1. Sooyoung Lee
Clinical and immunological characteristics of anchovy allergy in children

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Background
Allergic reactions to anchovy, a fish widely consumed in Korea, seem to be increasing in Korean children, but there is no previous report on anchovy allergy. We aimed to evaluate the clinical and immunologic profiles in Korean children with anchovy allergy.

Methods
We evaluated clinical and laboratory profiles of children who suspected clinically allergic or tolerant to anchovy (Ajou University Hospital, February 2021 to January 2023). Serum specific IgE to anchovy (anchovy-sIgE, Thermo Fisher Scientific/Phadia, Uppsala, Sweden) were measured. We produced 3 kinds of anchovy (small, middle and large sized of anchovy) extracts and underwent SDS-PAGE and IgE immunoblot analysis with patient sera.

Results
Twenty children had immediate-type reactions (allergic group) upon anchovy exposure (80% to broth). The median age of first symptom to anchovy was 1.9 years, and 80% had fish allergies other than anchovy. Cutaneous symptoms (90%) were most common, and 25% experienced anaphylaxis upon exposure to anchovies. The median levels of anchovy-sIgE in allergic group was 4.77 kU/L (0.04-49.60 kU/L). On SDS-PAGE analysis of 4 kinds of anchovy extracts, more than 18 bands were clearly identified. Five clean major IgE-binding bands were found on immunoblot analysis using pooled sera from clinical anchovy allergic children.

Conclusion
We hereby report the clinical and laboratory profiles in 20 anchovy allergic children. Furthermore, we visualize the IgE-binding patterns using immunoblot and individual sera of anchovy allergic children.
2. Walaa Hamadi
Garlic allergy might be more common than thought

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Background
Garlic (Allium sativum) is commonly used in cooking worldwide, but IgE-mediated allergic reactions to garlic are rarely reported. The Allium species also includes onion, shallot, leek, scallion, and chives. The only clinically relevant garlic allergen identified to date is alliin lyase. Garlic alliin lyase showed strong cross-reactivity with alliin lyases from other Allium species.

Methods
We used the Food Allergy Research & Education’s (FARE) Patient Registry to identify garlic allergic patients and characterize their clinical characteristics. Data collected from May 2017 to October 2021 were analyzed using descriptive statistics. Garlic allergy was identified in 132 patients of approximately 13,000 patients in the registry.

Results
34 of the 132 also reported an allergy to another allium species. Two-thirds were diagnosed by an allergist and most (74%) reported a positive skin prick test. In comparison to patients in the registry with a single food allergy other than garlic, garlic allergic patients were diagnosed later in life, had a higher rate of family history of food allergies and were more likely to have comorbid allergic rhinitis, asthma, or atopic dermatitis. About 56% of patients with a garlic allergy presented to the ER for a garlic-induced allergic reaction, 19% were hospitalized, and 6% were admitted to the ICU.

Conclusion
Data from this largest reported cohort to date of garlic allergic patients suggest that there is a need to evaluate sensitization to garlic and other allium species in people with food allergic reactions of unclear cause given its wide consumption and potential for serious allergic reactions.

References
Background
Flaxseed, specifically its seed storage proteins (e.g. Lin u 1), was identified as an emerging allergen in the context of increasing popularity as a superfood and egg-substitute. [1,2,3] Flaxseeds have poorly digested outer hulls and can be ingested in ground or whole forms. Antigen exposure and subsequent hypersensitivity reaction may depend on the form consumed. For instance, patients allergic to ground sesame were found to tolerate intact forms. [4] Our case series reports that hypersensitivity reactions occurred only with ground flaxseed and that one flaxseed allergic patient tolerated whole flaxseeds. Informed consents were obtained.

Methods
We identified pediatric patients at the BC Children’s Hospital Allergy Clinic and Allergy Victoria Clinic with confirmed flaxseed allergy. Their index reaction was reviewed, including the form of flaxseed (whole or ground) and prior or current tolerance to whole flaxseed.

Results
Four patients between the ages 10-21 months were identified to have flaxseed allergy based on history, positive skin test, and serum specific IgE. The index reactions to flaxseed included: generalized urticaria, vomiting, and/or altered level of consciousness. In all patients, index reactions were to ground flaxseed. One patient tolerated whole flaxseeds after the index reaction to ground flaxseed. Another patient consumed a cracker with whole and ground flaxseed with no reaction prior to their index reaction.

Conclusion
We report 4 cases of flaxseed allergy; all were associated with ground flaxseed with 1 demonstrating tolerance to whole flaxseed which may be due to the digestion-protective outer hull preventing antigen release. Allergists should inquire about reactions and tolerance to both forms of flaxseed, consider skin testing to both forms, and be cognizant of flaxseed as an emerging allergen.

References

<table>
<thead>
<tr>
<th>#</th>
<th>Sex</th>
<th>Age (months)</th>
<th>Form</th>
<th>Reaction</th>
<th>Skin Test (mm)</th>
<th>Serum sIgE (kUA/L)</th>
<th>Before Index Reaction</th>
<th>After Index Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>10</td>
<td>Ground – Used as egg substitute in vegan muffin.</td>
<td>Projectile vomit, mild lethargy, generalized urticaria within 15 minutes of ingestion.</td>
<td>12 x 6</td>
<td>51.1</td>
<td>Yes (multi-seed bread) – Tolerated</td>
<td>Yes (multi-seed bread) – Tolerated</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>21</td>
<td>Ground – Storebought flax almond cracker</td>
<td>With cracker: Vomit. With muffin: Facial rash.</td>
<td>9 x 4</td>
<td>Not done</td>
<td>Yes (homemade crackers with ground and whole flaxseed) – Tolerated</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>12</td>
<td>Ground – Added to banana and avocado (both currently tolerated).</td>
<td>Sudden onset hives, facial swelling.</td>
<td>10</td>
<td>2.77</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>12</td>
<td>Ground – Added to smoothie with peanut (currently peanut tolerant).</td>
<td>Generalized urticaria and reduced level of consciousness.</td>
<td>4</td>
<td>Not done</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

4. Kyung Hee Park
Clinical characteristics of Korean wheat dependent exercise induced anaphylaxis patients confirmed by challenge test

*Kyung Hee Park¹, Jae-Hyun Lee², Jung-Won Park³

¹Yonsei University College of Medicine, Republic of Korea

Background
Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a type of food allergy, but it is induced only when wheat containing food and augmenting cofactors are accompanied. Exercise, non-steroidal anti-inflammatory drugs and alcohol are known augmenting factors. WDEIA usually developed after ingestion of wheat based food followed by exercise. It is important to accurately diagnose WDEIA to prevent severe anaphylaxis because eating only wheat flour foods may not cause symptoms.

Methods
Subjects over 18 years of age WDEIA patients were enrolled. The concentration of specific IgE to wheat flour, gluten and ω-5-Gliadin was measured by ImmunoCAP assay. Skin tests were performed using wheat, glutenin, and gliadin. The co-factor that caused anaphylaxis and the severity of anaphylaxis was checked. For the wheat challenge test, dinner rolls were used, and aspirin, exercise, or both were used as cofactors. In the provocation test, allergic symptom and signs, tryptase levels and the amount of wheat causing allergic symptoms were detected.

Results
A total of 12 patients were enrolled. Cofactors that induced anaphylaxis were exercise (92%), alcohol (25%), and NSAIDs (8.3%). The sensitivity of the gliadin sIgE test was 100%. Levels of sIgE for ω-5-Gliadin was 7.2 kUA/L. In the gliadin skin test, the average wheal size was 5.5 mm. In the provocation test, allergy was only induced in 20% with bread alone, however cutaneous allergic reactions were occurred in all patients when bread ingestion was accompanied by aspirin or exercise. Respiratory or cardiovascular manifestations were occurred in 33.3%. The amount of bread required for the challenge test is about 218 g.

Conclusion
Gliadin sIgE test (serum, SPT) is highly sensitive when provocation test is difficult to perform. The amount of bread needed to challenge test is 218 g on average. Anaphylaxis can be happened by other cofactors without exercise, and the diagnosis cannot be ruled out even if tryptase elevation did not occur. Based on these points, it is important to suspect WDEIA and accurately diagnose it to prevent severe anaphylaxis.
5. Jennifer Protudjer
   Documentation of Allergies in Canadian Primary Care: New early introduction guidelines correspond to increases in allergy documentation, but not diagnoses

   Jennifer Protudjer¹, Leanne Kosowan¹, Elissa Abrams¹, Alexander Singer¹
   ¹University of Manitoba, Canada

   Background
   Allergic conditions confer a high burden of disease and as the first point of contact Primary Care Providers contribute to their prevention, diagnosis and management. In 2016, revised guidelines for the early introduction of solid foods at 4-6 months of age were adopted in Canada. We examined whether revised guidelines corresponded to fewer new food allergy diagnoses the subsequent years.

   Methods
   The analysis was conducted with a dataset derived from de-identified electronic medical records (EMR) obtained through physicians, nurse practitioners and community pediatricians participating in the Canadian Primary Care Sentinel Surveillance Network (CPCSSN). We captured the documentation of presentations for allergy-related conditions to primary care providers, including food allergy documentation, by age among active patients. The study period was from 1 Jan 2011-31 Dec 2021. Active patients were considered as having at least one visit between 1 Jan 2019-31 Dec 2021.

   We assessed proportions of new allergies within the cohort of patients that had a least one visit that year.

   Results
   Of the 1,690,058 CPCSSN patients, 1,173,145 (69.4%) were active patients, for whom allergy documentation was available for 47.5%. Of these, 57.6% (n=321,038) had allergy and 42.4% had no allergy.

   Regarding food allergy (14.1% of patients), mean age of first EMR documentation was 35.6±22.3y, albeit younger for peanut allergy (20.2±19.8y). While the proportion of new food allergy decreased over time, from 0.7% to 0.3%, new peanut allergy remained stable, at 0.1%. For children (<19y), mean age of first EMR-documented peanut allergy was 7.1±5.6y. For infants (<2y), peanut allergy increased between 2011-2015, from 0.2%-0.4%, then stabilised at 0.4%, despite increased EMR documentation.

   Conclusion
   Despite guidance to support early introduction, and increased presentations to primary care providers for concerns regarding food allergy, peanut allergy remained stable. This large dataset provides insights into the primary care provided to patients with allergic diseases.

6. Dong Keon Yon
   Food allergy and subsequent bone fractures in children (nationwide birth cohort study)

   Dong Keon Yon
   Kyung Hee University, Republic of Korea

   Background
   The prevalence of food allergy (FA) in children is increasing, however, no studies have investigated whether children with FAs are at increased risk of fracture and hence there is a need to determine the direct association between FA and fracture incidence during childhood.
Methods
We performed an exposure-driven propensity score-matched cohort study from a Korean nationwide birth cohort of children born 2008 to 2015 and further linked the dataset with the national health examination results for infants (total = 1,778,588). The primary outcome was first fracture diagnosis. We estimated adjusted hazard ratios (aHRs) from Cox regression to compare the risk of overall fractures in patients with and without FAs. Follow-up ended in December 2019.

Results
During follow-up of 1,778,588 children who completed the first national health examination for infants, 10,442 (0.59%) with FA (13,378,356 person-years). The incidence of first fracture was 41.84/1000 person-years in children with FA (reference: 36.60) corresponding to 1 extra fracture per 205 FA children and year. After propensity score matching, the risk of overall fractures was associated with children having FAs (aHR, 1.11; 95% CI: 1.05–1.17). This risk was pronounced according to the severity of FA. The earlier onset age of FA was associated with higher fracture risk.

Conclusion
In a birth cohort study of 1.78 million children, FA were linked to an increased risk of subsequent fractures. Our results provided an improved understanding of the osteoimmunology for FA in children and suggested that clinicians need to be cautious about sustaining musculoskeletal health.

7. Gabija Didžioikaitė
The prevalence of sensitization to the most common food allergens and their components in Lithuania: gender and age-related differences

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1Vilnius University, Lithuania, 2Institute of Clinical Medicine, Lithuania, 3Innovative Allergology Center, Lithuania

Background
Numerous studies have demonstrated that in the last decade the increasing prevalence of food allergies has become an important issue worldwide [1,2]. In Lithuania, sensitization to food allergens is also becoming an increasing concern. Nowadays there is a lot of research about food allergies, however epidemiological studies reporting the prevalence of sensitization to common food allergens obtained by molecular diagnostic methods in Lithuania are still lacking.

Methods
A retrospective descriptive analysis of data from 659 patients was performed. The patients were divided into groups by gender (females: 51.2%, males: 48.8%) and age (children under 18 y/o: 47.1%, adults: 52.9%). Molecular allergologic testing was performed with Allergy Explorer (ALEX) assay (MacroArray Diagnostics) – a diagnostic tool containing 157 whole extracts and 125 recombinant allergens. The ALEX measuring range for specific IgE is 0.3–50 kUA/L (quantitative) and the results are expressed from class 0 to 4. All patients agreed to participate in the retrospective study and signed a consent form (bioethics committee approval No: 2020/5-1221-716). Statistical analysis was performed using IBM SPSS Statistics 28.0.

Results
48.9% of all patients were sensitized to at least one food allergen. The most common sensitizations were found to nuts and seeds (31.9%) and fruits (29.9%) allergen groups. Dominating nuts and seeds allergens: Cor_a_1.0401 (22.9%), Hel_a (6.5%), fruits’ allergens: Fra_a_1+3 (22.2%), Mal_d_1 (21.3%). Men group was found to be more sensitized to nuts and seeds, fruits, legumes, vegetables, egg, fish and seafood allergen groups (p < 0.05). The most common sensitizations in children were to nuts and seeds (43.2%, mostly...
Cor_a_1.0401, Hel_a), fruits(38,4%, mostly Fra_a_1+3, Mal_d_3) and legumes(31,6%, mostly Gly_m_4). Boys’ group was found to be more sensitized to nuts and seeds and legumes’ allergen groups(p<0,05).

**Conclusion**
In this study, with the help of molecular allergy diagnostics, we specify the exact food allergen components, which dominates in causing allergic reactions to different age groups and genders. Lithuanians were found to be most frequently sensitized to nuts and seeds (with dominating Cor_a_1.0401), fruits (with dominating Fra_a_1+3 and Mal_d_1), legumes (with dominating Ara_h_8). When compared, sensitization to these food allergens, as well as to the majority of other food allergens, was more frequent in men’s group in comparison with women and the difference was statistically significant. Boys’ group was more sensitized to nuts and seeds and legumes allergen groups.

**References**

8. Carolina Gómez-Fariñas
Avocado anaphylaxis due to profilin

*Carolina Gómez-Fariñas*
*Complexo Hospitalario Universitario de A Coruña (CHUAC), Spain*

**Introduction**
Profilin is a panallergen located in almost all allergenic sources of plant origin. It is one of the responsible for the so-called Pollen-Food Allergy Syndrome (PFAS), a hypersensitivity reaction that occurs in patients with seasonal allergic rhinitis, who end up becoming sensitized to pollen profilin by inhalation, and who secondarily develop symptoms after coming into contact with plant foods[1]. Given its susceptibility to pepsin digestion, this thermolabile protein is usually involved in mild reactions limited to oral mucosa known as Oral Allergy Syndrome[2], and only a small percentage of patients develop anaphylaxis, such as in the case described below.

**Case Report**
We present a 45-year-old woman who had attended the Allergology department due to bothersome symptoms of seasonal rhinoconjunctivitis during spring and summer months, and later presented pruritus and generalized hives, facial erythema, dyspnea, and diarrhea within 30 minutes after ingesting an avocado, requiring urgent care and parental treatment. In addition, she had itchy hands when handling tomato, mango, and orange. Prick-Test with common aeroallergens in Northern Spain and fruits was positive for profilin, ribwort, birch and grass pollen. Prick-Prick with avocado, orange, mango and tomato was also positive. Specific Immunoglobulin E was negative for avocado but positive for pollen profilin.

**Conclusion**
Profilin sensitization is primarily associated with grass pollen. Although it more often produces mild symptoms, cases of anaphylaxis without oral symptoms have been described in the literature, assuming 3% of the total, so early diagnosis is essential[3]. There is no standard treatment established for FPAS by profilin except avoiding involved food. The evidence for immunotherapy is scarce, since profilin content in allergenic extracts is low and not enough to induce Immunoglobulin G against it, and consequently a resolution of the symptoms[1]. However, more research is needed to explore this field.
Food Allergy – Session B

1. Jessica O’Konek
   Immunization with a single peanut allergen and mucosal adjuvant protects against anaphylaxis in a mouse model of peanut allergy

   Oliva Benson\textsuperscript{1}, Jeffrey Landers\textsuperscript{1}, Katarzyna Janczak\textsuperscript{1}, James Baker\textsuperscript{1}, Jessica O’Konek\textsuperscript{1}

   \textsuperscript{1}University of Michigan, United States

Background

Many foods consist of multiple allergenic proteins, and patients are often sensitized to multiple allergens. It is not currently clear if immunotherapy with a single major allergen can suppress allergic reactivity in individuals sensitized to multiple food proteins. We have demonstrated that an immunotherapy protocol consisting of 2-3 intranasal immunizations with allergens formulated in a nanoemulsion mucosal adjuvant suppresses allergic responses and protects from allergen challenge in murine allergy models. Here we extend these studies to determine if similar vaccines can be formulated with a single major peanut allergen to suppress reactivity in a mouse model of peanut allergy.

Methods

C3H/HeJ mice were sensitized orally with whole peanut extract and cholera toxin. Mice were intranasally immunized three times with vaccines formulated with peanut extract or Ara h2 in nanoemulsion adjuvant. Mice were then subjected to oral challenges with peanut extract to assess reactivity. Peanut and Ara h2-specific IgG1 and IgE antibodies in the serum were measured by ELISA. Peanut-specific cytokine production was determined by an ex vivo recall response assay in splenocyte and lymph node cell cultures.

Results

Immunization with nanoemulsion-adjuvanted vaccines containing recombinant or natural Ara h2 markedly suppressed reactivity to oral peanut challenge. Vaccines containing the singular peanut allergen achieved similar protection compared with vaccines containing whole peanut extract. Protection from oral peanut challenge was achieved despite the persistence of peanut-specific IgE and was associated with strong suppression of peanut-specific Th2-polarized immune responses. Immunization with nanoemulsion adjuvant
alone did not alter the immune response or reactivity, suggesting a requirement for the presence of a peanut allergen in the vaccine.

Conclusion
These results demonstrate that immunization with a single major peanut allergen can be sufficient to suppress anaphylactic reactions driven by sensitization to and challenge with whole peanut extract. The ability to use single recombinant allergens may simplify the development of therapeutic vaccines for food allergies.

2. Christopher Mattison
In silico modeling, docking, and epitope prediction of human anti-Ara h 2 antibodies

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Background
Food allergies affect 1-10% of the global population [1]. The Ara h 2 peanut allergen is commonly recognized by allergy causing antibodies [2-5]. Peptide mapping has identified linear Ara h 2 epitopes [5-8], but there are only a handful of studies describing conformational Ara h 2 epitopes [9-11]. Similarly, only a few human anti-Ara h 2 antibody sequences have been made publicly available [12-15]. Here, published human anti-Ara h 2 antibody sequences were modeled and in silico docking experiments were used to predict and characterize potential Ara h 2 conformational epitopes.

Methods
All protein structure preparation steps, modeling, and docking were performed using Molecular Operating Environment (MOE, Chemical Computing Group, Montreal, Quebec, Canada). A crystal structure of recombinant Ara h 2 fused to maltose binding protein (MBP) (pdb 30B4) was used for docking following the deletion of the MBP moiety from the structure. Human anti-Ara h 2 antibody sequences were modeled in MOE using the antibody modeler function with the ‘best fit’ variable domains and complementarity-determining regions (CDRs). Docking was performed using the Protein-Protein Dock application within MOE.

Results
Two regions on the surface of Ara h 2 were commonly identified as conformation epitopes predicted to be recognized by human anti-Ara h 2 antibodies. The first predicted conformational epitope includes amino acids within alpha helix 4 and contributions from the amino-terminus and/or carboxy terminus. The second consists of residues that primarily reside in alpha helix 2 and 3 of Ara h 2 but may also include amino acids near the carboxy terminal loop.

Conclusion
The epitope prediction and modeling presented here indicates two conformational epitopes are commonly recognized by antibodies from independent human volunteers. This suggests the presence of particularly potent antigenic regions on Ara h 2, and these surfaces may provide hints to better understand what makes Ara h 2 such a potent allergen. Well defined Ara h 2 conformational epitopes may enable the development of biological-based drugs acting to prevent peanut allergen sensitization or reduce the severity of allergic reactions due to accidental peanut allergen contact.

References

3. Yuzhu Zhang

Mapping IgE binding epitopes with recombinant peptides and internal references

**Yuzhu Zhang**, Shilpa Bhardwaj, Ana Vilches, Andrew Breksa, Shu-Chen Lyn, Sharon Ghinthrajah, Kari Nadeau, Tengchuan Jin

**1USDA, United States, 2Stanford University, United States, 3University of Science & Technology of China, China**

**Background**

Linear IgE epitopes play essential roles in persistent allergies. Using chemically synthesized peptides attached to membranes and microarray experiments is one approach for determining predominant epitopes. However, the overall expense of this approach and the inherent challenges in scaling up the production and purification of synthetic peptides limited its adaptations by most research laboratories. There is a need for a cost-effective method for mapping linear IgE binding epitopes.

**Methods**

TL1A is a tumor necrosis factor (TNF) superfamily member. When recombinantly produced in bacteria without an expression tag, TL1A was present in high levels in both the soluble and insoluble partitions. Thus, TL1A was used as an expression tag to produce overlapping peptides derived from food allergens.
Results
A plasmid vector for expressing peptides sandwiched between an N-terminal His-tag and the trimeric TL1A was constructed. The vector was used to make overlapping peptides derived from a number of food allergens. The peptide fusions were present in both the soluble and the insoluble partitions, indicating the method’s potential utility in producing peptides with diverse properties. Peptides from peanut allergen Ara h were successfully expressed, purified, and used to identify IgE binding epitopes of Ara h 2 with patient sera. New and previously defined dominant IgE binding epitopes of Ara h 2 were identified.

Conclusion
TL1A could be used as a fusion partner to facilitate the production of peptides in E coli. The study developed a new method that offers another approach for researchers to obtain information about IgE binding epitopes of allergens for better diagnosis and prediction of the prognosis of allergies and for understanding better the allergenicity of proteins.

References

4. Charles Schuler
Transepidermal water loss rises before food anaphylaxis and predicts food challenge outcomes

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1University of Michigan, United States

Background
Food allergy (FA) is a growing health problem requiring physiologic confirmation via the oral food challenge (OFC). Many OFCs result in clinical anaphylaxis, causing discomfort and risk while limiting OFC utility. Transepidermal water loss (TEWL) measurement provides a potential solution to detect food anaphylaxis in real time prior to clinical symptoms. We evaluated whether TEWL changes during an OFC could predict anaphylaxis onset.

Methods
Physicians and nurses blind to TEWL results conducted and adjudicated the results of all OFCs. A study coordinator measured TEWL throughout the OFC and had no input on OFC conduct. TEWL was measured two ways in two separate groups. First, TEWL was measured using static, discrete measurements. Second, TEWL was measured using continuous monitoring. Participants who consented gave blood before and after OFCs for biomarker analyses.
Results
TEWL rose significantly during OFC-induced anaphylaxis and did not rise during non-reacting OFCs. Systemic increases in tryptase and interleukin-3 were also detected during reactions, providing supporting biochemical evidence of anaphylaxis. The TEWL rise occurred earlier in time and at lower food challenge doses than clinical evidence of anaphylaxis. Continuous monitoring detected a significant rise in TEWL that presaged positive OFCs, but no rise was seen in OFCs with no reaction, providing high predictive specificity for anaphylaxis against non-reactions.

Conclusion
During OFCs, a TEWL rise anticipates a positive clinical challenge. TEWL presents a novel monitoring modality that may predict food anaphylaxis and facilitate improvements in OFC safety and tolerability.

5. Derek Croote
Deconstructing the Human IgE Response in Peanut Allergy

Derek Croote¹, Joyce Wong¹, Paige Creeks¹, Ben Chung¹, Venu Aruva¹, Eric Mabery¹, Anmoldeep Kaur¹, Johanna Romero¹, Jessica Grossman¹, Roger Thomas¹, Henry Lowman¹

IgGenix

Background
The severity of peanut allergy and its increasing prevalence pose challenges to allergic individuals, their caregivers, and the healthcare industry. Despite extensive characterization of allergenic peanut proteins involved in mediating reactivity, a molecular understanding of how patient IgE interacts with specific epitopes on major allergenic proteins has been absent due to technological limitations of isolating human monoclonal IgE antibodies from allergic individuals.

Methods
IgGenix applied its SEQ SIFTER single-cell RNA-sequencing platform to discover monoclonal IgEs from a diverse cohort of peanut allergic individuals. Monoclonal IgG4 antibodies, re-engineered from monoclonal IgE antibodies, were screened for their specificity to peanut allergens Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8, and Ara h 9. A subset of antibodies were then characterized using affinity measurement and epitope binning. High affinity antibodies from unique epitope bins were then evaluated in functional assaying including plasma IgE blocking ELISAs, mast cell activation tests (MATs), and basophil activation tests (BATs).

Results
The repertoire of IgE antibody specificities discovered in an unbiased way was skewed strongly towards binding Ara h 2 and/or Ara h 6, in line with existing literature on the immunodominance of these allergenic proteins. At the molecular level, epitope binning revealed strong evidence for the immunodominance of particular Ara h 2 and Ara h 6 epitopes. The functional importance of these epitope bins was demonstrated in blocking ELISAs and cell-based assays that led to the design of an approach to significantly inhibit peanut-mediated cellular degranulation.

Conclusion
A molecular understanding of peanut allergy, developed through a methodical approach beginning with unbiased IgE discovery, can serve as the foundation for therapeutic design that addresses the drivers of allergic reactivity. Owing to the absence of adverse events associated with allergen administration, IgG4 antibody-based biologics are poised to become a promising treatment option for allergic individuals, especially those seeking a fast onset of action or don’t qualify for other treatment options.
6. Charlotte Castenmiller

Plant-based enveloped Ara h 2 Bioparticles display exceptional hypo-allergenicity and activate human dendritic cells to promote Th1 cell development

*Charlotte, Castenmiller*¹, Maria Stigler², Pascal Kroon¹, Mary Kirpas³,⁴, Serge Versteeg¹, Jaap, Akkerdaas¹, Glorismer Pena-Castellanos², Bart Blokhuys⁵, Stephen Dreskin⁶, Lydia Auger⁷, Réjean Desgagnés⁷, Caroline Martel⁷, Lucie Mirande⁸, Bertrand, Morel⁸, Virginie, Roberge⁷, Virginie, Stordeur⁸, Guy Tupper⁷ Louis Vézina⁷, Veronique, Gomord⁸, Esther de Jong¹, Frank Redegeld⁵, Wayne Shreffler³,⁴, Lorenz Aglas², Ronald van Ree¹

¹Amsterdam UMC, University of Amsterdam, The Netherlands, ²Paris Lodron University of Salzburg, Austria, ³Massachusetts General Hospital, United States, ⁴Harvard Medical School, United States, ⁵Utrecht University, The Netherlands, ⁶University of Colorado, United States, ⁷Angany Inc., Canada, ⁸Angany Innovation, France

**Background**

Currently, oral immunotherapy is the only immunotherapy for peanut allergy with market authorization for use in children from 4 to 17 years old. However, it is accompanied by frequent and sometimes severe side-effects, has to be adhered to for years and is high in cost. Here we examined a potential immunotherapy candidate, namely, plant-derived eBioparticles that express recombinant Ara h 2 (Ara h 2-eBPs) on the surface, and assessed both allergenicity and DC-mediated T cell polarization.

**Methods**

Allergenicity was assessed using 1) IgE binding potency (ImmunoCAP inhibition), 2) induction of effector cell triggering (using CD34+ stem cell-derived human mast cells (hMCs), rat basophil leukemia cells (RBL), and the basophil activation test (BAT) using human basophils), and 3) the capacity to form IgE-allergen immune complexes (FAB test). Flow cytometry was used to determine 1) Ara h 2-eBPs internalization by dendritic cells (DCs), 2) DC maturation markers, and 3) T cell polarization measuring intracellular IFNγ (Th1) and IL-13 (Th2), and CD25+CD127-Foxp3+ (Tregs). Finally, DC cytokine production was assessed by ELISA in the absence or presence of anti-TLR4.

**Results**

All three effector cell assays (RBL, BAT, hMCs) confirmed similar degrees of hypo-allergenicity, quantified by the RBL test to be > 14,000-fold. Ara h 2-eBPs proved to be incapable of forming IgE-Ara h 2 complexes (FAB test) and showed a 10,000-fold reduced capacity to bind IgE. Furthermore, Ara h 2-eBPs uptake by DCs was blocked by cytochalasin D. Also, DCs stimulated with Ara h 2 eBPs but not with nAra h 2 showed an increase in maturation markers (CD83, CD86, HLA-DR) and increased the ratio IFNγ+/IL-13+ T cells. Finally, blocking TLR4 reduced eBP-induced cytokine production.

**Conclusion**

Ara h 2-eBPs were exceptionally hypo-allergenic compared to natural Ara h 2 in multiple test using allergic effector cells. Furthermore, Ara h 2-eBPs were taken up by DCs via an active process of phagocytosis, induced DC maturation and cytokine production partly mediated by TLR4, and skewed the T cell response towards Th1 cells. Altogether, the combination of impressive hypo-allergenicity and Th1-skewed immunogenicity highlights the plant-derived Ara h 2 eBP as a promising candidate for peanut AIT.
Naoko Okishima

Search for hypoallergenic apples by Mal d 1 determination and oral challenge test

Katsuhiko Kobayashi1, Yumi Koike2, Yasuto Kondo3
1Kobayashi E.N.T. Clinic, Japan, 2Nagano Children’s Hospital, Japan, 3Fujita Health University, Japan

Background
We have shown the results of relative quantification of the mRNA of Mal d 1 in Japanese apple cultivars at WISC2018, and conducted an oral challenge test (OCT) on apple PFAS patients to search for cultivars that are asymptomatic at WAO2020. In this study, We compared several reported methods for the extracting Mal d 1 protein and constructed the ELISA system to quantify Mal d 1. By using the ELISA, Mal d 1 in Japanese cultivars that subjected to an OCT were quantified, to see the correlation between the oral symptoms and the amount of Mal d 1.

Methods
To determine the extraction efficiency, we compared the extract solutions of 1M sucrose, 10mM phosphate buffer, pH 6.8 and citrate buffer, pH 3.0 to extract the Mal d 1 protein from Fuji cultivated in Nagano prefecture. An ELISA system was constructed by combining a commercially available anti-Bet v1 mouse monoclonal antibody to immobilize the antigens and anti- Mal d 1 rabbit polyclonal antibody as an detection antibody. The placebo-controlled, double-blind OCT was conducted using apple and cabbage smoothies. The Mal d 1 was extracted from the remaining apple fruit used as the sample and quantified by the ELISA.

Results
To prepare the ELISA plates, the highest sensitivity and the lowest coefficient of variations were achieved by the overnight incubation of both samples and the antibody adsorption at 4°C. Of the three extraction methods were tested, the sucrose-based extraction solution gave the best result. Among 26 Japanese apple cultivars, the amount of Mal d 1 was significantly lower in 24 cultivars than in Fuji, which is the most produced apple in Japan. There was no correlation between the Mal d 1 contents in the apples used in the OCT and the oral symptoms.

Conclusion
The sucrose-based extract solution was the best to extract the Mal d 1 suitable for ELISA. Reports from other researchers suggested that one reason for the lack of correlation between Mal d 1 amounts in apples and oral symptoms was the involvement of polyphenols, which will be analyzed and reported in the future.

References

Peter Stoll

Tropomyosin - a highly cross-reactivity food allergen

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Background
In 2021 the European Food Safety Authority (EFSA) accepted mealworm Tenebrio molitor, as the first insect-based food source in the European Union. Exposure to new food sources always carries the risks of the
development of novel food allergies, often due to cross-reactions to already established food sources. Tropomyosin, an already known allergen in seafood, is suggested to play an important role in insect allergies, as well as in cross-reactions between insects and seafood. The aim of this study was to investigate the allergenic and cross-reactive potential of tropomyosin in insect and seafood allergies.

Methods
The IgE reactivity of sera from tropomyosin sensitized patients to extracts from Black Tiger prawn, Pacific oyster and Mealworm was evaluated in IgE immunoblots. Mass spectrometry experiments were performed to identify IgE-reactive proteins. cDNA codings for tropomyosins from Black Tiger prawn, Pacific oyster and Mealworm were cloned and the proteins recombinantly expressed in Escherichia coli. To verify the allergenic potential and analyze the cross-reactivity of the recombinant proteins, IgE immunoblots and inhibition IgE immunoblots with sera from tropomyosin sensitized patients were carried out.

Results
Tropomyosin sensitized patients recognized proteins of the molecular weight of 37 kDa in Black Tiger prawn, Pacific oyster and Mealworm extracts in IgE Immunoblots. Mass spectrometry experiments proved that the IgE reactive proteins indeed represent tropomyosins. The three proteins were recombinantly expressed in E. coli, purified to homogeneity and were shown to represent IgE-reactive proteins. Inhibition blots showed cross-reactivity of mealworm tropomyosin with tropomyosins of Black Tiger prawn and Pacific oyster.

Conclusion
We not only show that shrimp sensitized patients' display IgE reactivity respond to tropomyosins from oyster and mealworm, but also that tropomyosins from crustaceans, molluscs and insects represent cross-reactive molecules. Our results will contribute to a better understanding of allergic reactions to edible insects and potential cross-reactivity to seafood allergens.

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9. Nobue Takamatsu
Determination of Antigen Proteins Contained in Trace Amounts in Processed Foods Sold in Japan

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Background
In Japan, processed foods containing chicken eggs, milk, wheat, buckwheat, peanuts, shrimp, and crab are required to have allergy labeling. However, the labeling does not provide information on the amounts of the allergens present, leaving allergy sufferers unsure about the safety of these foods. To address this, a study measured antigenic proteins in commercially available processed foods and analyzed the approximate amounts present. The goal was to create reference materials for dietary guidance and to help allergy sufferers make more informed decisions about the foods they consume.

Methods
A total of 276 commercially available processed foods with allergy labels or "may contain" labels for chicken egg, milk, and wheat were included in the study. Measurements were performed using the "FASTKIT ELISA Series" manufactured by Nippon Ham Corporation, in accordance with the method notified by the Food Health Department, Pharmaceutical Affairs Bureau, Ministry of Health, Labour and Welfare.
Results
Processed foods sold in a typical supermarket in Japan were purchased. 121 foods were labeled "contains" and 155 foods were labeled "may contain", including 100 for eggs, 93 for milk, and 83 for wheat. The average antigenic protein concentration was higher in the "contains" label group than in the "may contain " label group (t-test: p<0.05), with 4.3% of the foods containing 10 μg/g or more. (10 "contains" labels and 2 "may contain" labels). The breakdown included processed meat products, noodles, and freeze-dried foods, 8 of which exceeded the detection limit of 20 μg/g.

Conclusion
Various factors such as extraction efficiency, food processing methods, and chemical reactions affect the accuracy of measuring allergens in processed foods. Based on the study, it is suggested that patients who can tolerate small amounts of allergens can consume processed foods labeled with "contains" or "may contain" labels. However, since there is no maximum limit for allergen labeling, the study recommends introducing such foods into the diet only if the measured values are clear.

10. Brian Goodman
Food-dependent exercise-induced anaphylaxis due to peach in a PR-10 sensitized patient

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Introduction
Food-dependent exercise-induced anaphylaxis (FDEIA) is a rare IgE-mediated hypersensitivity reaction, in which anaphylaxis is caused by exercise performed within a few hours after consumption of a specific food. Physical exercise alone or the food itself is not enough to cause anaphylaxis. Oral allergy syndrome (OAS) presents as allergic symptoms related to the oral mucosa and is due to IgE-mediated cross-reactivity between homologous peptides in specific pollens and certain nuts, fruits, and vegetables. FDEIA and OAS have rarely been reported to coexist. Here, we describe a case of FDEIA due to peach in a pathogenesis-related 10 (PR-10) sensitized subject.

Case Report
A 13-year old boy was referred for evaluation after experiencing anaphylaxis while playing basketball. He had a history of allergic rhinoconjunctivitis and oral allergy syndrome (apples, pears, peaches, cherries, nectarines, kiwis, and pecans). The patient ate 3 peaches followed by 1 hour of basketball. 1.5 hours after ingestion, the patient developed urticaria, abdominal pain, and bronchospasm requiring epinephrine and antihistamines. Prior ingestion of peaches resulted in oroapharyngeal symptoms alone. Percutaneous tests demonstrated sensitization to seasonal pollens, dust mite, cockroach, cat, dog, and mouse allergens. Serum specific IgE levels were measured. Birch IgE 41.30 KUa/L and peach IgE 7.65 KUa/L.

Conclusion
Cross-reactivity is common between Bet v1 in birch pollen and Bet v1 homologues, such as peach. Our patient previously only had oral pruritus after eating peach. However, by combining the consumption of multiple peaches with exercise, the patient developed anaphylaxis. Exercise is a known cofactor for anaphylaxis and may increase the permeability of the gastrointestinal barrier, leading to increased allergen uptake, and a subsequent increase in the bioavailability of the allergen. This is a rare case FDEIA due to peach in a PR-10 sensitized patient. It also demonstrates the capability of cofactors to influence the severity of allergic reactions.

References

**Food Allergy – Session C**

1. Yuri Takaoka
Diagnostic utility and safety of oral food challenge tests in children with suspected shrimp allergy

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**Background**
Shrimp allergy in children is relativity common. However, there are only a few reports on the clinical manifestation of shrimp allergy in Japanese children. We investigated the diagnostic utility and safety of combined oral food challenge (OFC) and blood tests for children with suspected shrimp allergy.

**Methods**
We conducted an OFC on Japanese children with suspected shrimp allergies using a multicenter protocol at the facilities of the Osaka Food Challenge Network. Blood tests and skin prick tests were performed before the OFC. Each child was administered boiled black tiger prawn or whiteleg shrimp in increments of 2-, 5-, and 10 g every 30 minutes for 1 hour (17 g total). Objective symptoms were judged as OFC positive. Only subjective symptoms, such as oral irritation, were withheld for judgment, and children were instructed to ingest the same dose repeatedly at home.

**Results**
A total of 67 children were enrolled. Of these, 17 had a positive OFC result, where the median total dose was 7 g. Seven children had mild symptoms, nine had moderate symptoms, and one child had severe symptoms that required intramuscular adrenaline administration. The median shrimp-specific immunoglobulin E (slgE) antibody titers in positive cases were significantly higher than those in negative cases (70.3 vs. 10.8 IUA/mL; p=0.00316). The optimal cutoff value of shrimp-slgE from the receiver operating characteristic curve was 26.9 IUA/mL (sensitivity: 76.5%, specificity: 72.7%).

**Conclusion**
An OFC combined with blood tests was performed on children with suspected shrimp allergy to clarify the clinical manifestation of shrimp allergy. Shrimp-slgE titer could predict OFC results to a certain extent; however, OFCs are recommended for the accurate diagnosis of shrimp allergy. It is necessary to perform OFCs with caution for severe symptoms, although most children were able to safely perform the OFC under...
this protocol. Further useful serological indicators are needed to predict severe symptoms and to improve the safety of OFC.

2. Yasuaki Matsumoto
Differences in eliciting doses between boiled eggs and processed products (homemade steamed bread) with eggs

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Background
Few studies have examined alterations in eliciting doses (EDs) owing to food matrix effects. In this study, we investigated whether boiled egg white and steamed bread with egg white alter EDs in patients with an egg allergy in Japan. We analyzed the results of oral food challenges (OFCs) performed in patients with a diagnosis of an egg allergy or in those suspected of having an egg allergy (based on clinical symptoms and laboratory findings) to determine a definitive diagnosis or a safe intake level to acquire tolerance.

Methods
We performed a cross-sectional study. We enrolled patients with an egg allergy who underwent OFCs of a boiled egg challenge or a steamed bread (mainly rice flour) challenge with egg white between November 2013 and October 2022 at the National Center for Child Health and Development (NCCHD), Tokyo, Japan. Egg white boiled for 15 minutes and steamed bread heated in a 500-W microwave oven for 5 minutes were used as each challenge food. We estimated a threshold distribution model and the ED for these challenge foods by interval-censoring survival analysis. The Ethics Committee of NCCHD approved this study.

Results
We included 852 boiled egg challenges and 201 steamed bread challenges with confirmed egg allergy. The median cumulative reacting dose of the boiled egg and steamed bread challenge was 452 mg (IQR: 119–1,187) and 505 mg (IQR: 101–2,020), respectively. The median ovomucoid-specific IgE was 11.85 kUA/L (IQR: 3.85–31.1) and 11.5 kUA/L (IQR: 3.78–35.3), respectively. The distribution curves were significantly different between the two groups. In the log-normal distribution model, the ED05 was 12.0 mg (95% CI: 8.9–16.2) for the boiled egg challenge and 49.9 mg (95% CI: 23.1–108) for the steamed bread challenge.

Conclusion
Significantly higher EDs were found for steamed bread than for boiled egg white, possibly due to the matrix effect. Steamed bread may be useful for a safer food challenge and oral immunotherapy. Additionally, the same amount of protein in a boiled egg as that in steamed bread may induce allergic symptoms.

3. Agnes Sze-Yin Leung
Reactions to Codfish in Double-Blind Placebo Controlled Food Challenges (DBPCFC)

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Background
Few studies have examined reaction characteristics to codfish. We aim to describe the symptoms and threshold doses in children with codfish allergy undergoing DBPCFCs. The severity and low dose reactor predictors were studied.

Methods
Paediatric patients aged 3 to 10 years with a history of fish-allergic reaction and positive codfish-specific IgE were referred for oral immunotherapy to codfish. All of them underwent double-blind placebo-controlled food challenges (DBPCFC) to codfish (cumulative 5000 mg fish protein). Codfish was blinded with herbs in mashed potatoe. Patients' skin prick test (SPT) and specific IgE (sIgE) levels to fish and fish components were evaluated.

Results
Among 27 participants aged 5.37 +/- 2.29 years, 26 (96%) reacted to codfish in DBPCFCs. Most participants were male (70%), had atopic dermatitis (85%) and other food allergies (89%). Common allergic manifestations were angioedema (74%), urticaria (74%) and erythema (33%). Most symptoms were mild (oFASS-5 grade 2-3)(89%), and no anaphylaxis was experienced. 40.7% reacted to below 0.1 gram of fish proteins; and SPT level to in-house grass carp extract was a predictor of threshold (P=.036). Reaction-eliciting dose was positively correlated with reaction severity (P=.031). There was no association between reaction-eliciting dose and symptoms severity with fish-specific IgE and SPT.

Conclusion
Children with codfish allergies in a DBCPFC setting mostly reacted with mild symptoms. Children who had positive codfish sIgE could tolerate codfish, which supports the need for DBPCFC to confirm eligibility in food immunotherapy studies. Severity of reaction is difficult to predict, and SPT to grass carp appears to predict low dose reactors.

4. Vanlaya Koosakulchai
Safe consumption of processed foods following negative medium-dose cow’s milk oral food challenge

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Background
Cow’s milk (CM) is one of the most common causative foods in children.1 Providing guidance on the types of products and serving sizes for children with cow’s milk allergy consumption at home can improve their quality of life.2 Although oral food challenge (OFC) is useful in CM allergy patients to avoid complete elimination, safety of reintroducing processed food containing CM is unknown.2-4 We aimed to investigate the safety of reintroducing processed food containing CM after a negative CM-OFC, in order to assist children with CM allergy in selecting safer products.

Methods
This study included CM-allergic children diagnosed by a history of immediate reactions to CM and tolerated to heated CM containing 850 mg of milk protein, at Sagamihara National Hospital from May 2015 to June 2018. We instructed children and guardians to consume a range of processed foods at home at least once a week, in amounts not exceeding 850 mg of milk protein after a negative result for CM-OFC containing 850 mg of milk protein. The children and their guardians were instructed to record all adverse reactions (AEs) on the given questionnaire which was collected 2 to 4 weeks later.
**Results**
From a total of 74 children, 17 (23%) reported AEs with a total of 25 events at home. All AEs were mild, and antihistamines were used in 8 events (32%). Milk chocolate and lactic beverage were the most common dairy foods that induced AEs: 7 and 6 events, respectively; meanwhile, bread and skimmed milk caused the least AEs. After all AEs were evaluated, no child required avoidance of all processed dairy foods. Children having had AEs at home had significantly higher levels of sIgE to CM, casein and total IgE (P = 0.006, 0.003 and 0.017, respectively).

**Conclusion**
This study revealed that all children having passed a CM OFC were able to consume some processed dairy-selected products, based on their protein content, the type of food matrix utilized, and the degree of heating process without experiencing significant serious AEs. However, children with higher sIgE to CM, casein, and total IgE levels may develop AEs and should be monitored.

**References**
5. Mika Ogata Safety of Oral Food Challenge for Individuals with Low Egg White and Ovomucoid-Specific IgE Antibodies

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**Background**
During an oral food challenge (OFC), there is a risk of adverse reactions, including anaphylaxis. Therefore, the physician conducting the OFC must be experienced. Although the levels of serum-specific IgE antibodies (sIgEs) to egg white (EW) and ovomucoid (OVM) are reliable predictors of hen’s egg (HE) allergy, the diagnostic accuracies of these biomarkers are limited.

**Methods**
A total of 2,058 individuals with low EW- or OVM-sIgE underwent HE-OFC at two Japanese general hospitals between January 1, 2017 and December 31, 2021, within 1 year of recorded sIgE measurements. The ImmunoCAP systems were used to measure sIgEs. The HE-OFC test was performed according to the Japanese guidelines for food allergy 2017 or 2020 in an open and unblinded method. We evaluated the OFC results in individuals with low levels of egg white (EW)- and ovomucoid (OVM)-specific immunoglobulin E (sIgE) and the safety of the hen’s egg (HE) OFC in these individuals.
Results
Five hundred-and-one individuals (24.3%) had low EW-sIgE levels (class 2 or lower), and 926 (45.0%) had low OVM-sIgE levels (class 2 or lower). Individuals with low EW-sIgE had lower total IgE and OVM-sIgE than did those with high EW-sIgE (greater than class 2). Those with low OVM-sIgE had lower total IgE and EW-sIgE than did those with high OVM-sIgE (greater than class 2). Among the individuals with low EW-sIgE, 86.4% (433/501 cases) passed the OFC without symptoms. Among the individuals with low OVM-sIgE, 82.6% (765/926 cases) passed the OFC without symptoms.

Conclusion
More than 80% of individuals with suspected IgE-dependent HE allergy with low levels of EW- or OVM-sIgE could tolerate at least a small dose of cooked HE, and approximately 50% could a 1/8 or more. Individuals with a history of anaphylaxis were at risk of developing anaphylaxis during the OFC. No subjects developed anaphylactic shock. HE-OFC for children with low OVM-sIgE can be safely performed and is acceptable for non-allergists.

6. Kyohei Takahashi
Examination of the probability of inducing allergic symptoms using the benchmark dose method: multicenter study

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Background
In some individuals with food allergies, even small amounts of allergens can induce symptoms, highlighting the importance of labeling food products with information on antigen presence. In Japan, it is not mandatory to label specific ingredients if the amount of total protein in the final product is very small, such as a few µg/g. However, this policy requires examination to ensure its appropriateness. The purpose of this study is to estimate the eliciting doses (EDs) for each food using the benchmark dose method based on data from oral food challenges (OFCs) at multiple facilities.

Methods
We analyzed data from 7817 food challenge test cases conducted at 9 facilities in 2019. We selected cases that met the following three conditions: (1) the amount of food intake could be calculated as a protein dose, (2) patients had a history of immediate-type symptoms, and (3) patients were completely eliminating the target food at the time of OFC. We collected information such as type of food product, total intake, amount of initial symptom onset, symptoms during OFC, blood test results, and other allergic comorbidities. The study was approved by the institutional review boards of Sagamihara National Hospital.

Results
The median age of the study population was 3.8 years (IQR: 1.8-6.8), with a male-to-female ratio of 6:4. Out of 556 hen’s egg OFCs, the ED at which a reaction occurred in 1% of cases (ED01) was 3.02 mg (95%CI: 1.45-5.09), and The ED05 were 17.7 mg (11.4-24.1). For the 513 milk OFCs, the ED01 and ED05 were 3.02 mg (1.45-5.09) and 17.7 mg (11.4-24.1). For the 214 wheat OFCs, the ED01 and ED05 were 0.39 mg (0.11-0.85) and 2.66 mg (1.24-4.50) For the 116 peanut OFCs, the ED01 and ED05 were 0.79 mg (0.16-1.96) and 4.63 mg (1.67-8.89).

Conclusion
Using the Bayesian benchmark dose method, we estimated the eliciting dose for each food and found that current food labeling was generally considered reasonable. We also investigated the factors associated with
EDs, such as specific-IgE and age. Our results suggest that the benchmark dose method is useful for predicting the probability of allergy symptoms and could provide valuable information for labeling and risk management.
7. Yumi Koike  
Low dose of wheat oral food challenge in patients with an immediate allergy and prognosis in patients with positive results

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**Background**

The Japanese Guidelines for Food Allergy 2021 recommend that an oral food challenge (OFC) test be performed using a low dose of wheat (1–3 g of udon noodles) for high risk wheat allergy patients. However, there are many severe cases in which even a small amount of OFC is positive. OFC should be performed using a lower dose to avoid complete elimination in patients with a positive result. In this study, we investigated the result of low dose of wheat OFC test at our hospital and performed close follow-up of patients with positive results.

**Methods**

Eighty-five wheat allergy patients with an immediate history of wheat consumption, who underwent a 2 g udon OFC from July 2014 to December 2022. We analyzed OFC test results and patients’ profiles (clinical and family history and allergy complications), laboratory findings (wheat and ω-5-specific immunoglobulin IgE levels and subsequent course of patients with positive results (Nagano Children’s Hospital Ethics Committee: S-03-7).

**Results**

OFC was performed at a median age of 3.0 (0.6–16) years. The OFC positivity rate was 27% (23/85), and the main provoked symptoms included skin (18/23, 78%), respiratory (16/23, 70%) and cardiovascular (1/23, 4%). Adrenaline was used in 1 case. Wheat-specific IgE levels were significantly higher in OFC-positive than in OFC-negative subjects (51.8 vs. 11.2 UA/mL). OFC-positive subjects underwent several OFC with an even lower dose. Ten of 17 (59%) who were able to follow the 3-year course after OFC were able to consume 0.5g of udon after 1 year, and 15/17 (88%) could avoid complete elimination after 3 years.

**Conclusion**

Even in patients with severe wheat allergy, the OFC could be safely performed using a small amount of wheat. Wheat-specific IgE levels were high in OFC-positive patients. Even in those with OFC positivity, complete elimination could be avoided with adjustment in the loading dose and repeating the OFC.

**References**

8. Noriyuki Yanagida
Nationwide survey of the status of the oral food challenge test conducted at hospitals during the coronavirus pandemic

Background
Spread of the Omicron variant of severe acute respiratory syndrome coronavirus 2 has significantly affected food allergy practice, particularly in implementing the oral food challenge (OFC) for food allergy. This nationwide survey was aimed at examining the number of inpatient OFC conducted at hospitals, infection control measures, frequency of positive OFC results for food allergy due to coronavirus disease (COVID-19), and nosocomial COVID-19 infections.

Methods
We asked 373 pediatric training facilities to fill out an online questionnaire on implementation of inpatient OFC from January 1 to June 30, 2022. The number of OFC conducted in shared and private rooms, COVID-19 testing at the time of OFC admission, and number of nosocomial COVID-19 infections in wards were investigated.

Results
Across the 177 facilities that conducted inpatient OFC, a total of 15,858 OFC tests were conducted, including 12,503 in shared rooms and 3,355 in private rooms. Thirty-two facilities conducted OFC only in private rooms, while 73% facilities conducted COVID-19 rapid antigen test or polymerase chain reaction for patients and 37% for patients and family members. The positive rate of COVID-19 testing was 0.5% of all patients and 0.1% of all family members. Significantly fewer OFC were performed (18.5 vs. 56.0) at institutions that performed COVID-19 testing (p = 0.001). No nosocomial infections in wards related to OFC were reported.

Conclusion
The results of the present study indicate that even during the COVID-19 outbreak, many facilities were able to perform inpatient OFC without inducing nosocomial infections.

9. Sakura Sato
Risk factors for needing multiple adrenaline injections during oral food challenges in a nationwide survey in Japan

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Background
Oral food challenges (OFCs) are necessary to diagnose and manage food allergies. However, OFCs can induce anaphylaxis (An) unexpectedly. When this occurs, patients may require multiple-dose adrenaline (Ad) injections. To date, there are few reports on the clinical characteristics of patients who required multiple-dose Ad injections during OFCs. In the present study, we aimed to clarify the risk factors for needing multiple-Ad injections due to severe reactions during OFCs in a nationwide survey in Japan.

Methods
In this cross-sectional study, patients who underwent OFCs between January and December 2017 were registered from 78 training and teaching facilities of the Japan Pediatric Society that provide OFCs in training and teaching facilities. Patients who developed severe symptoms during OFCs were included in this study. Patients with mild or moderate symptoms were excluded. We collected patients’ backgrounds, symptoms induced by OFCs, and treatment during OFCs from medical records. OFCs were performed using the
Japanese pediatric guideline for food allergy. Symptom severity was assessed according to Japanese anaphylaxis guidelines.

Results
Four-hundred ninety-five patients (median age, 5 years) who developed severe symptoms were included. Of these, 255 (52%) required Ad once, and 47 (9%) had multiple doses of Ad administered. Cashew nuts OFCs was the highest rate of patients requiring multiple-dose Ad (38%). Patients with multiple-dose Ad had the following symptoms: skin/mucosal (98%), respiratory (87%), cardiovascular (79%), neurological (77%), and gastrointestinal (66%). Moreover, 40% of patients had symptoms affecting multiple organs. Results from the multivariable logistic regression showed that the complete elimination of a causative antigen (odds ratio, 2.2; 95%CI, 1.0-4.8) was a risk factor for multiple-dose Ad.

Conclusion
In this study, 9% of patients had symptoms that require multiple doses of Ad during OFCs. The complete elimination of the causative antigen was a risk factor for multi doses of Ad among the patients who were administered Ad. However, it is not possible to predict the patients who will react with severe symptoms that require multiple doses of Ad before OFCs. Physicians should consider patient safety, choose an appropriate OFC implementation method, and carefully monitor for symptoms during OFCs.

10. Liudmyla Zabrodska
Anaphylaxis in a patient with comorbid pathology

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Introduction
During the diagnosis of drug allergy, which is a pathological immunological reaction of the body, the tryptase level is the basic diagnostic tool for anaphylaxis. This is especially necessary in severe anaphylaxis.

Case Report
Patient M. 62-year-old male with a severe course of bronchial asthma, NSAID intolerance, and hypertension was admitted to otolaryngology department for planned surgery. The operation was successful. After the surgery, an antibiotic was prescribed, which the patient had previously taken repeatedly.

After intravenous injection of the antibiotic, the patient lost consciousness. The intensive care team immediately started cardiopulmonary resuscitation, intravenous adrenaline, rapid infusion therapy, and artificial ventilation. The patient’s critical condition passed after an hour, and then we were able to collect blood to evaluate the level of tryptase. Monitoring of the patient’s condition due to circulatory instability was day.

Conclusion
The first result of the serum tryptase concentration was 186 μg/L (normal <11 μg/L), which corresponds to severe anaphylaxis. A repeat analysis was taken after 9 hours (20μg/l), and after 2 weeks the level of tryptase was 5μg/l - the baseline level of tryptase.

The level of tryptase increasing in the blood serum is an important marker for the diagnosis of anaphylaxis, especially in case of drug Allergy. Especially patients with complicated allergic history and comorbid pathology remain in the risk group for anaphylaxis and requires additional attention from the medical staff.
1. Stina Bodén
Diet diversity in pregnancy and early allergic manifestations in the offspring

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Background
It is important to disentangle the multi-factorial ethiology behind allergic diseases for which increasing incidences worldwide are evident. Maternal diet is suggested to be one determinant of early life allergy prevention since it may influence on the neonatal innate and adaptive immune system, even before birth. The aim of this study was to investigate if a more diverse diet during pregnancy is associated with subsequent decreased risk of early allergic manifestations in the offspring until the age of 18 months.

Methods
We utilized a diet diversity (DD) score including 40 food items or groups, based on the present dietary guidelines in Sweden, in 3200 pregnant women from the population-based NorthPop Birth Cohort Study. Associations to cumulative incidence of eczema, wheeze, asthma, and food allergy (FA) in the first 18 months of life were assessed using multivariable logistic regression models. For severity of eczema according to Patient Oriented Eczema Measure (POEM)-score), multinominal logistic regression models were used. Screening for sensitization to food and inhalant allergens was performed at 18 months of age in 1922 of the study participants.

Results
Higher diet diversity scores in pregnancy were associated with a decreased risk of physician diagnosed FA in infancy: OR per 1 unit increase in DD-score in Model 3: 0.96, 95% CI 0.92-1.00, P 0.038, and for quartile 4 of the DD-score, OR was 0.58, 95% CI 0.32-0.95 compared to quartile 1. There was an indication of an association between energy adjusted DD-scores and infant wheeze (0.97, 0.96-0.99, P 0.009) but it did not remain significant after further adjustments. No associations were found between diet diversity and offspring eczema or asthma risk or to sensitization status at 18 months of age.

Conclusion
A more diverse diet in pregnancy may reduce the risk of food allergy in early life and could be a promising strategy to reduce early childhood food allergy incidence and its associated individual and healthcare burden. More work is needed to elaborate robust measures of maternal diet diversity to disentangle its impact on early overall allergy risk. These results also indicate reason to further study the association between maternal diet and food allergy risk, potentially acting through both immune-regulated epigenetic imprinting and bacterial translocation from mother to fetus.

References


Table 1. Included food items (n=40) in the Dietary Diversity (DD) score in pregnant women in the Swedish NorthPop Birth Cohort Study. The DD score was adjusted for total energy intake using the residual method.

<table>
<thead>
<tr>
<th>Foods</th>
<th>Cutoff frequency or other measure</th>
<th>Foods</th>
<th>Cutoff frequency or other measure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fiber rich foods:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Fiber cereals</td>
<td>≥1-3 t/w = 1p</td>
<td>2 Fruits &amp; berries</td>
<td>1-2 t/day =1p</td>
</tr>
<tr>
<td>2 Fiber porridge</td>
<td>≥1-3 t/w = 1p</td>
<td>2 All fruits</td>
<td>1-2 t/day =1p</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 All berries</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>3 Fiber pasta</td>
<td>≥1-3 t/w = 1p</td>
<td>2 Red meat</td>
<td>1-3 t/w to 4-6 t/w</td>
</tr>
<tr>
<td>4 Brown rice</td>
<td>≥1-3 t/w = 1p</td>
<td>2 White meat</td>
<td>1-3 t/w to 4-6 t/w</td>
</tr>
<tr>
<td>5 Bulgur couscous/grains</td>
<td>≥1-3 t/w = 1p</td>
<td>Fish &amp; seafood</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>22 Fatty fish</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22 Lean fish</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td><strong>Fiber rich bread</strong></td>
<td></td>
<td>22 Sea food</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>6 Fiber rich soft bread†</td>
<td>If most common bread=1p†</td>
<td>22 Egg</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>7 Fiber rich crisp bread†</td>
<td>If most common bread=1p†</td>
<td>22 Pulses</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>8 Boiled potatoes</td>
<td>≥1-3 t/w = 1p</td>
<td>22 Soya bean products</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>9 Carrots</td>
<td>≥1-3 t/w = 1p</td>
<td>Dairy products</td>
<td></td>
</tr>
<tr>
<td>10 Root vegetables</td>
<td>≥1-3 t/w = 1p</td>
<td>22 Unpasteurized milk</td>
<td>If yes =1p</td>
</tr>
<tr>
<td><strong>Cabbage</strong></td>
<td></td>
<td>22 Cow’s milk</td>
<td>≥2 dl/day = 1p</td>
</tr>
<tr>
<td>11 Cauliflower</td>
<td>≥1-3 t/w = 1p</td>
<td>22 Milk replacement</td>
<td>≥2 dl/day = 1p</td>
</tr>
<tr>
<td>12 Broccoli</td>
<td>≥1-3 t/w = 1p</td>
<td>22 Soured milk unsweetened</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>13 White cabbage</td>
<td>≥1-3 t/w = 1p</td>
<td>22 Yoghurt unsweetened</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td><strong>Green vegetables</strong></td>
<td></td>
<td>22 Quark/cottage cheese</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>14 Lettuce</td>
<td>≥1-3 t/w = 1p</td>
<td>4 Nuts, all</td>
<td>≥1-3 t/w = 1p</td>
</tr>
<tr>
<td>15 Avocado</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 Cucumber</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other vegetables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 Frozen vegetables</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Sweet pepper</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Tomatoes</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 Corn</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 Onion</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 Garlic</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 Mushroom</td>
<td>≥1-3 t/w = 1p</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If ranked as the most common type of consumed bread (1 or 2 on a ranking scale of maximum 6) = 1p

Abbreviations: t/w, times/week; p, points; DD, Diet diversity
Figure 1. Association between diet diversity (DD) score in pregnancy and cumulative incidence of allergic manifestations until the age of 18 months (n=3200). Colored dots represent the odds ratio (OR) per 1 unit increase in DD score and colored lines represent the 95% confidence intervals.

*ORs produced with multinomial logistic regression with 'no eczema' as reference

1 According to POEM score 6-7
2 According to POEM score 8-28
3 Physician diagnosed
4 Sensitized to food mix (5x5) with cow’s milk, egg white, wheat, peanuts, soy, and cod. Sensitization was defined as positive IgE levels ≥ 0.35 kU/L.
5 Sensitized to inhalation mix (Phadiatop) for the allergens allergens birch, timothy, ragweed, cat, dog, horse, Chlaerosporium herbarum, Dermatophagoides pteronyssinus, and farina. Sensitization was defined as positive IgE levels ≥ 0.35 kU/L.

POEM, Patient Oriented Eczema Measure
2. Jonas Österlund

Earlier and more frequent consumption of allergenic foods among infants after the update of Swedish guidelines on complementary feeding

Jonas Österlund1, Gabriel Granäsen1, Stina Bodén1, Magnus Domellöf1, Anna Winberg1, Christina West1

1Umeå University, Sweden

Background

Studies have reported that early introduction of allergenic foods, such as peanuts and egg, can reduce the risk of food allergies in high-risk children. Many international guidelines recommend introduction in the first year of life. In June 2019 the Swedish National Food agency released revised guidelines but the population response is still unknown.

We aimed to examine if age at introduction and consumption frequency of allergenic foods have changed since the release of revised national guidelines on the introduction of solid foods in Sweden.

Methods

Comparison of two time periods, before and after the implementation of the revised guidelines with data from the longitudinal population-based birth cohort NorthPop. Data on food introduction were prospectively collected using web-based questionnaires.

The primary outcome was introduction of egg, fish, legumes, soy protein, peanut, almond, cashew nut, hazelnut, walnut and Brazil nut before 11 months of age. The secondary outcome was the consumption frequency of the aforementioned foods at 9 months. The primary outcome was analyzed using simple and multivariable logistic regression. The secondary outcome was analyzed using ordinal logistic regression. Adjustments for confounders were made.
Results
An increased proportion of infants had introduced egg, legumes, soy protein, peanuts, cashew nut and almonds during the first year of life after the implementation of revised guidelines. The largest change was seen for legumes (55.2% to 69.8% adjusted odds ratio (aOR) 1.90 (95% CI: 1.62-2.24) and peanuts (29.2% to 43.2% aOR 1.87 (95% CI: 1.55-2.24). The consumption frequency also increased for egg, legumes, peanuts, cashew nuts and almonds. Models were adjusted for allergic heredity, maternal country of birth, maternal education level, children in the household, gestational age and at 9 months history of reactions to food, eczema and wheeze.

Conclusion
Since the release of revised national guidelines, infants in the study population were introduced to egg, legumes, soy protein, peanut, cashew nut and almond earlier than before. The infants also consumed egg, legumes, peanuts, cashew nuts and almonds more frequently.

References
Figure 1: Flowchart over the inclusion of the study population and the division of the two study groups.
<table>
<thead>
<tr>
<th>Food Introduction</th>
<th>Previous guidelines</th>
<th>Revised guidelines</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>N [%]*</th>
<th>N [%] **</th>
<th>χ²</th>
<th>P-value</th>
<th>OR (95% CI)</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg introduction</td>
<td>Introduced</td>
<td>1175 (82.3)</td>
<td>1149 (88.7)</td>
<td>-0.001</td>
<td>1.647 (1.330-2.019)</td>
<td>1.661 (1.340-2.060)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Introduced</td>
<td>252 (17.7)</td>
<td>146 (11.3)</td>
<td>0.762</td>
<td>1.052 (0.729-1.539)</td>
<td>1.057 (0.726-1.539)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Legume introduction</td>
<td>Introduced</td>
<td>1368 (96.1)</td>
<td>1247 (96.3)</td>
<td>-0.001</td>
<td>1.918 (1.642-2.240)</td>
<td>1.902 (1.617-2.238)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>Not Introduced</td>
<td>51 (3.9)</td>
<td>48 (3.7)</td>
<td>0.009</td>
<td>1.328 (1.047-1.685)</td>
<td>1.309 (1.025-1.671)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Soy introduction</td>
<td>Introduced</td>
<td>191 (13.5)</td>
<td>911 (74.0)</td>
<td>-0.001</td>
<td>1.858 (1.552-2.215)</td>
<td>1.865 (1.551-2.243)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Introduced</td>
<td>776 (60.5)</td>
<td>384 (31.2)</td>
<td>0.009</td>
<td>1.422 (1.129-1.790)</td>
<td>1.399 (1.111-1.762)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Almond introduction</td>
<td>Introduced</td>
<td>161 (11.7)</td>
<td>203 (17.1)</td>
<td>0.047</td>
<td>1.322 (1.031-1.684)</td>
<td>1.319 (1.026-1.696)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Not Introduced</td>
<td>158 (86.3)</td>
<td>1092 (86.3)</td>
<td>0.413</td>
<td>1.190 (0.858-1.650)</td>
<td>1.143 (0.823-1.604)</td>
<td></td>
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</tr>
<tr>
<td>Hazelnut introduction</td>
<td>Introduced</td>
<td>81 (6.2)</td>
<td>91 (7.5)</td>
<td>0.089</td>
<td>1.435 (1.033-1.952)</td>
<td>1.396 (0.993-1.946)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not Introduced</td>
<td>133 (83.8)</td>
<td>1204 (92.5)</td>
<td>0.323</td>
<td>0.881 (0.613-1.267)</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table II: Introduction of solid foods at 9-11 months and comparison between the two time periods in relation to the revised guidelines. Statistically significant differences in bold. χ²: Pearson’s chi-squared test. OR: Odds ratio, aOR – Adjusted odds ratio. Odds ratios for comparison between the revised guidelines to the previous guidelines. Adjustment for heredity for food allergy, maternal country of birth, maternal education level, other children in the household, gestational age in weeks and at 9 months history of adverse reactions to food, eczema and wheeze respectively.

*Missing data for age of introduction for egg, fish, almond, peanut, almond, cashew, hazelnut, brazil nut (n=300 [28.9%]) and for soy and legume (n=938 [87.7%]) due to the question first added to the questionnaire in March 2018

** Missing data for all foods (n=466 [28.5%]).
3. Blaine Creasy
Living With Multiple Food Allergies: A Qualitative Study Of Social and Emotional Impact

Christina Ciaccio¹, Jessica Dunne², Andrea Bever², Alexis T. Mickle², Stacy Kowal³, Arpamas Seetasith³
¹University of Chicago Medicine, United States, ²Broadstreet Health Economics and Outcomes Research, Canada, ³Genentech, Inc., United States

Background
The impact of food allergies on quality of life (QoL) extends beyond severe reactions. Allergen avoidance is necessary to prevent allergic reactions, which permeates the daily lives of people with food allergies. To provide insight into the burden experienced by adults, teenagers, and children with multiple food allergies,
the objectives of this study were (i) to explore their lived experiences and (ii) to understand the impact on daily activities and QoL.

Methods
In this qualitative study in the United States, adults (≥18 years old; n=10), teenagers (13-17 years old; n=5), and adult caregivers of children (<13 years old; n=5) with multiple (≥2) food allergies participated in virtual semi-structured interviews (~1 hour each) from March to April 2022. Adult and teenager participants were asked to describe their own experiences of living with food allergies and the impact on QoL. Caregivers were able to provide insight into the life of their child with food allergies. Patterns in responses were explored using reflexive thematic analysis.

Results
Most participants were allergic to ≥3 foods (14/20). Participants described how allergen avoidance takes time and results in a loss of spontaneity, and how participation in society requires speaking up and trusting others. Caregivers recounted how children must learn to assume responsibility for their own safety. The emotional impact of living with food allergies varied based on personal factors including coping strategies. Teenage participants expressed feelings of sadness, embarrassment, guilt, and worry about their future. Children and teenagers were conscious about being different from their peers, experienced loneliness during school mealtimes, reported missed school days, and two participants were homeschooled.

Conclusion
People with multiple food allergies experience social limitations and restrictions on freedom. The emotional impact of food allergies includes anxiety related to food safety, the possibility of an allergic reaction, and social interactions; something that children with must learn to navigate at a young age.

4. Kumi Mizutani
The effect of consuming processed foods containing eggs for the treatment of egg allergy

Kumi Mizutani¹, Hikaru Sugita¹, Toya Kono¹, Saki Nishimoto¹, Kaoru Okamoto¹, Yuji Mori¹, Yoichi Nakajima¹, Yasuto Kondo¹
¹Fujita Health University Bantane Hospital, Japan

Background
Traditional guideline for food allergy (FA) is mainly avoidance of allergen. In Japan, patients are advised to ingest safe amount of allergen overtime, which is demonstrated by oral food challenge test (OFC). For FA patients, taking allergen is sometimes difficult because of dislike of target food, or traumatic due to past allergic reaction. In those cases, we suggest eating processed food containing target allergen so that they don’t have to take the allergen by itself. We aimed to evaluate the outcome of patients with hen’s egg allergy who eat boiled egg by itself and with processed food containing egg.

Methods
Annually, we publish a list of processed foods containing allergenic proteins (egg, milk, and wheat) measured by ELISA kits. We select safe-to-eat processed foods from the list and suggest to patients to eat them as treatment.

We enrolled 63 patients with hen’s egg allergy. 8 patients ate boiled eggs. 42 patients ate processed food containing egg. The remaining 13 patients were kept from eating egg as a control group. We evaluate the change of OVM, egg white IgE, and the amount of boiled egg patients could eat without any allergic reaction of the 3 groups in data gathered from OFC.
Results
In boiled egg group and processed food group, the amount of boiled egg they could take without reaction are both elevated. Both OVM IgE and egg white IgE in all 3 groups had no significant change.

Conclusion
Consumption of processed foods containing eggs may be as effective a treatment for egg allergy as consumption of eggs only. In addition, it has the benefit of alleviating stress of patients undergoing treatment, thereby facilitating the treatment more smoothly for patients and caregivers.

References
Motohiro Ebisawa, Komei Ito, Takao Fujisawa (Eds.)(2021) Japanese Guideline for Food Allergy 2021 Kyowa Kikaku

5. Jennifer Protudjer
An online, peer-mentored food allergy education program improves children’s and parents’ confidence

Ranjit Dhanjal¹, Kyle Dine¹, Jennifer Gerdzts¹, Kaitlyn Merrill², Tara Lynn Frykas², Jennifer Protudjer²
¹Food Allergy Canada, Canada, ²University of Manitoba, Canada

Background
Children with food allergy, and their families experience substantial psychological burdens because of efforts necessary to minimize the risk of allergic reactions. While healthcare provider-delivered food allergy education is important, peer-to-peer education may represent a novel way in which children develop skills to manage the burden of food allergy, while communicating with others who have similar lived experience. Food Allergy Canada offers an online, peer-to-peer mentoring program, termed Allergy Pals, for children aged 7-11 years. We aimed to determine if Allergy Pals contributed to increased child and parental food allergy competency and confidence, and to describe perceptions of the program.

Methods
From May 2020-May 2021, children and their parents were invited to participate in an online, anonymous mixed methods study about Allergy Pals, at pre-program, and post-program. Primary outcomes, which were described and compared using chi² or t-tests, as appropriate for the respective variables, included food allergy competence (epinephrine carriage, signs and symptoms of anaphylaxis) and food allergy confidence (e.g. feeling included). Secondary outcomes included child and parent qualitative perceptions of the program, which were analysed thematically.

Results
Overall, 17 and 11 children completed the pre-program and post-program surveys, respectively. Corresponding numbers for parents were 25 and 23. Food allergy competence was high pre-program, and remained so post-program. E.g. At pre- and post-program, nearly all (>90%) reported regular epinephrine carriage in various settings. Importantly, a higher proportion of children and parents reported recognizing signs and symptom of anaphylaxis post-program vs. pre-program (e.g. children: 100.0% vs. 68.8%). In contrast, food allergy confidence improved. E.g. A smaller proportion of children felt left out post-program vs. pre-program (30.0% vs. 41.7%, respectively). Child and parent qualitative themes supported improved food allergy confidence.
Conclusion
While competency in food allergy management is a necessary foundation, food allergy confidence provides those affected by food allergy to live full and meaningful lives, while confidently advocating for their needs. Allergy Pals, a unique, peer-to-peer, online mentorship program appears to increase food allergy confidence of both children and their parents. This confidence was attributed to greater feelings of empowerment, self-advocacy and community, and reduced feelings of isolation.

6. Jeongmin Lee
Behavior and parenting stress characteristics in young children with severe food allergy according to the severity score system

Jeongmin Lee¹, Jinhee Lee¹, Sanghwa Youm¹, Yeonjae Park¹, Sooyoun Lee¹
¹Yonsei University Wonju College of Medicine, Republic of Korea

Background
Food Allergy Severity Score System (FASS) has been developed recently. This study aims to analyze the usefulness of FASS for evaluating severity of FA in young children. Also, the emotional impacts of FA in young children/caregivers are evaluated according to the FASS for understanding vulnerable factors and further help for early intervention.

Methods
Patients/caregivers between 2-12 years of age who were diagnosed with FA by pediatric allergists and are on elimination diet of at least one causal food are enrolled. FA severity grouped using the ordinal FASS (oFASS; grade 1, mild; 2-3, moderate; 4-5, severe). Numeric FASS (nFASS) was calculated and according to the manual presented by using Zenodo, R software version 4.2.0 which classified into mild (1.07), moderate (2.01–3.98), or severe (4.07–7.75). Korean Parenting Stress Index (K-PSI) and Korean Behavior Assessment System for Children-2 (K-BASC-2) were used to analyze the relative risk of psychological factor for severe FA.

Results
Among the 75 patients (median: 54 months, range: 24–119), 64.0% had a previous history of anaphylaxis and 56.0% had multiple FAs. There were no differences in demographic and immunological findings between the groups. Patients/caregivers with severe nFASS (n=35) were associated with increased risks in 1 item of K-BASC-2 (adaptive skills) and 1 item of K-PSI-4 (life stress) compared to patients/caregivers with mild and moderate nFASS (n=40). A total of 160 cases of nFASS and oFASS were collected for 21 types of FA (mild, n=5; moderate, n=100; severe, n=55). Severity classification by oFASS and nFASS were consistent in all cases.

Conclusion
nFASS objectively evaluates the severity of FA in young children. By using the FASS, early intervention can be expected for screening emotionally vulnerable young children/caregivers with FA.

References

7. Noriko Hayashi
Survey on food allergy support for school lunches in Japan

Noriko Hayashi
Jumonji University, Japan

Background
Japan’s Ministry of Education, Culture, Sports, Science, and Technology (MEXT) has issued its "Guidelines for Food Allergy in School Lunches," with the main purpose of providing safe school lunches to students with food allergies (hereafter FA). The number of FA patients has increased in recent years, making it extremely difficult to accommodate FA in school lunches. Therefore, we conducted a survey on the actual situation of FA management in school lunches.

Methods
A self-administered questionnaire survey was conducted by mail from November 2021 to January 2022 among dietitians at elementary schools in Chofu City, Tokyo, and Sagamihara City, Kanagawa Prefecture. The survey items included the number of FA patients, elimination foods, details of FA management, and the equipment used for FA management.

Results
The survey questionnaires were distributed to 77 schools, of which 38 responded (for a valid response rate of 49%). A total of 29,917 meals were served daily, and 1,228 children with FA were enrolled. Their elimination foods were including hen’s eggs (19%), peanuts (15%), and walnuts (10%). In both cities, buckwheat and peanuts were banned, and the use of some nuts and kiwifruit was restricted. Facilities for FA included dedicated kitchens (21%), dedicated tableware (53%), and dedicated trays (89%). More personnel (61%), more facilities and equipment (55%), cooperation with medical institutions (45%), and FA management training (45%) were desired.
Conclusion
The data on initiatives taken in both cities to safely provide school lunches to patients with food allergy were examined. It is expected that staffing, equipment, and cooperation with medical institutions will be enhanced to ensure safe FA management in schools.

8. Melissa Engel
Teen Talks: An online video-based peer support program for adolescents with food allergies

*Melissa Engel¹, Christopher Warren², Ruchi Gupta²,³*
¹Emory University, United States, ²Feinberg School of Medicine, Northwestern University, United States, ³Ann & Robert H. Lurie Children’s Hospital of Chicago, United States

Background
Food allergies (FA) pose unique psychosocial difficulties for adolescents, yet food allergy research and interventions to-date have tended to focus on young children and their caregivers. As the prevalence of FA increases, and more and more children with FA become adolescents with FA, it is imperative to identify the psychosocial challenges faced by adolescents with FA and provide resources to address such challenges. This project (1) identifies the unmet psychosocial needs of adolescents with FA and (2) describes the development, feasibility, and acceptability of an online video-based peer support program for this population.

Methods
“Teen Talks” were developed in partnership with Food Allergy Research and Education (FARE) to allow youth with FA to connect and discuss shared experiences. Teen Talks have occurred monthly via Zoom, beginning in January 2021, and are open to all youth with FA aged 11-22 years. A Teen Talks Committee was created to generate monthly themes (e.g., Summer Travel, Back-to-School) and facilitate breakout room discussions. Unmet psychosocial needs of adolescents with FA were identified via thematic analysis of registration responses from January-September 2021. Feasibility and acceptability were assessed via monthly attendance and a program evaluation survey.

Results
Analysis of registration responses from 461 youth identified six psychosocial needs: meet other teens with FA (39.70%), share experiences (31.89%), learn how to navigate social situations (27.55%), cope with emotional challenges (11.93%), increase FA knowledge (11.50%), and gain confidence and communication skills (8.24%). Attendance across 16 months ranged from 40-91 participants, representing all major US geographic regions. Program evaluation data (n = 68 teens, 72 parents) suggest acceptability: teens (92.65%) and parents (91.89%) would recommend this program to others with FA. Quantitative and qualitative responses indicate that participants have developed friendships, feel less alone, and look forward to Teen Talks.

Conclusion
Adolescents with FA are in need of psychosocial support, including managing FA in various social situations (e.g., school, restaurants, dating), coping with emotional challenges (e.g., anxiety, bullying, guilt), developing communication strategies, and feeling less alone. It is important for allergists and pediatricians to be aware of the unique psychosocial challenges among adolescents with FA and provide resources to address these needs. Teen Talks are freely available nationwide, reducing barriers to patient access and promoting inclusion. Consistent high attendance and favorable evaluations by both teens and parents suggest that Teen Talks are feasible and well-accepted.
Program Evaluation Quantitative Responses from Teens and Parents

<table>
<thead>
<tr>
<th>Evaluative Statements (As a result of Teen Talks...)¹</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I would recommend Teen Talks to another teen (or parent of another teen) with food allergies</td>
<td>Teens: 4.43 (.78)</td>
</tr>
<tr>
<td>I (or my child) feel less alone</td>
<td>Teens: 4.31 (.82)</td>
</tr>
<tr>
<td>I (or my child) feel more supported</td>
<td>Teens: 4.21 (.89)</td>
</tr>
<tr>
<td>I (or my child) have learned how other teens manage their food allergies in different social situations (school, extracurricular activities, friends, restaurants, travel, etc.)</td>
<td>Teens: 4.43 (.83)</td>
</tr>
<tr>
<td>I (or my child) have seen how other teens cope with difficult emotions associated with their food allergies</td>
<td>Teens: 3.87 (1.02)</td>
</tr>
</tbody>
</table>

¹Participants respond on a Likert scale, ranging from 1 “Strongly Disagree” to 5 “Strongly Agree”

9. Fumiko Iwai
Current Status and problems of School Life Management and Instruction Chart in Mie Prefecture.

Fumiko Iwai², Rei Kanai³, Takahiro Nishida³, Takafumi Takase³, Tomoyuki Arima³, Shingo Yamada³, Mizuho Nagao¹, Takao Fujisawa¹

¹National Hospital Organization Mie National Hospital, Japan

Background
For proper management of food allergy in schools, utilization of the School Life Management and Instruction Chart (for allergic diseases), hereinafter the Chart, is essential. To know the problem to be solved, we reviewed the contents of the Chart written by physicians.

Methods
Descriptive statistics were performed for each item in the food allergy section of the Charts submitted to elementary and junior high schools in Mie Prefecture in 2020.
Results: The total number of submissions was 2387 and 2364 cases were analyzed, excluding cases other than food allergy (lactose intolerance, etc.).

Results
The eliminated foods were eggs, milk and dairy products, fruits, crustaceans, and nuts, in that order, which was different from hospital-based survey results previously reported. The percentage of the Charts stating two or more reasons for the necessity of elimination was 78% for eggs, 68% for wheat, and 64% for milk, but much lower percentages for other food, such as buckwheat (30%) and meat (15%). There was wide regional variability in the percentages. Contrary to the principle of elimination in school lunches, instructions for partial elimination were found in 8.7% of cases.

Conclusion
Problems with the Chart, such as food elimination instructions with little evidence, were revealed. It is important to educate physicians about the correct entry of the Chart.

10. Janet Luu
A meaty dilemma: recognizing delayed IgE-mediated hypersensitivity reactions in alpha-gal syndrome

Janet Luu
Santa Barbara Cottage Hospital, United States

Introduction
Alpha-gal syndrome is a remarkably unique allergy to the carbohydrate galactose-alpha-1,3-galactose (alpha-gal) found in the tissues of non-primate mammals. The sensitization to alpha-gal is strongly associated with tick bites which contain alpha-gal in their saliva. Alpha-gal syndrome classically has a delayed response of 3-6 hours after ingestion of non-primate mammalian meat and derived products which is atypical of usual IgE-mediated reactions.

Case Report
53-year-old-male, with past medical history of asthma and allergic rhinitis, presented to an outpatient allergy clinic two months after he had visited Tennessee where he was bitten a tick. Approximately one week after the bite, he began to experience intermittent hives to the hands and feet. On one incident, he developed full body hives, facial swelling, and esophageal discomfort necessitating emergency room treatment. The patient noted that these symptoms occurred hours after ingestion of red meat or milk products. He tested high for galactose-alpha-1,3-galactose IgE at 5.43 kU/L.

Conclusion
Alpha-gal syndrome is a unique food allergy that presents with a delayed onset of symptoms after ingestion of non-primate mammalian meat and derived products which is an atypical presentation of an IgE-mediated hypersensitivity reaction. It requires prompt recognition to prevent potentially life-threatening allergic reactions.

References


Food Allergy – Session E

1. Alexandra Hua

Evolution of FPIES index trigger foods and subsequent reactions after initial diagnosis

**Evolution of FPIES index trigger foods and subsequent reactions after initial diagnosis**

*Alexandra Hua¹, Mohamad El-Zataari¹, Elizabeth Hudson¹, Georgiana Sanders¹, Charles Schuler¹*

¹University of Michigan, United States

**Background**

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergy treated by trigger food avoidance and supportive care. Whether the prevalence of different trigger foods are changing with evolving food introduction patterns is unknown. The rate and nature of subsequent reactions after initial diagnosis has not been fully studied. We sought to characterize how trigger foods have changed to define the nature of subsequent reactions after initial diagnosis.

**Methods**

We collected data regarding patients’ FPIES reactions from 347 patients seen in the University of Michigan Allergy and Immunology clinic for FPIES from 2010 to 2022. Inclusion criteria consisted of pediatric patients diagnosed with FPIES by an allergist based on international consensus guidelines.

**Results**

Most foods including less commonly cited FPIES triggers increased in frequency over time. The most common index trigger was oat. 32.9% (114/347) of patients experienced a subsequent reaction after education on trigger avoidance and safe home introduction of new foods. Of those, 28% (32/114) experienced a subsequent reaction necessitating an emergency room visit. The most common new subsequent reaction triggers were egg and potato while peanut most commonly triggered reactions on oral food challenge.

**Conclusion**

The risk profile of FPIES triggers may be evolving over time, though high-risk FPIES foods remain common. The subsequent reaction rate after counseling indicates that home food introduction poses risk. This study highlights the need for improved safe and trigger food introduction and/or prediction methods for FPIES to help prevent potentially dangerous home FPIES reactions.

**References**

IgE-mediated immune responses to three types of Korean soy sauce in children sensitized to soybean and wheat

IgE-mediated immune responses to three types of Korean soy sauce in children sensitized to soybean and wheat

Jeongmin Lee1, Purevsan Gantulga2, Kyunguk Jeong2, Sanghwa Youm2, Sooyoung Lee2
1Yonsei University Wonju College of Medicine, Republic of Korea, 2Ajou University School of Medicine, Republic of Korea

Background
Soy sauces (SS) distributed in Korea are produced by various manufacturing methods, but studies on their antigenicity are scarce. This study aims to evaluate whether immunoglobulin E (IgE)-mediated immune response in children sensitized to soybean and/or wheat according to the different types of SS.

Methods
Sodium dodecyl sulphate–polyacrylamide gel electrophoresis (SDS-PAGE) was performed using three types of SS, and enzyme-linked immunosorbent assay (ELISA) analysis was performed according to the classification by immunological findings of 36 pediatric patients under 10 years of age.

Results
Guk-SS showed very faint protein bands. Protein bands corresponding to 6 and 25 kDa were observed in Yangjo-SS and those corresponding to 6, 25, and 65 kDa were observed in Jin-SS. By ELISA using pooled sera, all groups showed the lowest level of IgE binding to Guk-SS. In the individual ELISA, all of 4 patients sensitized to both wheat and soybeans showed significant levels of IgE binding capacity for all types of SS compared to those sensitized to wheat or soybean alone. Patients sensitized to only soybean showed slightly higher IgE-binding to Yangjo-SS compared to the control group.

Conclusion
Pediatric patients who have been sensitized to either wheat or soybean are likely to be able to consume Guk-SS and Jin-SS. Patients who are sensitized to both wheat and soybeans need to be cautious about all kinds of SS, but Guk-SS can be tried in a limited case.

References


3. Agnes Sze-Yin Leung
Predictors of severity and threshold of peanut-allergic reactions in Chinese children

Predictors of severity and threshold of peanut-allergic reactions in Chinese children
Agnes Sze-yin Leung1, Tik Wai Fu1, Christine Yee-yan Wai1, Ann Wing-shan Au1, Gary Wing-kin Wong1, Ting Fan Leung1
1The Chinese University of Hong Kong, Hong Kong

Background
Peanut is an important food allergen and one of the top triggers of food anaphylaxis. This study aims to identify potential predictors for severe peanut-allergic reactions and low dose reactors during peanut challenge.

Methods
Paediatric patients aged 1 to 17 years with a history of peanut-allergic reaction were referred for peanut oral immunotherapy. All of them underwent double-blind placebo-controlled food challenges (DBPCFC) to peanut (cumulative 4950 mg dose of peanut protein). Their skin prick test (SPT) and specific IgE (sIgE) levels to peanut and peanut components were evaluated.

Results
Among 132 participants, 95 (72%) failed DBPCFC to peanuts. Baseline demographics were comparable between peanut-allergic and tolerant groups with a median age of 5 (3.3-11) years, 67% male, 71% allergic to other foods, 88%, 71% and 29% had eczema, allergic rhinitis and asthma, respectively. Ara h 2 to total IgE ratio was the best diagnostic marker of peanut allergy (AUC 0.927, P=<.001). 36% reacted <0.1 gram and 30% had severe symptoms (oFASS-5 grade 4-5). SPT to peanut was the best individual predictor of threshold (AUC 0.628, P=.040), while age (β =1.208, P=.005) was the only predictor of severe peanut allergy.

Conclusion
Children with peanut allergies who experienced severe allergic reactions at low doses are not uncommon. SPT, as a conventional diagnostic tool, may identify low reactors but markers to predict children who will have a severe peanut-allergic reaction needs to be further investigated.
4. Arghya Laha
Revalidation of a food allergy predictive model for assessment of egg and milk allergies among Indians

Revalidation of a food allergy predictive model for assessment of egg and milk allergies among Indians

Arghya Laha1, Sanjoy Podder1
1The University of Burdwan, India

Background
The recent application of predictive models for the diagnosis of food allergy can envisage the outcome of oral food challenges (OFC), reducing cost and time. A logistic regression model was developed by DunnGalvin for children predicting OFC outcome using six predictors viz: sex, age, history, specific IgE, total IgE minus specific IgE, and skin prick test. This model was later updated by Klemans, reducing the number of predictors. Our aim was to revalidate both models for the assessment of egg and milk allergies among Indians in the age group 0–19 years and to determine regression coefficients for our study population.

Methods
The study protocol was approved by the Clinical Research Ethics Committee, Allergy and Asthma Research Center, West Bengal, India (CREC-AARC Ref: 004/17). Written informed consent was taken from the selected patients or from their parents. Revalidation was done at the Allergy and Asthma Research Center using OFC outcomes of 91 egg and 98 milk allergic patients. Precise values of the predictors were set up for which calibration (predicted against observed outcome) and discrimination (area under the curve [AUC] of receiver operator characteristic curve [ROC]) would be better.

Results
The Klemans model with a reduced number of predictors showed better accuracy, calibration, and discrimination than the DunnGalvin one. The best calibration for egg allergy was achieved in the Klemans model with a correlation coefficient (r²) of 0.90 and an accuracy of 97%. The AUC of ROC was 0.90. For milk allergy, the coefficient was 0.94 with an accuracy of 98%. The AUC was 0.91.

Conclusion
The present study indicated that the Klemans model may be suitable for use in our study area if the model parameters are modified suitably, even though the original model was constructed in different countries. The application of a predictive model may assist physicians in the diagnosis of food allergy in a non-invasive way that could save money and time. Moreover, this could become a highly important confirmatory test for food allergy. However, the universal validity of these models requires testing with larger datasets which could be possible with Artificial Intelligence or machine learning algorithms in near future.

5. Yu Bin Kim
Characterizations of food allergy patients under 3 years of age through endoscopic evaluation of eosinophil infiltration

Characterizations of food allergy patients under 3 years of age through endoscopic evaluation of eosinophil infiltration

Yu Bin Kim1, Soo Young Lee1
1Ajou University School of Medicine, Republic of Korea
Background
There is no uniform consensus on the diagnostic process for identifying non-IgE and mixed gastrointestinal food allergy. To confirm the usefulness of endoscopic evaluation, we conducted study to determine whether food allergy groups in infants under 3 years of age could be classified based on eosinophilic infiltration.

Methods
Upper gastrointestinal endoscopy, history-based specific IgE test, total IgE, ECP, and peripheral eosinophilia were retrospectively evaluated in patients younger than 3 years who complained of gastrointestinal symptoms caused by specific food trigger. Using 15/hpf of esophagus and >30 hpf of stomach/duodenum as criteria for eosinophilic infiltration, the clinical/biochemical characteristics of the patients were compared and analyzed.

Results
Of the 31 eligible cases, 19 patients were enrolled and analyzed.

Eosinophilic infiltration was confirmed in 10 patients, 4 esophageal infiltration, 1 esophageal and gastroduodenal infiltration, and 5 gastroduodenal infiltration. There were differences in clinical aspect gastrointestinal symptoms except vomiting, high IgE sensitization rate, low weight for height, allergic family history, and aeroallergen sensitization rate. On the laboratory aspect, the eosinophilic infiltration group demonstrates peripheral eosinophilia and high total IgE levels. The characteristics of the 9 patients without eosinophilic infiltration follow the typical clinical features of FPIEs. The most common trigger was egg, which was similar in both groups.

Conclusion
Endoscopic evaluation of eosinophilic infiltrates in children under 3 years of age identifies a food allergy population with characteristics different from FPIEs. Further studies on clinical course and non-invasive assessment tools, including treatment response, are needed in the future.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Eosinophilic infiltration (n=10)</th>
<th>No infiltration (n=9)</th>
<th>P (&lt;=0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7</td>
<td>4</td>
<td>0.26</td>
</tr>
<tr>
<td>Weight for Height(percentage)</td>
<td>18.9 (2.7-68)</td>
<td>62.3(13.2-92.3)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Symptom compatible IgE sensitization</td>
<td>4</td>
<td>0</td>
<td>0.04*</td>
</tr>
<tr>
<td>Gastrointestinal symptom except vomiting(pain, diarrhea)</td>
<td>7</td>
<td>2</td>
<td>0.037*</td>
</tr>
<tr>
<td>Aeroallergen sensitization</td>
<td>4</td>
<td>0</td>
<td>0.047*</td>
</tr>
<tr>
<td>Familial allergic history</td>
<td>8</td>
<td>2</td>
<td>0.038*</td>
</tr>
<tr>
<td>Associated Allergic disease</td>
<td>7</td>
<td>3</td>
<td>0.094</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.5(10.5-12.9)</td>
<td>12.5(11.4-14.2)</td>
<td>0.34</td>
</tr>
<tr>
<td>Peak Eosinophil (%)</td>
<td>8.5(3.0-29.0)</td>
<td>3.7(1.0-7.0)</td>
<td>0.025*</td>
</tr>
<tr>
<td>Total IgE (KU/L)</td>
<td>170(16-1566)</td>
<td>36(5-93)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Eosinophil catatonic protein (ug/L)</td>
<td>29.7(7.7-127)</td>
<td>22.8(4.1-37.9)</td>
<td>0.116</td>
</tr>
</tbody>
</table>
Molecular Diagnosis of Shrimp Allergy in Korean adults: identification of novel anaphylaxis specific allergen for Component Resolved Diagnosis

Bo Youn Choi¹, Eun-Mi Yang¹, Young-Min Ye¹
¹Ajou University School of Medicine, Republic of Korea

Background
Food allergy (FA) is an immunological hypersensitivity reaction caused by a specific food, and its prevalence has steadily increased, accounting for about 2.5% of the world population. In Korean adults, seafood is the most frequent cause of FA and more than half of the seafood-induced FA events presented as anaphylaxis. Shrimp extract or tropomyosin, hemocyanin have been reported as allergens to diagnose shrimp-induced FA. However, no allergenic components to differentiate anaphylaxis among shrimp-induced FA events has been noted. We aimed to identify specific allergenic components of white-leg shrimp, the main species of Korean shrimp to detect shrimp-induced anaphylaxis.

Methods
Enrolled 126 subjects with shrimp-induced FA were classified into two groups: anaphylaxis (n=52, mean age 38.8 years) and acute urticaria (n=74, 37.9 years). The specific IgE was measured by both ImmunoCap and homemade ELISA. IgE immunoblotting was performed using pooled serum from patients with anaphylaxis and acute urticaria according to the presence or absence of HDM allergy against raw shrimp extract. To identify and validate anaphylaxis specific allergen components, LC-MASS method and western blot was used.

Results
Specific IgE levels to shrimp extract measured by ImmunoCap system (9.14±17.4 vs 2.6±5.3 kU/L, P=0.022) and our homemade ELISA (1.1±1.1 vs. 0.7±0.9 AU, P=0.037) were higher in the anaphylaxis group compared with urticaria group. However, 26.7% of the anaphylaxis group and 12.9% of urticaria group had negative result on the ImmunoCap system to detect shrimp allergy. Even positive rate of Der. p10, HDM tropomyosin, was only 3.8% (anaphylaxis group) and 2.7% (urticaria) in Korean shrimp allergy patients. Regardless of HDM sensitization, MASS analysis and western blotting confirmed that hemocyanin was a specific allergenic component reacted in the shrimp-induced anaphylaxis group.

Conclusion
The false-negative rate of IgE against whole shrimp extract to determine the risk of anaphylaxis is greater than 25% in Korea. We identified and validated that the anaphylaxis specific shrimp allergenic component, hemocyanin in Korean adults with shrimp-induced FA. Further study to optimize shrimp hemocyanin for skin test or IgE assay are needed.

Clinical multidimensional assessment of patients with eosinophilic esophagitis: a prospective multicentric study for the validation of a novel patient-reported outcome

Sara Urbani

Clinical multidimensional assessment of patients with eosinophilic esophagitis: a prospective multicentric study for the validation of a novel patient-reported outcome
Background

Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease characterized by eosinophilic inflammation of the mucosa (≥ 15 eosinophils/HPF) and esophageal dysfunction symptoms [1]. EoE is associated with various allergological, nutritional, and psychological comorbidities.

In this scenario, EoE Disk (Figure 1) represents an innovative visual-analog patient-reported outcome tool for the multidisciplinary assessment of adult and adolescent patients with EoE. The study aims to validate the EoE Disk, by establishing its accuracy in predicting disease activity and its correlation with other symptomatic validated tools (EEsAI-PRO / PEESSv2.0)[2][3].

Methods

The EoE Disk was evaluated in adolescent (> 15 years) and adult patients from two centers, Fondazione Policlinico Gemelli and Bambino Gesù Pediatric Hospital of Rome. Patients with a diagnosis of EoE and with an endoscopy within 90 days were enrolled. All demographic, endoscopic, and questionnaire data were collected from March to September 2022.

To proceed with EoE Disk validation, all patients were simultaneously self-administered the EoE Disk and the EEsAI-PRO / PEESS v2.0 (depending on age). The Disk has been analyzed considering the total score and the score of the gastroenterological, allergological, psychological and nutritional domains.

Results

64 EoE-affected patients were included in the study, with a median age of 28.4 years. Clinical and demographical characteristics of patients are summarized in Table1. EoE Disk has proven as a moderately accurate tool in evaluating disease activity (AUC=0.71, sensitivity=77.4%, specificity=57.5%, cut-off values ≥27). The total scores of the disk have a strong correlation with EEsAI/PEESS v2.0 (rho=0.72; p<0.0001). The gastroenterological domain is significantly correlated with eosinophilia at biopsy (rho=0.39; p<0.01), EREFS (rho=0.39; p<0.01) and EEsAI/PEESS v2.0 (rho=0.76; p<0.0001). Higher scores, either in overall (p=0.029), or in the gastroenterological (p=0.003) and the psychological domains (p=0.044), were associated with active disease.

Conclusion

The EoE Disk proves to be a moderately accurate tool in predicting disease activity in EoE. It also shows an excellent correlation with already validated tools, in both adolescent and adult patients.

EoE Disk may be considered a valid novel instrument aiding clinicians in the rapid detection and assessment of comorbidities related to the disease.

To establish EoE Disk utility in clinical trials and patient monitoring, further evidence is needed, along with the inclusion of all patients as originally planned in the sample size calculation.

References


Table 1. Clinical and demographical characteristics of patients (N=64)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centre n (%)</td>
<td></td>
</tr>
<tr>
<td>Gemelli</td>
<td>42 (65.6)</td>
</tr>
<tr>
<td>OPGB</td>
<td>22 (34.4)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>49 (76.6)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (23.4)</td>
</tr>
<tr>
<td>Age, y (median, IQR)</td>
<td>28.4 (17.1–43.6)</td>
</tr>
<tr>
<td>15–18 y, n (%)</td>
<td>17 (26.6)</td>
</tr>
<tr>
<td>≥ 18 y, n (%)</td>
<td>47 (73.4)</td>
</tr>
<tr>
<td>Diagnosis n (%)</td>
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</tr>
<tr>
<td>De novo</td>
<td>9 (14.0)</td>
</tr>
<tr>
<td>Previous</td>
<td>55 (86)</td>
</tr>
<tr>
<td>BMI (median, IQR)</td>
<td>23.7 (21.5–25.4)</td>
</tr>
<tr>
<td>Smoke, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51 (79.7)</td>
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<tr>
<td>Yes</td>
<td>7 (11.0)</td>
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<tr>
<td>Alcol, n (%)</td>
<td></td>
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<tr>
<td>No</td>
<td>35 (54.7)</td>
</tr>
<tr>
<td>Yes/Occasional</td>
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<tr>
<td>Disease activity (eosinophils/HFF), n (%)</td>
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<tr>
<td>Remission (&lt;15)</td>
<td>33 (51.6)</td>
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<tr>
<td>Mild (15–50)</td>
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<tr>
<td>Moderate (51–60)</td>
<td>12 (18.8)</td>
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<td>Severe (≥ 60)</td>
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<tr>
<td>EEsAU/PEESSv2.0 (median, IQR)</td>
<td>12 (0–29)</td>
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<tr>
<td>Diagnostic delay, y (median, IQR)</td>
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<td>Disease history, y (median, IQR)</td>
<td>7 (4–13)</td>
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<tr>
<td>Allergy family history, a (%)</td>
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<td>Yes</td>
<td>43 (67.2)</td>
</tr>
<tr>
<td>No</td>
<td>21 (32.8)</td>
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<tr>
<td>Allergic comorbidities, a (%)</td>
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<td>IgE-FA</td>
<td>20 (31.3)</td>
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<tr>
<td>Rhinitis</td>
<td>43 (67.2)</td>
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<td>Asthma</td>
<td>17 (26.6)</td>
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<tr>
<td>Atopic dermatitis</td>
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<td>Nasal polyps</td>
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<td>Previous ITS, n (%)</td>
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<td>OIT</td>
<td>14 (21.9)</td>
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<td>SLIT</td>
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<td>Treatments, n (%)</td>
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<tr>
<td>PPI</td>
<td>43 (67.2)</td>
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<td>Topical steroids</td>
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<tr>
<td>Elimination diets</td>
<td>9 (14.1)</td>
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<tr>
<td>Dupilumab</td>
<td>2 (3.1)</td>
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<tr>
<td>Endoscopic dilatation</td>
<td>4 (6.2)</td>
</tr>
</tbody>
</table>

OPBG, Ospedale Pediatrico Bambino Gesù; Gemelli, Fondazione Policlinico Gemelli IRCCS, IQR, inter quartile range; BMI, body mass index; evo, eosinophilic; HFF, high power field; EEsAU, Eosinophilic Esophagitis Activity Index; PEESS v 2.0, Pediatric Eosinophilic Esophagitis Symptom Score; IgE-FA, IGE mediated food allergy; ITS, Specific immunotherapy; OIT, oral immunotherapy; SLIT, sublingual immunotherapy; PPI, proton pump inhibitors
Table 1. Clinical and demographic characteristics of patients (N=64)

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<td>15-18 y, n (%)</td>
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<td><strong>Alcol, n (%)</strong></td>
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<tr>
<td>Remission (≤ 15)</td>
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<tr>
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<tr>
<td><strong>Disease history, y (median, IQR)</strong></td>
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<td>Dupilumab</td>
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OPBG, Ospedale Pediatrico Bambino Gesù; Gemelli, Fondazione Policlínico Gemelli IRCCS, IQR, interquartile range; BMI, body mass index; eos, eosinophilic; HPF, hist power field; EEsAI Eosinophilic Esophagitis Activity Index; PESS v 2.0, Pediatric Eosinophilic Esophagitis Symptom Score; IgE-FA, IGE mediated food allergy; ITT, Specific immunotherapy; OIT, oral immunotherapy; SLIT, sublingual immunotherapy; PPI, proton pump inhibitors
The alternative bile acid pathway can predict food allergy persistence in early childhood

The alternative bile acid pathway can predict food allergy persistence in early childhood

8. So-Yeon Lee
The alternative bile acid pathway can predict food allergy persistence in early childhood

**Figure 1: EoE Disk.** The patients answer the questions referring to the three months prior to the interview. The answers are marked on the disk using a visual analog scale from (absolutely not) to 10 (definitely yes).
Background
Mechanisms underlying persistent food allergy (FA) are not well elucidated. However, no study has examined intestinal metabolites associated with FA persistence. The goal of this study was to investigate intestinal metabolites in early life that aid in determining the development and persistence of FA.

Methods
We identified metabolomic alterations in the stool of infants according to FA by mass spectrometry-based untargeted metabolome profiling. The targeted metabolomic analysis of bile acid metabolites was performed. Bile acid metabolite composition in infancy was evaluated by characterizing the subjects at the age of three into FA remission and persistent FA.

Results
In untargeted metabolomics, primary bile acid biosynthesis was significantly different between subjects with FA and healthy controls. In targeted metabolomics for bile acids, intestinal bile acid metabolites synthesized by the alternative pathway were reduced in infants with FA than those in healthy controls. Subjects with persistent FA were also distinguished from healthy controls and those with FA remission by bile acid metabolites of the alternative pathway. These metabolites were negatively correlated with specific IgE levels to egg white.

Conclusion
Intestinal bile acid metabolites of the alternative pathway could be predictive biomarkers for persistent FA in early childhood. These findings require replication in future studies.

Food-dependent exercise-induced anaphylaxis: 10 year follow up in an allergy department

Rita Aguiar

Food-dependent exercise-induced anaphylaxis: 10 year follow up in an allergy department

Raquel Pestana1, Rita Aguiar1, Filipe Benito-Garcia1, Mário Morais-Almeida1
1CUF Descobertas Hospital, Portugal

Background
Food exercise-induced anaphylaxis (FDEIA) is a rare clinical manifestation characterized by a chronological sequence in which food ingestion followed by exercise leads to anaphylaxis. There is a wide range of foods that trigger FDEIA, with lipid transfer proteins (LTP) being a major cause.

The authors reviewed the records of referred patients with FDEIA admitted to the Immunoallergy Department from January 2011 to January 2021 to assess the clinical characterization and incidence of this condition, and particularly the prevalence of LTP allergy in this disease, typically associated with the Mediterranean area, such as ours.

Methods
In this retrospective study, we analyzed the clinical characteristics and management strategies of 28 patients (aged 5-53 years) with a clinical history of FDEIA and proven sensitization (in vivo and/or in vitro testing) to the specific food implicated.

Results
Different food groups were associated with FDEIA cases, with vegetables being the most common trigger (41% of reactions), followed by fresh fruits (33%), tree nuts (18%), and seeds and milk-derived products (2% each). The majority of patients (61%) were sensitized to Lipid Transfer Protein (LTP) Pru p 3, and 32% had positive sensitization to ω-5-gliadin or specific IgE/ISAC (Immuno-Solid phase Allergy Chip) to Tri a 19.
Conclusion
FDEIA is a highly complex phenomenon, posing a significant diagnostic challenge. LTP allergy is highly implicated in this disease. Although it is a rare cause of anaphylaxis, it is increasing worldwide, emphasizing the need for a higher level of suspicion to avoid unnecessary evictions of potentially safe foods and improve the management of this potentially life-threatening condition.

10. Priyanka Timothy
Previously Healthy 2-Year-Old Male Presenting With Persistent Diarrhea Leading to Severe Protein-Losing Enteropathy, Anemia, Hypoalbuminemia, Anasarca, and Depressed IgG Levels

Introduction
Diarrhea, a common complaint in pediatric patients, has varied etiologies and is often treated conservatively. The persistence of diarrhea can be a result of immune dysregulation secondary to eosinophilic gastroenteritis which can proceed to severe protein-losing enteropathy. If untreated, sequelae include hypoalbuminemia with resultant anasarca, microcytic anemia, and depressed IgG levels. We present a previously healthy 2-year-old male from a rural community who presented to multiple facilities with non-bloody diarrhea which occurred 2 weeks after COVID-19. Symptoms then progressed to persistent diarrhea, periorbital edema, and anasarca prompting admission to the pediatric floor.

Case Report
Initial lab work revealed severe microcytic anemia thought to be due to increased milk intake. Patient's eosinophil count was elevated at 5,000 with negative infectious workup. Patient had decreased IgG 95, low IgM 28, and elevated IgE 1826. Flow cytometry revealed no evidence of a lymphocytic variant of hypereosinophilic syndrome. Normal tryptase and vitamin B12 levels made myeloid variant less likely. Patient underwent esophagogastroduodenoscopy/colonoscopy which was grossly normal. Pathology reports revealed >70 eosinophils per high power field in the antral stomach consistent with eosinophilic gastroenteritis. With the cessation of milk, patient had a resolution of diarrhea and clinical improvement.

Conclusion
Our case reflects how a common pediatric presentation of diarrhea can progress to multiorgan dysfunction, protein-losing enteropathy, severe hematological dyscrasias, and depressed level of immunoglobulins likely secondary to eosinophilic gastroenteritis related to milk ingestion. Other differentials of transient hypogammaglobulinemia of infancy, COVID-19-related diarrheal illness, and primary immunodeficiency are also considered. The patient has clinically improved with a strict milk-free diet. Repeat esophagogastroduodenoscopy/colonoscopy is scheduled to evaluate for histologic resolution. Given that diarrhea has resolved, we anticipate recovery of IgG levels with follow-up immune labwork pending.
1. Paul Turner
Desensitisation in cow’s milk-allergic children using oral immunotherapy (OIT) with sublingual OIT pretreatment: results from the SOCMA study

Desensitisation in cow’s milk-allergic children using oral immunotherapy (OIT) with sublingual OIT pretreatment: results from the SOCMA study

Paul Turner¹, Bettina Duca¹, Raphaëlle Bazire², Olaya Alvarez³, Marta Vazquez-Ortiz¹, Nandinee, Patel¹, Adnan, Custovic¹, Pablo Rodríguez del Río²
¹Imperial College London, United Kingdom, ²Hospital Infantil Universitario Niño Jesús, Spain, ³Universitario de Ferrol, Narón, Spain

Background
Desensitisation for cow’s milk (CM) allergy is clinically effective, but associated with a high rate of adverse events including anaphylaxis, compared to other food allergens. Data suggests that sublingual immunotherapy (SLIT) can also induce desensitisation in food allergy, but efficacy is typically lower than that achieved with oral immunotherapy (OIT). The SOCMA (Improving the safety of oral immunotherapy for cow’s milk allergy) study is a novel Phase 2b clinical trial in which we assessed whether SLIT pretreatment prior to OIT is an effective strategy to improve the safety and efficacy of OIT for CM allergy.

Methods
Children and young people with CM allergy confirmed at double-blind, placebo-controlled food challenge (DBPCFC) were randomised to one of three pretreatments for 6 months: (i) SLIT with CM protein; (ii) low dose OIT (using the same CM doses as for SLIT, but with participants immediately swallowing the dose); (iii) placebo. All subjects then underwent open CM-OIT for a further 6 months. Response was assessed by repeat DBPCFC at 6 and 12 months to assess response. Adverse events were recorded using a daily diary. Clinicaltrials.gov NCT02216175, NHS HRA Ethics approval 18/L0/1070.

Results
Sixty-eight children (6-18 years, 43% female) were randomised. Median maximum tolerated dose (MTD) at baseline was 44mg CM protein (IQR 14-144mg).

Following 6 months of SLIT pretreatment, this increased to 444mg CM protein and 144mg in those given the same doses but as OIT (p=0.04). There was no change in MTD in the placebo arm. Following a further 6 months of OIT, median MTD increased to to 4444mg CM protein (130ml milk). SLIT pretreatment was associated with a significantly lower rate of adverse events during OIT.

Conclusion
SLIT pretreatment was more effective than pretreatment with oral dosing in inducing desensitisation, and had a more favourable safety profile. Combination approaches using SLIT followed by OIT may be more effective at inducing desensitisation compared to OIT alone, as well as safer.

2. Kosei Yamashita
Optimal period for achieving sustained unresponsiveness in wheat oral immunotherapy

Kosei Yamashita¹, Takanori Imai¹, Aiko Hond¹, Chihiro Kunigami¹, Yuki Okada¹, Mayu Maeda¹, Taro Kamiya¹
¹Showa University School of Medicine, Japan
Background
Oral immunotherapy (OIT) can help children with persistent food allergy to achieve sustained unresponsiveness (SU). However, it is unclear whether the prolonged treatment period of OIT can increase the SU achievement rate. The aim of this study is to clarify the course of SU achievement in wheat OIT.

Methods
We retrospectively investigated the association between OIT period and achievement of SU. Patients who have received OIT for wheat between April 2012 to July 2020 were included. OIT protocol consisted of build-up, maintenance, and oral food challenge (OFC) for confirming SU. Patients increased the dosing up to maintenance dose, then maintained the dose at least for 5 months. SU was defined as a negative response to 100 g of udon noodles (2,650 mg of wheat protein) OFC after at least two weeks of complete avoidance. The analysis of OIT periods for SU achievement was evaluated using Kaplan-Meier survival analysis.

Results
There were 65 patients who underwent wheat OIT. The starting age of OIT was 6 (5-7) year-olds. Of those, 45 (69%) had a history of anaphylaxis to wheat. Specific IgE to wheat and ω-5 gliadin at OIT initiation were 75.0 (23.2-100) UA/mL and 6.0 (1.3-16.0) UA/mL, respectively. The mean observational period was 3.0 (2.2-5.6) person-years (PY). SU achievement rate was 50% in 3.0 PY, 58% in 3.5 PY, and 58% in 4.0 PY.

Conclusion
Although the rate of SU gradually increased with the period, the rate of SU achievement slowed down after 3.5 PY. When wheat OIT exceeds 3.5 PY, we should reconsider the treatment strategy.

3. Lianne Soller
What to do when peanut allergy oral immunotherapy fails: A case series of five preschoolers transitioned to sublingual immunotherapy

What to do when peanut allergy oral immunotherapy fails: A case series of five preschoolers transitioned to sublingual immunotherapy

Lianne Soller1, Brock A Williams1, Raymond T. Mak1, Stephanie C. Erdle1, Alanna Chomyn1, Brittany Tetreault1, Lisa Gaudet1, Kelly Morrison1, Ravinder Dhaliwal1, Edmond S. Chan1
1University of British Columbia, Canada

Background
Peanut oral immunotherapy (OIT) is safe and effective in preschoolers[1,2]. However, there is a subset of patients for whom OIT is not successful due to recurrent, sometimes severe, reactions during treatment. Unfortunately, these patients are often counseled by their allergist to revert back to avoidance. Although sublingual immunotherapy (SLIT) studies have shown lower effectiveness than OIT for similar duration of treatment, the safety profile and tolerability of SLIT are far superior to OIT[3], and the effectiveness of SLIT improves with increased duration[4]. The effectiveness of SLIT may be better than previously thought for preschoolers[5].

Methods
Patients were started on OIT at BC Children’s Hospital and transitioned to SLIT using a recipe which contained a mixture of commercially available peanut butter powder and water. After a brief buildup process (3 to 5 visits), the maintenance dose of 2mg peanut protein was reached. Age at start of OIT and grade of reactions[1], (including use of epinephrine), during baseline oral food challenge (OFC) (if applicable), OIT, and SLIT, were collected and presented below. These patients consented to their anonymous data being included in the FAIT registry (UBC REB: H20-02342).
Results
Between 2019-2021, five preschoolers (age range: 2-5 years) who started on OIT were transitioned to SLIT due to recurrent gastrointestinal symptoms (two patients), or reactions requiring epinephrine and emergency department visits (three patients). Four patients had baseline OFCs, two of which resulted in grade 4 (severe) reactions requiring multiple rounds of epinephrine, one requiring code blue resuscitation. During SLIT build-up, all patients experienced mild grade 1 or 2 symptoms such as oral itch and subjective abdominal pain (one patient opted to give epinephrine as a precaution), and successfully reached maintenance dosing with mild grade 1 symptoms during the maintenance phase.

Conclusion
This case series of predominantly severe phenotype preschoolers suggests that SLIT is a safe alternative to avoidance after failed OIT. These five patients will continue to be followed long-term to track adherence, safety, and effectiveness outcomes, including whether SLIT can be a bridge therapy to transition back to OIT in the future. Another question which requires further research is whether SLIT should be the destination therapy rather than simply a bridge to OIT.

References

4. Fatema Mollah
Oral Immunotherapy Competency-Based Assessments as a Tool for Fellowship Training

Fatema Mollah1, Ian F. Slack1, Anna Kovalszki1, Malika Gupta1
1University of Michigan, United States

Background
Allergy/Immunology fellowship programs are tasked with preparing trainees for independent practice. Competency-based assessments are used in training to evaluate trainee proficiency in a variety of Allergy/Immunology procedures to achieve an endpoint of independent clinical practice. Competencies are typically routed in consensus guidelines and evidence-based practice parameters. Consensus guidelines and practice-parameters have not been established for the practice of oral immunotherapy (OIT) in the US. There are a paucity of resources to educate and assess trainees in the practice of OIT.

Methods
Our working group sought to establish a competency based assessment for OIT to improve and standardize OIT education for Allergy fellows. A committee of academic Allergist/Immunologists at the University of Michigan iteratively generated a competency based assessment for OIT (table 1). The assessment was modeled on prior competency-based assessments assembled by the American Academy of Allergy, Asthma,
and Immunology. Considerations were given toward the longitudinal nature of OIT with specific focus on consenting, updosing, and maintenance phases.

Results
Domains of patient safety, fundamental desensitization principles, psychosocial impacts, and practical considerations throughout each OIT phase were included (figure 1). Special considerations were made to avoid prescriptive competencies and accommodate existing variation in OIT practice.

Conclusion
As demand for OIT increases, more Allergy practitioners will need to acquire the skills to practice OIT independently. However, nonstandardized practice can make OIT a challenge procedure to teach. Our competency-based assessment offers a framework to systematically evaluate Allergy fellows in OIT and tailor actionable feedback regardless of particular OIT protocols. The competency has undergone review by the AAAAI core curriculum committee and is available to fellowship program directors in the AAAAI PDA toolkit. We hope it is a first step toward a toolkit of resources for OIT education in Allergy/Immunology fellowships.

<table>
<thead>
<tr>
<th>Consent</th>
<th>Knowledge-based</th>
<th>Performance of the procedure</th>
<th>Interpretation of the data</th>
<th>Overall performance and competency</th>
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<tbody>
<tr>
<td>A/I Fellow identifies patients who would be appropriate candidates for OIT</td>
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<tr>
<td>A/I Fellow communicates appropriate goals of OIT</td>
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<td>A/I Fellow discusses medical risks of OIT</td>
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<tr>
<td>A/I Fellow outlines the economic and psychological burdens of OIT</td>
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<td>A/I Fellow reviews limitations of OIT and discusses alternative food allergy management strategies</td>
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<tr>
<td>A/I Fellow assesses the contraindications to OIT</td>
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<tr>
<td>A/I Fellow lists visit schedule for initial buildup, updosing, and maintenance phases</td>
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</tbody>
</table>

| Initial Buildup and Updosing                  |                |                              |                            |                                   |
| A/I Fellow explains procedure to patient and/or family |                |                              |                            |                                   |
| A/I Fellow identifies appropriate emergency resources including personnel, equipment, and medications during dosing |                |                              |                            |                                   |
| A/I Fellow appropriately confirms dosing with patient |                |                              |                            |                                   |
| A/I Fellow counsels patient on precautions necessary for home dosing |                |                              |                            |                                   |
| A/I Fellow appropriately recognizes and treats reactions to OIT dosing |                |                              |                            |                                   |
| A/I Fellow titrates dosing and/or supportive medications for patients with adverse reactions |                |                              |                            |                                   |
| A/I Fellow ensures adequate observation time following completion of dosing |                |                              |                            |                                   |

| Maintenance                                  |                |                              |                            |                                   |
| A/I Fellow ensures adherence with dosing schedule |                |                              |                            |                                   |
| A/I Fellow appropriately screens for adverse outcomes of OIT |                |                              |                            |                                   |
| A/I Fellow identifies signs and symptoms of eosinophilic esophagitis (EoE) in OIT patients |                |                              |                            |                                   |
| A/I Fellow establishes follow up surveillance |                |                              |                            |                                   |

Table 1: OIT Competency-based assessment
5. David Fleischer
VITESSE: phase 3, double-blind, placebo-controlled study of the efficacy and safety of epicutaneous immunotherapy in peanut-allergic children aged 4-7 years

David M. Fleischer¹, Dianne E. Campbell²,³, Katharine J. Bee, DBV Technologies, Montrouge, FrancePhilippe Bégin⁴, Jonathan Hourihane⁵, Antonella Muraro⁶, Pablo Rodríguez del Río⁷
¹Children’s Hospital Colorado, University of Colorado, United States, ²The Children’s Hospital at Westmead, Australia; ³DBV Technologies, France, ⁴Centre Hospitalier Universitaire Sainte-Justine, Canada, ⁵Royal College of Surgeons, Ireland, ⁶Padua General University Hospital, Italy, ⁷Hospital Infantil Niño Jesús, Madrid, Spain

Background
Epicutaneous immunotherapy (EPIT) with Viaskin Peanut 250 µg (VP250) is a novel approach to induce desensitization by delivering daily microgram quantities of peanut allergen (~1/1000th peanut) to the skin.¹⁻⁴ Post-hoc analysis of the PEPITES study of VP250 versus placebo in peanut-allergic children aged 4-11 years suggested a greater desensitization effect of VP250 in 4-7 year-old versus 8-11 year-old children. The size and shape of VP250 have since been modified, though the occlusion chamber and allergen dose have remained unchanged. This study (VITESSE) aims to assess the efficacy and safety of the modified VP250 patch among peanut-allergic children aged 4-7 years.

Methods
VITESSE is a Phase 3, multicenter, double-blind, placebo-controlled, randomized study in which eligible peanut-allergic children aged 4-7 years will undergo screening with a double-blind, placebo-controlled food challenge (DBPCFC) to peanut. Those that develop symptoms meeting stopping criteria at an eliciting dose (ED) ≤100 mg peanut protein will be randomized 2:1 to 12 months of daily treatment with VP250 or placebo, respectively. At Month (M) 12, a post-treatment DBPCFC will be performed escalating to 1000 mg (2043 mg cumulative dose). Immunological changes, safety, and adhesion of VP250 will also be assessed.

Results
Six hundred subjects are planned to be enrolled. The primary endpoint will be the percentage of treatment responders in the VP250 group vs placebo at M12, defined as DBPCFC M12 ED ≥300 mg if baseline ED ≤30 mg or M12 ED ≥600 mg if baseline ED >30 mg. Secondary endpoints will include cumulative reactive dose and ED at M12, maximum severity of allergic reactions on DBPCFC, and percentage of subjects with a M12 ED ≥600 mg and M12 ED ≥1000 mg peanut protein. Safety assessments will include overall adverse events, local site reactions, and systemic allergic reactions.
Conclusion
Young children are considered most likely to be responsive to allergen immunotherapy due to a potentially more modifiable immune system. Thus, this study of the efficacy and safety of a modified VP250 peanut patch is designed to recruit peanut-allergic children 4-7 years of age, who are more likely to benefit from EPIT. Patient screening is expected to begin in 2023 with topline results anticipated in 2025.

References

6. Raymond Mak
Bypassing escalation phase for oral immunotherapy in shrimp-allergic children is safe

Raymond Mak¹, Ann-Marie Schoos², Soller Lianne¹, Stephanie Erdle¹, Alanna Chomyn¹, Tiffany Wong¹, Edmond Chan¹
¹University of British Columbia, Vancouver, Canada, ²Herlev and Gentofte Hospital, University of Copenhagen, Denmark

Background
For oral immunotherapy (OIT), 300mg of food protein is a common target maintenance dose. However, the OIT escalation phase requires a series of time-intensive and costly "build-up" visits.

There are currently limited studies related to shrimp OIT. Previous studies have demonstrated that shrimp has a higher eliciting dose threshold compared with other allergenic foods. Only 4% of patients would react to less than 300 mg of shrimp protein[1]. The purpose of our case series is to explore the safety of directly administering maintenance OIT dose (300mg shrimp protein), bypassing the escalation phase of OIT for shrimp-allergic children.

Methods
Shrimp-allergic patients (ages 4-17 years) underwent a low-dose oral food challenge (OFC) to 300mg shrimp protein, with the goal of continuing to ingest this amount daily as a maintenance dose (300mg daily).

Patients needed to have either (1) a convincing objective IgE-mediated reaction and skin prick test ≥ 3mm or specific IgE level ≥ 0.35kU/L or (2) no ingestion history with a specific IgE level ≥ 5kU/L.

Parents were advised to record any adverse reactions and to use epinephrine auto-injector and seek immediate medical assessment in the emergency department in case of anaphylaxis. Follow-up was via ad hoc virtual visits.

Results
5 children (31%) were included based on sensitization criteria, 7 children (44%) had a history of a Grade 1 reaction to shrimp, and 4 (25%) had a history of a Grade 2 reaction with positive testing. 10 children (63%) had concurrent sensitization to house dust mite.

All 16 children completed the low-dose OFC. 9 (62%) experienced no reaction, and 7 (38%) had isolated oral pruritus. In follow-up, 15 (94%) continued OIT eating 300mg shrimp protein daily. 1 patient discontinued OIT because of significant side effects (oral pruritus). No patients developed anaphylaxis, needed epinephrine or emergency room visits related to immunotherapy.
Conclusion
Bypassing the escalation phase of OIT to shrimp may be a safe and cost effective strategy. Most patients will continue to tolerate the maintenance dose after the initial dose in follow up. However, given the high rates of concurrent house dust mite sensitization, and more mild index reactions for our patients, whether this strategy can be apply to more "severe phenotype" of shrimp-allergic individuals is yet to be known. Further studies are needed to evaluate the long term efficacy of ingesting 300mg of shrimp protein for treating shrimp allergy.

References

7. Felipe Benito-Garcia
Cow’s milk oral immunotherapy - a real-life 13-year follow-up study

Cow’s milk oral immunotherapy - a real-life 13-year follow-up study
Raquel Pestana¹, Filipe Benito-Garcia¹, Graça Sampaio¹, Mário Morais-Almeida¹
¹CUF Descobertas Hospital, Portugal

Background
Oral immunotherapy (OIT) dramatically changes the management of severe and long-lasting cow’s milk (CM) allergy. Once the maintenance dose has been achieved, patients should maintain a daily intake of CM to ensure tolerance. Clinical experience concerning long-term follow-up is scarce. The authors aimed to assess the long-term efficacy and safety of an OIT’s maintenance phase in real life.

Methods
Prospective study of children and adolescents, who underwent CM-OIT and were subsequently followed at our allergy centre on a maintenance dose (200mL daily) for at least 1 year after reaching the maintenance phase (from 2009 to 2022).

Results
78 patients were enrolled: 60% male, 22% with history of anaphylaxis and 53% with asthma. The median time follow-up was 8 years (range: 1-13 years) and median age at the last clinical evaluation was 15 years (range: 5-28 years). Regarding adherence to the protocol: 92% were on a free diet (at least 6-7g CM protein daily) and 6% withdrew with loss of CM tolerance. During maintenance, 32% developed mild (⅔) to severe allergic reactions (⅓), all associated with cofactors, mainly exercise. A positive correlation between the occurrence of allergic reactions and a previous history of anaphylaxis (odds ratio=2.57) was found.

Conclusion
This real-life study supports the long-term efficacy and safety of CM-OIT. Clinical tolerance depends on daily intake and eviction of the cofactors. The protective effect reached with OIT can be lost after CM withdrawal. History of anaphylaxis was a risk factor for the occurrence of allergic reactions during the maintenance phase.

Daily ingestion of the stipulated amount of CM or dairy (6-7g CM protein) enables a diet without restrictions, ensuring the maintenance of CM desensitization and decreasing the chance of a severe reaction upon accidental exposure. This intervention had a positive impact on both patients and their caregivers.
8. Makoto Nojo
The prevalence of allergic reactions after Pfizer-BioNTech (BNT162b2) COVID-19 vaccination in patients with severe food/drug allergy

Makoto Nojo1, Shintaro Suzuki1, Akihiko Tanaka1, Hatsuko Mikuni1, Yuto Miyata1, Hironori Sagara1
1Showa University, Japan

Background
Patients with allergies have strong concerns about the coronavirus disease (COVID-19) vaccine; thus, it is difficult to vaccinate these patients at walk-in vaccination centers. Although Japan has one of the highest vaccination rates in the world, 20% of the population has not received the vaccine[1], and one of the main obstacles to vaccine hesitancy is allergic concerns. Safe vaccination of patients with allergies is crucial for controlling the COVID-19 pandemic. In this study, we investigated the frequency and severity of immediate allergic reactions to vaccinations. The study was approved by Showa University Research Ethics Review Board(Approval number:21-113-B)

Methods
In this retrospective cohort study conducted from June 2021 to December 2021, we included patients at a high risk for anaphylaxis who were vaccinated at our hospital. At least two allergologists certified by the Japanese Society of Allergology determined the safety of the vaccinations. The vaccine was BNT162b2(Pfizer-BioNTech) and administered under the supervision of an allergist at our referral center for anaphylaxis or any adverse reactions to the vaccine. We recorded allergic reactions after the first and second doses of the vaccine and evaluated the number of patients who were discouraged from receiving the vaccine owing to allergic concerns.

Results
Forty-nine patients with high allergy could receive the vaccine. Among these, 26% (13/49) of the patients had very strong allergy concerns but were able to visit the hospital to receive the vaccine because of sufficient equipment and supervision by an allergist. Five patients had allergic-like reactions, and one had anaphylaxis. The patient had severe asthma and a history of anaphylaxis caused by aspirin and contrast agents. Anaphylaxis was diagnosed based on a cough and abdominal pain, which rapidly worsened 10 min after the administration of the second dose. The symptoms were moderate, and treated with antihistamines and steroids.

Conclusion
The rate of allergic reactions to the COVID-19 vaccine (2.0%) was higher in patients with a history of high-risk allergies than in the general population. However, even when symptoms occurred, the severity of reactions was low. This suggests that vaccination rates can be improved with sufficient equipment and supervision by an allergist, and that patients with allergies can receive vaccinations in a relatively safe manner.

References