Abstract Highlights

The following highlights spotlight selected abstracts presented at the 2023 European Academy of Allergy and Clinical Immunology (EAACI) Congress. They cover fascinating and timely topics, including the effect of infantile atopic dermatitis on maternal bonding, patient burden in hereditary angioedema, and the use of specific interleukins to reduce symptoms of allergic rhinitis.

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What Factors Contribute to FPIES Reactions at Oral Food Challenge?

A MULTICENTRE, prospective, observational study was led by researchers at Imperial College London, UK, to assess potential factors associated with reaction severity in food protein-induced enterocolitis syndrome (FPIES). The study aimed to outline the clinical symptoms and routinely available blood parameters in children experiencing reactions. There is currently limited knowledge surrounding the clinical and immunological symptoms experienced by patients with FPIES, and with a lack of diagnostic and prognostic biomarkers, oral food challenge (OFC) remains the current gold standard in its diagnosis.

The researchers conducted the study in children aged 0–18 years in 15 tertiary allergy clinics in France and Spain. The participants had been diagnosed with acute FPIES and were undergoing follow-up OFC to identify the cause of their reaction. OFCs were performed on either single day protocols with incremental doses, or 2-day protocols with a single dose of 25% of an age-appropriate portion on Day 1, with a reminder on Day 2.

Outcomes were interpreted using the FPIES consensus criteria, published in 2017, and children with a positive outcome were included. The researchers logged the participants' clinical characteristics and blood parameters at baseline, at the onset of reaction, and 4 hours later. Regression analyses were conducted for potential predictors of severe OFC reactions.

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This study found 81 children with positive OFC. Of this cohort 87.6% followed a 1-day protocol, and 70% had experienced previous severe reactions. Reaction severity was reported as mild in 11% of participants, moderate in 61%, and severe in 28%, with an increase in neutrophils and a reduction in eosinophils and lymphocytes remarked at OFC ($p<0.05$). Analyses showed that a 2-day OFC protocol correlated with reduced odds of severe reaction, and other factors including sex, age, and culprit foods were not associated with severity.

Overall, this study suggested that the 2-day protocol may be associated with less severity at FPIES OFC. The researchers highlighted the need for the development of safer FPIES diagnostics, given the high rates of moderate-to-severe reactions observed in this study.

Clinical Outcomes Following Allergen Exposure Chambers

ALLERGEN exposure chamber (AEC) is a diagnostic tool that permits exposure to allergenic and non-allergenic airborne particles. Used for diagnosing and for monitoring the effects of treatment, AECs provide a stable concentration of particles under controlled conditions, independent of external factors. The research team therefore sought to validate AEC-derived clinical outcomes of house dust mite (HDM) allergy immunotherapy (AIT).

Fifty patients with symptoms of HDM-triggered allergic rhinoconjunctivitis received skin prick tests, serum specific IgE, and basophil activation test to confirm the diagnosis. Allergy symptoms were then assessed using Combined Symptom and Medication Score (CSMS). AEC was used to assess patients both before and 12 months after treatment with subcutaneous HDM AIT. Standardised and lyophilised allergen extract particles were injected into the AEC through a computer controlled feeder during exposure. An optimal concentration of 5000 μ/m^3 of purified bodies of *Dermatophagoides pteronyssinus* was utilised for a challenge duration of 120 minutes. AIT efficacy was assessed using the Total Nasal Symptom Score (TNSS), Visual Analogue Scale (VAS), and objective parameters, such as peak nasal inspiratory flow, nasal secretion weight, and acoustic rhinometry.

Analysis suggested that constant environment conditions, including temperature, humidity, and carbon dioxide concentrations, were maintained for all challenges. Most importantly, TNSS was significantly reduced after one year of AIT ($p<0.005$) and a high reduction of nasal symptoms, such as peak nasal inspiratory flow and nasal secretion weight, were observed after a year of AIT ($p<0.05$). However, no statistically significant changes to acoustic rhinometry was seen following AIT. Finally, a strong correlation was observed between CSMS in field measured before treatment and nasal symptoms measured in AEC ($p<0.05$), using nasal secretion ($r=0.77$; $r=0.99$), peak nasal inspiratory flow ($r=0.80$; $r=0.75$), and VAS ($r=0.93$; $r=0.81$) before and after AIT, respectively.

Overall, the AEC is an effective, safe, and reproductible method for assessing HDM AIT outcomes in patients with allergic rhinoconjunctivitis. Future research and clinical practice would benefit from further validation of clinical endpoints using immunological biomarkers. ●

"AEC was used to assess patients both before and 12 months after treatment with subcutaneous HDM AIT."

Infantile Atopic Dermatitis and Maternal-Infant Bonding: A Mixed Methods Study

RESEARCH presented at the EAACI 2023 Congress explored infantile atopic dermatitis, a common, chronic skin condition characterised by the presence of dry, itchy, and inflamed skin. Previous studies and literature have delved into the impact of this condition on children and caregivers' quality of life; however, until recently, there has been little understanding of, or research dedicated to, the impact of the condition on the relationship between mothers and infants. This mixed-methods study aimed to assess the association between infantile atopic dermatitis and the maternal–infant bond.

The study used adjusted models with scores on the impaired bonding, pathological anger, and incipient abuse subscales, which did not significantly differ between case and controls. Further analysis demonstrated that mothers of infants with atopic dermatitis reported lower levels of infant-directed anxiety (β=-1.06; p=0.04). However, qualitative findings supported the idea that regular caregiving required for infants with infantile atopic dermatitis may strengthen the bond between some mothers and infants. The study participants had an average age of 30.80±4.36 years, and an average infant age of 7.60±4.20 months.

The researchers concluded that the mother–infant bond does not appear to be negatively impacted by the presence of infantile atopic dermatitis. On the contrary, analysis suggested that the requirement for the provision of routine care for infants with atopic dermatitis instead strengthens the bond between mothers and their infants. ●

"There has been little understanding of, or research dedicated to, the impact of the condition on the relationship between mothers and infants."

Symptom and Quality of Life Burden in Patients with Indolent Systemic Mastocytosis

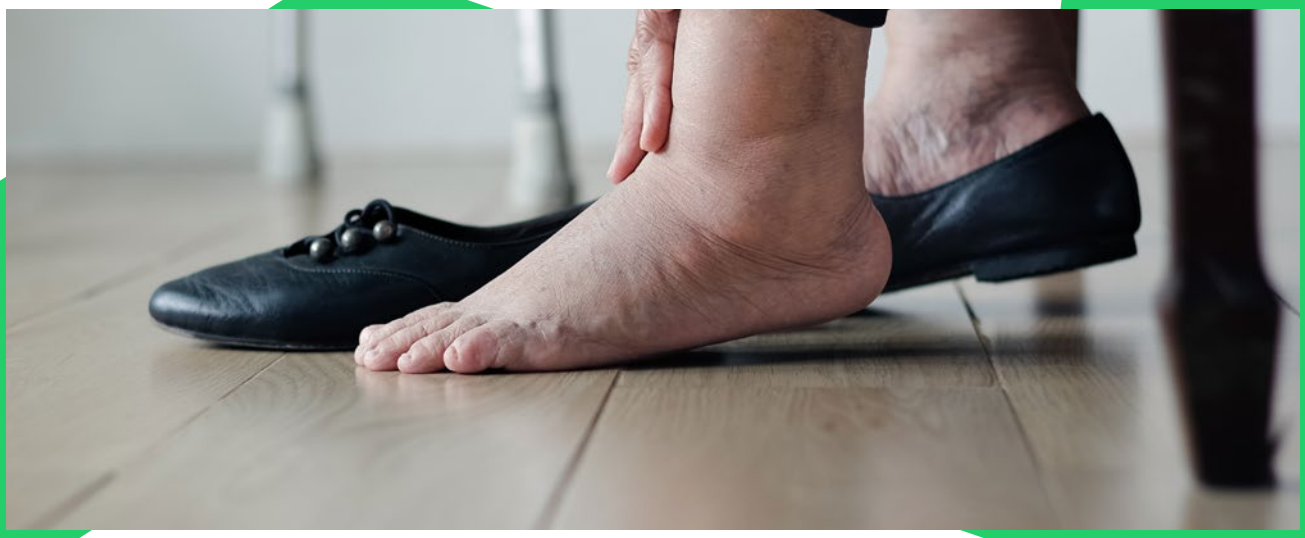
AT THE EAACI Congress 2023, Frank Siebenhaar, Charité – Universitätsmedizin Berlin, Germany, presented data from a registrational, randomised, double-blinded, placebo-controlled study. The study included patients with moderate-to-severe indolent systemic mastocytosis (ISM) with inadequately managed symptoms, despite receiving optimised treatment with two or more anti-mediator drugs.

The symptom burden was evaluated at baseline prior to the start of the study, using the ISM-symptom assessment form, which calculated the total symptom score (TSS) ranging from 0–110. The TSS was established based on a 14-day average of patient-reported severity for 11 ISM symptoms, with the scores ranging from 0 (referring to no symptoms) to 10 (indicating the worst imaginable symptoms). The patients were required to have a TSS ≥28 at screening to be eligible for inclusion. Various measures, including the 12-Item Short-Form Health Survey (SF-12), European Quality of Life 5 Dimensions (EQ-5D-5L), Mastocytosis Quality of Life Questionnaire (MC-QoL), and Patient Global Impression of Severity (PGIS), were utilised to assess patient health status and quality of life.

Prior to study initiation, enrolled patients (n=212) reported severe ISM symptoms. Multiple symptom-directed therapies were utilised, including H1 and H2 antihistamines (98.1% and 66.0%, respectively), and leukotriene receptor antagonists (34.9%); however, the mean TSS was 50.9. In comparison to general population norms, other chronic conditions, and cancers, the enrolled patients had lower scores, indicating worse physical and mental health. Notably, the mean physical component score of the SF-12 was 33.9, while the mean mental component score was 40.7. Additionally, the patients exhibited lower mean scores on the EQ-5D-5L index (0.62), compared to the general population (0.85).

"The symptom burden was evaluated at baseline prior to the start of the study, using the ISM-symptom assessment form."

The patients reported moderate disease severity based on MC-QoL, with a mean score of 57.5 on a range of 0–100, where ≥40 indicates moderate severity. When assessing symptom severity, patients rated their symptoms as very severe (22%), severe (33%), or moderate (36%) using the PGIS. The findings indicate that a substantial existing disease burden, and highlight the unmet needs of individuals with moderate-to-severe ISM.



Quality of Life and Patient Burden of Hereditary Angioedema in Resource-Limited Regions

HEREDITARY angioedema (HAE) data are prevalent across Europe and North America, but limited in other regions around the world, where healthcare systems are less well-developed, and access to treatments recommended in guidelines are limited. HAE, which causes sudden, painful, and recurrent swelling in patients, is a rare disorder that can be life-threatening.

Lead study author Rand Arnaout, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, embarked on this research topic with colleagues from Mexico, Singapore, and South Korea. The team carried out a cross-sectional, non-interventional, Internet-based survey in a patient cohort who had been diagnosed with HAE by a physician. Data was taken from four countries (Türkiye, Mexico, South Korea, and Saudi Arabia), with the starting point of 1st July 2022. Patients needed to be ≥18 years; have had ≥1 attack of HAE, or early warning symptoms of an attack within the last year; and have received medication for HAE within the last 2 years.

Researchers collected outcomes, patient-reported burden, and clinical characteristics data. They used the following outcome measures: the Angioedema Quality of Life (AE-QoL), the Hospital Anxiety and Depression Scale (HADS), and the Angioedema Control Test (AECT). The interim analysis ran until 31st January 2023.

In total, 116 patients were included (87 from Türkiye; zero from Mexico; 27 from South Korea; two from Saudi Arabia), with a mean age of 41.1 years. Of these, 59% were female, and 79% had Type I or II HAE. Median HAE onset age was 14.1 years, and diagnosis age was 27.1 years. Over the previous 12 months, 55% of these patients had >2 attacks per month on average, with 3% reporting ongoing attacks. These attacks were reported as severe or very severe in 61 out of 110 patients, 33% of whom were receiving long-term prophylaxis (most common: danazol [76%] and tranexamic acid [10%]), and 78% of whom were receiving on-demand treatment. Three-quarters of patients had AECT scores <10; the majority had AE-QoL scores ≥50; and 45% and 25% of patients had moderate-to-severe anxiety and depression, respectively, using the HADS score.

"Researchers collected outcomes, patient-reported burden, and clinical characteristics data."

Researchers concluded that in resource-limited regions, patients with HAE had a >10-year delay from onset to diagnosis, and also experienced severe attacks frequently. There was also found to be a substantial disease burden in this cohort. ●

Decreasing Allergic Rhinitis Symptoms with Low-Dose IL-2

LOW-DOSE IL-2 can decrease allergic rhinitis symptoms in patients, according to research presented at the EAACI Congress 2023. Researchers based in France performed a randomised, double-blind, placebo-controlled, parallel-group Phase IIA study to evaluate the efficacy of low-dose IL-2 on nasal response during birch allergen exposure.

A total of 24 patients, with a specific IgE to birch and a positive skin prick test, took part in the study. Their exposure to birch allergen was in an environmental exposure chamber, which the researchers deemed a good model to evaluate the efficacy of drugs on rhinitis symptoms in patients with allergies.

Firstly, patients were exposed to 25 ng/m^3 of Bet v I allergen to determine nasal response, and for the researchers to pick patients who had a positive nasal response, which was defined as a Total Nasal Symptom Score (TNSS) of ≥5 compared with baseline. The researchers also assessed rhinitis visual analogue scale (VAS) and asthma response, defined as a drop of ≥20 forced expiratory volume in 1 second.

After being randomised, the patients were either given a placebo or low-dose IL-2 (1 million IU/day) for 5 consecutive days. This was followed by a maintenance period, which either consisted of an injection of placebo or low-dose IL-2 for 4 weeks (from Day 15 to Day 36). Allergen exposure tests were performed after treatment on Days 8 and 40.

The results showed a decrease in TNSS in the IL-2 group, with an area under the curve of 8.03 at Day 40, compared with 3.27 for placebo. The area under the curve for rhinitis VAS was -32.31% compared with placebo. Patients on low-dose IL-2 also had a 1.5-fold increase in T regulatory cells, which play an important part in sustaining immune tolerance to allergens, and the researchers observed significant changes in spirometry.

In conclusion, low-dose IL-2 can decrease rhinitis symptoms, while increasing regulator T cells in an environmental exposure chamber. ●

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Do Comorbidities and Aeroallergen Sensitisation Affect Asthma Severity in Children?

ALLERGIC rhinitis and weed sensitisation have been identified as independent risk factors for low asthma severity in paediatric patients in a retrospective cohort study presented at EAACI 2023. The study aimed to investigate how comorbidities and aeroallergen sensitisation affect asthma severity in children.

Researchers collected data from a prospectively collected registry of 976 paediatric patients with asthma, who were enrolled in the National Pediatric Asthma Cohort Study between July 2016–January 2019. The team investigated baseline characteristics of all participants, including comorbidities, pulmonary function tests, and aeroallergen sensitisation with T helper 2 markers. Participants were classified into four groups. Group A included patients without comorbidities; Group B patients with atopic dermatitis (AD) only; Group C those with allergic rhinitis (AR) only; and Group D with AD and AR.

The team noted differences in asthma severity, initial fractional exhaled nitric oxide, and degree of sensitisation by aeroallergen group according to the comorbidities. Those in the AD only group had the highest proportion of moderate-to-severe asthma, while those in the AR only group had the lowest. Regarding fractional exhaled nitric oxide, this was lowest in the group without comorbidity, followed by the AD only group, and finally the group with both AD and AR. The AR group had high sum of skin prick tests wheels by each aeroallergen sensitisation group, except animal dander. Furthermore, total IgE and sum of skin prick tests wheels of weed were identified as predictors of AR and AD comorbidities in children with asthma. Multivariate logistic regression analysis showed that weed sensitisation and AR were negative risk factors for moderate-to-severe asthma.

"The team investigated baseline characteristics of all participants, including comorbidities, pulmonary function tests, and aeroallergen sensitisation with T helper 2 markers. "

The team concluded that AR and weed sensitisation were independent risk factors for low asthma severity in paediatric patients. The authors highlighted that this shows the need for reinterpretation of previous findings, which showed that most comorbidities associated with asthma adversely affect severity and prognosis. More studies, on a larger scale, are needed to further examine the definition of airway hyperresponsiveness, aeroallergen sensitisation, and the diagnosis of asthma according to comorbidities.

Allergic Rhinitis: Does Intranasal Phototherapy Improve Nasal Symptom Scores?

TOTAL nasal symptom score (TNSS) is a validated symptom-rating questionnaire used to quantify allergic rhinitis (AR) symptoms. Despite standard approaches, some patients have persistent symptoms. Intranasal phototherapy is a type of ultraviolet light therapy used alongside standard medical therapy to help treat AR.

To determine whether intranasal phototherapy improves AR symptoms in adolescent patients who failed to respond to standard treatment, a group of researchers from Birmingham, UK, conducted a retrospective analysis of data from all adolescent patients who underwent intranasal phototherapy for AR between July 2018–July 2022. In total, the analysis included 32 patients with AR. The mean age was 13.5 years and 26 were male. Most patients had a diagnosis of perennial rhinitis (81.8%).

The study revealed that intranasal phototherapy resulted in improved TNSS questionnaire results. The average pre-treatment TNSS was 8.7 (95% confidence interval [CI]: 7.5–9.9; range: 3.0–14.0), which reduced to 4.0 (95% CI: 2.8–5.2; range: 0.0–13.0), following intranasal phototherapy. The average difference pre- and post-treatment with intranasal phototherapy was 4.7 (95% CI: 3.3–6.0), translating to an overall TNSS improvement of 54%.

"The study revealed that intranasal phototherapy resulted in improved TNSS questionnaire results."

Whilst this study was performed in a small sample, and relied on self-reporting of TNSS questionnaires, the authors concluded that intranasal phototherapy improves AR symptoms, demonstrated by an improvement in TNSS. Research in larger cohorts, as well as studies to compare symptom responses to oral medications, including antihistamine and steroid treatment versus intranasal phototherapy, could be a potential focus for the future.

Reducing Inflammation in Chronic Rhinosinusitis with Nasal Polyps

WHILE exerting different effects on local immune pathways, mepolizumab, benralizumab, omalizumab, and dupilumab downregulated proteins and genes related to eosinophilic inflammation in patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

Type 2 nasal and sinus mucosa inflammation is common in patients with CRSwNP. It is characterised by high levels of IgE, IL-5, and eosinophilic cationic protein, as well as tissue eosinophilia. Up to 65% of these patients have comorbid asthma, and treatment involves drugs that treat severe, uncontrolled asthma. As knowledge of the local working mechanisms of these biologics is limited, Sharon Van Nevel, Upper Airways Research Laboratory, Ghent, Belgium, and colleagues studied how difficult biologicals modulate Type 2 airway inflammation.

Nasal polyp tissue was taken from patients before and during treatment, and immunohistochemistry stainings and protein measurements were performed. Patients were diagnosed with Type 2-high CRSwNP before treatment. Pre- and post-treatment samples from the same patients were then RNA-sequenced in bulk, with DESeq 2 (R4.2.0 [Bioconductor]) used to identify differentially expressed genes.

Patients were treated with mepolizumab (anti-IL-5), benralizumab (anti-IL-5-receptor), and omalizumab (anti-IgE), where eosinophils withdrew from the tissue and neutrophils were attracted locally. This was not present in dupilumab (anti-IL-4/13-receptor) treatment. Patients treated with mepolizumab showed a decrease in eosinophil markers, T cells, and apoptosis; however, there was an increase in mucus-related and neutrophilic genes. A similar downregulation of eosinophil-associated genes and upregulation of neutrophilic markers was seen with omalizumab treatment. However, this was not the case with dupilumab, where there were lower genes associated with eosinophils, and no upregulation of genes associated with neutrophils.

The researchers concluded that mepolizumab, benralizumab, omalizumab, and dupilumab resulted in the downregulation of eosinophilic inflammation-related proteins and genes. The upregulation seen during treatment with mepolizumab, benralizumab, and omalizumab suggests that there is a switch from eosinophilic to neutrophilic inflammation. However, this was not observed with dupilumab, which could explain the higher response rate in patients with CRSwNP. ●

"Nasal polyp tissue was taken from patients before and during treatment."

Are IgE Food Allergens Associated with Cardiovascular Disease?

SENSITISATION to food allergens and cardiovascular mortality risk were evaluated by a team of researchers from multiple centres across the USA. The team reviewed data from the cross-sectional National Health and Examination Survey (NHANES) and the Multi-Ethnic Study of Atherosclerosis (MESA) longitudinal cohort, both of which gathered detailed dietary information and food specific IgE data.

"Sensitisation to CM only was associated with significantly higher risk of cardiovascular mortality."

The NHANES survey included 4,996 adults, and included total and specific IgE to cow's mik (CM), egg, peanut, and shrimp, measured using ImmunoCAP™ (Thermo Fisher Scientific, Waltham, Massachusetts, USA), as well as linked mortality data up to 2019. MESA included adult patients with no clinical diagnosis of cardiovascular disease between 2000–2002. In a subset of this cohort, specific IgE for CM, alpha-gal syndrome, and peanut were measured using ImmunoCAP.

Cox proportional hazard models, adjusted for age, asthma, education, race/ethnicity, sex, and smoking history, were used to assess food sensitisation and cardiovascular death. Food sensitisation was defined as IgE >0.35 kU_A/L.

Results showed that 15% patients in the NHANES study were sensitised to at least one food, with 4%, 3%, 7%, and 6% being sensitised to CM, egg, peanut, and shrimp, respectively. Of the 960 patients in the MESA cohort, 4% were sensitised to CM, 0.8% to alpha-gal, and 7% to peanut. There were 264 cardiovascular deaths in the NHANES study, and 69 in the MESA cohort.

Sensitisation to CM only was associated with significantly higher risk of cardiovascular mortality in both studies (hazard ratio [HR]: 2.1; 95% confidence interval [CI]: 1.1–4.0; p=0.026 in the NHANES study, and HR: 3.8; 95% CI: 1.6–9.1; p=0.003 in the MESA cohort). In the MESA cohort, CM sensitisation was highly associated with non-atherosclerotic causes of cardiovascular mortality (HR:10.8; 95% CI: 3.5–32.4; p<0.001) and heart failure events, but not death due to atherosclerotic cardiovascular disease or myocardial infarction. Furthermore, an analysis limited to those who consumed a given food allergen in the NHANES study, unmasked shrimp sensitisation as a significant risk factor for cardiovascular mortality (HR: 2.9; 95% CI: 1.1–7.7; p=0.03).

From these findings, the authors concluded that sensitisation to food was associated with increased cardiovascular mortality, especially CM sensitisation. They highlighted that this association seems to be strengthened in regular consumers, which could indicate that even in the absence of symptoms, food sensitisation may not be benign.