**Oral Abstract Presentations**

**Respiratory and Skin Allergy – Session A**

1. Yuto Nakamura
   “Aspergillus sensitization in elderly patients with asthma: clinical features”

Yuto Nakamura¹, Kai Ryu¹, Kazuki Uchida¹, Yuichiro Kawasaki¹, Kentaro Watai², Akio Mori¹, Masami Taniguchi², Yuma Fukutomi¹, Yosuke Kamide¹, Kiyoshi Sekiya¹
¹Sagamihara National Hospital, Japan, ²Shonan Kamakura General Hospital, Japan

**Background**
Aspergillus fumigatus sensitization has been associated with asthma, especially severe and/or difficult-to-treat asthma, and allergic bronchopulmonary aspergillosis (ABPA) as complications. In addition, elderly patients with asthma have higher rates of morbidity and mortality directly attributable to their disease. However, the clinical features of aspergillus fumigatus sensitization in elderly asthma are unclear.

**Methods**
We performed a cross-sectional study of 234 consecutive elderly patients with asthma aged 60 years or older who visited Sagamihara National Hospital from February 2020 to November 2020, of whom 227 underwent aspergillus-specific immunoglobulin (Ig) E testing. Clinical characteristics of aspergillus sensitized and non-sensitized patients were compared. The study protocol (No. 2019-01) was approved by the Ethics Committee of Sagamihara National Hospital. All patients provided written informed consent.

**Results**
Aspergillus sensitization was identified in 63 of 227 elderly patients with asthma (27.8%) and 9 were diagnosed with ABPA (4.0%). Compared with aspergillus non-sensitized patients, those who were sensitized had asthma of significantly longer duration (p <0.001), with more oral corticosteroid use (p=0.006), more hospitalization due to asthma exacerbations (p=0.041), higher total IgE levels (P <0.001), higher peripheral blood eosinophil levels (P=0.043), and were more often male (P=0.040). In addition, the forced expiratory volume in 1 second (%) predicted and the body mass index were significantly lower than in non-sensitized patients (p=0.007, p = 0.008, respectively).

**Conclusion**
The proportion of elderly patients with asthma who are sensitized to aspergillus is high; such patients exhibit distinct clinical features. We need to consider aspergillus sensitization when we examine elderly patients with asthma who have the characteristic clinical features described here.
2. Stefanie Busold

“Toll-like receptor 4 and syk kinase shape dendritic cell-induced immune activation to major house dust mite allergens”

Stefanie, Busold¹, Jaap H., Akkervaas¹, Esther M., Zijlstra-Willems¹, Kees, van der Graaf², Sander W., Tas¹, Esther C., de Jong¹, Teunis B. H., Geijtenbeek¹, Ronald, van Ree¹

¹Amsterdam University Medical Centers, The Netherlands, ²Citeq Biologics, The Netherlands

Background

House dust mite (HDM) is a major cause of respiratory allergic diseases. Dendritic cells (DCs) play a central role in orchestrating adaptive allergic immune responses. However, it remains unclear how DCs become activated by HDM. Biochemical functions of the major HDM allergens Der p 1 (cysteine protease) and Der p 2 (MD2-mimick) have been implicated to contribute to DC activation.

Methods

We investigated the immune activating potential of HDM extract and its major allergens Der p 1 and Der p 2 using monocyte-derived DCs (moDCs). Maturation and activation markers were monitored by flow cytometry and cytokine production by ELISA. Der p 1 depletion and proteinase K digestion were used to investigate the involvement of proteins, and in particular of the major allergens. Inhibitors of Toll-like receptor 4 (TLR4) and of C-type lectin receptors (CLRs) were used to identify the involved receptors.

Results

HDM extract induced DC maturation and cytokine responses in contrast to the natural purified major allergens Der p 1 and Der p 2. Proteinase K digestion and removal of Der p 1 did not alter the immune stimulatory capacity of HDM extract. Blocking TLR4 signalling reduced the HDM-induced IL-10 and IL-12p70 induction, but not IL-6. In contrast, antibodies against the CLRs Dectin-1, Dectin-2, and DC-SIGN did not affect cytokine responses. Strikingly, spleen tyrosine kinase (Syk) inhibition partially reduced IL-6, IL-12 and completely blocked IL-10.

Conclusion

Our data strongly suggest that HDM-induced immunity is neither dependent on Der p 1 nor Der p 2, but depends on Syk and TLR4 activation, suggesting crosstalk between Syk and TLR4 pathways. Our data further
indicate that a Syk-dependent receptor other than Dectin-1 and Dectin-2 might be involved in immune activation by HDM.

3. Sandra Pfeiffer
“Patterns Of IgE Cross-Reactivity Between Enolases”

Sandra Pfeiffer1, Clio-Melina Sperl1, Katharina Nöbauer2, Margarete Focke-Tejkl3, Katja Sterflinger4, Ines Swoboda4
1Campus Vienna Biocenter, Austria, 2University of Veterinary Medicine, Austria, 3Medical University of Vienna, Austria, 4Institute of Natural Sciences and Technology in the Arts Academy of Fine Arts Vienna, Austria

Background
Enolases can cause respiratory, food, and contact allergies and are further unique in that they can represent allergens in the three major kingdoms animals, plants, and fungi. The fact that they are highly conserved, ubiquitous enzymes suggests potential cross-reactivity among enolases. The purpose of our study was to analyze the cross-reactive potential of enolases from various allergen sources including molds, plant pollen and foods, with the aim to gain a better understanding of the enzymes’ pan-allergenic character.

Methods
Protein extracts were prepared from plant pollen and animal-derived foods, and recombinant enolases were produced from important allergenic mold species (Alternaria alternata, Cladosporium herbarum, Aspergillus fumigatus, Penicillium chrysogenum, Paecilomyces variotii). IgE-reactivity and cross-reactivity were then investigated by ELISAs, immunoblots, and inhibition experiments with sera from polysensitized patients.

Results
IgE immunoblots and ELISAs, performed with the protein extracts and the recombinant enolases, showed that polysensitized patients reacted with enolases from multiple allergen sources. Interestingly, IgE inhibition experiments revealed that IgE cross-reactivity only occurred between enolases from closely related species, but not between enolases from distantly related organisms. Inhibition experiments further demonstrated also in case of highly homologous enolases the presence of cross-reactive, but also of species-specific IgE-epitopes.

Conclusion
It was shown that IgE antibodies from polysensitized patients recognized enolases from different molds, pollen, and food sources. However, IgE cross-reactivity was only seen between enolases from closely related species, whereas enolases from distantly related organisms seem to lack cross-reactivity. Our findings will contribute to an improvement of allergy diagnosis and patient-tailored prevention strategies.

4. Gwang Cheon Jang
“Air pollution, pollen and allergic diseases: Analyzed based on artificial intelligence algorithm”

Gwang Cheon Jang1, Seong-Yun Jeon1, Jeong Wook Kim2, Young-Jin Choi3, Jae-Won Oh3
1NHIS ILSAN Hospital, Republic of Korea, 2Seoul School of Integrated Sciences and Technologies, Republic of Korea, 3Hanyang University Guri Hospital, Republic of Korea

Background
Allergic diseases are affected by genetic and environmental predisposition. Allergic diseases are on the rise all over the world, and this increase is affected by the continuation and exacerbation of the disease by
environmental factors such as pollen and air pollution as well as genetic factors. So we investigated the air pollution and pollen as environmental factors.

**Methods**

Allergic diseases of the National Health Insurance Corporation’s claim data, pollen data and the Ministry of Environment air environment data (SO2, O3, NO2, PM10, CO) were analyzed based on artificial intelligence algorithms, between Jan, 1 2011 and Dec. 31 2015. A total 463,091 patients was included, after regional matching.

**Results**

The importance of environmental factors affecting the number of outpatient for atopic dermatitis was in the order of SO2, O3, NO2, PM10, CO (AUC: 0.74). In the time series analysis, pollen concentration 7 days before was correlated with current hospitalization for asthma (p <0.0001). PM10 concentration 12 days before was correlated with current hospitalization for asthma (p=0.0002). The importance of atmospheric environmental factors affecting hospitalization for asthma was in the order of SO2, PM10, NO2, CO, and O3 (AUC: 0.69).

**Conclusion**

Pollen concentration and PM10 was correlated with current hospitalization for asthma. Air pollution affecting the number of outpatient for atopic dermatitis. Among the environmental factors, there are many research results on NO2, but in this study, SO2 is so important that further research is needed.

5. Marianna Kulka

“Substance P analogs devoid of key residues fail to activate human mast cells via MRGPRX2”

*Marianna Kulka*, Shammy Raj1, Stepan, Hlushak2, Narcy, Arizmendi2, Andriy, Kovalenko1

1Nanotechnology Research Center, Confirm Country, 2University of Alberta, Canada

**Background**

Mast cells play an important role in the disease pathogenesis by secreting immunomodulatory molecules. Mast cells are primarily activated by the crosslinking of their high affinity IgE receptors (FcepsilonRI) by antigen bound immunoglobulin (Ig)E antibody complex. However, mast cells can also be activated by mas related G protein-coupled receptor X2 (MRGPRX2), in response to a range of cationic secretagogues, such as substance P (SP) which is associated with pseudo-allergic reactions. We have previously reported that the in vitro activation of mouse mast cells by basic secretagogues is mediated by the mouse orthologue of the human MRGPRX2, MRGPRB2.

**Methods**

To further elucidate the mechanism of MRGPRX2 activation, we studied the time-dependent internalization of MRGPRX2 by human mast cells (LAD2) upon stimulation with the neuropeptide SP. In addition, we performed computational studies to identify the intermolecular forces that facilitate ligand-MRGPRX2 interaction using the known peptide agonist, substance P (SP). The computational predictions were tested experimentally by activating human mast cells (LAD2) with SP analogs that were missing key amino acid residues.

**Results**

Our data suggest mast cell activation by SP causes internalization of MRGPRX2 within 1 min after stimulation. Hydrogen bonds (h-bonds) and salt bridges govern the biding of SP to MRGPRX2. Arg1 and Lys3 of SP are key residues that are involved in both h-bonding and salt bridge formations with Glu164 and Asp184 of MRGPRX2, respectively. In accordance, SP analogs SP1 and SP2 devoid of key residues failed to activate MRGPRX2.
degranulation. However, both SP1 and SP2 caused a comparable release of chemokine CCL2. Further, SP analogs SP1-5 did not activate tumor necrosis factor (TNF) production.

**Conclusion**

The results provide important insight into the events that result in mast cell activation through MRGPRX2 and highlight the important physiochemical characteristics of a peptide ligand that facilitates ligand-MRGPRX2 interactions. The results and important in understanding the activation through the MRGPRX2 and will aid in designing novel therapeutics.

**References**


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Mohammad Farazuddin

“The inhibition of retinoic acid signaling in innate immune cells paradoxically suppresses respiratory syncytial virus infection through enhanced antiviral immunity.”

Mohammad Farazuddin, Grant Acker, Joseph Zouro, Pamela Wong, Susan Morris, Andrew Rasky, Chang Kim, Nicholas Lukacs, James Baker

University of Michigan, United States

**Background**

Respiratory syncytial virus (RSV) infection is a major cause of morbidity and mortality in children. It is also associated with enhanced Th2 immunity and asthma. Vitamin A deficiency causes deficient mucosal immunity because of the central role of retinoic acid (RA) in generating mucosal immunity and enhancing immune cell function. We therefore sought to evaluate the effect of RA signaling deficiency on immune responses to RSV infection.

**Methods**
We blocked RA signaling in dendritic cells and alveolar macrophages (two cells thought to be crucial to RSV innate immunity) using transgenic mice expressing a dominant negative form of retinoic acid receptor α (RARα) under the CD11c promoter (CD11c-dnRARα). These animals were infected with RSV and compared to wild-type WT littermates.

**Results**
Unexpectedly, RSV infected CD11c-dnRARα animals had significantly lower viral burden, reduced pathology and more Th1 polarized immunity than WT mice. In addition, when bone marrow derived dendritic cells (BMDCs) from CD11c-dnRARα mice were infected with RSV, we found enhancement in the expression of genes related to innate and Th1 adaptive immunity, particularly interferons, while genes associated with Th2 immunity and viral replication were significantly down-regulated. In contrast, viral replication was enhanced when RA was added to cultured WT BMDCs infected with RSV.

**Conclusion**
These findings indicate that RA enhances RSV infection in innate cells. Inhibiting RA signaling in these cells improves immunity against RSV infection and decreases RSV pathology, while also reducing Th2 skewing. The results have potential implications for treating RSV infection and in RSV vaccine development.

7. Sung Weon Cho
“The induction of histamine synthesis from mouse immature mast cells with cytokines”

*Sung-weon Cho*, *Bong Jun Sur*, *Kyung Sook*¹
¹*Korea University College of Medicine, Republic of Korea*

**Background**
Histamine is the amines produced mainly by mast cells and raises allergic diseases including even anaphylaxis. To comprehend the allergic disease raised with histamine from mast cells, histamine synthesis is necessary to be investigated in vitro. The cell lines used for mast cell study was not appropriate for histamine production. However, bone marrow derived mast cells (BMMC) are the immature mast cells prepared with bone marrow cells in the presence of cytokines of IL-3 and stem cell factor (SCF) and regarded to produce low level histamine. Mouse BMMC (M-BMMC) was investigated for histamine synthesis whether affected by cytokine concentrations.

**Methods**
Bone marrow cells are harvested from Balb/c mouse femor and cultured in the presence of each concentration of IL-3 and SCF (50 ng/ml as high or H, 10 ng/ml as low or L) for 28 days. The cells were supplied with fresh media by 7 days and maintained in cell population rate of 5.5 x 10⁵/ml (high-cell population, H-C) or 1.1 x 10⁵/ml (low-cell population, L-C). The cells were washed and then dissolved in perchloric acid. The lysate was washed through hexane to remove histidine. The histamine was labeled with o-phenylene diamine for fluorescence assay.

**Results**
In the H-C, the histamine level at culture day 28 was 4.12 pg/cell both with high IL-3 (H-3) and with high SCF (H-SCF), and that was 4.59 pg/cell with low IL-3 (L-3) and H-SCF. However, that was 1.83 pg/cell with L-3 and L-SCF. In the L-C, that was 0.97 pg/cell both with L-3 and with H-SCF, and 0.86 pg/cell with L-3 and L-SCF. That was 0.64 pg/cell with non-cultured BMC.

**Conclusion**
These results indicated that mouse stem cell factor is the cytokine to enhance histamine production of mouse bone marrow derived mast cells prepared in the high cell population rate.

8. Ricardo Martinez Tenopala
   “Expression of HIF-1α in pediatric asthmatic patients”

Ricardo Martinez-Tenopala¹, Victor Gonzalez-Uribe¹, Alejandra Osorio-Martinez¹, Jimena Prieto-Gomez¹, Christian Alcocer-Arreúin²
¹Facultad Mexicana de Medicina de Universidad La Salle, Mexico, ²Sin Alergia GDL, Mexico

Background
Asthma presents airway remodeling; is explained by the morphological changes involving cells and tissue that constitute bronchioles. Different studies have implied that Hypoxia-inducible factor 1α (HIF-1α) plays a key role in the physiopathology of asthma since the inflammatory process and bronchoconstriction promote hypoxia. HIF-1α acts as a central regulator of cellular oxygen levels, therefore, playing a critical role in inflammatory and immune responses

Methods
A descriptive, cross-sectional, and comparative study was held, in 133 patients, between 6 to 17 years of age, with previous diagnosis of asthma, in two Pediatric Hospitals in Mexico City, Mexico. HIF-1α levels was measured by immunocytochemistry. The glass slides were analyzed by microscope and the positive cells, were quantified in 4 fields per glass slide using an image analyzer.

Results
HIF-1α and HIF levels were significantly higher in patients with asthma and even higher in patients with asthma attacks with p < 0.0001 (95% CI).
No significant difference was found between the percentage of expression of the transcription factor HIF-1α between the groups with intermittent asthma and the groups with mild persistent asthma, nor in the expression of the transcription factor between asthma and asthma crisis groups.

Conclusion
The expression of nuclear HIF and HIF-1α is increased in peripheral mononuclear cells in patients with asthma and even more elevated in patients with asthma crisis compared to healthy patients, suggesting the importance of this factor in the pathogenesis of this disease.

References


Respiratory and Skin Allergy – Session B

1. Nandini Ghosh
   “Study of cross-reactivity among different pectate lyase allergens and designing multi-epitope vaccine”

   Nandini Ghosh¹, Gaurab Sircar², Sudipto Saha³, Swati Gupta Bhattacharya³
   ¹Vidyasagar University, India, ²Presidency University, India, ³Bose Institute, India

   Background
   A large proportion of the population across the continents is found to be allergic to pectate lyase allergens from different sources. Asteraceae pollen grains harbor pectate lyase as major allergen. Pectate lyase allergens are also present among Cupressaceae pollen grains. This study aims to find out the cross-reactivity among different allergenic pectate lyases reported from Asteraceae pollen grains and to design a candidate vaccine against pectate lyase.
Methods
The cross-reactivity among different pectate lyase allergens, such as Hel a 6, Amb a 1, and Art v 6 was studied through inhibition ELISA, inhibition western blot, and histamine release assay. Their B cell epitopes were predicted using ABCpred and BCEpred servers. The sequence conservation of predicted and reported IgE epitopes of various pectate lyases was compared. Epitopes with more than 55% sequence conservation were used to design in silico multi-epitope chimeric vaccine. Multiple epitopes were joined with a carrier molecule. Different carrier molecules and combinations of peptides were used and their properties were studied bioinformatically.

Results
Around 60-80% cross-reactivity was found between Hel a 6, Amb a 1, and Art v 6 through inhibition ELISA. Cross-reactivity among them was also confirmed by inhibition blot as well as through mediator release from Hel a 6 sensitized effector cells, cross-stimulated with Amb a 1 and Art v 6. Conserved IgE epitopes were taken to design the vaccine construct. PreS protein of hepatitis B virus and Cholera toxin B (CTB) along with fractions of tetanus toxoid (TTFr) were used as carrier molecules. CTB and TTFr-linked molecules showed greater stability. Both constructs were capable of inducing a protective response.

Conclusion
Multi-epitope vaccine designing is a novel approach for the treatment of pectate lyase allergic patients. Pectate lyase is a pan-allergen. The IgE epitope sequences of different pectate lyases are more or less conserved. So patients allergic to pectate lyase allergens may be given relief by using a single candidate vaccine against all pectate lyases.

2. Hyemi Jee
“Differences in clinical characteristics between adults and children with allergen immunotherapy for allergic rhinitis in Korea”

Hyemi Jee1, Ju Hee Kim2, Young Hyo Kim3, Jung-Won Park4, Youngmin Ahn5, Jeong-Hee Choi6, Hey-Sung Baek2, Mi-Ae Kim5, Hwa Young Lee7, Seon Tae Kim5, Kyung Hee Park4, Man Yong Han1

1CHA Bundang Medical Center, CHA University School of Medicine, Republic of Korea, 2Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Republic of Korea, 3Inha University School of Medicine, Republic of Korea, 4Yonsei University College of Medicine, Republic of Korea, 5Jang’s Woman’s Hospital, Republic of Korea, Hallym University Dongtan Sacred Heart Hospital, Republic of Korea, 7College of Medicine, Seoul St Mary’s Hospital, The Catholic University of Korea, Republic of Korea, 8Gil Medical Center, College of Medicine, Gachon University, Republic of Korea

Background
We aimed to analyze the similarities and differences of clinical characteristics between adults and children patients receiving allergen immunotherapy (IT) for allergic rhinitis.

Methods
A multicenter study in South Korea has been conducted with 172 patients diagnosed with allergic rhinitis and undergoing IT, consisting of 87 children (mean age: 9.9 years) and 85 adults (mean age: 31.6 years). Clinical characteristics were obtained from face-to-face interviews and questionnaires.

Results
There are 61 (70.1%) children and 68 (80.0%) adults of subcutaneous IT, and 26 (29.9%) children and 17 (20.0%) adults of sublingual IT (P = 0.134). The comorbidity of atopic dermatitis is more prevalent in children (20.7% vs 9.4%, P = 0.039). Oral allergy syndrome (OAS) in children is similar in adults and children in prevalence, but there are more food types of OAS and more systemic symptoms of OAS in children.

**Conclusion**
This study showed the differences in the severity of allergic rhinitis, drug use, comorbidity, OAS, and the concentration of sIgE of D. farinae and pattern of IT prescription between adults and children as subjects of IT.

3. Noémi Anna Nagy
“Nanocarriers containing tolerogenic adjuvants for the treatment of allergy induce regulatory circuits in human dendritic cells

Noémi Anna Nagy1,2, Fernando Lozano Vigario3, Rinske Sparrius1,2, Toni M. M. van Capel1,2, Sander W. Tas1,2, I. Jolanda M. de Vries4, Teunis B. H. Geijtenbeek1,2, Bram Slütter3, Ronald van Ree1,2, Esther C. de Jong1,2
1Amsterdam UMC, University of Amsterdam, The Netherlands, 2Amsterdam Institute for Infection & Immunity, The Netherlands, 3Leiden Academic Center for Drug Research, The Netherlands, 4Radboud University Medical Center, The Netherlands

**Background**
Nanomedicine features promising methods for tolerogenic manipulation of dendritic cells (DCs) and the ensuing regulatory adaptive immune response. In nanocarriers, such as liposomes, tolerogenic adjuvants can be combined with allergens to simultaneously target DCs in tissue and achieve allergen-specific tolerance in vivo.

**Methods**
To select an optimal vaccine carrier, we examined the uptake and functionality of six different liposome formulations by human monocyte-derived DCs (moDCs) and skin DCs (Langerhans cells and dermal DCs). In addition, we loaded liposomes with vitamin D3 (VD3) or retinoic acid (RA), two adjuvants possessing potent immune tolerizing potential. We investigated the tolerogenic effect on liposome-primed moDCs and skin DCs by extensive phenotyping and assessment of regulatory function of CD4+ T cells raised by our modulated DCs.

**Results**
Imaging flow cytometry measurement revealed that cationic formulations were internalized less effectively by DCs than neutral or anionic formulations. Strikingly, RA and VD3-liposome treated moDCs induced the growth of FoxP3+ and IL-10+ regulatory CD4+ T cells that inhibited bystander memory T cell proliferation. Skin injection of vitamin-loaded liposomes selectively stimulated the migration of CD14+ skin DCs, which also fostered the development of suppressive, FoxP3+ T cells. The induced FoxP3+ T cells had higher expression of the inhibitory markers TIGIT, ICOS, PD1, or CTLA-4. Furthermore, liposome adjuvant-primed moDCs abrogated inflammatory T helper 1 and T helper 17 type responses.

**Conclusion**
These results suggest that anionic liposomes would be more suitable as vaccine carriers for dermal application. Most importantly, nanoparticulate VD3 and RA appear to be potent tolerogenic adjuvants for DC-mediated induction of regulatory T cell responses, serving as a promising platform for allergen-specific treatments.

4. Jun-Pyo Choi
“Lactic acid bacteria strains showed different therapeutic effects according to the types of airway inflammation”
Heon Cho, Sae Hun Kim, Yoon-Seok Chang

Seoul National University Bundang Hospital, Republic of Korea, Seoul National University Medical Research Center, Republic of Korea, College of Life Science and Biotechnology, Korea University, Republic of Korea, Seoul National University College of Medicine, Republic of Korea

Background
Asthma is a chronic inflammatory airway disease with increasing prevalence in worldwide. Potential therapeutic effects of probiotics have been reported. However their role in airway inflammation has not been fully elucidated. In this study, we aimed to investigate the immune-regulatory effects of the lactic acid bacteria strains in the eosinophilic or neutrophilic airway inflammation.

Methods
Different types of airway inflammation were induced by intranasal stimulation of ovalbumin (OVA) after sensitization of OVA with alum or double-stranded RNA (dsRNA) using C57BL/6 mice. At the same time, 4 kinds of lactic acid probiotics (PG1, PG2, PG3, and PG4, 1x10⁹ CFU/mouse) were delivered intragastrically from the start to the end of OVA stimulation. Airway inflammation and immunological parameters were evaluated 24 hours after last OVA stimulation.

Results
In the eosinophilic airway inflammation model induced by OVA with alum, PG1 and PG2 administration induced decrease of neutrophil and eosinophil infiltration. PG3 and PG4 groups also showed decreased tendency of airway inflammation, which was not significant. PG1, PG2, and PG3 administration decreased IL-4, IL-5, IL-13, IL-17, and eotaxin. In the neutrophilic airway inflammation model induced by OVA with dsRNA, PG3 and PG4 administration decreased airway inflammation. In addition, PG3 and PG4 groups showed decreased OVA-specific IgG2c, IP-10, and MCP-1. Interestingly, administration of PG4 induced elevation of IL-4 and IL-13.

Conclusion
This study showed the potential therapeutic effects of lactic acid probiotics which could be affected by the type of airway inflammation and species of lactic acid bacteria.

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5. Jeong-Hee Choi
“A meta-analysis of direct comparison between Subcutaneous and Sublingual immunotherapy in perennial allergic rhinitis”

Hyemi Jee, Ju Hee Kim, Young Hyo Kim, Jung-Won Park, Youngmin Ahn, Jeong-Hee Choi, Hey-Sung Baek, Mi-Ae Kim, Hwa Young Lee, Seon Tae Kim, Kyung Hee Park, Man Yong Han

CHA Bundang Medical Center, CHA University School of Medicine, Republic of Korea, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Republic of Korea, Inha University School of Medicine, Republic of Korea, Yonsei University College of Medicine, Republic of Korea, Jang’s Woman’s Hospital, Republic of Korea, Hallym University Dongtan Sacred Heart Hospital, Republic of Korea, College of Medicine, Seoul St Mary’s Hospital, The Catholic University of Korea, Republic of Korea, Gil Medical Center, College of Medicine, Gachon University, Republic of Korea

Background
A meta-analysis of head-to-head comparisons of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) for perennial allergic rhinitis (AR) has not been performed. This study aimed to compare the efficacy, safety, and adherence of SCIT and SLIT in patients with house dust mite (HDM)-sensitized AR through a meta-analysis of head-to-head comparative studies.

Methods
A meta-analysis of head-to-head comparisons of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) for perennial allergic rhinitis (AR) has not been performed. This study aimed to compare the efficacy, safety, and adherence of SCIT and SLIT in patients with house dust mite (HDM)-sensitized AR through a meta-analysis of head-to-head comparative studies.

Results
Six RCTs and three NRS scores were analyzed. No statistically significant difference was noticed in improvement of symptoms and medication scores between SCIT and SLIT groups. Systemic adverse events occurred more frequently in SCIT than in SLIT in both RCT (RR 3.97, 95% Confidence interval (CI) 0.50–31.57) and NRS (RR 5.48, 95% CI 1.94–15.50). SCIT showed significantly higher adherence than did SLIT (RR 1.16, 95% CI 0.92–1.47).

Conclusion
No significant difference in efficacy was noticed between the two modalities for HDM-sensitized AR. However, SLIT had relatively low number of systemic adverse reactions, and SCIT had comparatively preferable adherence.

6. Krisztina Moric
“eHealth - another benefit of sublingual immunotherapy”

Krisztina Moric¹, Katalin Balogh¹, Laszló Babai², Tünde Szobonya¹, Péter Ilosvai², Balázs Szilágyi²
¹Prima Medica, Budai Allergiaközpont, Hungary

Background
Allergen immunotherapy is the most effective and single-cause treatment for IgE-mediated allergies, known today to invert the excessive immune response to allergens to a normal immune response. However, this therapy must be continuous to be successful. The COVID-19 pandemic has changed many aspects of medicine, like going to the doctor’s office. There were examples for cases when subcutaneous immunotherapies had to be changed to sublingual immunotherapies due to the pandemic, but there were cases when because of the pandemic the immunotherapy was delayed or stopped.

Methods
Between February 2020 and February 2023 there were 121 active patients in our clinical register, whose condition was assessed at the annual follow-up after the end of the given year during the years of immunotherapy, and with the help of the register, we could contact patients who did not report during the pandemic.

There were altogether 467 telemedicine visits during these 3 years. We used telephone consultations (30 min long) for the telemedicine visits. Patients’ therapy was solved with EESzT system (Elektronikus Egészségügyi Szolgáltatási Tér = National eHealth Infrastructure) Patients were informed about the process and verbal consent was obtained.
Results
A total of 467 telemedicine visits has been made in the past 3 years, 83.51% during the pandemic (1 Febr 2020 – 31 May 2022), 35.76% in 2020, 31.90% in 2021, and 32.33% in 2022.
We have had 88 active patients in our clinical register during the pandemic, average age was 37.4, 41 telemedicine (13.22%) and 269 (86.77%) personal visits were made.
We have had 33 active patients in our clinical register after the pandemic (1 June 2022 – 18 January 2023), average age was 35.9, 5 telemedicine (12.19%) and 38 (92.68%) personal visits were made.

Conclusion
At the beginning of the Covid-19 pandemic most elective outpatient care was suspended, including allergen immunotherapy. Telemedicine applications provided an opportunity for efficient patient care, and in allergology they significantly facilitated everyday clinical practice. Sublingual immunotherapy drops are used at home by patients, who do not need to be at the doctor's office, due to which patients who were being healed by these drops did not have to discontinue their immunotherapy during the pandemic. Their conditions could be traced with telemedicine applications. We did not have to interrupt ongoing immunotherapy in any case due to pandemic.

7. Gabriel Mendoza
“Baker’s asthma in a warehouse worker allergic to cultivated wheat: a case report”

Gabriel Mendoza
University of Washington, United States

Introduction
Baker’s asthma is a type of sensitizer-induced occupational asthma (OA) caused by inhalation of grain such as wheat, rice, oat, maize or barley. High-molecular weight sensitizers in grains also include enzyme additives (amylase, cellulose), storage and house dust mites, and fungal alpha-amylase [1]. There are no clear guidelines on the role of skin testing and in vitro assays in diagnosis. We report a case of a tortilla warehouse worker who developed Baker’s asthma, with initial work-up negative for wheat on in vitro assay, but who was positive for wheat on skin testing and cultivated wheat on in vitro assay.

Case Report
The patient is a 44-year-old man who worked at a tortilla warehouse and developed new-onset asthma symptoms after 1 month at his new job. Occupational asthma remained undiagnosed until the patient’s symptoms improved after missing work for 2 weeks. Asthma was diagnosed with a positive bronchial challenge to methacholine. Initial testing included in vitro assays positive to various pollens including timothy grass and negative to wheat. Follow-up skin testing was positive to wheat, oat, corn and barley; in vitro assay to cultivated wheat IgE was positive. Medical management includes daily inhaled corticosteroids and as needed bronchodilators and muscarinic antagonists.

Conclusion
This case illustrates the importance of obtaining an occupational history when determining the diagnosis and management of new-onset asthma among the adult working population. The patient was a warehouse receiver of packaged grains and not a baker, the typical working population considered for baker’s asthma. The patient was initially found to be negative to in vitro testing to wheat IgE, but was found to be positive to wheat on skin testing and cultivated wheat on in vitro testing; this suggests the importance of doing both skin testing and aeroallergen in vitro testing when determining the diagnosis of baker’s asthma.
References

8. Toshinobu Nakatake 
“A 13-year-old patient who developed anaphylactic shock following sublingual cedar immunotherapy”

Toshinobu Nakatake
Osaka Habikino Medical Center, Japan

Introduction
Allergen immunotherapy is the only treatment that has the potential to modify the course of allergic disease. In Japan, many patients are allergic to cedar pollen. Sublingual immunotherapy (SLIT) is often administered for the common cedar pollen allergy, which rarely improves spontaneously. SLIT results in fewer anaphylactic symptoms compared with subcutaneous immunotherapy (SCIT); especially cedar SLIT has almost no anaphylactic symptoms. Here, we report a case of anaphylaxis associated with initial SLIT administration for cedar pollen allergy.

Case Report
A 13-year-old girl presented with severe rhinitis and hyperemia every year during the cedar pollen season and had been taking antihistamines. Ten minutes after she was administered Cedacure® 2000JAU sublingually, she developed a feeling of airway obstruction, peripheral coldness, and somnolence. The patient required three rounds of intramuscular epinephrine injections, saline boluses, inhaled beta-agonists, and further administration of antihistamines.

Her symptoms gradually improved, and she subsequently gained consciousness. Peripheral coldness and subjective symptoms also disappeared.

Conclusion
Regarding anaphylaxis, caution should always be observed, even during SLIT treatment, which is considered relatively safe. Further accumulation of cases is needed to clarify the cause of anaphylaxis.

Respiratory and Skin Allergy – Session C

1. Nataliia Liakhovska 
“Peculiarities of Allergic Pathology During Warfear”

Nataliia Liakhovska1,2
1Poltava State Medical University, Ukraine, 2Rockefeller University, United States

Background
The issue of neural regulation of immune response processes is gaining more and more publicity. Modern scientific institutions pay considerable attention to the study of signaling pathways, cytokine, epigenetic factors at various stages of stress and behavioral characteristics. The effect on neuroimmune interaction is considered as one of the promising directions of allergic disease's treatment. The war in Ukraine once again emphasized the need for a more in-depth study of these issues, including in patients with an allergic profile.
Methods
The study was conducted February-May 2021 and in 2022. General clinical tests, including allergens sensibilisations and the level of IgE were done for all patients. The questionnaires survey was conducted. The first of the questionnaires was about COVID-19 infection, second one determined the psychological state of the patients. We modified questionnaires of Quality of Life, Cognitive Abilities and stress scale. We added some questions to the survey during warfare in 2022. We calculated the number of drugs needed to achieve disease control. The total number of respondents was 240 people.

Results
45.5% of patients with allergic disease suffered from a COVID-19 infection. Mild forms got 60.9% patient’s and moderate severity of the disease 26.6%. Only 12.6% of patients indicated the appearance of an allergy related to COVID-19. The number of patients that was hospitalized at the has increased by 1.5%, since the beginning of 2022 comparing with 2021. More than 30% of patients dedicated that first symptoms of allergy were revalidated to stress. The severity of allergic diseases increased, during the war. The numbers and doses of drugs to relieve the exacerbation of the disease are grows up in 2022.

Conclusion
Our other study clearly indicates the relationship between psychological factors and the allergic pathology. Transmission of an infectious disease has less effect on the development of allergic pathology than stress. The development of tactics for the treatment of allergy, taking into account the psycho-emotional state, is an extremely important issue, especially during military operations. The combination of drugs aimed at correcting the psycho-emotional state together with basic therapy leads to a faster reduction of clinical signs of exacerbation of the pathology. A positive effect was also noted during the work of a psychologist and classical therapy.

2. Yu-Kyoung Hwang
“Department paramedics Changes in the awareness on anaphylaxis and asthma after the education for 119 emergency”

Yu-Kyoung Hwang1,2, Jeong-Eun Yoon1,2, Moon Hee Choi, Sae-Hoon Kim1,2, Yoon-Seok Chang1,2
1Seoul National University Bundang Hospital, Republic of Korea, 2Seoul National University College of Medicine, Republic of Korea

Background
Anaphylaxis and asthma exacerbations are emergency condition that can even lead to death. 119 rescue members arrive at the scene for the first time in such emergency conditions. It is important to increase the awareness on allergic emergency conditions for 119 rescuers so that they can provide first aid or communicate with emergency medical specialists.

Methods
In Gyeonggi-do province, 119 paramedics have been given lectures on asthma exacerbation and anaphylaxis since 2011. An allergy specialist conducted a 90-minute training session for anaphylaxis and asthma exacerbation, including hands-on workshops on self-injectable epinephrine. To evaluate the changes in the awareness on each emergency conditions, the same questionnaire was filled out before and after the education. Online education was conducted for 3 years from 2020. We analyzed the results of the pre- and post-education awareness survey accumulated from 2017 to 2022.

Results
A total of 1769 (male 1028) 119 rescuers participated. After education, the overall awareness score for anaphylaxis has been increased from 48 to 83% (62 to 79% after online education). The awareness on asthma after education has been increased from an average of 82 to 93% (90 to 94% after online education). The overall baseline awareness before education was also increasing: Compared by every three years, anaphylaxis awareness score before education has been increased from 43 to 60% (2017-2019) and 60 to 65% (2020-2022). The asthma awareness score before education has been increased from 80 to 85% (2017-2019).

**Conclusion**

We demonstrated the effectiveness of education by evaluating the awareness scores before and after the education on anaphylaxis and asthma. The study also showed a general trend of increasing baseline awareness on asthma exacerbation and anaphylaxis among 119 rescuers for recent years.

3. Linda Cox  
“The Art and Science and Healing Power of Dance and Visual Arts”

*Linda Cox*  
*Nova Southeastern University, Nova Scotia*

**Background**

The purpose of this review is to evaluate the health benefits of dance and dance therapy in various health domains. Dance interventions included movement therapy with certified therapists, common dances such as ballroom dancing, salsa, and cha-cha as well as ethnic dances, such as the Chinese Guozhuang Dance and the Native American Jingle Dance. The health domains included depression, cognitive function, neuromotor function, dementia, balance, neurological growth factors, subjective well-being, etc.

**Methods**

Recent Findings: National Library of Medicine, Congress of Library were searched using the terms: Dance, Dance Movement Therapy, Health, Cognitive Function, Healing, Neurological Function, Neuromotor Function, and Affective Disorders. 2591 articles were identified. Articles were selected if they provided information on the health benefits of dance in one or more of the above domains as compared to a ‘non-dance’ control population. Studies included systematic reviews, randomized controlled studies, and long-term prospective studies. Many subjects in the studies were considered ‘elderly,’ generally defined as 65 years or older. However, the benefits on Executive Function was demonstrated in primary school children.

**Results**

Summary: Overall, the studies demonstrated that DI provided benefits in several physical and psychological parameters as well as Executive Function as compared with regular exercise alone. Impressive findings were that dance was associated with increased brain volume and function and neurotrophic growth function. The populations studied included subjects who were ‘healthy’ older adults and/or children who had dementia, cognitive dysfunction, Parkinson’s Disease, or depression, other affective disorders, and respiratory conditions.

**Conclusion**

As the evidence demonstrating dance interventions are associated with measurable improvements in objective and subjective parameters continues to emerge, it is likely that dance, whether in the form of dance movement therapy or dance itself, will eventually become an integral part of traditional Westernized medicine, instead of being a homeopathic alternative approach. Initially, it will become an accepted therapy for specific conditions. Over time, dance interventions will likely be employed as a proven preventive measure, much like daily aspirin is prescribed for coronary artery disease prophylaxis.
References

Dance as a Healing Art References


4. Nami Yamada
“Clinical effects of a three-day inpatient education program for children with atopic dermatitis”

Rei Kanai¹, Takahiro Nishida¹, Takafumi Takase¹, Tomoyuki Arima¹, Fumiko Iwai¹, Shingo Yamada¹, Mizuho Nagao¹, Takao Fujisawa¹
¹National Mie Hospital, Japan

Background
Atopic dermatitis (AD) is a chronic inflammatory skin disease and is treated by skin care and topical anti-inflammatory drugs. To achieve and maintain good control of AD, patients need good self-management skills.
and adherence to the treatment under shared decision-making, thus, patient education is essential. Various education programs have been reported. However, standardized programs are yet to be established. We sought to develop an efficient and effective education program for AD.

Methods
A single-center, retrospective study. Clinical records of children under 16 years with AD were retrieved. The intervention was the three-day inpatient education program (IPE) consisting of AD knowledge introduction by pediatricians, and hands-on instructions on topical treatment and skincare by nurses for both parents and children during the hospital stay. As controls, the records of age-, gender-, and severity-matched patients who had conventional outpatient education (OPE) were retrieved. The Eczema Area and Severity Index (EASI) score was evaluated before treatment (visit 0), less than 4 weeks after treatment (visit 1), and more than 4 weeks after treatment (visit 2).

Results
Clinical data were collected from 33 patients who received IPE and 61 patients who received OPE. The median (IQR) EASI score before treatment was 11.6 (9.5-16.8) in the IPE group and 11.6 (9-17.3) in the OPE group, decreasing to 3.1 (1.6-8.0) and 6.0 (2.5-9.8) in visit 1 and to 2.4 (1.0-6.0) and 5.2 (2.7-11.5) in visit 2. EASI scores at visit 2 in the IPE group were significantly lower than in the OPE group. Further, the proportion of patients in the IPE group who achieved an EASI < 6 at visit 2 was significantly higher than in the OPE group.

Conclusion
The three-day IPE program for AD produced better clinical results than a traditional OPE program. Intensive education in a short period of time is effective for good control of pediatric AD.

5. Yazid Imoru
“Increasing knowledge and awareness of respiratory diseases through an educational programme for nursing students in rural Ghana.”

Yazid Imoru
Family Health Medical School

Background
Respiratory Diseases and allergies are on the rise in developing countries and Ghana is not an exception. In rural Ghana, there is massive indoor air pollution and lack of awareness and education on these diseases which contributes to a high morbidity and disease burden. However, no official focus has been made towards these conditions. Hence, the Respiratory Diseases and Allergy Organization, Ghana was established in 2022 to improve respiratory health and well-being of Ghanaians through awareness, advocacy, education and research activities.

Methods
We performed an educational programme at the Bolgatanga Nurses Training School, Gumioko Junior High School, Concordia Junior High School and Bolgatanga Central Market focusing on awareness on common respiratory problems in these settings through public health education, Games and a radio programme to improve respiratory health.

After the World Lung Day activities were carried-out, a total of 79 students of Bolgatanga Nurses Training College were interviewed through questionnaires to determine the impact of the activities on respiratory health organized in the rural Ghana by the Respiratory Diseases and Allergy Organization, Ghana.
Participation in the programme and answering questionnaires was voluntary.

Results
79 participants responded the questionnaire, evenly distributed throughout the 3 years of nursing education and a median age between 21-25 years. Responders reported a significant increase in their knowledge on respiratory diseases, increasing from a moderate level to a good level of knowledge after participating in the educational programme. Major focus shifted to awareness of tuberculosis as a major health problem in the rural setting.

Conclusion
Our educational programme for the World Lung Day 2022 increased knowledge and awareness of respiratory diseases among nursing students in rural Ghana (Upper East Region). We will continue to provide education on respiratory health through awareness creation, education, advocacy and research.
6. Jaime Sosa

“The first report of concomitant immediate-type I hypersensitivity reaction and delayed-type IV hypersensitivity reaction to p-Phenylenediamine, case report.”

Jaime Sosa
Colombia

Introduction
Most reactions reported in literature are delayed-type IV hypersensitivity reactions, with just few immediate-type I hypersensitivity reactions reported, but no case of both concomitant hypersensitivities have been reported.
p-Phenylenediamine (PPD) is an organic compound derivative of aniline. It is mainly used as a component of engineering polymers and composites like kevlar but is also an ingredient in hair dyes and is occasionally used as a substitute for henna and it is the main cause of allergic contact dermatitis regarding hair dyes (1). PPD requires a secondary ingredient such as a developer or oxidizer to produce the black color(2)

Case Report
After dyeing her scalp hair with black dye, felt generally unwell within 10 minutes, and developed severe itching of the scalp, hives and lip angioedema, 5 minutes later she started with shortness of breath and wheezes; she attended the emergency department at the local hospital, where she was found to have urticaria, wheezes, and to be hemodynamically unstable, presenting with shock (BP 70/55 , 120 BPM) so anaphylaxis diagnosis was made, and she was treated with epinephrine 0,5 mg subcutaneous. The patient came to private consultation because of chronic contact dermatitis, severe itching of the scalp, and micro-papular eczematous rash

Conclusion
The inadequate treatment given for the anaphylaxis that the patient presented, demonstrates the shortcomings in the identification and correct treatment of anaphylaxis, and is consistent with what was reported in a study carried out in Medellín city, where 92.2% of non-allergists surveyed knew that adrenaline was the drug of choice, 76.5% knew the time of administration, however, there was less knowledge in other aspects such as the appropriate route of administration as 45.2% who did NOT choose intramuscular route of administration of epinephrine (5)
An accurate diagnosis and successful treatment of anaphylaxis will allow complications to be avoided

References
7. Anfal Alshaya

“HLA-A*32:01 and Carbamazepine-induced DRESS: a Coincidence, or is There More?”

Anfa Alshaya
University of British Columbia, British Columbia, Canada

Introduction
Carbamazepine-induced adverse reactions occur in up to 10% of patients. Although severe cutaneous adverse reactions (SCARs) are rare, they carry high mortality and morbidity. Several high-risk Human Leukocyte Antigen (HLA), particularly HLA-A*31:01 and HLA-B*15:02, have been linked to increased risk of carbamazepine-induced SCAR in different ancestries. To prevent SCARs, the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) recommends routine screening for these alleles in carbamazepine-naive patients where the allele is common, its frequency unknown, or whose origin is unknown. We report two pediatric patients who developed Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) with carbamazepine despite negative HLA-A*31:01 and HLA-B*15:02 testing.

Case Report
Two pediatric patients were started on carbamazepine for epilepsy. Both patients tested negative for HLA-A*31:01 and HLA-B*15:02. Patient 1, a 6-year-old girl of Afghan ancestry developed a maculopapular rash with facial swelling, cervical lymphadenopathy, fever, atypical lymphocytes, liver dysfunction, and eosinophilia three weeks into carbamazepine exposure. Patient 2, a 14-year-old girl of European ancestry presented with a generalized maculopapular rash, fever, cervical lymphadenopathy, peripheral eosinophilia, and moderate-severe liver injury four weeks after carbamazepine exposure. Both patients were diagnosed with carbamazepine-induced DRESS. Carbamazepine was stopped. After treatment failure with steroids, intravenous cyclosporine led to clinical improvement. Expanded HLA genotyping revealed HLA-A*32:01.

Conclusion
It is not common to find reports in the literature of both hypersensitivity reactions occurring concomitantly. Both mechanisms are completely different, and it is not usual for them to be present at the same time as both reactions must be identified separately.

It draws attention to the inadequate treatment given for the anaphylaxis that the patient presented, and demonstrates the shortcomings in the identification and correct treatment of anaphylaxis, and is consistent with what was reported in a study carried out in Medellin city, where 93.2% of non-allergic surveyed knew that adrenaline was the drug of choice. 76.5% knew the time of administration, however, there was less knowledge in other aspects such as the appropriate route of administration as 45.2% who did not choose intramuscular route of administration of epinephrine [5].

In addition, it has been reported that less than half of the doctors indicated adrenaline in the discharge plan of the patient with anaphylaxis, as recommended by the guidelines, and 10.7% admitted that they do not know how to do it [6]. These results correspond to what was found in a previous study carried out in Medellin, Colombia, where of 989 patients referred to allergy with a presumptive diagnosis of anaphylaxis, less than 50% had prescribed adrenaline [6].

An accurate diagnosis and successful treatment of anaphylaxis will allow complications to be avoided. Once again, the shortcomings in the treatment of life-threatening reactions are demonstrated, for which reason continued medical education constitutes a fundamental strategy to consolidate and maintain the necessary knowledge to manage anaphylaxis among non-allergists doctors.

References

Anfal Alshaya
University of British Columbia, British Columbia, Canada

Introduction
Carbamazepine-induced adverse reactions occur in up to 10% of patients. Although severe cutaneous adverse reactions (SCARs) are rare, they carry high mortality and morbidity. Several high-risk Human Leukocyte Antigen (HLA), particularly HLA-A*31:01 and HLA-B*15:02, have been linked to increased risk of carbamazepine-induced SCAR in different ancestries. To prevent SCARs, the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) recommends routine screening for these alleles in carbamazepine-naive patients where the allele is common, its frequency unknown, or whose origin is unknown. We report two pediatric patients who developed Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) with carbamazepine despite negative HLA-A*31:01 and HLA-B*15:02 testing.

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An accurate diagnosis and successful treatment of anaphylaxis will allow complications to be avoided. Once again, the shortcomings in the treatment of life-threatening reactions are demonstrated, for which reason continued medical education constitutes a fundamental strategy to consolidate and maintain the necessary knowledge to manage anaphylaxis among non-allergists doctors.

References
We present two pediatric patients who developed DRESS from carbamazepine. Expanded HLA genotyping identified HLA-A*32:01 in both patients. HLA-A*32:01 is an allele strongly associated with vancomycin-induced DRESS in Europeans. Its relationship with carbamazepine-induced SCAR has not been previously described. Whether this finding is incidental or whether HLA-A*32:01 is associated with carbamazepine-induced DRESS due to shared peptide binding properties is still to be validated in larger populations. Furthermore, the population prevalence of this genotype is unknown. Further studies are needed to fully understand the relationship between HLA-A*32:01 and carbamazepine-induced SCAR.

References
Table 1: Results of Genetic Testing

<table>
<thead>
<tr>
<th>HLA variant</th>
<th>Drug</th>
<th>cADRs</th>
<th>Odds ratio (range)</th>
<th>Specific populations studied</th>
<th>Patient result</th>
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<tr>
<td>1</td>
<td><em>HLA-A</em>54:02</td>
<td>Lamotrigine</td>
<td>MPE, DRESS, SJS/TEN</td>
<td>3.2 – 44.3</td>
<td>Han Chinese, Spanish, Korean, Norwegian</td>
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<tr>
<td>2</td>
<td><em>HLA-A</em>31:01</td>
<td>Carbanazepine</td>
<td>DRESS, SJS/TEN</td>
<td>3.6 – 57.6</td>
<td>European, Spanish, Japanese, Korean, Han Chinese, Indian, North African</td>
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<tr>
<td>3</td>
<td><em>HLA-A</em>32:01</td>
<td>Vancomycin</td>
<td>DRESS</td>
<td>(403)</td>
<td>European</td>
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<tr>
<td>4</td>
<td><em>HLA-A</em>55:05</td>
<td>Allopurinol</td>
<td>DRESS, SJS/TEN</td>
<td>3.2 – 105</td>
<td>European, Japanese, Korean, Han Chinese</td>
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<tr>
<td>5</td>
<td><em>HLA-B</em>13:01</td>
<td>Dapsone</td>
<td>DRESS</td>
<td>35.4 – 122</td>
<td>Han Chinese, Thai, Malay</td>
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<td>6</td>
<td><em>HLA-B</em>15:02</td>
<td>Carbanazepine</td>
<td>SJS/TEN</td>
<td>12.4 – 2,504</td>
<td>Han Chinese, Thai, India, Malay, Singaporean, Vietnamese, European, Spanish</td>
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<td></td>
<td>Phenytoin</td>
<td>SJS/TEN</td>
<td>3.4 – 18.5</td>
<td>Han Chinese, Thai, Malay, Singaporean, Vietnamese, European, Spanish</td>
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<td></td>
<td></td>
<td>Oxicarbazepine</td>
<td>MPE, SJS/TEN</td>
<td>6.6 – 49.0</td>
<td>Han Chinese, Taiwanese, Greek, Portuguese</td>
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</tbody>
</table>

8. Myong-Hwan Karm

“Allergic reaction due to Methylprednisolone administered preoperatively”

Myong-Hwan Karm

School of Dentistry and Dental Research Institute, Seoul National University, Republic of Korea

Introduction

Methylprednisolone is routinely prescribed before dental treatment, such as orthognathic surgery and surgical extraction, to prevent nerve damage(1,2). Corticosteroids are drugs used to alleviate allergic reactions. Recently reported in the literature, the percentage of type I steroid hypersensitivity is about 0.3-0.5%(3). When an allergic reaction occurs in a drug-administered patient, the first thing to suspect is an antibiotic allergic reaction. An antibiotic skin test (AST) before antibiotic intravenous injection administration is already widely used as a protocol because of the risk. This paper is a case of a patient allergic to other medication despite receiving an antibiotic AST.
Case Report
A female patient had no allergic history. The day before the surgery, antibiotic skin test for amoxicillin was performed, and it was confirmed negative. On the day of orthognathic surgery, methylprednisolone 250mg and amoxicillin 1.2g were administered intravenously. Afterward, the patient complained of swollen eyes and stuffy nose. The patient’s symptoms worsened, such as severely swollen eyes, nasal congestion, and throat tickling. Dexamethasone 5mg and chlorpheniramine 4mg were injected. After about 140 minutes, improvement of symptoms was confirmed. The patient later visited the allergy department and performed the injectable drug induction test. An allergic reaction to methylprednisolone was finally confirmed.

Conclusion
Corticosteroids are drugs commonly used to neglect and treat asthma, allergic reactions, autoimmune diseases, and nerve damage. Allergic or hypersensitivity reactions to steroids are so rare that it is not easy to attribute corticosteroids to allergic reactions when they do occur. However, as it is a drug whose effectiveness for pain and prevention of nerve damage has recently been recognized, and its usage is increasing in various fields, including dentistry, it is necessary to be alert. This case shows that allergy test for other medications is critical before IV administration in addition to antibiotics.

References

9. Gabija Didziokaite
“Gender and age differences in molecular allergy profile to inhalant allergens in Lithuania”

Gabija Didziokaite¹, Gabija Biliute¹, Aida Kuznecovaite¹, Inga Cesnaviciute¹, Violeta, Kvedariene¹,²
¹Vilnius University, Lithuania, ²Innovative Allergology Center, Lithuania

Background
Allergies tend to be more common in childhood and decrease after the first 20 years of lives [1]. Determining the age and gender distribution of allergens in certain areas is important and relevant for the effective diagnosis and treatment of allergic diseases [2]. There is a lack of epidemiological studies on the prevalence of common allergens obtained by molecular diagnostic methods. The aim of our study was to evaluate the prevalence of common inhalant allergens and molecular profile of lithuanian patients and to investigate the gender and age differences.
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
72.8% of all subjects were found to be sensitized to at least one allergen: females - 70.9%, males - 74.5%. Sensitization to pets and tree pollen was diagnosed the most frequently: 38.9%(dominating allergens - Bet_v_1 (33.6%), Fag_s_1 (27.4%)) and 38.6%(dominating: Fel_d_1 (31.2%), Can_f_5 (17.5%), accordingly. Slightly lower rates were found to house dust mites (35.1%, mostly Der_f_2, Dep_p_2), grass pollen (34.5%, mostly Phl_p_1, Lol_p_1). Males were sensitized to pets, tree and grass pollen more frequently (p<0.05). The most common sensitizations in children were to tree pollen (43.9%, dominating: Bet_v_1) and pets (40.0%, dominating: Fel_d_1, Can_f_1) – both allergens’ rates were higher in children’s group (p<0.05).

Conclusion
In this study, with the help of molecular allergy diagnostics, we specify the exact inhalant allergen components, which dominate in causing allergic reactions to different age groups and genders. Lithuanians were found to be most frequently sensitized to tree pollen, mostly to Bet_v_1 and Fag_s_1 and pets with dominating Fel_d_1 and Can_f_5. Males were found to be sensitized more frequently to pets, tree pollen and grass pollen than females. Children were found to be sensitized most frequently to tree pollen and animals and sensitization rates of these allergen groups were higher for children in comparison with adults.

References

Respiratory and Skin Allergy – Session D

1. Chizuko Sugizaki
“Comparison of pediatric allergic disease prevalence with a 12 year interval (Sagamihara Allergy Cohort study the 4th report)”

Chizuko Sugizaki1, Fumiko Goto1, Sakura Sato1, Noriyuki Yanagida1, Kyohei Takahashi2, Motohiro Ebisawa1
1National Hospital Organization Sagamihara National Hospital, Japan

Background
We had followed up a birth cohort in Sagamihara-city to clarify profiles of allergic diseases during the first 7 years of life from 2002. We began to follow the same cohort again from 2014 with a 12 year interval. The purpose of the current survey is to clarify changes in prevalence of allergic diseases and environmental factors, compared with data from 2002 survey.
Methods
Using the mass medical examination system at the age of 4 months (m), we obtained consent and basic profile information on subjects from January 1st, 2014 to December 31st, 2014. We have followed up the subjects whose parents had agreed to participate in this survey at the ages of 8 m, 12 m, 1 year(y), 3 y, 5 y and 7 y. We applied the same questionnaire on atopic dermatitis (AD), food allergy (FA), bronchial asthma (BA) etc. that was used in 2002 survey.

Results
A survey of 7 y was conducted from September 2020 to August 2021. We analyzed 2332 cases in the 2014 survey and compared 2219 cases in the 2002’s. The incidence of eczema with suspected AD was 15.3% (13.8% in 2002’s) and diagnosed AD was 8.5% (7.1%). “Reported FA” includes a case with eliminating foods or using special milk due to FA. The rate of “Reported FA” was 6.3% (3.1%) and diagnosed FA was 6.6% (3.2%). The rate of diagnosed cedar pollinosis increased significantly 33.6% (21.1%) and diagnosed BA decreased significantly 10.5% (15.0%).

Conclusion
For AD, both surveys result showed a discrepancy in the ratio of suspected to diagnosed cases. For FA, the ratio of suspected to diagnosed cases matched after age 3 years; the 2002 survey showed a subsequent downward trend, while the 2014 survey showed a slight increase. PFAS (pollen-food allergy syndrome) and nut allergies in these age groups may have contributed to the increase. Cedar pollinosis increased significantly and BA decreased significantly compared to 12 years ago.

2. Abbos Nazarov
“Clinical course and characteristics of dust bronchial asthma in the Covid-19 pandemic.”

Abbos Nazarov
Israel

Background
Plant dust affects the mucous membrane of the upper respiratory tract and the mucous membrane of the eyes, causing a common disease - pollinosis.
Due to the fact that the etiology and pathogenesis are the same, this group of diseases is collectively called pollinosis. Dust allergy is also known as hay fever, dust allergy, dust rhinopathy, and dust bronchial asthma. During the course of work, a general practitioner and an allergist make up a large part of their practice in the diagnosis and treatment of long-term chronic diseases of the respiratory tract.

Methods
In the Republic, the period of increasing the concentration of dust in the air is divided into 3 periods: 1) From the end of February to the beginning of March - larch, poplar, willow plants bloom. 2) From the end of April to the middle of June - acacia, walnut, maple, as well as spiky plants are in the flowering period. 3) From August to October - sunflowers and sorrels bloom. Pathogenesis of the disease takes place in 3 immunological steps (interaction of allergen and antibody in target organs); pathochemical (release of biologically active substances and mediators into the blood);

Results
The clinical presentation of dust bronchial asthma often begins with rhinoconjunctival syndrome. Patients complain of itching and redness of the eyelids, feeling of a foreign body falling into the eye, fear of cracks, lacrimation, and in severe cases, blepharospasm. At the same time, patients are disturbed by itching in the upper palate, throat, nasal mucosa, and earlobes. Patients are disturbed by severe runny nose, non-stop attacks of snoring, and nasal breathing disorders. These phenomena are usually accompanied by "dust intoxication": quick fatigue, loss of appetite, profuse sweating, nervousness, irritability, sleep disturbances are observed.

**Conclusion**

Patients are unable to work during this period. The disease acquires the most severe manifestations when the lower part of the respiratory tract, i.e. the bronchi, is damaged. The disease is often develops after or together with repeated seasonal rhinitis. The patient complains of itching in the throat and dry swallowing, which worsens after contact with dust. Gradually, it becomes difficult to breathe through the nose, and the clinic of bronchial asthma develops. Patients are bothered several times during the day by attacks of shortness of breath during the flowering season of sensitive plants.

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4. Rei Kanai “Adult outcomes of severe childhood asthma in the pre-ICS era

Rei, Kanai1, Mayumi Matsunaga1, Mizuho Nagao1, Sankei Nishima2, Hiroshi Odajima2, Toshiyuki Nishimuta3, Hiroko Watanabe3, Minako Tomiita3, Takao Fujisawa4

1National Hospital Organization Mie National Hospital, Japan, 2National Hospital Organization Fukuoka National Hospital, Japan, 3National Hospital Organization Shimoshizu National Hospital, Japan

**Background**

Asthma is a lifelong disease and the status of asthma in childhood may have an impact on the long-term outcomes in later life. In the days before the guideline-based inhaled corticosteroid (ICS) therapy (in the pre-ICS era), severe asthma in children was far more prevalent than in the current ICS era. In Japan, national hospitals were in charge of treating those children with severe asthma, and long-term inpatient therapy, mainly by non-pharmacological measures, was administered to them. Long-term adult outcomes of the patients are not well known and the relationship between childhood status and current outcomes may provide new insights.

**Methods**

Children with hospitalized severe asthma from the 1970s to 2000s were identified from the hospital admission registers. A primary questionnaire survey by mail and a secondary survey by visits to the hospital was performed.

**Results**

A total of 998 patients were identified and 187 patients responded to the primary survey. The secondary survey included 101 patients who underwent lung function tests and chest CT scans. The current average age of 46.2 years, 54% of them had wheezing symptoms in the last 12 months, 42% were treated with inhaled steroids, and 33% had no symptoms without inhaled steroid therapy during the last 12 months. Overall, there was a tendency
to improve with advancing age. Patients with current persistent asthma or emphysema lesions were more severe with poorer control during childhood hospitalization than those in current remission.

Conclusion
Asthma control during childhood is vital to improving long-term prognosis.

4. Mizhuo Nagao
“Factors associated with requirement of inhaled corticosteroid therapy in 1-year-old children with recurrent wheezing”

Mizhuo Nagao\textsuperscript{1}, Noriyuki Yanagida\textsuperscript{2}, Motohiro Ebisawa\textsuperscript{3}, Yohei Watanabe\textsuperscript{4}, Chiho Tatsumoto\textsuperscript{5}, Tadashi Matsuda\textsuperscript{6}, Takao Fujisawa\textsuperscript{1}

\textsuperscript{1}National Hospital Organization Mie National Hospital, Japan, \textsuperscript{2}National Hospital Organization Sagamihara National Hospital, Japan, \textsuperscript{3}National Hospital Organization Sendai Medical Center, Japan, \textsuperscript{4}Atsuta Pediatric and Allergy Clinic, Japan, \textsuperscript{5}Aozora Pediatric Clinic, Japan, \textsuperscript{6}Matsuda Pediatric Clinic, Japan

Background
Recurrent wheezing in early childhood can be caused by a variety of pathophysiology. Some of them may develop asthma later in life and it is important to identify them early as a target to be treated. We sought to characterize phenotypes of early wheezers to identify the treatable trait by prospectively observing the clinical course of them.

Methods
One-year-old children with two or more episodes of wheezing who visited a pediatric clinic or hospital specializing in allergy were included in this study. The parents completed an online questionnaire every month regarding the course of wheezing symptoms of their children and treatment; and after two years, a physician diagnosed the child with or without asthma and confirmed treatment details. Multivariable logistic regression analysis was performed to determine the factors associated with use of inhaled corticosteroids.

Results
A total of 251 children were enrolled, of whom 88% completed 2-year follow-up, and 43.5% had inhaled corticosteroid prescribed during the 2-year period. History of hospitalization for wheezing at the time of enrollment (OR 2.60, 95%CI 1.32-5.13), eczema in infancy (OR 0.45, 95%CI 0.25-0.83), high sensitization to house dust mite (OR1.56, 95%CI 1.03-2.36) and milk (OR 1.83, 95%CI 1.07-3.12), and total IgE levels (OR 0.59, 95%CI 0.40-0.87) were significantly associated with ICS use.

Conclusion
Severity of wheezing and type 2 immune response-trait may have prompted physicians to administer ICS.

5. Tai Tran-Quoc
“Combination of fractional exhaled nitric oxide and spirometry/impulse oscillometry in the initial diagnosis of asthma”

Tai Tran-Quoc\textsuperscript{1}, Lan Le Thi Tuyet\textsuperscript{1}

\textsuperscript{1}University Medical Center, Ho Chi Minh City, Vietnam
Background
An asthma diagnosis is challenging because the patient’s symptoms fluctuate. In stable disease, most patients are completely asymptomatic and have normal lung function. Fractional exhaled nitric oxide (FENO) is a non-invasive measurement of eosinophilic airway inflammation and could guide the diagnosis and treatment of asthma, according to GINA (1). However, data on the combination of FENO and lung function testing (spirometry or impulse oscillometry-IOS) are still limited. This study was conducted to determine the role of adding FENO to lung function testing in the initial diagnosis of asthma.

Methods
Retrospective study of 102 medical records of patients with persistent respiratory symptoms suspected of asthma visiting the Community Health Care Center in Ho Chi Minh City, Vietnam, from 2018 to 2022. These patients had their first FENO measurement and spirometry with a bronchodilator test. Thirteen patients who could not perform acceptable spirometry were then indicated IOS with a bronchodilator test. The study collects the doctor's final diagnosis. FENO, spirometry and IOS are interpreted according to the latest recommendations (2-4).

Results
The study enrolled 102 patients with an average age of 34.5 years (95%CI 30.9-38.2), females accounted for 60%. 65 cases were diagnosed with asthma or suspected asthma. These patients had a significant difference in FENO value: 37.7 ppb (95% CI 29.2-46.1) vs. 14.2 ppb (95%CI 11.5-16.9), p<0.001; elevated FENO (FENO >= 25ppb) 52% vs. 11% (p<0.001); obstructive impairment 43% vs. 14% (p = 0.002), positive bronchodilator response 37% vs. 3% (p<0.001), abnormal spirometry 54% vs. 16% (p<0.001), and at least one abnormal test 72% vs. 24% (p<0.001) when compared to the group with no asthma diagnosis.

Conclusion
FENO or lung function testing (spirometry, IOS) alone is suggestive enough of the initial diagnosis of asthma. Combining FENO and spirometry/ IOS will provide more evidence to support the diagnosis of asthma.

References

6. Deepti Vellaichamy Manian
“Coagulation function in patients with Aspirin exacerbated respiratory disease”

Deepti Vellaichamy Manian1, Erin O’Brien1, Janalee Stokken1, Garret Choby1, Rajiv Pruthi1, Rohit Divekar1
1Mayo Clinic, Currently at Stormont Vail Health, United States

Background
The purpose of this study was to better characterize how pathways involved in Aspirin Exacerbated Respiratory disease (AERD) impact coagulation pathways. Previous studies suggest that dysregulation of the coagulation cascade at the tissue level contributes to the pathogenesis of the disease. It is unknown if similar coagulation dysfunction is present systemically. AERD is an underrecognized disease. If a systemic coagulation dysfunction is confirmed, it could serve as a biomarker for better diagnosis of the disease. This was a follow on study to our
pilot that showed significantly higher fibrinogen and activated partial thromboplastin time (APTT) levels in AERD patients.

**Methods**
We prospectively enrolled 26 patients (18 with a strong clinical suspicion of AERD and 8 control patients) from the Allergy/Immunology and Otolaryngology clinics after obtaining informed consent. Patients with Chronic rhinosinusitis with nasal polyps (CRSwNP), asthma, and without Aspirin (ASA) sensitivity were excluded from the study. Pregnant patients, patients desensitized to Aspirin, currently on Zileuton, anticoagulation, or systemic steroids were excluded. Blood samples were collected to measure eosinophil & platelet counts, fibrinogen, APTT, prekallikrein, and high molecular weight kininogen (HMWK). SNOT-22 scores and Lund Mackay scores were calculated by chart review. Urinary Leukotriene E4 levels (LTE4) were collected if available.

**Results**
The median age of the AERD group was 57 (Range: 19-78 years), and a majority were female. The median eosinophil count was higher in the AERD group. The median Lund-Mackay and SNOT 22 scores were also higher in the AERD group.
Some patients (10/18 AERD, 1/8 controls) had urinary LTE-4 documented. All the AERD subjects with a urine LTE-4 obtained prior to sinus surgery had elevated levels (>104 pg/mg creatinine), consistent with aspirin hypersensitivity as previously reported.
The AERD subjects had higher fibrinogen levels compared to the controls. APTT levels were similar in both AERD and Control groups.

**Conclusion**
The study was done with the hypothesis that AERD patients may have coagulation factor abnormalities given the pathways involved in the disease. While the study showed higher disease burden and higher levels of biomarkers in AERD patients when compared to the controls - the differences were not statistically significant. Limitations of our study include small sample size and a lack of age/sex-matched controls. A limited number of coagulation factors were only obtained. We hope that our study can serve as a reference for future studies with an improved design and higher power to better identify biomarkers for AERD.

7. Jaime Sosa
“Clinical and sociodemographic characteristics of the population with angioedema diagnosis, attended in a reference center in Medellín-Colombia, 2013- 2018”

*Jaime Sosa*, Fernando Fuentes, Catalina Gomez, Victor Calvo, Libia Diez, Ricardo Cardona
1*Universidad de Antioquia, Colombia*

**Background**
Angioedema understood as a disease but not as a symptom, has particular characteristics and defined subtypes. In Colombia there are no descriptions of the clinical and sociodemographic characteristics of patients with angioedema. The aim of this study is to describe the clinical and sociodemographic characteristics of the population diagnosed with angioedema, treated at a reference center in Medellín-Colombia; period 2013-2018.

**Methods**
A retrospective descriptive observational study was carried out in patients treated at the IPS Universitaria, in Medellín, Colombia.

**Results**
3744 clinical records were collected; of which 309 corresponded to patients diagnosed with angioedema. The univariate and bivariate distribution of the different sociodemographic and clinical characteristics are described in this article (sociodemographic aspects; clinical, paraclinical and therapeutic characteristics in patients with angioedema; frequency of presentation of angioedema in the study population; distribution of sociodemographic, clinical and therapeutic aspects taking into account the classification of the different subtypes of angioedema; relationship of sociodemographic and clinical data with histaminergic angioedema).

Conclusion
Knowledge of the characteristics of a disease in specific populations allows directing public health policies to reduce the impact of diseases, additionally allows acquiring knowledge to generate new research proposals.

8. Sandeep Sakaria
“A rare case of sinonasal Rosai-Dorfman-Destombes disease in a patient with common variable immunodeficiency”

Sandeep Sarkaria1,2,3
1Case Western Reserve University, United States, 2University Hospitals, United States, 3Allergy Immunology Associates, United States

Introduction
Rosai-Dorfman-Destombes disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a rare form of non-Langerhans cell histiocytosis with a prevalence of 1:200,000. Extranodal involvement of the nasal cavity and paranasal sinuses are uncommon and occur only in 11% of RDD cases (1). Patients with sinonasal RDD may present with rhinitis, sinusitis, nasal obstruction, epistaxis, nasal dorsum deformity, facial asymmetry, and aural fullness (1,3,4). Although the etiology is unknown, it is commonly associated with autoimmune disease, viral infections, and hematologic malignancies, which may suggest that it occurs due to immune dysfunction (1,2).

Case Report
Patient is a 45 YO female with a history of common variable immunodeficiency (CVID) on monthly intravenous immunoglobulin infusions who presented with nasal obstruction with recurrent epistaxis. Evaluated several times by ENT for the nasal mass, biopsy was recommended; however, the patient refused. A year later, developed epistaxis initially in the setting of a traumatic nasogastric tube placement which continued intermittently for 2 years. Eventually underwent surgical debulking, and was diagnosed with granulomatous disease. Symptoms did not resolve with standard medical therapy, and she underwent an additional surgery. Tissue pathology demonstrated +S100, +CD68, and -CD1a histiocytes, consistent with RDD.

Conclusion
We present the first reported case of sinonasal RDD associated with CVID. Though the disease is generally self-limiting, surgical-debulking is required for symptom improvement and diagnosis (2). Prompt diagnosis of extranodal RDD may prevent unnecessary treatment and impairment of quality of life. For our patient, prompt diagnosis and complete excision of her nasal mass could have prevented recurrence, use of unnecessary resources, and additional surgeries. Although the etiology of RDD remains unclear, its presumed association with immune-dysfunction highlights the importance of including RDD on the differential diagnosis in CVID patients who present with lymphadenopathy, extranodal masses, and recurrent epistaxis (1,2).

References

Respiratory and Skin Allergy – Session E

1. Ana Caraballo
   “Type 2 inflammatory response in patients with chronic rhinosinusitis and its clinical relevance according to nasal challenge test”

Ana Caraballo1, Leidy Alvarez2, Jorge Sanchez1
1Hospital “Alma Mater de Antioquia”, University of Antioquia, Colombia, 2SURA Company, Colombia

Background
BACKGROUND: Inflammation in Chronic rhinosinusitis (CRS) is heterogeneous but is mainly characterized by type 2 (T2) inflammation with high levels of specific IgE (sIgE) and eosinophils in serum and nasosinusal mucosa. Whether sIgE is associated with clinical symptoms has yet to be explored in detail.

OBJECTIVE: To describe T2 inflammation in CRS and explore its possible association with clinical symptoms using nasal challenge tests.

Methods
We identified T2 inflammation using markers including total IgE, serum sIgE (SsIgE) and nasosinusal sIgE (NsIgE) against Der p, Der f, Blo t, Can f, Fel d, Staphylococcus enterotoxin A, and enterotorixin B in patients with CRS, allergic rhinitis (AR), and a control group. Anti-Der p IgE was the highest allergenic source in this population. We performed nasal challenge tests (NCT) with Dermatophagoides pteronyssinus in 4 groups of patients: CRS with SsIgE (CRS SsIgE+, n = 32), CRS without SsIgE (CRS SsIgE-, n = 30), allergic rhinitis (AR, n = 28), and control subjects (control, n = 20).

Results
Out of 62 patients with CRS, 68% had T2 inflammation. The presence of nasal polyps, asthma comorbidity, NSAID hypersensitivity, and smell loss were significantly associated with the presence of T2 inflammation. The prevalence of NsIgE and positive NCT was 74% and 64% among CRS SsIgE+, 45% and 18% among CRS SsIgE-, 82% and 84% among AR, and 15% and 0% among controls, respectively. The prevalence of SsIgE among the AR and control group was 100% and 15%, respectively. There was no significant association between NCT and the presence of polyps or asthma.

Conclusion
Type 2 inflammation is frequent among patients with CRS and seems to be associated with some clinical characteristics that create the most frequent endophenotype in CRS. However, the presence of SsIgE or NsIgE has less clinical relevance than that observed in patients with allergic rhinitis. These results should be considered when choosing medical treatments in CRS, for example, the application of allergen immunotherapy.

2. Dong Kyu Kim
“Long-term Effects of Turbinate Surgery on Allergic Rhinitis”

Sang Chul Park², Hyun Jung Kim², Dong-Kyu Kim³,
¹Hallym University College of Medicine, Republic of Korea, ²Korea University College of Medicine, Republic of Korea

Background
Turbinate surgery is an effective treatment for allergic rhinitis refractory to medical treatment. However, a systematic review and meta-analysis of the long-term effects of turbinate surgery have not yet been performed. Therefore, we investigated the long-term efficacy and safety of turbinate surgery in allergic rhinitis under a meta-analysis.

Methods
Medline, Embase, the Cochrane Library, and ClinicalTrials.gov were searched through September 2020. Studies on the long-term therapeutic effect of turbinate surgery in allergic rhinitis refractory to medical therapy that assessed clinical outcomes were selected. 18 studies of 1411 patients were included. Descriptive and quantitative information was extracted; the weighted mean difference (WMD) was synthesized under a random effects model. Heterogeneity was assessed by using the Q statistic and the I² metric.

Results
We observed significant reductions in nasal obstruction (WMD 4.60, 95% confidence interval [CI] 3.43–5.76), rhinorrhea (WMD 3.12, 95% CI 1.97–4.28), sneezing (WMD 2.64, 95% CI 1.74–3.54), itching (WMD 1.75, 95% CI 1.20–2.30), nasal resistance (WMD 0.16, 95% CI 0.08–0.24), and total nasal volume (WMD 0.96, 95% CI 0.73–1.19). There was no significant difference in the occurrence of any complication. More than 1 year after surgery, the improvements in nasal obstruction (WMD 5.18, 95% CI 3.00–7.37), rhinorrhea (WMD 3.57, 95% CI 1.78–5.37), sneezing (WMD 2.95, 95% CI 1.58–4.32), and total nasal volume (WMD 0.96, 95% CI 0.73–1.19) were maintained.

Conclusion
Turbinate surgery is effective in allergic rhinitis and maintains its effect during long-term follow-up. The rate of complications is also low.

3. Duy L. Pham
“The roles of FeNO in predicting asthma and sensitization to common aeroallergens in patients with allergic rhinitis”

Bao Thai Nguyen¹, Duy L. Pham¹
¹University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

Background
FeNO is an indicator for Th2-dependent airway inflammation, which is used in evaluating airway inflammation in asthma patients. The roles of FeNO in diagnosing comorbid asthma and sensitization to common aeroallergens (AA) in allergic rhinitis (AR) is not clearly understood. This study aimed to evaluate the role of FeNO in predicting comorbid asthma and sensitization to AA in patients with allergic rhinitis.

**Methods**

This is a cross sectional study. We recruited 30 patients with AR only (Group I) and 30 patients with AR and asthma comorbidity (Group II) at the University Medical Center Clinic 1 at Ho Chi Minh City. Asthma comorbidity was diagnosed according to GINA 2020 guideline. FeNO levels and serum specific IgE antibodies to 20 AA were measured.

**Results**

52/60 (86.67%) patients were sensitized to at least one AAs. FeNO levels in Group II (50.09 ± 31.76 ppb) was higher compared to Group I (19.81 ± 18.59 ppb, P<0.001). AUC of FeNO in identifying asthma comorbidity was 0.853 (P<0.001). In addition, FeNO levels in AR patients sensitized to at least 1 tested AA (37.59 ± 30.73 ppb) was higher than unsensitized patients (17.15 ± 16.36 ppb, P = 0.02). AUC of FeNO in identifying sensitization to AAs in AR patients was 0.755 (P=0.001).

**Conclusion**

FeNO levels were increased in AR patients with comorbid asthma and/or sensitization to aeroallergens. Elevated FeNO level was an independent risk factor of asthma comorbidity in AR patients.

4. Ana Caraballo
   “Autoallergy response in patients with chronic rhinosinusitis and its clinical relevance according to its severity”

   Ana Caraballo¹, Leidy Alvarez², Jorge Sanchez¹

   ¹Hospital “Alma Mater de Antioquia”, University of Antioquia, Colombia, ²SURA Company, Colombia

**Background**

BACKGROUND: Inflammation in chronic rhinosinusitis (CRS) is characterized by type 2 (T2) inflammation with high levels of sIgE and eosinophils in serum and nasosinusal mucosa. Although IgE autoimmunity has been studied in different allergic diseases, it has not been explored in detail in CRS. Understanding this may guide medical therapies (e.g., the election of anti-IgE, anti-IL4R/13 or anti-IL5/5R).

OBJETIVE: To describe IgE autoimmunity in CRS against eosinophils huma proteins; eosinophil peroxidase (EPX) and eosinophil cationic protein (ECP).

**Methods**

We recruited patients with CRS and healthy controls to compare the prevalence and levels of IgE autoantibodies against EPX (anti-EPX-IgE) and ECP (anti-ECP-IgE). We also explored the potential role of IgE autoantibodies and clinical phenotypes (polyps, eosinophil serum levels [ESL], SNOT22 score, asthma, and Aspirin-exacerbated respiratory disease [AERD]).

**Results**

In the CRS group, prevalence of anti-EPX-IgE and anti-ECP-IgE were higher than the control group (30%, 28% and 6%, respectively). Among those with CRS, there was a moderate correlation between anti-EPX-IgE and anti-ECP-IgE (r=0.488, p=0.03), between anti-EPX-IgE and ESL (r=0.588, p=0.02), and between anti-ECP-IgE and ESL
There was no correlation between IgE autoantibodies and total IgE. There was a significant association between IgE autoantibodies and polyps (OR [95 CI] 2.44 [1.2, 5.33], p=0.02), SNOT22 score (OR [CI 95], 1.8, [1.01, 2.04], p=0.03), and AERD (OR [CI 95] 4.04, [2.67, 7.45], p<0.01) but not with asthma.

Conclusion
We described a new possible endophenotype with IgE autoantibodies against eosinophil human proteins with clinical relevance as a biomarker of disease severity. These results could be important when choosing medical treatments in CRS.

5. Agnes Nemeth
“Long-term follow-up of post-COVID patients and their sleep disorders”

Agnes Nemeth¹, Árpád Kovács¹, Marta Ranyák¹, Balint Egyed¹, Nikolett Beniczky¹, Judit Hervay¹, Sara Dobner¹, Eva Hosszú¹, Annamaria Palinkas¹, Zsuzsanna Rikker¹, Attila Szabo¹, Gabor Kovacs¹
¹Semmelweis University, Hungary

Background
Long-COVID syndrome (LCS) presenting with various symptoms after the acute condition associated with the SARS-CoV-2 virus emerged in 2019 causes a significant challenge to the health care system. According to recent literature data, the LCS evolves in 14% of children infected by SARS-CoV-2.

Methods
In LCS, (i) SARS-CoV-2 infection was confirmed by microbiology tests or suspected based on the disease course, (ii) the symptoms of COVID-19 still persist at least 3 months after the acute infection, and (iii) the patient has had complaints for at least 2 months and there is no alternative diagnosis. In 50% of patients, only one symptom persists, but the multisymptomatic disease is also frequent. A co-segregation analysis identified symptomatology associations in LC: fatigue and vitamin D deficiency (p=0.021), as well as sleep disorders and rheumatologic, cardiac or neurologic symptoms (p=0.003, 0.016, 0.040, respectively).

Results
Respiratory symptom presented in half of the patients. Spirometry was carried out at all patients above the age of 5, and abnormal values were seen in 10%. An ECG was performed and consulted by cardiologist in every case, echocardiography, Holter ECG monitor were in selected cases. Headaches and dizziness led to thorough neurological examination in one third of the patients. In certain cases, this resulted in the diagnosis of migraine, polyradiculopathy, vestibular neuritis or multiple sclerosis. A thorough gastroenterological examination was necessary in less than 10% of patients because of vomiting, diarrhea, hair loss, loss of appetite, abdominal pain.

Conclusion
From June 2021 to December 2022, 286 children presented at our long-COVID outpatient unit. The sex ratio was equal, and the presentation of children above the age of 10 was predominant. The most frequent symptoms were fatigue, loss of taste and smell, abdominal issues, cough and drowning. In summary, based on our 1.5-year experience, the extensive examination and specific treatment of children with LCS is of raised importance, which is not feasible without the cooperation of diverse specialists.

6. Misako Higashida-Konishi
“Characteristics of hydroxychloroquine allergy”
Background
Hydroxychloroquine is widely used to treat autoimmune diseases such as systemic lupus erythematosus. However, the use of hydroxychloroquine is sometimes difficult due to allergy to the side effects of hydroxychloroquine. Our objective was to be able to evaluate the susceptibility to allergy before taking hydroxychloroquine by comparing patients who were allergic to hydroxychloroquine with those who were not allergic to hydroxychloroquine.

Methods
We retrospectively studied patients prescribed hydroxychloroquine for autoimmune diseases at our hospital between 2016 and 2023. Patients who were prescribed hydroxychloroquine but did not take it internally at their own discretion were excluded. Patients who stopped taking hydroxychloroquine for reasons other than allergy, such as retinopathy, were also excluded. Patients who developed allergy after taking hydroxychloroquine were compared with those who did not develop allergy after taking hydroxychloroquine. Baseline data at diagnosis and treatment of autoimmune disease at the start of hydroxychloroquine were performed for patients in both groups.

Results
There were 122 patients in our study; 15 patients with allergy and 107 patients without allergy were enrolled. The median dosing period was 20 and 1289 days (p<0.05). Patients with allergy stopped taking hydroxychloroquine when the hydroxychloroquine allergy occurred. While there were no significant differences in autoantibodies at diagnosis, dose of prednisolone at the start of hydroxychloroquine was significantly lower in patients with allergy than without allergy (median 0.0 mg/day with allergy and 5.0 mg/day without allergy) (p<0.05). At the start of hydroxychloroquine, 46.7% of patients with allergy and 70.1% of patients without allergy were taking prednisolone (p = 0.08).

Conclusion
Patients with hydroxychloroquine allergy received less prednisolone at the start of hydroxychloroquine than patients without hydroxychloroquine allergy. Hydroxychloroquine induction may be better performed when the patient takes prednisolone and the dose of prednisolone is high.

7. Leila Alenazy
“Omalizumab-induced delayed prolonged bronchospasm and asthma exacerbation despite administration through desensitization in an asthmatic patient: A case report”

King Saud University, Saudi Arabia

Introduction
Omalizumab is a humanized monoclonal antibody that contains a 5% murine sequence, generally well tolerated but carries a risk for anaphylaxis at an incidence of 0.09%.1-2 Hypersensitivity reactions (HSRs) to Omalizumab are believed to be due to murine immunogenic structure, which can be recognized as non–self–epitopes inducing cellular and humoral immune responses.1-3 Clinically, most patients with immediate Ig-E-mediated and delayed mild cutaneous HSRs have tolerated Omalizumab re-administration through desensitization protocol.1-2 We present a first case of an asthmatic patient who failed Omalizumab desensitization due to delayed and prolonged bronchospasm.
Case Report
A 37-year-old female with severe noneosinophilic steroid-dependent asthma was previously well-controlled on Omalizumab for three years before experiencing erythema, chest tightness and a 20% decline in FEV1. Omalizumab was re-administrated through desensitization (DS) after Dupilumab failure. During the early DS steps of the 7-step protocol,1 she exhibited cough, chest tightness, and dose-dependent reduction in FEV1, improved with bronchodilators. However, delayed bronchospasm persisted for 7-10 days after DS and necessitated treatment with bronchodilators and systemic steroids. Tryptase levels remained remarkably stable. Despite modifying the premedication, DS protocol, and 50% dose reduction, bronchospasm persisted; thus, Omalizumab was stopped after 5 DS sessions.

Conclusion
Delayed HSRs to biologics, including Omalizumab, were previously described as serum sickness-like reactions, maculopapular rash, or severe cutaneous adverse reactions.1-2 We present a new phenotype of Omalizumab HSRs: Omalizumab-induced delayed prolonged bronchospasm despite administration through DS. Beyond producing drug-specific IgE, biologics could also cause immediate and delayed HSR related to the formation of antidrug antibodies and the cell-targeted release of proinflammatory cytokines besides T-cell and other cell-mediated delayed reactions.3 The underlying cellular mechanism of Omalizumab-induced delayed prolonged bronchospasm remains unknown and further studies are required.

References

Respiratory and Skin Allergy – Session F

1. Shoko Matsui
“Allergy in IgG4-related disease”

Shoko Matsui1, Seisuke Okazawa1, Kotaro Tokui1, Aki Matsui1, Yu Matsui1, Chihiro Taka1, Shingo Imanishi1, Kenta Kambara1, Minehiko Inomata1
1University of Toyama, Japan

Background
IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory disease. It has been reported that lesions of IgG4-RD present Th2 dominant immunity. The aim of this study was to investigate allergic disorders in patients with IgG4-RD.

Methods
We conducted a retrospective study of 80 patients with IgG4-RD treated in Toyama University Hospital between 2010 and 2021. Diagnosis of IgG4-RD was made based on comprehensive diagnostic criteria (2011, 2020). We
investigated patients’ history of allergy, symptoms, organ involvement, levels of serum IgG, IgG4, and IgE, the specific IgEs for aeroallergens, and analyzed relationships among them.

**Results**

Of the 80 patients, 54 had allergic conditions (rhino-sinusitis, bronchial asthma, and skin allergy) in their past or present history (AA+group), and 26 did not (AA-group). AA+group was younger than AA-group (P=0.0334), had lacrimal and salivary gland involvement (P=0.0198), and showed rhino-sinusitis on imaging findings (P=0.0344). Eosinophils in blood, levels of serum IgG, IgG4, IgE, IL2-R and the specific IgEs for aeroallergens did not significantly differ between groups. Serum IgG4 levels did not correlate with serum IgE levels, but did show a remarkable correlation with blood eosinophil counts (P<0.0001)

**Conclusion**

The results of our study suggest that 70% of patients with IgG4-RD have airway allergic involvement, and that eosinophil counts on peripheral blood and levels of serum IgG4 are strongly correlated in such patients. Although we observed no IgEs directed against any specific aeroallergen, innate immunity may be involved in the pathogenesis of IgG4-RD. Further analysis of allergic manifestations might be helpful in elucidating the pathogenesis of IgG4-RD.

2. Bábara Kong Cardoso

“Asthma, atopic diseases, and cardiovascular diseases/risk factors: a Portuguese nationwide study”

**Background**

Lifestyle changes have been associated with an increase in cardiovascular (CV) diseases/risk factors (RF) as well as atopic diseases, including asthma. While the epidemiological link between obesity and asthma has been well studied, the evidence regarding CV diseases/other CV RF and atopic diseases is much scarcer. We aimed to analyse the association between the frequency of atopic diseases (asthma, rhinitis, and eczema) and CV diseases/RF in a population-based study.

**Methods**

A cross-sectional, nationwide study of Portuguese adults (2012-2014) included participants randomly selected from the national list of primary care settings. Data was obtained from face-to-face interviews and weight, height, and waist circumference measurement. Associations between the study variables were investigated by regression models.

**Results**

Of 1688 subjects, 50.2% were male, mean age of 50.17±18.32 years. Asthma was reported by 7.2% participants, rhinitis by 10.8%, and eczema by 3.9%. After adjusting for potential confounding factors, eczema was associated with angina pectoris (OR 8.801; 95%CI 2.789-27.772). Eczema, asthma, and rhinitis were not independently associated with other CV diseases/RF. However, abdominal obesity was more frequent in asthmatic men (OR 2.695; 95%CI 1.562-4.650). Asthmatics with excess weight were older (OR 1.041; 95%CI 1.008-1.074) and had hypertension more frequently (OR 4.061; 95%CI 1.139-14.478) than lean asthmatics.
Conclusion
This population-based study supports a link between asthma as well as eczema, and CV diseases/RF. Further analysis, with a physician-confirmed diagnosis of atopic diseases, may be necessary to better address this issue, aiming to enhance their prevention and management.

3. Ulus Atasoy
“RNA binding protein HuR controls CD4+ T cell cytokine production in allergen driven mouse airway inflammation and human asthmatic endotypes”

Fatima Fattahi1, Jason Ellis1, Michael Sylvester1, Kristin Bahleda1, Njira Lugogo1,
1University of Michigan, United States

Background
The RNA-binding protein HuR (ElavI) positively regulates the expression of its mRNA targets by increasing transcript stability and translation. Its expression is cell cycle regulated. Th2 and Th17 related genes play critical roles in airway inflammation in both mouse and human. Using in vitro and in vivo studies, we have previously shown that HuR is required for and regulates both Th2 and Th17 differentiation in mice and humans.

Methods
We hypothesized that HuR is required for allergic airway inflammation and conditionally ablated HuR in T cells (distal Lck-cre HuRfl/fl) and used the ova challenge model of allergic airway inflammation to determine whether HuR plays a role in airway inflammation. We further hypothesized that HuR might similarly regulate lung inflammation in human asthma via control of CD4+ T cells gene expression.

Results
We found significant decreases in Th2 differentiation, cytokine production, and lung inflammation in the ovalbumin model of allergic airway inflammation. Immunized HuR KO mice had essentially nil lung inflammation. Using peripheral CD4+ T cells from asthmatic subjects, we found that HuR-specific inhibitors CMLD-2, as well as an AMPK activator (acadesine aka AICAR), decreased Th2/Th17 signature cytokines (mRNA and protein). Asthmatics were classified into type 2 high or non-type 2 high based on their blood eosinophil and FeNO levels. Surprisingly, IFNγ (mRNA and protein) were also markedly decreased by HuR inhibition.

Conclusion
Taken together, our mouse and human data suggest that HuR plays a crucial permissive role in both allergen and nonallergen-driven airway inflammation by regulating key genes via stabilization of cytokine mRNA transcripts and that interfering with its function may be a novel way to treat asthma.

The study protocol was approved by the Institutional Review Board of the University of Michigan.

4. Sundus Bhatti
“Use of Mepolizumab for Chronic Cough due to Eosinophilic Bronchitis”

Sundus Bhatti
University of Texas Medical Branch at Galveston, United States

Introduction
Eosinophilic bronchitis (EB) is an eosinophilic airway disease (EAD) and can be a key feature of bronchial/cough variant asthma and atopic/isolated cough. EB is defined as eosinophilia of >2.5% in sputum or >1% in BAL.1 The prevalence of EB is unknown but is less than asthma. The prevalence of EB in asthma is 65-100%.1 EB was seen in 10-30% of cases of isolated chronic cough (CC) in tertiary referral clinics.2

Allergen induced IL-5 recruits eosinophils to sensitize airway nerves, increasing spontaneous cough.3 Unlike asthma, EB does not cause airway hyperreactivity, due to the characteristic absence of mast cells.2,6,7

Case Report
A 65-year-old female with allergic rhinitis, presented for evaluation of severe, progressive, coughing episodes since 2012, complicated by two episodes of post-tussive syncope. Treatment with multiple intranasal sprays, antihistamines, PPIs, and inhalers (ICS-LABA + SABA) provided no benefit. Cough improved on OCS but recurred on discontinuation. Spirometry showed no obstruction and bronchoalveolar lavage (BAL) showed 2% eosinophils. Recent CBC demonstrated peripheral eosinophilia of 500/µL (normal eosinophils from 2004-2021).

CT thorax revealed areas of peripheral articulation, architectural distortion and volume loss. We suspected EB, based on elevated bronchial eosinophils and started Mepolizumab. She reported miraculous improvement in cough.

Conclusion
This case shows improvement in refractory CC due to EB with mepolizumab. The MUCOSA trial (NCT04765722) is investigating if mepolizumab reduces objective cough frequency and airway eosinophilia in patients with non-asthmatic EB with CC. CC with EB may lead to asthma, airway remodeling, and chronic obstruction. The prognosis of EB is unknown. Early recognition and effective treatment may prevent the development of asthma.1

The management of refractory EAD is an unmet need for clinicians. Even long-term low-dose OCS have adverse effects. Tapering OCS results in high relapses. Physicians should consider biologics in patients with refractory EAD.3

5. Sara Urbani
“Nasal Polyps in Children: a multidisciplinary approach”

Maria Cristina Artesani, Sara Santarsiero, Emanuela Sitzia, Sara Urbani, Fabio Majo, Giovanni Cristalli, Alessandro Giovanni Fiocchi
1Bambino Gesù Children’s Hospital – IRCCS, Italy

Background
Nasal Polyps (NPs) are rare in pediatric age with a frequency of 0.1% in children younger than 10 years old [1]. However, many cases of adult NPs might represent the manifestation of a process likely to have started in childhood: in fact most of the published studies on NPs refer to children with underlying systemic diseases [2], such as cystic fibrosis (CF), primary ciliary dyskinesia (PCD), and immunodeficiencies. So we have set up a NPs clinic including the coordinated activity of otorhinolaryngologists, pulmonologists, allergists and CF experts to compose a multidisciplinary Chronic Rhinosinusitis Allergo-Rhinologic Team (CRART) in our hospital.

Methods
CRART evaluate the following aspects: phenotypic and endotypic identification of patients with NPs; clinical classification of nasal pathology (endoscopic/radiological signs); nasal cytology; sensitization status with prick test (SPT) and/or specific IgE. Blood tests for immunodeficiency and vasculitis were performed, such as sweat test and molecular analysis of CFTR and PCD genes.

Patients’ clinical phenotypes were classified in non-type2 or type2 according to EPOS 2020’s cut-off levels (tissue eos ≥10/hpf, OR blood eos ≥250, OR total IgE ≥100) [2].

Ethic Committee authorized us to review the clinical records of children corresponding to our inclusion criteria.

Results
In 25 children with NPs (Table 1) endotype 2 was identified in 10 children (Table 2) with neutrophils in their rhynocytogram, while eosinophils were observed in 9 patients and mast cells in 3 patients. The incidence of inhalant allergic sensitization was 50%. Only half of them presented involvement of lower airways.

15 patients were non-endotype 2 (Table 3): neutrophils were detected in 14 cases, eosinophils in 8 and mast cells in 3. Lower airway pathology was detected in all these patients, but allergy was remarkably rarer (4/15). Chi-square for allergy in endotype 2 vs. non-endotype 2 is 2.9231 (p .087321).

Conclusion
In conclusion, pediatric NPs is a variable phenotype caused by a complex interaction of different factors, not all understood until now. A well-designed, multidisciplinary approach is mandatory for NPs management in children. The strong cooperation between different specialists is fundamental to reach personalized diagnostic tools and target therapies.

References

Table 1. Demographic and general characteristics of 25 pediatric patients with NPs

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CRSwNP’s patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>25</td>
</tr>
<tr>
<td>M/F</td>
<td>13/12</td>
</tr>
<tr>
<td>Mean age, median age range (y)</td>
<td>12.08, 12, 5-18 y</td>
</tr>
<tr>
<td>Sensitized to aeroallergens</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Lower airway disease*</td>
<td>20/25 (80%)</td>
</tr>
<tr>
<td>AERD</td>
<td>0/25</td>
</tr>
</tbody>
</table>

*Chronic bronchitis, bronchiectasis and/or asthma
AERD: Aspirin-exacerbated respiratory disease
Table 2. Patients with NPs and endotype 2.

<table>
<thead>
<tr>
<th>Patient no, age, gender</th>
<th>Allergy</th>
<th>Nasal Cytology</th>
<th>Sweat test</th>
<th>Lower Airway Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1, 12 yo, F</td>
<td>No</td>
<td>NEU3+, EOS1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#2, 12 yo, F</td>
<td>No</td>
<td>NEU4+, EOS1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#3, 9 yo, M</td>
<td>Yes</td>
<td>NEU 4+, EOS3+</td>
<td>negative</td>
<td>asthma</td>
</tr>
<tr>
<td>#4, 12 yo, F</td>
<td>Yes</td>
<td>NEU3+, EOS2+, MAST1+</td>
<td>negative</td>
<td>asthma</td>
</tr>
<tr>
<td>#5, 13 yo, M</td>
<td>Yes</td>
<td>NEU4+, EOS2+, MAST1+</td>
<td>borderline</td>
<td>none</td>
</tr>
<tr>
<td>#6, 9 yo, F</td>
<td>No</td>
<td>NEU4+, MAST1+</td>
<td>negative</td>
<td>chronic bronchitis</td>
</tr>
<tr>
<td>#7, 9 yo, M</td>
<td>Yes</td>
<td>NEU4+, EOS4+</td>
<td>negative</td>
<td>none</td>
</tr>
<tr>
<td>#8, 15 yo, M</td>
<td>No</td>
<td>NEU4+, EOS2+</td>
<td>negative</td>
<td>none</td>
</tr>
<tr>
<td>#9, 14 yo, M</td>
<td>Yes</td>
<td>NEU2+, EOS2+</td>
<td>negative</td>
<td>none</td>
</tr>
<tr>
<td>#10, 18 yo, M</td>
<td>No</td>
<td>NEU4+, EOS2+</td>
<td>negative</td>
<td>none</td>
</tr>
</tbody>
</table>

*NEU: neutrophils; EOS: eosinophils; MAST: mast-cells. Inflammatory cells count was performed by a semiquantitative, standardized method from Gelardi et al. [30]. In particular, cells’ count was defined as grade 0 (not visible), grade 1+ (occasional groups), grade 2+ (moderate number), grade 3+ (easily visible), grade 4+ (elevated number).

Table 3. Patients with NPs and non-type 2 endotype

<table>
<thead>
<tr>
<th>Patient no, age, gender</th>
<th>Allergy</th>
<th>Nasal Cytology</th>
<th>Sweat test</th>
<th>Lower Airway Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>#11, 5 yo, M</td>
<td>No</td>
<td>NEU1+, EOS1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#12, 6 yo, F</td>
<td>No</td>
<td>NEU1+, EOS1+, MAST1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#13, 6, M</td>
<td>No</td>
<td>NEU3+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#14, 14 yo, F</td>
<td>No</td>
<td>NEU2+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#15, 15 yo, F</td>
<td>No</td>
<td>NEU1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#16, 18 yo, M</td>
<td>No</td>
<td>NEU3+, EOS1+</td>
<td>Positive</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#17, 5 yo, F</td>
<td>Yes</td>
<td>NEU4+, EOS1+, MAST1+</td>
<td>Negative</td>
<td>asthma</td>
</tr>
<tr>
<td>#18, 10 yo, M</td>
<td>Yes</td>
<td>NEU3+, EOS1+</td>
<td>borderline</td>
<td>asthma</td>
</tr>
<tr>
<td>#19, 18 yo, F</td>
<td>Yes</td>
<td>MAST1+</td>
<td>Negative</td>
<td>asthma</td>
</tr>
<tr>
<td>#20, 11 yo, F</td>
<td>Yes</td>
<td>NEU4+, EOS1+</td>
<td>Negative</td>
<td>chronic bronchitis</td>
</tr>
<tr>
<td>#21, 11 yo, M</td>
<td>No</td>
<td>NEU4+, EOS2+</td>
<td>Negative</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#22, 13 yo, M</td>
<td>No</td>
<td>NEU4+</td>
<td>Negative</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#23, 18 yo, M</td>
<td>No</td>
<td>NEU2+</td>
<td>Negative</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>#24, 11 yo, F</td>
<td>No</td>
<td>NEU4+, EOS2+</td>
<td>Negative</td>
<td>reactive airway disease</td>
</tr>
<tr>
<td>#25, 18, M</td>
<td>No</td>
<td>NEU3+</td>
<td>Negative</td>
<td>bronchiectasis</td>
</tr>
</tbody>
</table>

*NEU: neutrophils; EOS: eosinophils; MAST: mast-cells. Inflammatory cells count was performed by a semiquantitative, standardized method from Gelardi et al. [30]. In particular, cells’ count was defined as grade 0 (not visible), grade 1+ (occasional groups), grade 2+ (moderate number), grade 3+ (easily visible), grade 4+ (elevated number).