epidemiology

What is food allergy?

Lars K. Poulsen, PhD, Dr. Med.

Professor, Head of Research
Copenhagen University Hospital at Gentofte
Hellerup, Denmark

The symptomatology of food allergy is quite variable, and often symptoms originate from more than a single organ among: *the oral cavity*: oral allergy syndrome; *the skin*: urticaria and exacerbation of atopic eczema; *the respiratory system*: rhinitis and asthma; *the gastrointestinal system*: nausea, vomiting, abdominal pain, diarrhea; with additional symptoms being conjunctivitis, angioedema, and generalized anaphylaxis. It is generally believed that whole food allergen proteins either act on the mucosa in the intestinal tract or may be absorbed systemically in a bioactive form. Patients' reactivity to ingestion of allergic foods experienced in the community are extremely difficult to describe, but it is generally assumed that the threshold dosages that can be determined in clinical settings are the most reasonable approximation, even though many cofactors of real-life (infections, allergic co-morbidities, exercise, matrix in which the food is given, alcohol, drugs) may alter the patient's reactivity to challenges.

The most important single factor in food allergy is specific IgE directed against the food allergens. IgE is situated on mast cells, and by allergen cross-linking, mediators are released which form the basis of the acute symptoms. The diagnosis of food allergy is a response to two important questions: Does the patient have a food allergy? And if confirmatory: Which foods will elicit allergic symptoms?



Session 1. Food Allergy: Mechanisms, Diagnosis and Epidemiology

How is food allergy diagnosed?

Montserrat Fernández Rivas, MD, PhD

Allergy Department
Hospital Clínico San Carlos
Madrid, Spain

The diagnosis of IgE-mediated food allergy is based on a three-step approach. The first step comprises the collection of a medical history that allows the practitioner to establish the link between symptoms and food intake, identify the potential culprit food(s) and whether an immunological mechanism is involved, and guide the diagnostics tests to be performed and the evaluation of their results. The second step consists of the performance of IgE testing on the food(s) under investigation by means of skin prick tests (SPT) and/or serum determinations using whole foods extracts and individual allergens. The sensitivity of whole extracts is reduced when labile allergens are involved, something that may be overcome with individual component testing. Specificity of IgE testing is hampered by cross-reactivity among foods or between foods and inhalant allergens, and this can only be overcome with oral food challenges. Therefore, to establish the clinical relevance of the sensitization to the food, it is necessary to perform, as a third step, an oral food challenge. This test confirms or rules out the patient's reactivity to the food, although it has the inherent risk of inducing allergic reactions that may be severe and has a high cost.

Reference:

Muraro et al. 2014. EAACI Food Allergy and Anaphylaxis Guidelines: diagnosis and management of food allergy. *Allergy*. doi: 10.1111/all.12429. [Epub ahead of print].
Open access: <http://onlinelibrary.wiley.com/doi/10.1111/all.12429/pdf>



Session 1. Food Allergy: Mechanisms, Diagnosis and Epidemiology

Food allergy and different socio-economic backgrounds

Prof. dr. Maria Yazdanbakhsh
Head, Parasite Immunology Group
Leiden University Medical Center
Leiden, The Netherlands

Co-authors:

Abena Amoah^{1,2}, Elias Asuming Brempong^{1,2}, Firdaus Hamid^{1,3}, Sitti Wahyuni³,
Daniel Boakye², Taniawati Supali⁴, Ronald van Ree⁵

¹ Department of Parasitology, Leiden University Medical Center, Leiden, The Netherlands

² Department of Parasitology, Noguchi Memorial Institute for Medical Research, Legon, Accra, Ghana

³ Department of Parasitology and Microbiology, Hassanudin University, Makassar, Indonesia

⁴ Department of Parasitology, University of Indonesia, Jakarta, Indonesia

⁵ Department of Experimental Immunology and Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands

The prevalence of allergic disorders is often reported to be higher in urban compared to rural areas of developing countries. Within urban centres of countries undergoing economic transition, there is considerable variation in lifestyle and socioeconomic status and this appears to be an important predictor of allergy. The prevalence of allergies as defined by skin prick test positivity to allergens is higher in the urban rich than in urban poor. However, the IgE responses can show very different patterns. IgE responses to allergens are high in the rural compared to urban areas. However, IgE in urban poor is lower than in urban rich. Using both the ISAC biochip and glycan arrays, we have gained more insight into the molecular targets of the IgE from different geographical areas as well as from populations with different socioeconomic status and have suggestions for why IgE can at times not be directly associated with skin prick test positivity or clinical symptoms.



Session 1. Food Allergy: Mechanisms, Diagnosis and Epidemiology

Specific mammalian allergens and symptoms of allergic disease: Fel d 1 vs. alpha-gal

Adnan Custovic, DM, MD, PhD, FRCP
Professor of Allergy
Institute of Inflammation and Repair
University of Manchester
University Hospital of South Manchester
Manchester, United Kingdom

[abstract not available]



Session 2. Food and Respiratory Allergy in Eastern Africa

Asthma and allergy-related disease in Uganda

Prof. Alison Elliott

Harriet Mpairwe, MBChB, MSc, PhD

Research Unit on AIDS

Medical Research Council / Uganda Virus Research Institute

Entebbe, Uganda

Very little research has been conducted on asthma and allergy-related disease in Uganda. However, these conditions are increasingly recognised as important, especially among the region's rapidly expanding middle classes.

The combination of an environment in which exposure to infectious diseases, including helminths, is still common and the current, rapid transition to an urban lifestyle provide unique opportunities for research to understand the relationship between allergy-related conditions and the environment.

We will report upon recent clinical and epidemiological studies of asthma and atopy in Uganda, and upon the effects of early life infectious exposures on allergy-related outcomes in this setting.



Session 2. Food and Respiratory Allergy in Eastern Africa

Food and respiratory allergy in Kenya

Dr. Evans Inyangala Amukoye

Director

Centre for Respiratory Diseases Research

Kenya Medical Research Institute

Nairobi, Kenya

Food is an important cause of anaphylaxis, intolerance and allergies. Less than 6% of respiratory allergies are due to food. Studies done in Kenya in this area are few. Allergy to cow's milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish constitutes the majority of food allergy reactions worldwide, but reliable estimates of their prevalence are lacking. Allergies in general are common and, in the ISAAC studies done in the 1990s, Africa and Latin America had higher incidences of eczema. For the age group 13 to 14 years, and using data on 663,256 participants from 230 centers in 96 countries, Odhiambo et al. showed prevalence values ranging from 0.2% in China to 24.6% in Columbia, with the highest values in Africa and Latin America. 'Current eczema' in the same study was lower for boys than girls.

Asthma was a common occurrence in Nairobi, Kenya, recording 18% prevalence among the age group 13 to 14 years. Several studies have shown rural urban differences with higher rates reported in urban areas. This has been attributed to life style and pollution. This difference is now narrowing.

The role of helminthes and micronutrient such as Vitamin D will be discussed.



Session 2. Food and Respiratory Allergy in Eastern Africa

Food and respiratory allergy in Tanzania

Dr. Nohrasco Mang'ondi

Lecturer and Dermatovenereologist

Bugando Medical Centre

Catholic University of Health and Allied Sciences (CUHAS)

Mwanza, Tanzania

Tanzania is a large country in east Africa with a general population of 45 million and many different tribes with diverse cultural practices. Food and respiratory allergies are a common known problem, but definition and knowledge of allergic disease differ from one tribe to another and from rural to urban areas.

Food allergy is mostly suspected by many people when they have any chronic or recurrent skin problem which failed to be treated in Hospital, while any dry cough with recurrent nature is attributed to respiratory allergies.

No studies have been done so far to assess the magnitude of food or respiratory allergies, but a few studies have been done in special groups like children. Atopic dermatitis revealed a prevalence of food allergy ranging from 1.4% - 36.5% in some areas of the country. Respiratory allergy ranges from 1.2% - 18.6% in asthmatic and industrial worker populations.

Common food allergies are peanuts, cow's milk, hen egg, and fish, but currently no specific respiratory allergies have been studied.

Conclusion

Food and respiratory allergy are a common problem although may be differently interpreted by different communities. The burden of allergenic diseases in Tanzania is increasing due to urbanization and industrialization.



Session 3. Food and Respiratory Allergy in Western Africa

Food and respiratory allergy in Ghana

Ms. Abena Amoah

Department of Parasitology
Noguchi Memorial Institute for Medical Research
University of Ghana
Legon, Ghana

Over the past few decades, there has been a sharp global increase in the prevalence of allergic disorders, particularly among children. We conducted a cross-sectional study to investigate the prevalence of markers of aeroallergy and food allergy among urban and rural children in Southern Ghana. Of particular interest were sensitization to aeroallergens based on specific immunoglobulin E (IgE) levels and skin prick test reactivity, as well as reported symptoms of asthma and wheeze. In addition, food allergy was determined based on reported adverse reactions to food, as well as food sensitization to selected food allergens that included peanut. The effects of factors such as parasitic infections, body mass index, and area of residence on our allergy outcomes were also investigated.

We observed notable urban-rural differences in our allergy outcomes, as well as elevated levels of allergen-specific IgE that did not translate into skin prick test positivity or reported symptoms. Further in-depth analysis demonstrated that helminth-induced IgE cross-reactivity may explain in part the lack of skin reactivity to allergens such as peanut in the face of elevated allergen-specific IgE. Overall, our investigation demonstrates the complexities underlying the rise in allergic diseases in rapidly developing countries such as Ghana.



Session 3. Food and Respiratory Allergy in Western Africa

Risk factors for food adverse reaction reporting in Lambaréné, Gabon

Ayola Akim Adegnika, MD, PhD

Co-Director and Group Leader

Immuno-Epidemiology of Parasitic Infections (IEPI)

Centre de Recherches Médicales de Lambaréné (CERMEL)

Hôpital Albert Schweitzer

Lambaréné, République of Gabon

Allergy disorders constitute a major public health problem in developed countries. In developing countries, data for allergy disorders are mainly available on inhalant allergy, while few data are available on food allergy disorders. In these countries, allergy disorders are negatively associated with poor hygiene and microbial infections, including helminths infections.

Lambaréné is a semi-urban city in Gabon which is endemic for parasitic infections including helminths parasites, and is composed of different socio-economic groups, geographic areas (rural, semi-urban and rural), and diverse food intake. Lambaréné was chosen to conduct a nested case-control study to assess factors associated with food adverse reaction reporting.

Data were collected on self-reported adverse food reactions in 2,679 participant at a cross-sectional level. The number of participants reporting the adverse food reaction was 353 (13.2%). From this cross-sectional cohort, 105 cases and 216 controls were selected for further assessment of factors associated with food adverse reaction, including parasitic infection, socio-economic status, and confirmatory tests including skin prick test as well as a measurement of specific IgG-E with reported food adverse reaction.

It was found that independent risk factors for food adverse reaction reporting included infection with schistosomiasis (OR (95%CI)) (0.44(0.22-0.55)) and living in the administrative area (OR (95%CI)) (4.15(1.63-11.16)). However there is no statistically significant correlation or association between specific IgE, as well as specific skin prick test positive, with food adverse reporting.

This population-based study reports for the first time food adverse concerns in Lambaréné and surrounding population, but fails to confirm so far a single true food allergy using existing and validated tools. Further investigations are needed to alleviate this discrepancy.



Session 4. Food and Respiratory Allergy in Southern Africa

Food and respiratory allergy in Zimbabwe

Professor Elopy Sibanda, MD

Asthma, Allergy & Immune Dysfunction Clinic
Harare, Zimbabwe

Diseases that result from allergic reactions are common worldwide. Their frequency and associated triggers are rarely documented in Africa. We have summarized the findings of an audit of laboratory test results of 981 patients referred to a specialist allergy clinic in Harare, Zimbabwe. The test panels included eleven inhalants (house dust mites, pollen, animal hair and molds) and twenty-two food allergen sources. The food allergen sources included egg, milk, grains, nuts, fruits and vegetables.

Serological reactivity to allergen sources was found in all age groups tested. The majority of the patients were children or young adults. A steep increase in the numbers of allergic patients was noted in individuals born in the last 20 years. The numbers of people with moderate to severe allergic diseases more than doubled with each decade from 1980 to 2010. The most significant inhalant allergen sources were house dust mites and pollen. House dust mite sensitization exceeded 50% in some age groups. Grass pollen was more frequently diagnosed than tree and weed pollen. Patients with grass pollen allergy reached 30% in certain age groups. The numbers of people with food allergen sensitization were lower than those with house dust mite or pollen allergy. The most prominent food allergen sources were potato and peanuts. Allergy to milk and seafood was infrequent. This study confirms the persistence of inhalant allergic diseases in Zimbabwe and reports the increasing prevalence of food allergy. The study also notes that in some cases (peanut, potato), sensitization does not always translate to clinical manifestations of disease.



Session 4. Food and Respiratory Allergy in Southern Africa

Food allergy in South Africa

Prof. Michael Levin

Head, Division of Asthma and Allergy
Department of Paediatrics
Red Cross Children's Hospital
Cape Town, South Africa

There is a paucity of information about food allergy in South Africa. Recent and ongoing studies are starting to cast light on the epidemiology of food allergy.

SAFFA STUDY

Primary researchers: Mike Levin, Maresa Botha, Wisdom Basera, Claudia Gray

Introduction: There are no data on the prevalence of food allergy (FA) in unselected South African children, a shortfall which this study addresses. The South African Food sensitisation and Food Allergy (SAFFA) study aims to determine the prevalence of IgE-mediated food sensitisation and food allergy in unselected 12-36 month old urban South African children.

Methods: This cross-sectional study recruited 12-36 month old toddlers from randomly selected registered crèches in Cape Town. Parents of eligible children in the crèche completed a questionnaire and the children had skin prick tests (SPT) for cow's milk, egg, soya, wheat, peanut, hazelnut and fish (cod). Participants with SPT test > 1mm, who were not tolerant to that food had an oral food challenge (OFC) to assess for IgE-mediated food allergy. Parents choosing not to participate completed a non-participant questionnaire to control for bias.

Results: Of 435 eligible participants, 281 responded (65% response rate) and 253 of 263 enrolled participants completed the study (96% completion rate). Of 10 children meeting the criteria for OFC, 7 completed challenges. Participants were black African (42.3%), Caucasian (13.0%), and Mixed Race (44.7%).

The prevalence for SPT \geq 1mm to any food was 11.9% (95% CI: 7.9-15.9%), SPT \geq 3mm 9.8% (95% CI: 6.2-13.6%), \geq 7mm 4.0% (95% CI: 1.5-6.4%), and OFC confirmed food allergy 1.2% (95% CI: 0.2-3.4%) (3 food challenges remain to be done meaning that 1.2% is a minimum value for the prevalence of FA).

The most common sensitisation was to egg and then peanuts. Sensitisation \geq 1mm to fresh egg was 8.3%, 7.5% \geq 3mm, 4.0% \geq 7mm with 2 (0.8%) positive OFCs. Sensitisation \geq 1mm to peanut was 4.7%, 3.6% \geq 3mm, and 1.2% \geq 7mm with 2 (0.8%) positive OFCs. Sensitisation \geq 1mm for soya was 2.0%; wheat 1.6%; and for cow's milk, fish, and hazelnut 1.2% each. 4.7% of participants were poly-sensitised.

In general, sensitisation in Black African and Mixed Race children were slightly higher than in Caucasian participants, viz at SPT \geq 1mm 12.8%, 11.6%, and 9.8%, respectively; SPT \geq 3mm 11.9%, 8.0%, and 9.7%, respectively; and SPT \geq 7mm 4.6%, 3.5%, and 3.2%.



Conclusion: This is the first food challenge proven prevalence of FA determined in unselected children in Africa and provides a basis for further monitoring of a population possibly only at the beginning of the food allergy epidemic.

Although not statistically significant, the higher sensitisation rates in Black African and Mixed Race children are similar to the high rates of aeroallergen sensitisation seen in unselected and allergic populations. Further expansion in the next phase of the study will compare the prevalence of sensitisation and food allergy between urban Caucasian, Mixed Race and Black African children and between rural and urban Black African Xhosa children, and will generate population-specific cut-off levels for SPT and Immunocaps with 95% positive predictive values.

RXH FOOD CHALLENGE AUDIT: OVERVIEW

Primary researchers: Talita Van Der Watt, Mike Levin

Introduction: The diagnosis and confirmation of food allergies can be challenging. The gold standard for diagnosing food allergy is the double-blind, placebo-controlled oral food challenge; however, open oral food challenges (OFC) are useful to exclude food allergies.

Methods: This is a retrospective, descriptive study of children who presented to Red Cross Children's Hospital's tertiary Allergy clinic with food allergies and subsequently had OFC during the 39 month period from February 2011 to April 2014.

Results: Two hundred and two OFCs were performed on 142 children (age 9 months to 14 years). Challenges were done to 18 different foods. Egg, peanut, baked egg, and cow's milk made up the largest number at 64, 37, 29, and 25 respectively.

Ninety four (66.2%) children had a single OFC, while 39 (27.5%) had 2 challenges and 9 children had more than 2 challenges.

Thirty eight (18.8%) challenges were positive with reactions varying from mild rash to wheeze. The rate of positive reactions increased significantly over the study period from 11.6% (n=5/43) in 2011 to 14.5% (n=10/69) in 2012, 21.5% (n=14/65) in 2013, and 36% (n=9/25) in 2014 (p=0.01). The most common reaction was urticaria in 23 (60.5%) and angioedema in 11 (28.9%). Three (7.9%) had wheezing.

Fourteen percent of egg challenges (n=9/64), 35.1% of peanut challenges (n=13/37), 17.2% of baked egg challenges (n=5/29) and 20% of cow's milk challenges (n=5/25) had a positive outcome. There is a significant difference between the median age at challenge (egg 53 months, peanut 67 months, baked egg 38 months and cow's milk 29 months) (p=0.01). Baked egg challenges with positive outcomes occurred in younger children than those with negative food challenges (13 vs 44 months) (p=0.04).

Co-morbidities were common in our population: atopic dermatitis was present in 73.9% (n=105/202), asthma in 37.3% (n=53/202), allergic rhinitis in 45.8% (n=65/202), and allergy to multiple foods in 62.7% (n=89/202). Co-morbidity prevalence was significantly different between groups with positive and negative OFC outcomes (p<0.01).

Conclusion: Oral food challenges are necessary to accurately diagnose children with food allergies. With increased utilization of OFCs, increased numbers of true food allergy diagnoses are made. The prevalence and age of food allergy varies with different foods tested. Peanut allergy was the most common food allergy diagnosed. The presence of other atopic diseases had a significant impact on the outcome of food challenges.



RXH FOOD CHALLENGE AUDIT: SPECIFIC IgE ANALYSIS

Primary researchers: Talita Van Der Watt, Mike Levin

Introduction: Sampson determined 95% positive predictive values (95% PPVs) for food challenge outcome in children in a first world country. These values are used worldwide in decision making processes regarding oral food challenges and in the diagnosis of symptomatic food hypersensitivity. Predictive values for African children have not been determined. Decision points determined include IgE to egg of 7kU/l and 2kU/l for children above and below 2 years of age, IgE to cow's milk of 15kU/l and 5kU/l for those above and below 2 years of age, and IgE to peanut above 14kU/l. We aim to compare the applicability of international 95% PPVs for IgE levels in the African setting to determine whether significance of specific IgE levels differs from international standards and varies with ethnicity.

Methods: This is a retrospective, descriptive study of children who presented to Red Cross Children's Hospital's tertiary Allergy clinic with food allergies and subsequently had open oral food challenges (OFC) over the 39-month period from February 2011 to April 2014.

Results: Two hundred and two OFCs were done on 142 children between the ages of 9 months and 14 years. Egg, peanut, and cow's milk made up the largest number of challenges at 64, 37 and 25, respectively. Thirty-eight (18.8%) challenges had a positive outcome.

The majority of challenges were done in children of mixed race (84.1%), with black African and white children accounting for 12.9% and 3%, respectively. The rate of positive food challenges differed for children of different ethnicity.

Challenges had a positive outcome in 18.8% (n=32/170) of challenges in children of mixed race, 15.4% (n=4/26) of black African, and 33.3% (n=2/6) of those done in white children. Median age at challenge was 47 months for mixed race children, 42 months for black African and 117 months for white children. There was a significant difference in the median ages at challenge (p=0.007). Further analysis was not performed on white children as numbers are too small.

IgE levels for each food and each challenge outcome were compared to the published 95% PPVs. In challenges to egg, 36.1% (17/47) mixed race and 42.9% (3/7) black African had negative OFCs with IgE above the 95% PPV. In cow's milk challenges, 40.0% (6/15) mixed race and 80.0% (4/5) black African children had negative OFCs with IgE above the 95% PPV. For peanut challenges, 21.7% (5/23) mixed race children had negative OFC outcomes with IgE above the 95% PPV. Black African did not have negative OFCs with IgE above the 95% PPV (0/1).

Conclusion: In this setting, large numbers of patients have negative challenges despite IgE levels above the internationally derived 95% PPVs. A higher proportion of Black African children have negative egg and milk challenges despite IgE levels above the internationally derived 95% PPVs; however, the converse is true with regards to peanut challenges.

FOOD ALLERGY IN CHILDREN WITH ECZEMA

Primary researchers: Claudia Gray, George Du Toit, Mike Levin

Introduction

In 2009, South African infants with atopic dermatitis were shown to have frequent sensitisation to foods, most commonly egg white (47.1%), cow's milk (28.4%), and peanuts (26.8%). This study did not, however, explore clinical food allergy. In 2011, the South African food allergy-eczema study showed children attending a tertiary dermatology clinic for atopic dermatitis were shown to



have even higher sensitisation rates (66% to at least one food), most commonly to egg (54%), peanuts (43%), and cow's milk (27%). This latter study had stringent criteria for defining food allergy, with incremental oral food challenges where indicated, and found 40% of patients to have an IgE-mediated food allergy (25% were allergic to egg, 24% to peanut and 2% to cow's milk).

Age of onset of eczema below 6 months was a significant risk factor for food allergy, with much higher prevalence of food sensitisation (86%) and food allergy (66%) in children with eczema onset before 6 months compared to those with onset between 6-12 months or after 1 year. The study confirmed that in our local population, age of assessment affects allergy prevalence with 50% of patients under the age of 2 years at the time of study having a food allergy, compared with 25% of patients above the age of 4 years. Greater severity of eczema is also associated with higher risk of food allergy.

We then compared peanut sensitisation patterns, true peanut allergy, and peanut component patterns between South African children with atopic dermatitis (AD) of Black (Xhosa) origin and children of mixed race to determine whether there are ethnic differences in peanut sensitisation and peanut allergy patterns in South African children with AD.

Methods: 100 children (6 months to 10 years) with moderate to severe AD were randomly selected from a dermatology clinic at the Red Cross Children's Hospital in Cape Town. They underwent food allergy screening by questionnaire and skin prick tests, and allergen specific IgE was assessed with ISAC 103 component microarray testing. Those who were sensitised to peanut (n=43) had additional ImmunoCAP tests for components rArah 1,2,3,8 and 9. Patients with any uncertainty regarding clinical peanut allergy (n=25) underwent incremental open oral food challenges. Sensitisation was defined as SPT \geq 3mm or ISAC $>$ 0.3Units, and allergy as positive food challenge or convincing recent history of reaction with positive SPT/specific IgE above the "traditional" 95% positive predictive values for peanut allergy (8mm for SPT, 14kU/L for specific IgE).

Results: Overall, 43% of patients were peanut sensitised (53% mixed race and 37% Xhosa, $p=0.1$). Peanut allergy rates were high overall (24%), though significantly lower in the Xhosas (15%) compared with mixed race (38%, $p=0.01$), despite comparable baseline characteristics. Traditional 95% positive predictive values for SPT (\geq 8mm), peanut specific IgE (\geq 14 kU/L) and ImmunoCAP rArah2 (\geq 0.35 kU/L) fared well in the mixed race group (88%, 90%, and 93%, respectively), but poorly in the Xhosa group (80%, 57%, and 53%).

Component tests had a similar pattern in both ethnic groups with Arah2 being most strongly associated with peanut allergy in both ethnic groups. However, the likelihood of allergy with a positive rArah2 (\geq 0.35 kU/L) was significantly lower in Xhosa than mixed race patients (53% v 93%, $p=0.01$). Arah 3, 8, and 9 were more commonly positive in tolerant patients in both ethnic groups with Arah9 having the strongest association with tolerance of any single component.

Conclusion: In Xhosa patients, sensitisation to peanut (including Arah2) is significantly less likely to equate to true allergy than in mixed race patients. Traditional 95% PPV for peanut allergy perform poorly in Xhosa patients. The component Arah2 is the most valuable for differentiating sensitisation from allergy in both ethnic groups; Arah9 is associated with asymptomatic sensitisation.

EOSINOPHILIC OESOPHAGITIS IN CAPE TOWN, SOUTH AFRICA

Primary researchers: Mike Levin, Cassim Motala

Introduction: Eosinophilic oesophagitis has been described in patients from all ethnic backgrounds in studies originating in all continents apart from Africa.



Methods: This is a descriptive study of children who were diagnosed with eosinophilic oesophagitis at Red Cross Children's Hospital's tertiary Allergy clinic during 2009 to 2010.

Results: A cohort of 8 patients (3 boys, 5 girls) identified at Red Cross Hospital during 2009-2010 is described:

Average age: 7 years (1yr 11 months to 15 years 10 months)

Ethnicity: 2 Caucasian, 5 mixed, 1 Black African

Age of onset: mean 3 years, median 1 year 4 months

Age of diagnosis: mean 6 years 3 months; median 3 years 9 months

Time to diagnosis: mean 3 years 3 months, median 6 months, IQ range 5 months to 6 years.

Presenting symptoms in order of prevalence are reflux (7/8), long time to eat (6/8), difficult swallowing (6/8), growth failure (5/8), food refusal (5/8), and painful swallowing (4/8). Associated atopic diseases comprised immediate food allergy (6/8), eczema (6/8), rhinitis (6/8), asthma (3/8) and urticaria (2/8).

Total of 26 biopsy specimens; mean 3.25 per patient. Only 4/8 confirmed peak eosinophil count >15/hpf, 7/8 had minor features present. Food skin prick tests 152 (19 per patient). Positive skin tests ≥ 1 mm 57 (13 per patient). The most commonly identified foods are peas, wheat, milk, egg white, banana, and egg yolk. Skin tests ≥ 3 mm 32 (7 per patient). Most commonly identified foods by SPT > 3mm are egg yolk, egg white, peas, soya, rye, rice, carrot, and green beans. Patch tests 167 (21 per patient). 30 positive, average of 4.3 per patient. Most commonly identified foods are beef, peanut, lamb, chicken, soy and ham.

All commenced on initiation of short course of oral steroids. All put on targeted elimination diet. All had clinical improvement. 3 controlled and acceptable symptoms, 2 some symptoms and difficulties, 2 very symptomatic with poor control, 1 defaulted.



SPEAKER ABSTRACTS

AGRICULTURAL BIOTECHNOLOGY SAFETY ASSESSMENT



Agricultural Biotechnology Safety Assessment

Agricultural biotechnology background in Africa

Jacoba Adriana ('Kobie') de Ronde, PhD
Regulatory Affairs Country Manager
Syngenta
Gauteng, South Africa

Agricultural productivity has a crucial role to play in ensuring food security in Africa. Because biotechnology holds great promise, African countries are increasingly considering genetically modified (GM) crops as a potential tool in the agricultural toolbox. The adoption of new and emerging technologies is, however, slow in most countries, mainly due to the status of biosafety regulatory frameworks, which include policies, laws and regulations. The development and implementation of a functional regulatory framework to move from research to commercialization of biotechnology crops varies greatly between countries. Africa accounts for about 3.5 million hectares of GM crops, planted only in Burkina Faso, Egypt, North Sudan and South Africa. Various countries are performing confined field trials or are involved in biotechnological research. I will provide a brief overview of the progress made in Africa regarding the adoption of regulatory frameworks and, consequently, the cultivation of biotechnology crops.



Agricultural Biotechnology Safety Assessment

Safety assessment process in support of the regulatory approval of agricultural biotech products

Laura Privalle, PhD
Bayer CropScience
Research Triangle Park, NC
USA

Crops produced through modern agricultural biotechnology are the most highly studied foods consumed. Even before identification of the elite event that is going to be taken commercial, the safety assessment begins. An evaluation using *in silico* techniques is undertaken to confirm that the gene of interest does not encode a protein that has similarity to known toxins or allergens. Once technical proof of concept in the crop is demonstrated, a preliminary evaluation of the digestive sensitivity is examined. After the commercial event is selected, an extensive safety assessment is conducted that includes studies on the safety of the newly expressed protein, molecular characterization of the insert, impact of the insert on plant performance and composition, environmental impact, and wholesomeness of the crop (Codex Alimentarius Commission, 2003). The registration dossiers are scrutinized by regulatory agencies around the world in both producing countries (those that will grow the crops) and in importing countries. Approval is granted only if the biotech crop has been demonstrated to be as safe as the conventional crop as food or feed and for the environment. This technology has been rapidly adopted by growers in all parts of the world and, in the almost twenty years since these crops have been grown and consumed, there have been no incidences of food safety attributed to them. Furthermore, the many benefits to the environment and for the grower have resulted in a very rapid adoption of this technology.



Agricultural Biotechnology Safety Assessment

Crop composition as part of the GM crop safety assessment

Philip Brune, PhD

Product Safety

Syngenta Crop Protection, LLC

Research Triangle Park, NC

USA

The fastest adopted new crop technology to date is that of genetically modified (GM) crops because their use has led to reduced crop inputs, convenience and flexibility in crop management, and increased yield and quality. However, many countries require a safety assessment of novel GM crops before they can be grown within the country or before consumption of food and feed from the GM crop. Nutritional composition studies of GM crops are an important component of the overall safety assessment of novel GM crops. These studies compare the GM crop to an appropriate comparator in order to assess the nutritional status of food and feed originating from the novel GM crop, and to identify any possible unintended changes due to insertion of the transgene(s) or its products. If the levels of a nutritional component in the GM crop are not statistically significantly different than those in the comparator, then no further assessment is needed. If levels are statistically significantly different, then these changes are placed in the context of the natural variability within the traditional crop that is considered to be safe.



Agricultural Biotechnology Safety Assessment

Molecular/protein characterization of GM products

Scott McClain, PhD
Product Safety
Syngenta Crop Protection, LLC
Research Triangle Park, NC
USA

The evaluation process for genetically modified (GM) crops begins with a molecular characterization of the DNA inserted into host plants which drives the expression of the GM trait(s) and selectable marker proteins. The process relies on asking key questions: 1) What DNA was put into the crop? 2) How many expressible genes were put into the crop? 3) What were the source organisms of the DNA? 4) Where in the host genome is the inserted DNA located? 5) Is expression of the gene(s) stable? Similarly, characterization of the trait proteins themselves relies on answering fundamental questions to support these products from a food and feed safety perspective: 1) Is the transgenic-expressed trait protein produced in the plant in a stable manner? 2) Are the biophysical properties of the protein consistent with a safe protein? 3) Is there a history of safe use of the protein or its homologues in other species? 4) Is the recombinant protein equivalent to the GM plant protein? 5) Is the purified trait protein suitable for human and environmental toxicity studies? 6) How much of the protein is expressed? Studies are designed that support these questions and the data are then used to assemble a risk assessment.



Agricultural Biotechnology Safety Assessment

Assessment of potential allergenicity of GM crops

Gregory S. Ladics, PhD, DABT, Fellow ATS

Research Fellow

DuPont Pioneer Agricultural Biotechnology

Wilmington, DE

USA

Unlike conventionally bred crops, a thorough safety assessment process exists for genetically modified (GM) crops. The goal of this process is to demonstrate that the GM crop is “as-safe-as” non-GM crops in the food supply. One of the issues for GM crops is the evaluation of the expressed novel protein for allergenic potential. The purpose of this assessment is (1) to protect allergic consumers from exposure to known allergenic or cross-reactive proteins, and (2) protect the general population from potential risks associated with the introduction of genes encoding proteins that are likely to become food allergens *de novo*. A food allergy is a reaction of the immune system to an otherwise harmless protein in food. Importantly, allergic reactions to food are relatively rare. The incidence of food allergy ranges from approximately 1 to 2% in adults and 6 to 8% in young children. Currently, no single endpoint or response is recognized as a predictor of protein allergenicity. Consequently, a weight-of-evidence approach, which takes into account a variety of factors for an overall assessment of allergenic potential, is conducted [Codex Alimentarius Commission, 2003]. This assessment is based on what is known about allergens, including the history of exposure and safety of the gene(s) source (i.e., whether the gene source for the new protein is known to induce allergy); similarity to known allergens (*in silico* amino acid sequence identity comparisons to a database of allergens); stability to pepsin digestion *in vitro*; processing effects [heat stability]; and, when appropriate, specific IgE binding studies.



Agricultural Biotechnology Safety Assessment

Assessment of potential toxicity of GM crops

Gregory S. Ladics, PhD, DABT, Fellow ATS

Research Fellow

DuPont Pioneer Agricultural Biotechnology

Wilmington, DE

USA

An extensive safety assessment process exists for genetically modified (GM) crops. The goal of this process is to demonstrate that the GM crop is “as-safe-as” non-GM crops in the food supply. As part of the mammalian safety assessment, GM crops are evaluated for their toxicological potential. This is accomplished by employing a holistic approach where the host plant, gene, gene product (i.e., protein), and GM crop are evaluated. Some relevant questions initially asked include: 1) Does the host plant have inherent toxicity? and 2) Does the source of the gene(s) have a history of safe use (i.e., whether the gene source for the new protein is known to induce toxicity)? To evaluate the transgenic protein(s), a weight-of-evidence approach, which takes into account a variety of factors for an overall assessment of toxicological potential, is conducted [Codex Alimentarius Commission, 2003]. This assessment is based on what is known about the transgenic protein and protein toxins, including similarity to known toxins (*in silico* amino acid sequence identity comparisons to protein databases); stability to pepsin digestion *in vitro*; processing effects [heat stability]; acute toxicity evaluation, mode of action and specificity; and expression level and dietary intake. The GM crop (i.e., the part consumed by humans [typically grain]) is further evaluated for unintended effects by conducting repeat-dose feeding studies in rodents where general health and food consumption, clinical chemistry, hematology, and histopathology are evaluated. When necessary, hypothesis-based toxicology studies may also be conducted.



Agricultural Biotechnology Safety Assessment

Regulatory and safety assessment perspectives for genetically modified food in Kenya

Prof. Theophilus M. Mutui, PhD
Chief Biosafety Officer
National Biosafety Authority
Nairobi, Kenya

Consumption of any food (conventional, genetically modified (GM), or organic) may present some risk of hazard due to the presence of proteins or other naturally occurring chemicals such as glycoalkaloids that might cause allergies or other harmful effects to humans. GM food safety assessment is the evaluation of known or potential adverse health effects resulting from human consuming GM foods. The safety evaluation of GM food is science-based, conducted on a case-by-case basis, and generally follows a comparative approach involving a step-wise process. The process is comprised of assessment of possible allergenicity (hypersensitive reaction initiated by immunologic mechanisms caused by allergens), toxicity, compositional analysis of key ingredients, food processing, and nutritional modification. Additional risk characterization may involve a toxicological assessment in a rodent model, depending on the outcomes of the previous risk evaluation steps. This paper describes the Kenyan regulatory and safety assessment process for GM food with a view to ensuring the safety of human health and providing adequate levels of protection of the environment.



Agricultural Biotechnology Safety Assessment

Regulatory and safety assessment perspectives: South Africa

Liesel Michelle Gouws, PhD

Project Manager

Biosafety South Africa

South Africa

The safety of foods derived from genetically modified (GM) crops has been a subject of significant interest and discussion between technology developers, consumers, and policy-makers. A number of national and international regulations govern the use of genetically modified organisms (GMOs). The primary aim of these regulations is to ensure that any activities with GMOs are assessed with regard to their potential risks to human health and the environment. In South Africa, GMOs are primarily governed by the GMO Act (Act 15 of 1997), which provides measures to promote the responsible development and use of GMOs. South Africa has a rigorous regulatory framework, which has been fully functional for more than 14 years. GM crops approved for commercial release in South Africa have undergone extensive safety assessments and have met all the stringent requirements set by the national and international regulatory framework.