Abstract Highlights

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The following selected highlights explore several groundbreaking abstracts presented at the European Academy of Allergy & Clinical Immunology (EAACI) Congress 2024. Topics covered include a novel strategy to detect asthma with nanosensors, the impact of pollution on rhinitis, and advancements in treatment of hereditary angioedema.

Benefit of Synbiotics in Infants with Cow's Milk Allergy

INFANTS with cow's milk allergy (CMA) who consume an amino acid-based formula with added synbiotics exhibit beneficial changes in their gut microbial composition, reports a study presented at EAACI 2024.

Researchers assessed the impact of amino acid-based formulas with (AAF-S) and without (AAF) synbiotics on faecal short-chain fatty acids (SCFA) and branched SCFA (BCFA) over a period of 12 months.

> **Researchers assessed the impact of amino acid-based formulas with and without synbiotics**

The study analysed faecal samples from children aged ≤13 months, all of whom had IgE-mediated CMA and were participants in the PRESTO study (NTR3725). Samples were collected at the start of the study, and again at 6, 12, 24, and 36 months. All samples were taken at least 60 minutes after feeding. The concentrations of SCFA and BCFA in these samples were measured using gas chromatography, and statistical comparisons between the AAF and AAF-S groups were performed using the Wilcoxon rank sum test.

Out of 169 randomised infants, faecal samples were collected from 161 (95%), with 85 (53%) assigned to the AAF group and 76 (47%) to the AAF-S group. The average age of the infants at baseline was 9.35±2.56 months. After 6 months of consuming the formula, children in the AAF-S group showed significantly lower median faecal propionate concentrations and a lower percentage of propionate relative to the total SCFA (acetate, butyrate, propionate) compared to the AAF group. Additionally, the AAF-S group had lower median faecal concentrations of valerate and BCFAs isobutyrate and isovalerate. Conversely, the percentage of acetate from the total SCFA was significantly higher in the AAF-S group. No significant differences in faecal butyrate concentrations were observed at 6 months, nor were there differences in SCFA or BCFA at baseline or at 12, 24, and 36 months.

The study concluded that the inclusion of synbiotics in an amino acid-based formula results in faecal microbial metabolite profiles that closely resemble those observed in healthy, exclusively breastfed infants. The observed effects on SCFA and BCFA concentrations were transient, appearing only 6 months after starting AAF-S. This may be due to reduced consumption of AAF-S and increased intake of complementary foods as children grow older.

Novel Breath Test Improves Accuracy of Asthma Diagnosis

RECENT findings presented at EAACI 2024 demonstrate the potential of a novel point-of-care (POC) breath test for asthma diagnosis, utilising deep neural networks (DNN) and nanosensors to provide a non-invasive and accurate diagnostic tool.

> **The method shows promise for diagnosing paediatric asthma, which could enhance early intervention strategies**

Standard asthma diagnosis relies heavily on detailed clinical history and physical examination, processes that can be subjective and inconsistent. To address the need for a more objective diagnostic method, researchers developed a breath test that analyses volatile organic compounds (VOC) in exhaled breath, combined with advanced machine learning techniques.

The study's cohort included 25 individuals, comprising 15 diagnosed with asthma and 10 healthy controls with no history of respiratory disease. Researchers collected end-tidal breath samples and analysed 13 VOC parameters using nanosensors. Principal component analysis was employed to identify key parameters that would inform the algorithm's learning process. The primary component of the diagnostic tool was a 13-layer deep neural network (DNN) model. This model was trained on a dataset of 688 data points, encompassing patient information, VOC biomarkers, and lung function parameters. The comprehensive dataset of a diverse range of parameters facilitated nuanced learning, enabling the DNN to classify respiratory health accurately.

The study's results indicate a high level of accuracy, with the model achieving a 93% accuracy rate and an area under the curve value of 0.95. These findings demonstrate the model's effectiveness in distinguishing between asthmatic and non-asthmatic individuals. Beyond its diagnostic capabilities, this breath analysis approach holds potential for asthma phenotyping and identifying the underlying drivers of inflammation. Researchers noted that the breath test could lead to the development of targeted therapies, including biologic treatments, offering more personalised care for asthma patients. Moreover, the method shows promise for diagnosing paediatric asthma, which could enhance early intervention strategies.

These findings led the authors to conclude that the integration of nanosensor technology with deep learning algorithms represents a significant step forward in asthma diagnosis. Furthermore, the VOC breath test not only improves diagnostic accuracy, but also has the potential to inform more tailored treatment approaches, thereby enhancing patient care and management.

Olfactory Training in Chronic Rhinosinusitis with Nasal Polyps

NOVEL research conducted at The First Affiliated Hospital of Nanchang University, China, has identified key factors that influence olfactory recovery in patients undergoing endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps (CRSwNP).

The research presented at EAACI 2024 highlights the potential benefits of combining glucocorticoid therapy with olfactory training (OT) to improve post-operative outcomes.

The study enrolled 213 patients with CRSwNP who had undergone endoscopic sinus surgery, and divided them into two groups: those who experienced olfactory recovery (99 patients) and those who continued to suffer from olfactory dysfunction (114 patients). The research aimed to develop a predictive model for olfactory recovery using logistic regression and support vector machine approaches.

Within the olfactory dysfunction group, patients were randomly assigned to three treatment subgroups: glucocorticoid therapy alone (GC group, 38 patients), olfactory training alone (OT group, 36 patients), and a combination of both therapies (GCwOT group, 34 patients). Follow-up assessments were conducted at 1, 3, and 6 months post-therapy, evaluating outcomes with various clinical scores, including the Total score for Threshold, Discrimination, and Identification (TDIS).

Results indicated that combination of glucocorticoids and OT significantly improved olfactory function in patients with eosinophilic CRSwNP (ECRSwNP) and reduced olfactory fluctuations. Notably, in the ECRSwNP group, the GCwOT group showed higher TDIS improvements at 3 and 6 months compared to the GC group. However, there was no significant difference compared to the OT group alone. For patients with non-eosinophilic CRSwNP, the GCwOT group showed better TDIS improvements at 1 month compared to the OT group alone.

The study concluded that age and olfactory cleft scores are critical factors influencing post-operative olfactory recovery. The researchers also emphasised that persistence in olfactory training for 6 months can yield significant improvements, particularly for patients unable to use steroids.

This research underscores the importance of personalised treatment plans for patients with CRSwNP and the potential of combining therapies to enhance recovery outcomes. The use of machine learning in developing prediction models marks a significant advancement in understanding and treating olfactory dysfunction post-surgery.

> **Combination of glucocorticoids and OT significantly improved olfactory function in patients with eosinophilic CRSwNP**

Air Pollution Impacts Respiratory Health in Patients with Rhinitis

AIR pollution has a detrimental impact on respiratory health, particularly in individuals suffering from allergic rhinitis (AR) and non-allergic rhinitis (NAR), according to a recent study presented at EAACI 2024.

The study, conducted at Kirikkale University Faculty of Medicine, Türkiye, included 58 participants to explore the effects of air pollution during both clean (summer) and polluted (winter) seasons (45 patients with rhinitis; 13 healthy controls; age distribution: 30.4+9.4 years). Of individuals with rhinitis, one-third reported dyspnoea, and the other third had completely controlled symptoms. Participants underwent pulmonary function and bronchial provocation tests (BPT), alongside clinical and laboratory evaluations, to measure bronchial airway hypersensitivity, serum oxidant-antioxidant stress levels, and nasal symptoms.

Key findings from the study revealed that during winter, when air pollution levels were higher, the forced expiratory volume in 1 second (FEV1%) decreased across all groups. Notably, the decline was more significant in the NAR group compared to the AR and control groups. In winter, the NAR group experienced a reduction in FEV1% from 93.9±10.4 to 90.6±11.3 (P=0.026) and a decrease in total antioxidant stress levels from 1.6±0.2 to 1.51±0.15 (P=0.041) compared to the summer. Similarly, FEV1% following BPT was shown to be lower in winter (P=0.020).

Despite the AR group showing a higher rate of positive BPT during polluted periods, the increase was not statistically significant. The study also found a negative correlation between changes in total nasal symptom scores and antioxidant stress indicators (r=-0.284; P=0.039), suggesting that worsening nasal symptoms were associated with decreased antioxidant defences.

The research underscores the adverse effects of air pollution on respiratory health, particularly in individuals with rhinitis. This is the first study to evaluate the relationship between AR and NAR phenotypes and bronchial hyper-responsiveness through the oxidant-antioxidant pathways influenced by air pollution. The findings highlight the need for increased awareness and measures to protect vulnerable populations from the harmful effects of polluted air, which deteriorates respiratory function not only in patients with rhinitis, but also healthy individuals.

> **This is the first study to evaluate the relationship between AR and NAR phenotypes and bronchial hyper-responsiveness through the oxidant-antioxidant pathways**

Real-World, Long-Term Effectiveness and Safety of Lanadelumab for Hereditary Angioedema

THE ENABLE study is an ongoing Phase IV, non-interventional, prospective, multicentre investigation evaluating the long-term effectiveness of lanadelumab in patients with hereditary angioedema (HAE) in real-world clinical settings.

Results from this interim analysis were presented at the 2024 EAACI Congress.

This interim analysis covers data from December 11th 2019–April 17th 2023, expanding on previously reported 24-month findings. The study involves patients aged ≥12 years with HAE Type I/II from 18 sites across Austria, Germany, Israel, Italy, Kuwait, Spain, and Switzerland. Participants are monitored for up to 24 or 36 months based on their enrolment date. The primary measure is the incidence rate ratio of HAE attacks post-lanadelumab initiation compared to the baseline period, while safety is assessed through treatment-emergent adverse events (TEAE).

Out of 140 enrolled patients (129 with Type I; 10 with Type II; 1 undifferentiated), 138 received lanadelumab. The mean age was 41 years, with a majority being female (62.3%) and White (97.8%). The mean time from HAE symptom onset to diagnosis was 8.8 years, and the average duration on lanadelumab was 603.6 days. Initially, 97.1% of patients were started on a biweekly dose, with 43.1% reducing to a monthly dose by month 36. The HAE attack rate dropped significantly from 3.70 attacks/month at baseline to 0.35 on treatment, with 65.2% experiencing a ≥90% reduction. Most TEAEs (84.0%) were mild or moderate, and unrelated to lanadelumab. There were no deaths or serious treatment-related TEAEs. The study confirms lanadelumab's long-term efficacy in reducing HAE attacks, and a safety profile consistent with prior research.

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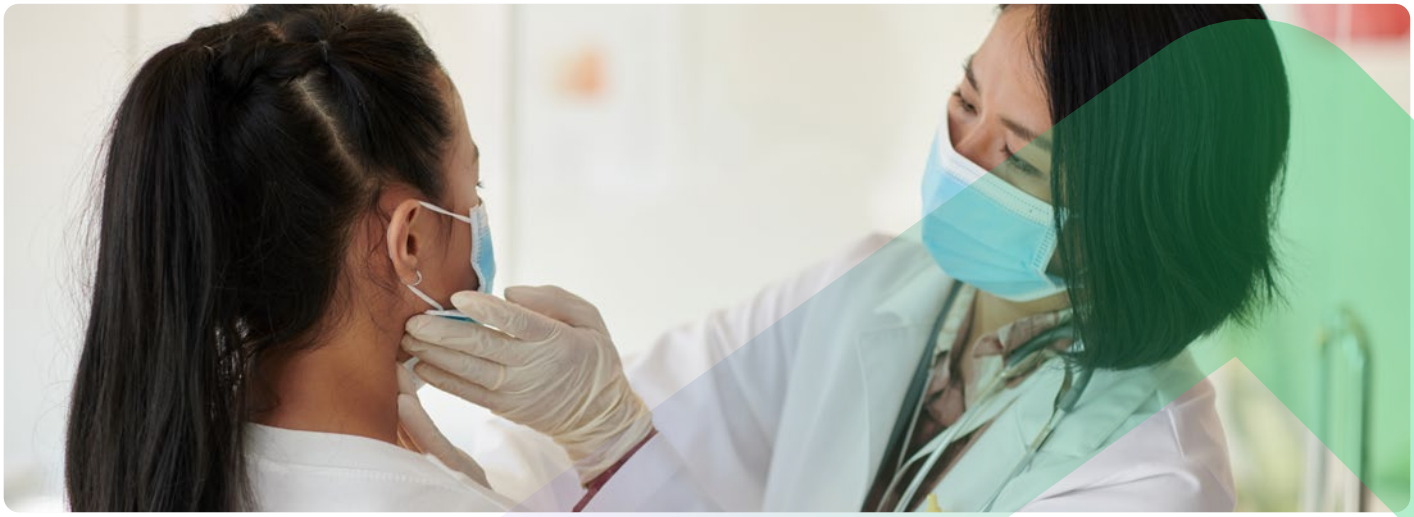

Early-Life Infections: Risk of Asthma and Adverse Lung Function

REDUCING the number of common infections experienced in early-life could be a strategy for paediatric asthma primary prevention, according to research presented at EAACI 2024.

Whilst the development of asthma has been linked to infections of the respiratory tract in early-life, details on the subtypes and burden of these infections, and their role in asthma development, are lacking.

> **Those who experience a higher infection burden (>16) had a significantly increased risk for developing asthma**

Researchers from Copenhagen Prospective Studies on Asthma in Childhood (COPSAC), Gentofte, Denmark, used data from the $COPSAC_{2010}$ birth cohort and generalised estimating equations to evaluate the association between early-life infections and their subtypes, with the risk of asthma in those aged 3–10 years, and lung function at 10 years.

In total, 662 children with prospectively registered daily diary entries of acute otitis media, acute tonsilitis, cold, fever, gastroenteritis, and pneumonia, between the ages of 0–3 years, with a diagnosis of asthma between the ages of 3–10 years, were included in the study.

The analysis found that, on average, between the ages of 0–3 years, children experienced 16 infections, and those who experience a higher infection burden (>16) had a significantly increased risk for developing asthma between 3–10 years (adjusted odds ratio: 3.61; 95% CI: 2.39–5.45; P<0.001). This was driven by cold, fever episodes, gastroenteritis, and pneumonia (P<0.050), but not by acute otitis media or acute tonsillitis. This association between infections and asthma risk was higher in children with a diagnosis of allergic rhinitis at 6 years of age (P-interaction=0.046). Additionally, the study identified that increased infection burden was associated with reduced lung function and a greater fractional exhaled nitric oxide by the age of 10 years.

From the study findings, the authors concluded that primary prevention of paediatric asthma could include strategies aimed at reducing the burden of early-life infections.

Drug Allergy: Severity and Impact on Quality of Life

NEW data from the BIOGRIAL study were presented at EAACI Congress 2024.

The study set to explore the severity of drug allergy and quality of life (QoL) for the individuals involved.

Utilising data from 18 allergy-referral centres involved in the BIOGRIAL study in Spain, the authors analysed the frequency and severity of immediate allergic reactions to drugs in 337 patients. In total, there were 436 reported reactions, of which 54.1% (n=236) were secondary to non-steroidal anti-inflammatory drugs (NSAID), 30.2% occurred following β-lactam antibiotic use, and 15.4% occurred as a result of other drug classes.

Reaction severity was graded using the Drug-adapted version of the Food Allergy Severity Score (D-FASS). Severe reactions were defined as Grade 4 (bronchial/laryngeal involvement) and Grade 5 (cardiovascular/neurological involvement). QoL was measured using the drug hypersensitivity questionnaire (DrHy-Q).

The findings revealed that severe reactions secondary to β-lactams were more common than severe reactions resulting from NSAID use. In the β-lactam group, 60.6% of reactions were severe, with 43.2% classified as Grade 5, compared to 38.6% of reactions being severe in the NSAID group, where 19.1% were classified as Grade 5. These differences in severity were significant (P<0.01).

> **Those with severe drug reactions had a worse QoL, particularly in the fear and insecurity domains**

In terms of QoL, 145 individuals with NSAID allergy, 123 with β-lactam allergy, and 59 with other drug allergies completed the DrHy-Q questionnaire. This highlighted that those with severe drug reactions had a worse QoL, particularly in the fear and insecurity domains. Responses to the DrHy-Q questionnaires also revealed that QoL was worse for those with β-lactam allergic reactions than for those with other drug allergies (P=0.03).

The authors concluded that reaction severity is different between those with β-lactam and NSAID allergies, and that irrespective of drug type, those with severe allergic reactions have a worse QoL.

Deucrictibant: A New Therapeutic Option for Hereditary Angioedema

PROMISING results from a recent Phase II study pesented at EAACI 2024 have shown that deucrictibant, a selective antagonist of the bradykinin B2 receptor, may be effective for the treatment of hereditary angioedema (HAE), both as a preventative measure and on-demand.

HAE attacks, which are caused by excess bradykinin activating bradykinin B2 receptors, can significantly impact patients' quality of life. Therefore, these findings offer a valuable new therapeutic option for patients.

The CHAPTER-1 study (NCT05047185) evaluated the efficacy and safety of deucrictibant for long-term prophylaxis of HAE attacks. Conducted in two parts, the study involved 34 participants from Canada, Europe, UK, and USA. In part 1, participants received a double-blinded treatment with either a placebo or one of two doses of deucrictibant (20 mg/day or 40 mg/day) for 12 weeks. In part 2, participants had the option to continue with an open-label treatment of deucrictibant at 40 mg/day.

Health-related quality of life (HRQoL) was a key focus, assessed through the Patient Global Assessment of Change (PGA-change) and the Angioedema Quality of Life questionnaire (AE-QoL). The PGA-change measures overall changes in HRQoL on a five-point scale from 'much worse' to 'much better'. The AE-QoL questionnaire, specifically validated for HAE, evaluates HRQoL across four domains: 'nutrition', 'fatigue/mood', 'fear/shame', and 'functioning'.

In part 1 of the study, deucrictibant showed significant improvement in HRQoL. At Week 12, 80% of participants on 20 mg/day, and 78% on 40 mg/day reported feeling "much better" in the PGA-change assessment, compared to just 13% in the placebo group. All participants (100%) receiving 40 mg/day of deucrictibant reported improvement, while 63% of the placebo group reported "no change." Additionally, the AE-QoL scores showed marked improvements. Participants on 20 mg/day and 40 mg/day of deucrictibant saw their scores improve by 19.0 and 25.9 points, respectively, compared to an 11.9-point improvement in the placebo group. The domains 'fear/shame' and 'functioning' showed the greatest improvement with deucrictibant treatment.

The CHAPTER-1 trial results indicate that prophylactic treatment with oral deucrictibant for 12 weeks can lead to clinically meaningful improvements in the quality of life for individuals with HAE. The significant enhancements in HRQoL measures highlight deucrictibant's potential as an effective long-term treatment option for HAE.

Health-related quality of life was a key focus

Effect of Air Pollution Exposure in Pregnancy on DNA Methylation

MODULATION of the immune system, pulmonary disease exacerbation, and cardiovascular disease are known consequences of exposure to ambient air pollution.

However, the effect of this exposure on health in pregnant persons is sparse. New research presented at EAACI Congress 2024, endeavoured to explore the association between PM2.5 (particulate matter <2.5 µM) and DNA methylation in pregnancy.

When controlling for pregnancy status, 321 differentially methylated CpGs were found to be associated with PM2.5

In a case-control analysis, researchers looked at data from 54 pregnant individuals and 84 age-matched non-pregnant individuals. Using US Environmental Protection Agency data and an individual's zip code, PM2.5 was calculated. Following extraction of DNA from peripheral blood mononuclear cells, DNA methylation was assessed via a custom asthma and allergy array that targeted functional CpG sites. After quality control and processing, the researchers looked at the relationship between PM2.5 and DNA methylation, pregnancy status, and the interaction between them.

When controlling for pregnancy status, 321 differentially methylated CpGs were found to be associated with PM2.5 levels. While controlling for PM2.5 levels, 17 differentially methylated CpGs were found to be associated with pregnancy. Interaction term for pregnancy and PM2.5 was found to be associated with 107 differentially methylated CpGs. Moreover, genes located closest to the PM2.5 differentially methylated CpGs were enriched for microRNA pathways.

Overall, these preliminary results highlight associations between PM2.5, DNA methylation, and pregnancy; and indicate that pregnancy status modifies the PM2.5-DNA methylation association. The team concluded that further analysis and epigenetic research is needed to understand the mechanisms that underly microRNA dysregulation in pregnancy.