

Oral Abstract Session 8

Reshaping Allergy Practice: Atopic Dermatitis, Food Allergy, Urticaria and Anaphylaxis

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The Environmental and Perinatal Risk Factors of Food Allergy and other Allergic Diseases in Taiwanese Young Children

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Purpose: Food allergies (FAs) are immune-mediated adverse reactions to food. World-widely estimated prevalence of FAs ranged from 1–10%. But the prevalence of FAs in children, particularly before 3 years old, in Taiwan remains unknown. We hypothesize that the increased prevalence of FAs in children may be associated with hereditary factors, maternal diet during pregnancy, feeding patterns of children, and environmental factors.

Methods: We used (Southern Taiwan Allergy Research Alliance, STARA) FAs questionnaire to conduct random questionnaire-based survey for the self-reported prevalence rate and type of FAs in children, aged 1–3 years. This questionnaire survey was performed in well-baby clinics of 4 medical centers located in Southern Taiwan. In each medical center, we expected to have about 250 subjects. STARA-FA questionnaire consisted of 99 questions to investigate the association with FAs. Chi-square test was used to identify the risk factors for these FAs children.

Results: According to our collected 903 subjects, the prevalence rate of food allergy in Southern Taiwan was 10.5%. The most common food allergens were egg (2.9%), milk (2.4%), fruit (1.4%), and seafood (1.3%). There was no significant different risk of FAs between different gender, gestational age, birth weight of children, children's feeding patterns > 6 M/O and the maternal diet during pregnancy. Children with eczema had significant higher risk of FA. Besides, children with family history of allergic disease had 3.16-fold higher risk of FA.

Conclusions: The prevalence of FA in children aged 1–3 years in Southern Taiwan was 10.5%, and the most common food were egg (2.9%) and milk (2.4%). Children with eczema and family history of allergic disease had higher risk of FA.

Cluster Analysis of Pediatric Atopic Dermatitis

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Rationale: All patients with AD do not have the same clinical characteristics and natural courses. We aimed to identify several distinct clusters in Korean children with AD by cluster analysis.

Methods: We retrospectively reviewed the medical records of 592 children with AD who visited pediatric allergy clinic in Samsung Medical Center between June 2007 and September 2017. Hierarchical cluster analysis was performed with 5 variables for unsupervised classification. The variables include age of onset (≤ 2 years, > 2 years), sensitization to inhalant allergens, sensitization to food allergens, severity estimated by initial SCORing Atopic Dermatitis (SCORAD) index (≤ 25 , 25–50, > 50), and family history of allergic diseases.

Results: We identified three clusters. Cluster 1 (n=287; 48.4%) was characterized by early onset age (≤ 2 years; 94.4%), low sensitization rate to inhalant and food allergens (1.0%, 55.1%), low severity (≤ 25 ; 55.4%, 25–50; 39.0%, > 50 ; 5.6%) and strong association with family history (83.6%). Cluster 2 (n=265; 44.8%) demonstrated early onset age (≤ 2 years; 100.0%), high sensitization rate to inhalant and food allergens (55.1%, 95.5%), high severity (≤ 25 ; 47.9%, 25–50; 37.4%, > 50 ; 14.7%) and weak association with family history (35.1%). Cluster 3 (n=40; 6.8%) was related with late onset age (> 2 years; 100.0%), high sensitization rate to inhalant allergens (77.5%), low sensitization rate to food allergens (7.5%), high severity (≤ 25 ; 37.5%, 25–50; 52.5%, > 50 ; 10.0%) and weak association with family history (42.5%).

Conclusions: Pediatric AD can be classified into 3 distinct phenotypes. Early-onset, mild AD is associated with family history of allergic disease. Early-onset, moderate-to-severe AD is associated with male sex, food allergy and sensitization to inhalant allergens. Mid- or late-onset AD is more likely to have allergic rhinitis and associated with sensitization to inhalant allergens.

Key Words: Pediatric atopic dermatitis, Cluster analysis

Trajectories of Class-Switching Related Egg and Cow's Milk Allergen-Specific Immunoglobulin Isotype Formation and Its Modification by Eczema with Low and High-Affinity IgE during Early Infancy

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Introduction: Allergen-specific immunoglobulin isotype formation associated with immunoglobulin class-switching during the lactation period is the immunological background for food allergy in infants. But, to our knowledge, no detailed data in the serial changes of immunoglobulin during the lactation period are available at present.

Purpose: The aim of the present study was to analyze the serial changes in the production of feeding type-related egg- and milk-specific immunoglobulin isotypes from birth to 6-months of age with or without eczema in infants.

Methods: Allergen-specific IgG1, IgG2, IgG3, IgG4, IgA and IgE levels of hen's egg and bovine milk were measured in cord blood and blood samples from infants at 2, 4 and 6 months of age by the densely carboxylated protein microarray.

Results: This study included 84 infants and their mothers. Formula and mixed feeding were associated with rapid increase in cow's milk allergen-specific immunoglobulins and feeding type-related significant differences in casein-specific immunoglobulin levels were detected. Breast and mixed feeding were associated with slow but significant increase in ovalbumin-specific IgG1 and IgE levels, but not other immunoglobulins. We found two different immunoglobulin isotype formation at 6-months of age with low- or high-affinity IgE against ovalbumin. One isotype formation pattern had relatively high ovalbumin-specific IgG1 levels, detectable IgG2 and low-affinity IgE, while the other had low ovalbumin-specific IgG1 levels, undetectable IgG2 and high levels of high-affinity IgE. The incidence of eczema was significantly higher in the latter pattern (84.6%), compared with the remaining infants (42.2%).

Conclusions: Feeding practice-related allergen sensitization and immunoglobulin isotype formation were identified during the lactation period. The development of eczema during the lactation period could potentially modify the immunoglobulin isotype formation with high levels of high-affinity IgE.

Prenatal Maternal Meat Dietary Pattern May Promote Offspring's Atopic Dermatitis through Cord Blood Metabolites

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Background: Atopic dermatitis (AD) risk has been linked with a variety of environmental factors during pregnancy, including the maternal diet. This prospective study examined the relationship between maternal dietary pattern during pregnancy and the risk of AD in offspring aged 6, 12 months and whether the mechanism is mediated by cord blood metabolites.

Methods: Subjects were mother-child pairs from Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA). We analyzed 916 of these mother-child pairs with complete food frequency questionnaire data, feeding type assessments during infancy, and clinical assessments. Cord blood metabolites were measured using untargeted liquid chromatography-mass spectrometry.

Results: There were no associations found between dietary patterns and offspring AD at age 6 and 12 months. However, lactating mothers with a higher meat intake during pregnancy had a higher risk of offspring AD at 6 and 12 months (aOR 2.07 [95% CI, 1.05-4.09]; aOR 2.06 [95% CI 1.04-4.10]). Among the 318 diet-specific and 232 AD-specific mass ions, the levels of 20 compounds including phosphatidylcholines, sphingolipids, fatty acids and bilirubin differed according to the maternal dietary patterns. Phosphatidylcholines, sphingomyelin and ganglioside GM3s were decreased in the AD offspring with a maternal meat dietary pattern compared with the healthy control infants with a maternal healthy dietary pattern (P < .05).

Conclusion: The maternal meat dietary pattern during pregnancy is associated with change in cord blood metabolites and the risk of offspring's AD.

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Key Words: Prenatal maternal diet, Cord blood, Metabolites, Atopic dermatitis

Presence of Past History of Immediate Reactions to Peanut Alters Probability Curves of Specific IgE

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Background/Purpose: Peanut-specific IgE (sIgE) and Ara h 2 sIgE levels and a history of immediate reaction to causative foods are associated with outcomes of oral food challenge (OFC) to peanut.

This study aims to assess the association of a combination of these on the results of OFC to peanut.

Methods: We retrospectively analyzed the data of children aged <18 years who underwent inpatient OFC to 3 g peanut (=750 mg peanut protein) between March 2010 and March 2016.

Results: Among 128 children, 39% failed in OFC. A statistically significant association was observed between a history of past immediate reaction, peanut sIgE, and Ara h 2 sIgE levels (p values: <0.0001, 0.038, and <0.0001, respectively). We drew fitted predicted probability curves for the positive outcome of OFC at a given peanut and Ara h 2 sIgE level and subdivided them by the presence of a history of immediate reaction. Peanut and Ara h 2 sIgE levels in patients with a history of past immediate reaction, indicative of a 95% predictive decision point (PPV), were 96.3 and 38.4 kU_A/L, respectively. A 95% PPV couldn't be obtained in patients without a history of past immediate reaction.

Conclusions: This is the first study to report two different probability curves for peanut allergy with or without the presence of the history of immediate reaction. A combination of the presence of a history of immediate reaction and sIgE levels more accurately predicts the results of OFC to peanut than sIgE alone.

Prenatal PM Exposure Combined with Skin Barrier Dysfunction is Associated with AD and Its Severity in Early Life: COCOA Study

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Background: Exposure to particulate matter (PM) during the critical period affects the development of allergic diseases. Skin barrier dysfunction is the key pathophysiology of AD. However, there have been no studies on the combined effect of the two factors during the critical period. In the present study, we identified the effect of exposure to PM during prenatal period on AD combined with skin barrier dysfunction in early life.

Methods: This study enrolled 468 infants from the Cohort for Childhood Origin of Asthma and allergic diseases (COCO). Levels of outdoor PM_{2.5} and PM₁₀ during the prenatal period were estimated by land-use regression models based on national monitoring system. Levels of indoor PM_{2.5} and PM₁₀ at 36 weeks of gestation were measured using a particle discriminator (Model GT-331; SIBATA Co., Japan). Levels of trans-epidermal water loss (TEWL) were measured at age 1. AD was diagnosed on the basis of parents-reported physician diagnosis with measurement of SCORAD score at ages 1.

Results: Exposure to higher levels of indoor PM_{2.5} at 36 weeks of gestation and outdoor PM_{2.5} at the first trimester was increased the risk of AD at age 1 in infants with higher levels of TEWL (aOR 3.23, 95% CI, 1.18–8.82; aOR 3.03, 95% CI, 1.25–7.32, respectively). Exposure to higher levels of outdoor PM₁₀ at the first and third trimester increased the risk of AD at age 1 in infants with higher levels of TEWL (aOR 2.75, 95% CI, 1.07–7.03; aOR 3.51, 95% CI, 1.03–9.46). SCORAD score at age 1 was increased in infants with high levels of TEWL combined with exposure to higher levels of outdoor PM_{2.5} and PM₁₀ during the prenatal periods.

Conclusion: Prenatal PM exposure is associated with AD in early life, when combined with skin barrier dysfunction. Avoidance of PM exposure during prenatal period and enhancement of skin barrier function might be helpful to prevent the development of AD in early life.

Key Words: Atopic dermatitis, Particulate matter, Skin barrier function

Wheat Oral Immunotherapy (OIT) Can be Successfully Carried Out in Thai Children with Severe Wheat Allergy

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Introduction: Wheat allergy is a major food allergy among Thai children. Natural tolerance can occur but persistence can be observed in those with high wheat sensitivity. We aim to study the outcome of wheat OIT in Thai children with severe wheat allergy.

Method: Retrospective data of 34 patients with severe wheat allergy, who underwent wheat OIT at the Samitivej Allergy Institute (SAI) between February 2016 to February 2019, were studied. All patients underwent PRACTALL double-blind, placebo-controlled food challenge to wheat powder beginning at 1 mg and end with at 3000 mg. Eliciting dose of wheat powder was determined and ED-1 was chosen as a starting OIT dose. Twenty percent dose increment was carried out every 2 weeks in the office. Blood were drawn for the measurement of SpIgE to wheat and omega-5-gliadin before OIT and at 1-3 year after starting the OIT.

Results: There were 19 females and 15 males with mean age 6.3 years at the time of OFC/OIT. The mean age of onset of wheat allergy was 9 months (range 3-15 months). The median eliciting dose was 20 mg of wheat protein (range 1-1200). The mean SpIgE to wheat at the beginning of OIT was 271.45 kUA/l (range 0.1-1628) with SpIgE to omega-5-gliadin of 32.92 kUA/l (range 0.04-200). SpIgE to wheat and omega-5-gliadin after 1-3 years of OIT declined with the mean of 47.5 % Std Dev 32.9 % and 65.8% Std Dev 22.7% respectively.

There were 13 patients who currently reached maintenance (MT) dose of 1 slice of bread/day (1500 mg of wheat protein). The mean time to reach MT was 11 months. There were 18 patients who are still in the build-up phase. 3 patients dropped out due to severe eczema (1), GI side effect (1), and loss to follow up (1). 23 patients required adrenaline during DBPCFC. Using a modified World Allergy Organization Systemic reaction grading system, all patients developed adverse reactions (6 patients had grade 1, 15 had grade 2, 12 had grade 3, 1 had grade 4 reaction). No fatal or near-fatal reaction was observed.

Conclusion: In this study, wheat OIT can be carried out even among patients with severe degree of wheat sensitivity. Our study showed that 13/34 (38%) of patients have reached MT phase so far. All patients developed some degree of adverse effects which can be successfully controlled. Further follow up of these patients is required.

PTGR2 Expression in Gut Epithelial Cells and Fine Mapping Analysis of Polymorphisms in Atopic Dermatitis

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Atopic dermatitis (AD) is a common and chronic inflammatory skin disease affecting up to 20% of children and 3% of adults worldwide. The gut microbiome is linked to immune development and immune responses, and can play an important role in development of allergic diseases including AD. Our result of a global gene expression profile in the colonocyte from fecal samples identified PTGR2, a gene involved in prostaglandin catalysis and inflammatory responses, as a potential risk factor for AD. To investigate the association between PTGR2 genetic variants and AD, a fine mapping using 17 single nucleotide polymorphisms (SNPs) of PTGR2 was performed in 864 Korean subjects (420 AD patients and 444 unaffected controls). As a result, several SNPs and a haplotype showed significant associations with AD in the case-control analysis (minimum $P=0.026$ at rs1968105, $P=0.02$ at haplotype ht2), suggesting that genetic polymorphisms and haplotype may be related to this disease. In additional linear regression analysis, five SNPs (rs9646165, rs1962795, rs17782239, rs8005140, rs8020630) and two haplotypes (ht2, ht3) showed significant effects on the SCORing AD (SCORAD) values (minimum $P=0.006$ at rs17782239 and $P=0.02$ at ht3 under an additive genetic model) in AD patients. Although further functional evaluations are needed, our findings suggest that genetic variations and haplotypes of PTGR2 may be associated with the risk of AD and its SCORAD.

Key Words: Atopic dermatitis, PTGR2, Single nucleotide polymorphism

Wheat Anaphylaxis Can Occur Despite Very Low Level of Specific IgE to Wheat

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Purpose: To describe demographic data, symptom and its severity of wheat anaphylaxis among 3 patients who had low-very low specific IgE to wheat.

Methods: A retrospective review of medical records from three children (aged from 2 to 9 years) who presented with wheat anaphylaxis and with low to very low level of wheat specific IgE were undertaken. Demographic data, laboratory profiles and result of wheat challenge test were described.

Results: Three patients with wheat anaphylaxis and with low-very low level of specific IgE to wheat were identified. All developed first symptom of wheat allergy upon wheat ingestion since age 8-12 months. Reactions occurred 15-30 minutes after wheat ingestion. The most common manifestation was skin rash (urticaria, angioedema). Concomitant allergic rhinitis and egg allergy were presented in 2 cases and one of them was allergic to tree nut. All parents had allergic rhinitis. All patients had positive results of skin prick test to wheat extract with 3.5-5 mm in mean wheal diameter and had low-to-very low level of specific IgE to wheat (0.1-0.3 KUA/L). Case no.1 reacted to 3000 mg dose of wheat oral challenge. Eliciting dose in case no.2 was 36 mg of wheat powder. These two cases were placed on our oral immunotherapy of wheat program. Eliciting dose of the last patient was 937 mg of wheat powder.

Conclusions: Wheat anaphylaxis could occur despite low-to-very low level of specific IgE to wheat and omega gliadin. This could be due to low wheat sensitivity among these patients or due to the generation of neoallergen in the gastrointestinal system. In some of these patients, higher dose of wheat is needed to elicit allergic manifestation.

Two-Year Results of the Multicenter Web-based Anaphylaxis Registry in Korea: Causes, Clinical Characteristics, and Severity

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Purpose: We have developed the first multicenter web-based registry of anaphylaxis in Korea to collect more precise and standardized data including severity of anaphylaxis. Here we report the first 2-year results from the registry.

Methods: Twenty-two departments from 16 hospitals participated in patient registration from November 2016 to December 2018. Anaphylaxis events within 3 months from the visit date with the exact date of occurrence identifiable were included.

Results: During 2 years, 558 cases of anaphylaxis were registered. The age of registered patients ranged from 2 months to 84 years, and 60% were less than 18 years old. In children, foods (84.8%) were the most common cause of anaphylaxis followed by drugs (7.2%), whereas in adults, drugs (58.3%) were the most common cause, followed by foods (28.3%) and insect venom (8.1%). The onset time was ≤ 10 minutes in 37.6%. The most common place of occurrence was home (51.4%), followed by restaurants (7.3%). Among the 351 cases registered via the emergency department (ED) of participating hospitals, epinephrine was administered in 63.8% (61.3% in adults, 66.7% in children). Among those who received epinephrine in ED, 13.8% required 2 or more shots of epinephrine. Of the total registered cases, severe anaphylaxis accounted for 23.5% (38.1% in adults, 13.7% in children). By cause, the proportion of severe anaphylaxis was highest among those triggered by insect venom. The significant risk factors for severe anaphylaxis were increasing age, past history of anaphylaxis, presence of cardiovascular symptoms, and presence of co-factors.

Conclusion: This multicenter anaphylaxis registry would provide a better understanding of anaphylaxis, especially in predicting risk factors for severe anaphylaxis, to help prevent and manage the disease more effectively. [This research was supported by a fund by Research of Korea Centers for Disease Control and Prevention (2018E6702-00).]

Key Words: Anaphylaxis, Korea, Registry

Association of Parasite Infection with Chronic Urticaria in Vietnamese Patients

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Background: Chronic urticaria (CU) is one of the most common allergic diseases in Vietnamese people. The causes of CU are difficult to identified. This study aimed to investigate the associations of parasite infections with CU in Vietnamese patients.

Methods: 60 patients with CU and 30 patients with other skin diseases (disease control group) were recruited in Ho Chi Minh City Hospital of Dermatovenereology. CU severity was evaluated by severity score of Breneman et al. ELISA was used to measure the serum IgG levels against 5 common infectious parasites in Vietnamese (*Toxocara spp.*, *Gnathostoma spp.*, *Strongyloides stercoralis*, *Entamoeba histolytica*, *Fasciola spp.*).

Results: Females were predominant in both CU (65%) and control group (60%). The median age of CU group [28 (24–36.25)] were not significantly different from the one of control group [26.5 (25–34.5), $p=0.807$]. The prevalence of positive results in at least 1 serology tests againts the 5 parasites were significantly higher in CU group (76.7%) compared to the control group (50.0%, $p=0.011$). The positive serology test to each parasite in the CU group tended to be higher than that of the control group (*Toxocara spp.*, 63.3% vs 43.3%; *Strongyloides stercoralis*, 16.7% vs 3.3%; *Fasciola spp.*, 13.3% vs 10.0%; *Gnathostoma spp.*, 3.3% vs 3.3%; *Entamoeba histolytica*, 3.3% vs 0%, respectively); however, no significant differences were observed ($p>0.05$ for all comparisons). CU patients with at least 1 positive serology tests had significantly lower severity score (8.17 ± 1.52) compared to the control group (9.29 ± 1.2 , $p=0.015$). There were no associations of serology test results with age of onset, duration of disease, and the coexistence of angioedema in CU patients.

Conclusions: Parasite infections could be associated with CU in Vietnamese patients; however, it may not affect the disease severity. Screening tests and appropriate treatment for parasite infections should be considered in Vietnamese CU patients.