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## ABSTRACTS

SUNDAY, 27 MAY 2018

TPS 01

ASTHMA: FROM BENCH TO BEDSIDE

### 0630 | Development and characterization of effective DNAzymes against human rhinoviruses

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**Background:** Infections with human rhinoviruses (RVs) are responsible for millions of common cold episodes and the majority of asthma exacerbations, especially in childhood. No drugs specifically targeting RVs are available. We aimed to develop a specific antirhinoviral therapeutic based on DNAzyme technology.

**Method:** A total of 226 candidate DNAzymes were designed against highly conserved regions of RV RNA genome, 5'-untranslated (5'-UTR) and cis-acting replication element (CRE), by use of three representative strains, RVA1, -A16, and -A29. All DNAzymes were screened for their cleavage efficiency against *in vitro*-expressed viral RNA. Those showing any catalytic activity were subjected to bioinformatic analysis of their reverse complementarity to (coverage of) 322 published rhinoviral genomic sequences. Further molecular optimization was conducted for most promising candidates. Cytotoxic and off-target effects were excluded in HEK293-cell-based systems. Antiviral efficiency was analyzed in infected human bronchial BEAS-2B cells and *ex vivo*-cultured human sinonasal tissue.

**Results:** Screening phase generated DNAzymes characterized by either good catalytic activity or by high RV strain coverage but no single molecule representing a combination of those two features. Modifications in length of the binding domains of two lead candidates, Dua-01(-L12R9) and Dua-02(-L10R11), improved their cleavage efficiency to an excellent level with no loss in strain coverage (about 98%). Both DNAzymes showed highly favorable cytotoxic/off-target profiles. Subsequent testing of Dua-01-L12R9 in BEAS-2B cells and sinonasal tissue demonstrated its significant antiviral efficiency.

**Conclusion:** Effective and specific management of RV infections with Dua-01-L12R9 might be useful in preventing asthma exacerbations.

### 0631 | Characterisation of Aspergillus niger and *A. tubingensis* related allergens relevant to asthma

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**Background:** Colonisation and IgE sensitisation to *Aspergillus fumigatus* is associated with decreased lung function in asthmatics. Our recent high-throughput sequencing data of the mycobiome in the lungs of patients with asthma and healthy subjects showed that higher quantities of fungal sequences from *Aspergillus* section *Nigri* were present in the lungs of asthmatics compared to healthy controls. This suggests that these black fungi could contribute to the asthma phenotype.

**Method:** To get a better understanding of this contribution, we investigated the IgE response to well characterised clinical isolates from two strains of the black fungi, which were most frequently

recovered from clinical samples of asthmatics, *A. tubingensis* and *A. niger*. Strains from *A. fumigatus* served as a positive control. Protein extracts of these fungi were used for immunoblots performed with sera from asthmatics with varying IgE-levels to *A. fumigatus* (0-66 kU/L, as determined by ImmunoCAP).

**Results:** Immunoblots showed that only those patients who were highly sensitised to *A. fumigatus* (≥17 kU/L) showed IgE-reactivity towards *Aspergillus* section *Nigri*, though the reaction was weaker than to the *A. fumigatus* controls. Six allergens with molecular weights of 15, 18, 23, 35, 50 and 100 kDa were recognized in *Aspergillus* section *Nigri*. Cross-reactivity between the different *Aspergillus* species was indicated by inhibition blots, where *A. fumigatus* proteins could inhibit IgE-reactivity towards *Aspergillus* section *Nigri* allergens. To identify the cross-reactive allergens, inhibition immunoblots were performed with available recombinant allergens of *A. fumigatus* (Asp f 3, 4 and 6). The fact that Asp f 3 and 6 inhibited IgE-binding to the three low molecular weight proteins allowed identification of these proteins as novel cross-reactive black fungi allergens. Peptide mass fingerprinting, performed to identify the remaining *Aspergillus* section *Nigri* allergens, yielded many potential candidates, which will be narrowed down by other techniques such as two-dimensional IgE immunoblots or immunoprecipitation followed by mass spectrometry analysis.

**Conclusion:** In conclusion, several allergens of the *Aspergillus* section *Nigri* were identified with some cross-reactivity to allergens found in *A. fumigatus*. Further characterisation of these allergens is ongoing.

## 0633 | Preventive and therapeutic effects of vitamin D in a mouse model of allergic asthma

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**Background:** It is known that vitamin D has anti-allergic effects to control the inflammation of asthma. We investigated whether vitamin D has anti-allergic and anti-inflammatory effects on sensitization and challenge stage of asthma development in murine model.

**Method:** Five groups of mice were designed according to ovalbumin (OVA) and vitamin D (VD) administration: control group, OVA group, preventive VD group (100 ng of VD injection before OVA sensitization), therapeutic VD group (100 ng of VD injection after OVA challenge), both VD group (100 ng of VD injection before OVA sensitization and after OVA challenge). Each group is evaluated for allergic and inflammatory markers such as airway hyper-responsiveness (AHR), cell counts in bronchoalveolar lavage fluid (BALF), cytokines in BALF, total IgE and OVA-specific IgE in BALF. Cytokines in lung lysate and major basic protein stained cell (eosinophil) in lung tissue are also evaluated.

**Results:** At the concentration of 50 mg/mL of methacholine, AHR was lesser in therapeutic VD and both VD group than in OVA group. Eosinophil, neutrophil, IL-5 in BALF and IL-4, TGF-β in lysate were decreased by preventive, therapeutic and both VD administration compared to OVA group. While, lymphocyte, macrophage, IL-4 in BALF and IL-5 in lysate were decreased by therapeutic and both VD administration and not influenced by preventive VD use. These anti-allergic effect of VD was most distinct when VD was administered for both preventive and therapeutic purpose.

**Conclusion:** According to these results VD may have the preventive and therapeutic effects on development and exacerbation of asthma in murine model.

## 0634 | Toxicity and adjuvant effect of silver nanoparticles in airway allergic inflammation

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**Background:** The effects of silver nanoparticles (SNPs) on airway disease have been remained as a controversy. In this study, we investigated the effect of inhalation toxicity on the size of silver nanoparticles and the effect on bronchial allergic inflammation.

**Method:** Female BALB/c mice and two different sized of SNPs (10 nm and 100 nm) were used for this study. First, to evaluate toxicity of SNPs itself, particles were administered intra-nasally for 4 weeks. Second, to evaluate the adjuvant effects of SNPs, we administered SNPs with or without ovalbumin (OVA) intra-nasally for 4 weeks. Body weight, airway hyper-responsiveness (AHR), cytology of broncho-alveolar lavage fluid (BALF), histology with immunochemical staining of lung, immunologic cytokines (interleukin-5, 13 and interferon-gamma), OVA—specific immunoglobulin titers (IgE, IgG1, IgG2a) were measured.

**Results:** Intra-nasal administration of SNPs (both 10 nm and 100 nm) alone did not make difference in AHR, histology, Th2-related cytokines between sham and SNP administered groups. But 100 nm SNPs induced significant increase in the number of total inflammatory cells, macrophages and neutrophils in BALF. Body weights of SNP-treated groups were less than sham group which was not significant. OVA specific IgG1 were elevated significantly in the 100 nm SNP group compared with 10 nm SNP group. In the second experiment model, nasal administration of OVA alone could not induce asthma. However, when administered with both OVA and SNP 100 nm particles, asthmatic bronchial inflammation was marked. Peri-bronchial and peri-vascular infiltration of eosinophils, neutrophils and macrophages were significant. Respiratory goblet cell hyperplasia was observed and specific IgG1, G2a to OVA were also elevated. The results of 100 nm SNPs were more prominent than

those of the 10 nm group. However, AHR and body weight did not show statistical difference between groups.

**Conclusion:** SNPs can act as adjuvants in bronchial allergic inflammation development in murine model. The effects are more prominent at 100 nm SNPs than at 10 nm SNPs.

## 0635 | The effects and uptake of gold nanoparticles in asthmatic mice

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**Background:** Nanoparticles are increasingly used as an advanced strategy for drug delivery and different medical therapies. The impact of nanomaterials in healthy and asthmatic models is still under investigation. Our aim is to investigate the uptake, influence and distribution of nanoparticles in BALB/c ovalbumin (OVA) asthma mouse model.

**Method:** Dispersions of citrate/tannic-acid-coated (citrated) 5 nm gold nanoparticles and polyethylene-glycol-coated (PEGylated) are given to asthma and control groups intranasally. Allergic airway resistance and airway inflammation are measured. Nanoparticle uptake into extrapulmonary organs is quantified by inductively coupled plasma mass spectrometry.

**Results:** The asthmatic precondition augments nanoparticle uptake. Furthermore, systemic uptake is more elevated for PEGylated gold nanoparticles compared to citrated nanoparticles. We also revealed that nanoparticles prevent both airway hyperreactivity and inflammatory infiltrates, especially citrated gold nanoparticles. PEGylated and Citrated NP-treatments in allergic asthma mice models significantly inhibit a strong increase of the macrophage population. More precisely, we found out that both types of NPs do not make any effect on M1 and M2 macrophages polarization.

**Conclusion:** Gold nanoparticles may have antiinflammatory effects in asthmatic mice. Asthmatic situations raises systemic uptake of gold nanoparticles.

## 0637 | Epidemiological survey of asthma based on the data of health insurance claims and specific health checkups for metabolic syndrome

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**Background:** Although many studies conducted in Western countries have shown that obesity is a risk factor for incident asthma, few reports have occurred in Asian countries. Although metabolic syndrome is a well-known risk factor for many non-communicable diseases, its contribution to asthma remains controversial. In 2008, metabolic syndrome-specific health checkups were started for all residents with public health insurance coverage in Japan. We aimed to clarify the relationships of obesity and metabolic syndrome with incident asthma among middle-aged adults in Japan.

**Method:** Data were collected and analyzed from health insurance claims and metabolic syndrome-specific health checkups at three large health insurance societies from April 2011 to March 2015. Among the subjects without asthma from April 2011 to March 2013, multivariate logistic regression analyses were performed to investigate the relationships between obesity and metabolic syndrome in the 2012 fiscal year compared with incident asthma from April 2013 to March 2015 (n = 9888). In order to compare the impact of obesity measures and metabolic syndrome on incident asthma, both obesity measures and metabolic syndrome were simultaneously entered into the statistical models as independent variables. All analyses were separately performed in men and women considering possible sex differences in relationship between obesity and risk of asthma. A $P$ value of $<0.05$ was considered statistically significant.

**Results:** Two hundred thirteen out of 5915 men and 211 out of 3973 women developed asthma. In women, BMI 25-29.9 kg/m$^2$ or $\geq$30 kg/m$^2$, waist circumference $\geq$90 cm, and waist-to-height ratio $\geq$0.5 were shown to be significant risk factors for incident asthma, with adjusted odds ratios (95% CI) of 1.93 (1.35-2.76), 2.24 (1.23-4.09), 1.89 (1.30-2.75), and 1.54 (1.16-2.05), respectively. The significance remained even after adjustment for metabolic syndrome. To be classified as metabolic syndrome preliminary group (abdominal obesity plus one of the following: hyperglycemia, hypertension, or dyslipidemia) was shown to be a risk factor for incident asthma only in women, but the statistical significance disappeared after adjustment for BMI. In addition, there was no significant relationship

(either in men or women) between metabolic syndrome and incident asthma.

**Conclusion:** This study confirmed the significance of obesity as a risk factor for incident asthma. Moreover, obesity appeared to be a stronger risk factor than metabolic syndrome.

## 0638 | Relationship between helminth infection, blood eosinophils and asthma symptoms in a rural community from the tropics

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**Background:** Immune response to helminths shares many features with the allergic response. In tropical regions where helminths are highly prevalent, asthma is still a major public health burden. Large clinical cohorts suggest that high blood eosinophils (HBE=>400 cells/mm$^3$) are associated with asthma exacerbations. However, the association between HBE and asthma severity in rural communities with prevalent helminthic infections is unclear.

**Method:** Patients with wheezing symptoms in the last year living in a rural tropical community (Santa Catalina, Colombia) where helminths are highly prevalent, were recruited for this study. Blood eosinophils were assessed by complete blood count. Parasitic infection was evaluated with two serial coprological exams (Kato-Katz method) and skin prick tests were conducted to determine reactivity to Ascaris.

**Results:** Seventy-three patients (mean age: 21; range: 2-64 years old) were recruited in this study. *A. lumbricoides* and *T. trichuria* active infection (47.9% and 16.4%, respectively) were not related to age or gender. A positive SPT to Ascaris extract, ABA-1 and *D. pteronyssinus* was observed in 23%, 18.4% and 34.2%, respectively. Mean eosinophil count was 621 cells/mm$^3$; 43.9% had HBE. Rate of patients with at least one emergency department visit was 61.9% and hospitalization, 21.9%. Blood eosinophil counts (as a continuous variable) were inversely associated with age ($P = 0.03$) and higher in helminth infection ($P = 0.002$). In crude univariate analysis, exacerbations (ER and/or hospitalization) were associated with age (OR: 0.96; 95% CI: 0.93-0.99, $P < 0.01$) and HBE (OR: 2.9; 95%CI: 1.1-7.8, $P = 0.04$), but not with helminth infection. For a better definition of asthma, multivariate analysis done in those >7 years old indicated that HBE, helminth infection and positive Ascaris SPT were not associated with asthma exacerbations.

**Conclusion:** Uncontrolled asthma is common in rural places of the tropics. Since helminth infection influences eosinophilia, the clinical value of HBE to predict exacerbations is limited in helminth-endemic populations.

## 0641 | Association of 19-bp del/ins dhfr polymorphism with bronchial asthma

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**Background:** The bioavailability of NO and endothelial homeostasis depends on the functional polymorphism of 19-bp Del/Ins within intron-1 of DHFR (*Dihydrofolate reductase enzyme)* (rs70991108) that could interfere in the regeneration of BH4 (tetrahydrobiopterin) from BH2 (7,8-dihydrobiopterin) and contributes to endothelial dysfunction in asthma.

**Method:** Asthmatics (n = 123) compared with control group (n = 50).The polymorphism was analyzed by PCR. Control of asthma assessed by (ACQ7 and PAQLQ). Statistical analysis with SPSS 23.0 establishing a significance level of $P < 0.05$.

**Results:** There are 80 women and 43 males in asthmatics and 39 women and 11 males in controls ($P = 0.137$). In asthmatics: age ($\bar{x}$ ± SD): 38.26 ± 19.24; and in control group: age ($\bar{x}$ ± SD): 51.50 ± 13.34. The genotype frequencies in asthmatics are: DD (6.5%); ID (66.7%); II (26.8%); in control group: DD (12.0%); ID (64.0%); II (24.0%); there is no statistical difference between groups ($P = 0.478$). The allelic frequencies in asthmatics are: allele D (39.8%); allele I (60.2%); in control group: allele D (44%); allele I (56%); there is no statistical difference between groups ($P = 0.476$).

The genotype frequencies in the uncontrolled asthmatics are: DD (0.0%); ID (61.1%); II (38.9%); in the controlled asthmatics are: DD (9.4%); ID (68.2%); II (22.4%); there is statistical difference between groups ($P = 0.047$). Genotypes ID and II are more frequent in the uncontrolled asthmatics. The allelic frequencies in the uncontrolled asthmatics are: allele D (30.6%); allele I (69.4%); in the controlled asthmatics are: allele D (43.5%); allele I (56.5%); there is a trend to have differences between groups ($P = 0.059$). Allele I is more frequent among uncontrolled asthmatics.

The uncontrolled asthmatics are older than the controlled asthmatics ($P < 0.001$). There is no differences in gender distribution ($P = 0.903$).

The genotype II confers a risk of being uncontrolled asthmatic of 2.950 times when compared with controlled asthmatics and adjusted for age: OR$^b$: 2.950 [1.117-7.789]; $P = 0.029$.

**Conclusion:** In this hospital based population we have demonstrated that this polymorphism is related with more severe asthma. Uncontrolled asthmatic patients are more frequent among those that express allele I. Homozygous II confers a risk of 3 times of being uncontrolled asthmatic when adjusted for age.

## 0643 | The advantage of periostin as the traditional markers of allergic inflammation in bronchial asthma

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**Background:** Allergic asthma very common phenotype in childhood. Introduction to clinical practice of monoclonal antibodies to IgE - omalizumab, IL 5 - reslizumab and in the future lebrikizumab (anti IL 13) requires the selection of patients for therapy. Effector cells and serum proteins are proposed for the role of markers of specific inflammation. Serum periostin (SP) is a protein produced by fibroblasts under the action IL 13. It is known, that SP predictor of lebrikizumab efficacy in clinical studies in adult patients.

**Method:** The study included 75 children (6-17 years) with uncontrolled asthma. The group of mild asthma - 51 people, moderate asthma - 24 people. The patients were examined: serum eosinophils (EOS), SP, spirometry. The cut off $0.4 \times 10^9$ was chosen for high eosinophilia. Patients are divided into 2 groups with high and low periostin by median - Me (Q1; Q3). Analyses included descriptive statistics, logistic regression, Spearman correlation.

**Results:** The level of SP was in the range 0.17-22.6 ng/mL, Me—3.93 (1.96; 7.80) ng/mL. In the group of mild asthma patients with high SP - 40.0%, in the group with moderate periosteum 72.7% ($P = 0.02$). Medians for mild asthma was 3.14 (1.80; 5.42), for moderate asthma 5.71 (3.52; 10.53). Differences are significant ($U = 790.5$, $P = 0.003$).

Patients with serum EOS $> 0.4 \times 10^9$ in the group with mild and moderate asthma were not statically different (29.2% vs 33.3%, $P = 0.79$).

There were no significant Spearman correlation between eosinophils, SP, $FEV_1$, $FEV_1$/FVC in children with asthma.

Logistic regression analysis showed that SP is the best predictor severe asthma, odds ratio 1.22 CI 95% (1.07-1.42), $P = 0.004$.

**Conclusion:** Serum Periostin significant predictor of severe and moderate asthma. IL13—associated is widely represented in the children's population. Monoclonal antibodies to IL 13 may be promising for the treatment of childhood asthma.

SUNDAY, 27 MAY 2018
TPS 02
CLINICAL ASPECTS OF ASTHMA

## 0645 | Asthma in a gas station worker

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**Background:** Although several large epidemiological studies have demonstrated a strong association between exposure to motor vehicle traffic emissions and allergic symptoms and reduced lung function, the evidence for the development of allergic sensitization from hydrocarbons is less abundant than for the aforementioned associations

**Method:** We present a 35-year- old patient with allergy and seasonal asthma in childhood. Worker of a gas station, required long sick leaves during which he remained asymptomatic, worsening with serious exacerbations in the work environment despite treatment with high doses of ICS-LABA and rescue SABA.

We performed a forced spirometry with bronchodilation test at baseline and the study of occupational asthma without working after discontinuing the treatment: non-specific bronchial provocation with methacholine before and after the specific bronchial provocation and specific bronchial provocation in the inhalation chamber with hydrocarbons.

**Results:** Baseline spirometry: FVC 86%, FEV1 86% TI 83 FEF 75/25 78.1%

Occupational asthma study:

- Non-specific bronchial provocation with methacholine after specific bronchial provocation: PC 20 1.43 mg/mL
- Non-specific bronchial provocation with methacholine after specific bronchial provocation: PC 20 0.5 mg/mL
- Specific bronchial provocation in inhalation chamber with hydrocarbons (diesel and gasoline): Drop in the FEV1 of 18.5% at the end of the test maintained for 6 hours, reverts with B2 agonist.

**Conclusions:** Occupational asthma, by direct inhalation of fuel, has not been extensively studied in the literature. We confirmed the diagnosis of presumption of moderate-severe persistent asthma with exacerbation of occupational origin by hydrocarbons in a gas station worker by occupational asthma study in the inhalation chamber.

## 0646 | Case-report: The combination of recurrent papillomatosis of the trachea and bronchial asthma

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**Case report:** The patient (33-y.o. woman) appealed with complaints of dyspnea, cough and sharp difficulty breathing at swallowing. The patient gives history of the bronchial asthma since 2001 with basic treatment by *formoterol/budesonide 4.5/160* μg; since 2012 she had pollinosis. Early in April 2014 the symptoms of seasonal rhinoconjunctivitis, dry paroxysmal cough, hoarseness have appeared, the basic therapy didn't give effect. The spirometry was not run during the pulmonologist visit, the patient condition was diagnosed as neurotic, the anxiolytics were prescribed. During the treatment the symptoms increased, discomfort during swallowing, distant whistling rales in the chest has joined; inhalation of *formoterol/budesonide 4.5/160* μg and short-acting β2-agonists gave not effect. During the examination heard the distant wheezes over the trachea and larynx, there was the participation of auxiliary muscles in breathing; during the auscultation there were a lot of buzzing wheezing, which was regarded as wired. In conducting of spirometry the data for the obstructive changes was not received: FEV1 113%, FVC 120%, the sample with *salbutamol 400 μg* was negative. The discrepancy between the clinical symptoms and data of physical and instrumental methods of examination were taken in account and the bronchoscopic examination was run. Data of the bronchoscopy: in the middle third of the trachea is visualized tumor formation up to 1.5-2 cm in diameter with new formations up to 2 mm in the mucosa joined to the basic growth. The removal of papillomas with electropathy was run under local anesthesia; small papillomas were removed with use of photodynamic therapy. After operation the symptoms fully has stopped. The spirometry figures were in the normal range (FEV1 135%, FVC 134%). It was the reason for basic therapy changes: the use of *formoterol/budesonide of 4.5/80* μg in SMART. Resume: lack of attention to anamnesis data and knowledge according to the problem of primary care physicians were cause for untimely necessary instrumental examinations and, as a result, prescribing of the various medicamental treatments without effect. It caused further growth and spread of papillomas. This case-report demonstrates the necessity for regular monitoring of bronchial permeability by spirometry and/or peak flow as well as long-term observations of patients by one doctor. This allows to identify the symptoms changes and apply all necessary diagnostic and therapeutic steps.

## 0647 | Effects of viral infections for asthma development in wheezy children

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**Background:** Viral infections especially rhinovirus and respiratory syncytial virus (RSV) infections may affect asthma development in wheezy children. In this study we aimed to evaluate the effects of viral infections on asthma development.

**Method:** We evaluated 33% girl, 67% boy 1013 atypic (30%) and typic (70%) wheezy children's respiratory virus panels for viral infections retrospectively.

**Results:** Average ages, ages of first attack and attack times per year were 11 ± 8 years, 26 ± 14 months, 4 attack/year respectively. Half of the patients had attacks at winter. We isolated virus in 45.2% of the patients (54% typic, 46% atypic). The most common viruses were rhinovirus (16.2%), RSV (15.8%), parainfluenza virus (8.3%), influenza A virus (8.3%), adenovirus (3.9%). There wasn't any statistical difference between atypic and typic wheezy patients according to viruses. Virus was isolated in 45.5% of the typic wheezy patients. The most common viruses in these patients were rhinovirus (17.2%), RSV (14.8%) and parainfluenza virus

Forty percent of these wheezy children developed asthma. Virus isolation rate for these patients was 51%. Twenty-five percent of the virus isolated patients had developed asthma. When we compared patients with and without asthma we didn't find any difference for virus isolation and isolated virus types. There wasn't also any difference between atopic and nonatopic asthma. Rhinovirus was mostly isolated in the patients with poor income.

**Conclusion:** In conclusion we didn't found viral infections as a risk factor for asthma in wheezy children.

## 0649 | Clinical and functional features of patients with bronchial asthma

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**Background:** Purpose: conduct a study on clinical and functional features of patients with bronchial asthma.

**Method:** 195 patients with BA Steps 2 and 3, who have been using "on-demand" short-acting beta2-agonists, and who did not take basic medical drugs in the last 3 months (glucocorticosteroids, long-acting beta2 agonists), were examined. 95 patients (49%) were found to have BA Step 3, and the other 100 patients (51%) BA Step 2. The duration of disease amounted to 10.62 ± 0.43 years (3-20 years). As per results of the Asthma Control Test (ACT), the symptom control level recorded a score of 17.09 ± 0.14 (11-20) on an average out of the maximum 25. Twenty healthy volunteers comprised the control group. Condition of the patients was assessed subjectively based on a five-point scale (1-5) and on the daily requirement for short-acting B2-agonists; whereas, objective assessment was conducted based on the figures of the external respiratory function (ERF) and diurnal variation in peak expiratory flow rate (PEFR).

**Results:** At the time of inclusion of patients in the study, the diurnal variation in PEFR was 24.58 ± 0.19%, ERF figures (6 parameters) and accurately decreased when compared to CG ($P < 0.001$). Moderately severe obstruction was detected in 126 patients, moderate obstruction (FEV1 60-63% of the due) in 45 patients, apparent obstruction (FEV1 47-49% of the due) in 24 patients. Assessment of the condition of patients on the choking intensity in points also revealed an accurate difference between groups, with a high degree of choking among patients with asthma BA Step 3 ($P < 0.001$). Dynamics of bronchial obstruction was fairly higher among patients with BA Step 3 compared to patients with BA Step 2 ($P < 0.001$ for both figures). Velocity and volume figures of ERF in patients with BA Step 3 were lower compared to patients with BA Step 2 ($P < 0.05$, $P < 0.001$). The frequency distribution of patients in groups based on the obstruction levels revealed that patients with BA Step 3 of apparent obstruction fairly dominate the group compared to patients with BA Step 2 ($P < 0.01$).

**Conclusion:** The study showed that BA patients with an increased step of disease experience an increase in the dynamics of bronchial obstruction, which determined based on the diurnal variation in PEFR, a decrease in the velocity parameters of the ERF, and an increase in the choking intensity; the remaining subjective data does not depend on the step of disease.

## 0651 | Physician beliefs about asthma diagnosis: Results of an electronic survey to identify specialty-specific knowledge-gaps versus a transculturized evidence-based clinical guideline recommendations

Larenas-Linnemann DE[1]; Luna-Pech JA[2]; Rodriguez-Gonzalez M[3]; Fernandez-Vega M[4]; Del Rio-Navarro BE[5]; Cano-Salas MDC[4]; Ortega-Martell JA[6]; Romero-Lombard J[7]; Lopez-Estrada EDC[4]; Salas-Hernandez J[4]

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**Background:** Diagnostic strategies for asthma have been improved in past years favored by a better understanding of its

physiopathology and the emergence of evidence-based clinical guidelines. However, variation still exists among some diagnostic aspects of asthma in real life. It is unknown to what degree diagnosis is affected by the treating physician's medical specialty.

**Method:** An online survey of general practitioners (GPs) and board-certified physicians of 4 medical specialities about their knowledge about diagnostic criteria, phenotyping and classification of asthma was performed. The replies were analyzed per specialty against the newly-developed 2017 Mexican Asthma Guideline's (MAG) evidence-based recommendations. Response proportions were contrasted with chi square.

**Results:** A total of 62 GPs, 239 pediatricians, 364 allergists, 161 pulmonologists and 34 otolaryngologists (ORLs) replied. Although for general application of diagnostic clinical criteria all physicians rated similarly, in general accordance with the MAG suggestions, a third of non-pulmonologist practitioners don't recognize chest discomfort as one of the clue symptoms of asthma, but they erroneously believe crackles are ($P$ = 0.01). We found agreement in almost half of all physicians to erroneously believe that viral illness' induced wheezing in non atopic children predisposes asthma. Conversely, 75-85% are aware that allergic sensitization predisposes to asthma. Most specialists -except pulmonologists ($P$ = 0.02)- incorrectly listed FEV1 as the best parameter to identify airflow obstruction (AO) and FEV1/FVC to assess AO severity. 20% of GPs do not know peak expiratory flow (PEF) measurements could be valuable, and 75% of all specialists are not aware that changes in PEF can also be used to confirm AO reversibility. To classify asthma, only pulmonologists adequately considered the level of control in similar proportion than severity (81% and 83%, respectively), which is uniformly the preferred method by most other specialists.

**Conclusion:** Although in general many clinical aspects of asthma diagnosis seem to be accurately assessed, there is a wide speciality-specific variation regarding some aspects of phenotyping and classification, diverging from MAG's recommendations. As such, our results can help to detect knowledge-gaps and to guide the development of more focused specialty-specific learning tools to improve clinical impressions, process medical evidence, and apply it to patient care.

## 0652 | Issues, continuous medical education on treatment of acute asthma, exercise induced asthma and asthma in pregnancy should include, per medical specialty

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**Background:** To unify and improve the management of asthma, including asthma exacerbations, the Mexican Guideline on Asthma (Guía Mexicana del Asma -GUIMA 2017) was developed, as a transculturization of the highest scoring internationally available asthma guidelines (BTS/SIGN, GEMA, GINA). Just prior to the GUIMA launch, knowledge of physicians was evaluated as part of the guideline dissemination plan and to detect specialty-specific knowledge

| % of correct answers (%) | GUIMA R = recommends S = suggests | Allergist (N = 364) | Pulm (N = 161) | Pediatr (N = 239) | ENT (N = 34) | GP (N = 62) |
|---|---|---|---|---|---|---|
| 1. The first-choice initial treatment of every mild-moderate, asthma exacerbation without complications is: | R: SALB MDI 2-4 puffs or Nebulized SALB every 20 min (NOT: SALB+Ipratropium Br) | 66<br>45<br>49 | 80<br>46<br>43 | 78<br>53<br>50 | 50<br>50<br>36 | 71<br>53<br>42 |
| 2. The initial treatment of every patient with an asthmatic crisis includes systemic corticosteroids | S: yes | 31 | 30 | 30 | 14 | 21 |
| 3. In a severe crisis salbutamol + ipratropium bromide combined nebulization is more effective than solely salbutamol | S: yes | 75 | 69 | 70 | 79 | 61 |
| 4. Recommendation of several add-on medications for crisis | Of all correct add-ons, % ticked: | 8-70 | 12-80 | 12-79 | 0-57 | 5-71 |
| 5. Can Dexamethasone IM or PO substitute prednisone? | R: yes | 70 | 61 | 63 | 86 | 82 |
| 6. Exercise induced asthma can be treated with… | R: Inhaled salb (or montelukast) | 87<br>36 | 90<br>25 | 88<br>24 | 86<br>36 | 90<br>32 |
| 7. During pregnancy, which ICS is recommendable? | R: Budesonide | 46 | 46 | 44 | 36 | 38 |

gaps that might lead to a more specialty-directed teaching of GUIMA concepts.

**Method:** An online questionnaire, Surveymonkey® was sent out to board-certified members of National Societies of four specialties (allergists, pulmonologists, paediatricians, ENTs) and GPs. Results for treatment of acute asthma, exercise induced asthma and asthma in pregnancy are presented here and compared with GUIMA recommendations. Pearson's Xi-square was used to detect differences between specialties.

**Results:** We had a total of 860 replies, see table 1. For severe acute asthma, allergists and ENTs knew less about magnesium sulphate than PED and PULM ($P$ = 0.001). Less than 1/5 of allergists and ENTs knew about heliox. Theophylline is still mentioned by half of all physicians, though it is no longer recommended for acute asthma. Only a third knew budesonide is 1st choice ICS in pregnancy.

**Conclusion:** In general, several areas sensible for improvement could be detected, but with no clear specialty-dependent difference. Continuous medical education in acute asthma should contain the following messages: (i) frequent inhaled SABA is the first line of treatment, leaving more expensive double-bronchodilator treatment for severe cases; (ii) early introduction of systemic corticosteroids; (iii) theophylline does not form part of the treatment of acute asthma; (iv) there are several add-on treatment options for severe asthma exacerbations (e.g. heliox, magnesium sulphate). For exercise induced asthma montelukast is a treatment option, and budesonide is the ICS of choice in pregnancy.

## 0654 | Smoking in adolescents in Latin America – A sad reality

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**Background:** Smoking in Latino America (LA) is very common in adults. Despite the anti-smoking prevention programs, many teens start smoking at school age. We evaluated the prevalence of smoking in adolescents living in LA.

**Method:** A prospective study conducted in adolescents (N = 5847; 12-19 years; mean = 14.5 years), enrolled in municipal schools in 8 cities from 5 countries (Argentine, Brazil, Cuba, Mexico, Paraguay) in LA, who answered a self-administered questionnaire on smoking *(California Tobacco Survey*)*

**Results:** Although 75.3% of adolescents in Latin America are told by their parents not to smoke, 39.5% have had tobacco experimentation (ever tried a cigarette, even one or two puffs), and 22.7% smoked at least once in the last month. 36.3% of those have had tobacco experimentation started smoking before 12 years of age.

Teens reported having ease in getting cigarettes (66.7%), although 92.6% believe that smoking at least one cigarette / day is harmful to their health, 43.8% have a smoker friend and 27.3% would smoke a cigarette if it were given to them, 26.1% believe they are more respected because they smoke, and 30.7% believe that smokers have more friends, 49.4% have tried to quit smoking, 32.2% stated that they would smoke if there was a less toxic cigarette, 63.5% knew the electronic cigarette, 57.1% know about hookah. 45.0% are prohibited from smoking at home and 25.3% have no restriction on smoking at home.

**Conclusion:** The prevalence of smoking among adolescents in LA is high. The implementation of measures to reduce/stop tobacco use and its new forms of consumption, such as electronic cigarettes and hookah in schools are urgent and imperative.

## 0656 | Role of community pharmacists in educating patients with asthma

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**Background:** In asthma, the preventive measures taken by patients play an important role in improving life span and quality of life. This can be done more efficiently by community pharmacists by providing patient counseling and improving knowledge of patient about disease, risk factors, medication management and preventive measures to control asthma.

The objective of the study was to evaluate the contribution of community pharmacists in improvement of life span and quality of life of asthma patients.

**Method:** The study was performed from Mid September to Mid-December 2016 in the city of Lezhe, Albania. Data were collected by using a structured face to face questionnaire with randomly selected different community pharmacies. The questionnaire composed of different closed questions about the action plan of pharmacists in asthma management and factors that affect the counseling of asthma patients by the pharmacists.

**Results:** It is noteworthy to observe that, in general, pharmacists are sufficiently knowledgeable and competent to counsel their asthma patients effectively.

**Conclusion:** The present study has revealed a number of salient points. Firstly, community pharmacists believe that, on the whole, their patients' level of asthma management is optimal. In an attempt to improve this situation, there is a need to broaden pharmacists' perceptions of their role in asthma management beyond counseling primarily on the medications dispensed. However, as time is a major factor influencing pharmacists' ability to counsel, significant changes

are needed within community pharmacy that will facilitate pharmacists using their professional skills to become more actively involved in patient care and disease management and moving away from the traditional role of medication supply.

## 0659 | Authorizations process analysis of an immunotherapy prospective cost-effectiveness study in asthma patients sensitized to mites: The ITACA study (Late Breaking Abstract)

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**Background:** Few studies evaluate the cost-effectiveness of immunotherapy for allergic disease, until now mainly based on pharmacoeconomic models and not on the analysis of data collected prospectively in real world setting. Immunotherapy is clinically effective, but we must know if it is also from the economic perspective. To cover this need a study adjusted to "real life" was designed. The objective of this communication is to show a temporal metric of the authorizations management of the study and to evaluate the administrative difficulties with which the post-authorization studies of prospective follow-up are found in Spain.

**Method:** This is an observational cost-effectiveness study post-authorization of prospective follow-up. Fifty centers with national representation were selected in 14 Autonomous Communities. Patients with confirmed diagnosis of asthma with or without rhinoconjunctivitis due to sensitization to mites with indication of treatment with specific immunotherapy would be included. Patients would be observed for six months before starting immunotherapy, and followed up to six years, with a total duration of follow-up of six and a half years.

**Results:** Fifty eight percent of the selected centers (29) finally participated in the study. The mean time from the acceptance of the study by the researcher until the signing of the contract with the center was 130 days (IC 95% 95-164). The mean time from the request for authorization to the Autonomous Communities to the approval of the study was 73 days (95% CI 39-108). Two autonomous communities did not authorize the study and as a consequence 11 centers (22%) were withdrawn from the study.

**Conclusion:** Pos authorization prospective studies face great administrative difficulties, in spite of their importance since they constitute a real reflection of the results of the effectiveness of the treatments. These difficulties should be solved by the health authorities in order to promote the knowledge of effectiveness in real life.

SUNDAY, 27 MAY 2018
TPS 03
OCCUPATIONAL ALLERGY, ASTHMA AND RHINITIS

## 0660 | Evaluation of wheat flour sensitivity and respiratory symptoms in a bread factory in Ankara, Turkey

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**Background:** Baker's asthma (BA) is one of the most common causes of occupational asthma. The prevalence in our country is reported as 5%. The main allergen causing BA is wheat flour. The aim of study was to determine respiratory symptoms and allergic sensitization to wheat flour in workers of a bread factory in Ankara.

**Method:** All steps of the study were carried out in the workplace by the research team who made regular visits to the bread factory. A survey was conducted to determine the presence of respiratory symptoms and its relation with the occupation. Skin prick tests with respiratory allergens (house dust mites, storage mites, grass pollen mix, aspergillus] and food allergens [wheat, rye, oats and barley flour, egg white, egg yolk) were performed. Pulmonary functions were measured by a portable spirometer.

**Results:** A total of 162 patients (F/ M: 3/159, mean age 38.25 ± 7.8 years) were included in the study. The mean working period was 11.23 ± 7.38 years. Eighty-four workers (51.9%) were smokers. Family history of asthma was positive in 7 (4.3%) individuals. There were 118 (71.7%) employees who had exposure to flour. Of the 99 workers (61.1%) who described symptoms, 88 (88.8%) had nasal, 57 (57.5%) had respiratory and 35 (35.3%) had eye symptoms. In 71 (72.4%) employees, the symptoms began after starting work. The symptoms increased at workplace in 68 (69.4%) and decreased at off-work period in 54 (55.1%) workers. Of the 68 employees who described increase in symptoms at workplace, 51 (68.4%) had an increase with flour exposure and 11 (16.1%) with flour plus additives. Prick skin tests were positive in 43 (26.5%) employees. Sensitivity to wheat flour was present in 23 (14.2%) subjects among all workers. Wheat flour sensitivity was positive in 19 (19.2%) of 99 employees with respiratory symptoms and in 13 (25.5%) of 51 employees who stated increased symptoms with flour exposure. Among all workers 9 (5.5%) employees were diagnosed as asthma and 7 (4.3%) workers were diagnosed as BA.

**Conclusion:** Wheat flour sensitivity is high among workers who are exposed to wheat flour, however the prevalence of BA is similar to the previous data in the literature.

## 0661 | Occupational allergy to transglutaminase in a chef—A case story

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**Background:** Enzymes are well known as sensitizers and causes of occupational allergy primarily in the industries producing and using the products. We present a case of occupational contact urticaria, rhino-conjunctivitis and asthma in a 32 year male chef who was using a transglutaminase enzyme powder obtained from fermentation of *streptomyces mobaraense* as meat glue in processing of fine culinary dishes. This transglutaminase has been used for protein food preparation in industrial settings since 1992 to improve the texture of protein rich foods such as surimi or ham. In this case it was used in small scale in a gastronomy restaurant kitchen spraying enzyme powder with a sieve over raw meat without any protective equipment in contrast to the producer's recommendation. The chef was also found allergic to dried, edible mushrooms also forming part of the meat dish prepared with the transglutaminase enzyme powder. In one occasion he experienced an oral reaction with itching and swelling of the mucosa in the mouth, stridor, angioedema of the face, and urticaria after ingestion of beef meat treated with transglutaminase and rolled in horn of plenty dried mushroom powder.
No other symptoms of food allergy were reported but a known cat allergy was.

**Method:** Skin prick test, Histamine Release Test, Peak flow measurements and pulmonary function tests.

**Results:** Skin prick tests (SPT) were positive to saline solutions of two transglutaminase enzyme powders and mushroom powders of (horn of plenty (*craterellus cornucopioides*), porcini (*boletus edulis*), dotted stem bolete (*boletes luridiformis*), king trumpet (*pleurotus eryngii*) and cat. SPT were negative to meat from cow, pig, lamb, other mushrooms, common food allergens, pollens, dog, horse, house dust mites and moulds.
SPT were negative to additive components of the transglutaminase enzyme powders (maltodextrin, miprodane and lactonate). SPT with the transglutaminase enzymes was negative in a control subject.
Histamine Release Test with two transglutaminase enzyme powders and horn of plenty were highly positive in the patient.
Peak flow measurements during weekdays showed a 21% variation with reduced values at the end of workweeks. FeNO 27.9 ppb. Normal FEV1 and FVC.

**Conclusion:** We present to our knowledge the first case of enzyme allergy to transglutaminase used in molecular gastronomy.

## 0662 | Three case of work-related rhinitis in a pathology unit

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**Background:** Formaldehyde and xylene are occupational skin and respiratory irritant and/or sensitizer, exposure to those may be associated with dermatitis, rhinitis and asthma. Health care workers, as nurses, laboratory technicians, doctors could be exposed in different tasks in operating rooms, endoscopy and in pathology laboratory.

We describe three cases of work-related rhinitis in technicians employed in the same unit of hospital pathology .

**First case:** A woman of 38 years old underwent medical examination in our occupational allergy unit because allergy respiratory symptoms. She has been working for 8 years in pathology laboratory and was exposed to xylene and formaldehyde. She developed rhinitis, rhinosinusitis, hyposmia and cough with sputum after 5 years started work. She had negative skin prick test for common aeroallergens. Lung function was normal with a FEV1/FVC ratio of 80% of predict. Blood cells count reveled 15% of eosinophils (980/mmc) with 6550 total leucocytes.

**Second case:** A Woman of 40 years old was affected by moderate persistent allergic rhinitis with positive skin prick tests to house dust mite, dog and cat. In the last year rhinitis symptoms worsened in relation to work and improved during vacation. When she was exposed mostly to formaldehyde during shift at the end of it she usually experienced face skin and conjunctival erythema. She developed work-related symptoms after 14 years of exposure in the pathology unit.

**Third case:** A woman of 38 years old, who has been working for 14 years in the pathology unit and was exposed to formaldehyde and xylene, in the last year developed moderate-severe persistent rhinitis with hyposmia and chronic cough. She referred to otorhinolaryngologist and an irritant induced rhinitis was diagnosed. She had negative skin prick test for common allergens and normal lung function.

**Results and conclusion:** The workers experienced respiratory symptoms in relation to work exposure to formaldehyde and xylene. The suspected causal agents were monitored in the work environment and an exceeding of the recommended limit values was found. Preventive measure were adopted with a reduction of exposure and symptoms improve only in the second and third case.

## 0663 | The usefulness of the mannitol challenge test for occupational asthma in bakers—preliminary results

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**Background:** Diagnosis of occupational asthma (OA) requires methods of high specificity and sensitivity to exclude false positive and false negative results. The specific inhalation challenge test (SICT) remains the reference method for the diagnosis of OA. Monitoring of SICT comprises evaluation nonspecific bronchial responsiveness (NSBHR) measured at baseline and after SICT. Inhalant challenge test with mannitol is considered to be more specific than test with methacholine. Also, duration of procedure is shorter and safer. Therefore the study aim was to compare the usefulness of these two tests in monitoring of SICT.

**Method:** Four bakery workers with suspicion of OA underwent single-blind, placebo-controlled SICT with workplace allergens accompanied by evaluation of NSBHR with mannitol and methacholine before and after SICT. Clinical examination, spirometry, skin prick tests (SPTs) to common aeroallergens and occupational allergens, serum specific IgE antibodies to occupational aeroallergens were also performed.

**Results:** Positive SPTs results to occupational aeroallergens were found in all bakery workers, specific IgE to flours were detected only in two subjects.

Three out of the four patients displayed positive SICT reaction (in two cases early spirometric response). In all of these 3 patients, airway response to methacholine increased significantly. In the first two patients also airway reaction to mannitol was significant, whereas in one subject with early reaction there was no increase in NSBR after mannitol inhalation. The patient with negative SICT results did not reveal any changes in NSBR before and after the test, neither to methacholine nor mannitol.

**Conclusion:** Preliminary results indicate the need of further investigations to evaluate the usefulness of mannitol challenge test in the diagnostics of occupational asthma.

## 0664 | Occupational rhinoconjunctivitis and asthma caused by allergy to buckwheat flour

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**Background:** Buckwheat *(Fagopyrum esculentum)* is a herbaceous plant of the *Polygonaceae* family, originated from Central Asia. There

is an increasing use of buckwheat flour since it is marketed as a healthy, gluten-free substitute for patients with celiac disease and is also used in "organic or ecological" food. IgE-mediated allergy to buckwheat by inhalation and ingestion of its flour has been described previously.

**Method:** A 45-year-old male baker with a history of mild allergic rhinitis to mites presented with 8 months of coughing, wheezing, dyspnea, sneezing, rhinorrhea and ocular pruritus when his co-worker kneaded buckwheat flour. Symptoms disappeared when he performed his usual work, kneading wheat flour and rye, and when he was at home.

A skin prick-test with aeroallergens and food (including flours) was performed. Testing included a prick-prick test with buckwheat flour and a prick test with an extract of this flour at 5% w/v prepared by ALK-Abelló. Further workup included specific IgEs to flours (ImmunoCAP™), immunoblotting, methacholine challenge test and specific bronchial challenge (SBC) with buckwheat flour by exposure in a challenge chamber.

**Results:** Skin tests were positive for dust mites and buckwheat flour extracts. Total IgE was 187 KU/L with specific IgE to *Dermatophagoides pteronyssinus*, *Lepidoglyphus destructor*, buckwheat, and cereal flours of 10.1, 1.98, 15.4 and <0.1 KU/L respectively. Immunoblotting detected several IgE-binding bands against different proteins of buckwheat extract (9-75 KDa). Methacholine test was positive. After 4 minutes of exposure to buckwheat (SBC), he developed rhinoconjunctivitis with a 30% reduction in his FEV1.

**Conclusion:** We present a case of occupational rhinoconjunctivitis and asthma from IgE-mediated allergy to buckwheat flour in a baker. Due to the increased consumption of "organic" and gluten-free food, we will likely see a higher prevalence of allergy to this flour.

## 0665 | Two cases of occupational fish allergy caused by percutaneous sensitization

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**Background:** Occupational hand eczema is a common health problem in food handlers and cooks. Recently, it has been recognized the importance of percutaneous allergen sensitization through damaged skin. Direct exposure to food allergens through damaged skin could lead to develop food allergies among food handlers and cooks with hand eczema. It has not been well-documented whether percutaneous exposure to food allergens through damaged skin is a significant risk factor for the development of food allergy in adults or not.

**Case:** Two 26-year-old women (case 1 and case 2) with hand eczema visited our department because of fish allergy and eczema. They are dietician of our hospital, and daily handled raw fish for cooking without groves. Case 2 had atopic dermatitis. They had no history of food allergy before being employed. Their hand eczema appeared after starting their work, and they subsequently started to experience food allergy symptoms such as intraoral itchiness or dyspnea after ingestion of raw or cooked fish. During cooking of fish, they presented urticaria, eyelid swelling, dyspnea, and cough. The specific IgE antibodies were detected for many fishes in both cases. They need to avoid fish at this time.

**Conclusion:** Hand eczema is a risk factor for occupational food allergy, so we should recommend food handlers to avoid direct contact exposure to fish. The treatment of eczema and use of gloves while handling fish, which contribute to avoid percutaneous sensitization to fish allergens, are important to prevent fish allergy. More attention should be paid to the risk of occupational food allergy by percutaneous sensitization.

## 0666 | Allergic reaction to calving: A-galactose as a new occupational allergen

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**Background:** Many non-primate mammalian cells, glycoproteins and glycolipids contain galactose-α-1,3-galactose (α-Gal) motif in their glycosylation. Various sources of α-Gal have already been reported, as red meat, organ meat (especially pork kidney) and dairy products, gelatin-containing foods and drugs, immunoglobulins, biologics and xenograft tissues (ie. porcine bioprosthesis).

**Case report:** Here, we report the case of a 36-year-old male farmer with tick-bite history, who have experienced a recurrent acute urticaria since several years. He first presented a generalized urticaria after consuming an aspic containing pork gelatin. Then, he noticed other similar episodes and suspected pork meat dishes as the only shared factor. He also experienced several localized urticarial eruptions 30 minutes after contacts with bovine placenta and amniotic fluid when assisting during calving; some of these reactions were secondarily generalized. No cofactor has ever been identified. The patient gave his written consent for the publication of the clinical details and images of this communication.

**Results:** Skin prick tests (SPTs) were performed to aeroallergens and common food allergens, all negative. SPTs to meats have only resulted in a positive test for veal raw meat and an isolated erythema without wheal for pork kidney. The α-Gal allergy was confirmed by ruling complementary SPTs and blood samples; SPT to Cetuximab was positive, and IgE ($kU_A/L$) to α-Gal was 2.74 to bovine thyroglobulin and 0.21 to bovine serum albumin.

**Conclusions:** Lately, presence of α-Gal has been noticed in many bovine placenta and amniotic fluid glycoproteins. A recent spanish publication has reported the cases of 3 known α-Gal-allergic patients who experienced allergic contact urticaria on exposure to amniotic fluid when assisting during calving. One of them also presented a lower respiratory tract involvement, probably due to inhalation of amniotic fluid proteins. The medical history of these cases is not suggestive of a calving-induced sensitization.

This new occupational exposure to α-Gal could have some legal implications and should lead to specific recommendations for α-Gal allergic subjects working in cattle or veterinary workplace.

## 0667 | A case of dimethyl fumarate causing a multisystem occupational allergic reaction

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**Background:** Dimethyl fumarate (DMF) is a mould-growth inhibitor and potent sensitizer commonly found in sachets contained in furniture, or in boxes for footwear, clothing, and leather-based accessories. Type IV delayed hypersensitivity reactions to DMF in the form of allergic contact dermatitis have been well established, and have led the European Union (EU) to ban the importing of products containing this chemical in 2009. However, immediate type I hypersensitivity reactions to DMF are rare, and reports are scant in the literature. The compound is not banned in countries outside the EU.

**Objective:** We report a case of a healthy 35-year-old female retail worker who had developed generalized pruritus, a sensation of throat constriction, and urticaria to her face, trunk, and upper extremities. Her reactions occurred while unpacking new clothes and while steaming clothes that were shipped in boxes that contain desiccant sachets with DMF.

**Methods:** Patch testing was performed to the North American Contact Dermatitis Group (NACDG) and textile series. DMF was tested with open patch testing. A literature search was performed to review reports of hypersensitivity reactions to DMF, including immediate hypersensitivity reactions causing multisystem symptoms.

**Results:** This patient developed localized urticaria with no respiratory involvement within 30 minutes of an open patch test with DMF. Her symptoms abated within an hour with the use of cetirizine. Due to the immediacy and severity of the reaction with open patch testing, we did not proceed with skin prick testing with DMF due to the risk of provoking a systemic reaction. Her patch test to the NACDG and textile series was negative.

**Conclusion:** To our knowledge, there have been no reports of rapid onset diffuse urticaria with upper respiratory symptoms due to DMF exposure. In addition to allergic contact dermatitis, the potential for immediate allergic reactions and anaphylaxis reinforces that DMF should be considered a hazardous compound. Regulation of this compound should be strongly considered in countries where restrictions have not already been imposed. In regions where the compound is restricted, physicians may still encounter cases of allergic reactions to DMF, including anaphylactic-type reactions, due to DMF-containing goods that are either illegally imported or purchased abroad.

## 0668 | Rice-induced occupational anaphylaxis and socio-economic impact-case report

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**Background:** Few cases of IgE-mediated hypersensitivity to rice were published despite its wide consumption. Inhalation of rice flour or steam of cooked rice caused rhinoconjunctivitis, bronchial asthma or generalized urticaria and in same cases anaphylactic reaction. The same reactions may occur also in occupational exposure to foods. Lipid transfer protein (LTP) as in peach/apple was a relevant allergen of rice-induced anaphylaxis. We present a case of a cook experienced anaphylaxis after occupational inhalation of rice cooking vapors.

**Case report:** In October 2015 a 27 year old boy, non atopic, smoker (2.5 pack year) started working as cook head match instructed to cook every day 4 kg of vialone rice and 2 kg of venus and basmati rice. Few months later he developed pruritus and tingling lips within minutes of eating rice so he avoided it from his diet. Between February 2016 (first event) and may 2017 he had 9 episodes of oral and nose itching, stuffy nose, conjunctival erythema, cough, lipotimia, vomit and abdominal pain few minutes after inhalation of rice vapors. Episodes required access to the emergency department and administration of epinephrine, steroids and antihistamines.

He referred to our Occupational Allergy Unit after the 9 episodes of systemic reactions, physical examination revealed an healthy status, with normal lung and thyroid function, blood cell counts and normal autoimmunity markers. Total serum IgE level was 44, 2 KU/L and serum tryptase 2.6 Ug/L. Skin prick tests to commercial common aeroallergens, cereals (including rice, maize, wheat, rye, oat, soy) and α-amylase were performed with negative results. The results of skin prick-by-prick tests with cooked and raw rice were both positive (wheal ≥ 7 mm). Serum specific IgE were 0.30 kUA/L for brown rice, 1.23 kUA/L for rPru p3, 0.97 kUA/L for rCor a 8, 1.11 kUA/L for rAra h9, 1.22 kUA/L for rJug r3.

**Conclusions:** After the diagnosis of allergy to rice and occupational anaphylaxis the worker changed his task from cook to the management of restaurant with loss of qualification, income and regret for professional missed career. This case report demonstrated the work disability in a rare case of occupational anaphylaxis.

## 0669 | A diphencyprone allergy "epidemic" at a dermatology department

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**Introduction:** Diphencyprone (DCP) is a chemical agent commonly used as topical immunotherapy in the treatment of alopecia areata (AA). It acts through type IV sensitization of affected areas, stimulating hair follicle growth. A 2% solution of DCP is usually applied to a small area of the scalp, intended to sensitize the patient. Treatment is started 1–2 weeks with the application of a 0.001% concentration of the DCP to the affected areas. As DCP is a potent allergen but cases of occupational allergy to DCP are rare.

**Case description:** Three years after starting to use DCP in the treatment of AA, 2 nurses started to complain of skin erythema and pruritus in the face, neck, dorsum of both hands and wrists. The 1st nurse reported that, initially symptoms begin 2–3 days after working with DCP; with repeated exposures, the reaction became more rapid, starting about 6 hours after exposure, and more extensive, affecting the arms, face and neck. The 2nd nurse reported similar symptoms but, with repeated exposures, started to have symptoms just by staying in the same room where DCP was previously used.

The diagnosis of occupational airborne contact dermatitis was suspected and both nurses were subjected to patch tests to DCP 0.2% and presented an extreme positive bullous reaction.

**Conclusion:** DCP is a potent sensitizer and is this property that fundaments its use in the treatment of AA. However, as a potent sensitizer, it can pose risk to healthcare workers handling it, as occupational exposure to DCP can result in airborne contact dermatitis. DCP needs to be handled with proper care and wearing protective gloves and a mask its mandatory; also handling it in a safety cabinet has been recommended.

In this case, avoidance of work with DCP has been challenging as of now only 2 elements of the nursing team is not presenting with symptoms of DCP allergy.

## 0670 | Case report: Stylist with allergic contact dermatitis to paraphenylenediamine, eyebrow tattoo carrier

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**Background:** Paraphenylenediamine (PPD) is a substance that has a high sensitizing power. It is used in multiple products, especially dyes hair dyes, gums, lacquers, skins, tissues, eye shadows or bitumen. It has also been used as an antioxidant for plastics, printing inks, fax machines, photography products. In the specific case of hairdressing, PPD is the main contact sensitizing agent, followed by its derivatives such as para-aminodiphenylamine (PAD), o-nitro-p-phenylenediamine (ONPPD) and para-toluenediamine (PTD). At present, PPD continues to be a frequent and relevant sensitizing agent for occupational contact dermatitis in stylists.

**Case presentation:** 48-year-old female, occupation stylist for over 15 years. No personal history of atopia. Antecedent of eyebrow tattoo 3 years ago.

Starts 2 years ago, with dermatosis disseminated to eyelids, and hands, characterized by intense pruritus, macules and papules; 4 months later with palpebral edema in upper eyelids, bilateral. Valued by Dermatologist, treatment with systemic steroid, topical, and antihistamines, partial improvement.

Sent to Occupational Contact Dermatitis Clinic: Patch Tests, positive for Paraphenylenediamine; change of working area is indicated, as well as eyebrow tattoo pigment removal and treatment with topical calcineurin inhibitor, antihistamines and skin care, with improvement.

**Discussion:** The majority of PPD sensitization occurs through contact with hair dyes, both in hairdressers and users. In the case of hairdressers, awareness-raising occurs at the earliest stages of their professional career and in most cases forces them to leave the profession.

Favorable factors have been the existence of a previous irritant dermatitis of the hands by detergents, lotions and the action of humidity. In fact, the professional dermatosis that is most frequently observed among hairdressers is irritant dermatitis. Other sources of sensitization increasingly important are temporary tattoos, in which PPD is used as a substitute for henna and sensitization to textile dyes.

**Conclusion:** PPD continues to be a frequent sensitizing agent in our environment, it is essential to continue maintaining it in the standard battery. A fundamental part of the treatment is the avoidance of exposure to said compound, and as preventive measures the use of protective equipment, as well as proper hygiene.

## 0671 | The role of questionnaire and appropriate diagnostic tests on natural rubber latex allergy among Albanian dental students

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**Background:** Latex allergy is a usual occupational disease among healthcare workers. In vivo allergic tests, self-administrated questionnaire and physical examination are largely used to assess data about natural history and risk factors. The aim of the present study was to determine the prevalence of allergy to latex gloves among dental students and the association between questionnaire items and diagnostic tests.

**Method:** In this prospective study, a total of 240 students completed a self-administrated questionnaire that comprised different questions and gave information about the participants and their glove use, working habits, signs and symptoms related to these gloves, precautions taken to minimize it, etc. Skin prick test is performed through commercial extract latex gloves (Stallergenes), while patch test is prepared through latex gloves and adhesives. Two types of gloves are used: gloves that contain latex and gloves without latex (vinyl gloves), which are used also as e negative control.

**Results:** Questionnaire items and diagnostic tests revealed that one-fourth of subjects were suspicious for latex gloves hypersensitivity. Their mean value for skin reactions like irritant or allergic dermatitis or contact urticaria was between 10% and 14%, while for other symptoms the mean value was under 5%. Logistic regression analysis revealed an association between different questionnaire items and positive allergy tests among suspected cases and diagnosed cases of latex allergy.

**Conclusion:** These findings suggest that among different mechanisms and their interaction during sensitization processes, the respiratory exposure plays an important role. The clinical phenotype and the questionnaire in combination with positive diagnostic tests lead to an accurate diagnosis.

## 0672 | Occupational food allergy: review of 11 cases

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**Background:** Workers in the food industry are exposed to a variety of food derived protein allergens that may lead to food induced occupational allergies. However, they are often underreported and, consequently, underdiagnosed.

**Objective:** To assess the medical history, professional background and diagnostic approach of patients diagnosed with allergy to food allergens present in their workplace, as well as the clinical and occupational implications.

**Method:** Review of all clinical records of patients evaluated in the food allergy unit of a university hospital with diagnosis of food allergy associated to their occupation between 2010 and 2017.

**Results:** Eleven patients were included (64% female); all worked in the food industry (5 cooks, 1 baker, 1 fish monger, 1 waiter, 1 supermarket employee, 1 hotel management student) with the exception of one personal trainer. The median age of onset was 25, interquartile range [15; 42] years. All were new onset disease with only one with work-exacerbated childhood fish allergy. The period between the first professional exposure and the development of symptoms ranged from 3 months to 15 years.

The most common implicated foods were: fresh fruits (n = 5), shellfish (n = 4) and fish (n = 3). Eight patients were atopic; one had atopic dermatitis (AD) and 3 had hand eczema at the time of diagnosis.

All patients had mucocutaneous manifestations and anaphylaxis was the clinical presentation in 4. Ten patients had symptoms with ingestion, 7 with skin contact and 3 with inhalation. Sensitization to LTP was present in 80% of patients with fresh fruit allergy.

One patient changed her occupation and one was on extended sick leave due to symptoms in the workplace.

**Conclusion:** Clinicians should be aware of food related occupational allergies in individuals employed in the food industry. The high degree of exposure to allergens, either by cutaneous contact including skin barrier disruption or inhalation could be important risk factors for food allergen sensitization in an occupational setting.

In work-related allergic reactions, avoiding professional exposure is often difficult, removal from the workplace may not be feasible and a career change may have significant socio-economic impact.

## 0673 | Innovative nasal filters allow for measurement of exposure to laboratory animal allergens

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**Background:** Laboratory animal allergy (LAA) is an occupational disease which can develop as a result of exposure to animal allergens and may manifest as an allergic hypersensitivity response. Approximately 20% of people who work with laboratory animals experience some allergic symptoms and about 10% of animal technicians go on to develop serious symptoms of asthma. UK government guidelines state that employers must prevent or adequately control exposure of employees to animal allergens and should undertake monitoring to ensure that suitable controls remain effective. The most widely used monitoring method is personal IOM filters. However, these need to be attached to a pump and carried by the technician which can be cumbersome and awkward. Previous data has demonstrated that allergens from dust mite, cat, dog and pollen could be captured and quantified by a novel type of nasal filter. In this current study, we sought to assess the feasibility of using the nasal filters for the assessment of exposure to mouse allergen in a laboratory facility.

**Method:** Technicians working in a laboratory animal facility were asked to wear the filters during normal routine work. For comparison, they were also asked to wear an IOM filter for the same duration. Allergen was extracted from nasal and IOM filters by gentle rocking in PBS-Tween for two hours. Levels of the major mouse urinary protein (Mus m 1) were quantified using our multiplex array technology, which is highly sensitive and allows for quantification of Mus m 1 down to 0.01 ng/mL.

**Results:** Significant levels of Mus m 1 were detected in the nasal filter extracts and these levels correlated with the type of activity that was being performed by the technician, as well as the housing environment of the mice. Levels were compared to the suggested 'safe' limit of allergen exposure of 5 ng/m$^3$. We also found that the technicians grew accustomed to the nasal filters quickly and found them far more practical for every day monitoring that wearing the IOM filter and pump.

**Conclusion:** These data indicate that nasal filters may be considered a simple and easily wearable method for monitoring laboratory animal allergen exposure. Future studies are planned to assess the feasibility of wearing the filters for analysing exposure to other laboratory animal allergens from rat and guinea pig.

## 0674 | Prevalence of sensitization to aeroallergens in librarians and archivists at Havana University

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**Background:** There is a scarcity of studies on aeroallergen sensitization in Cuban workers occupationally exposed to stored paper documents in archives and libraries, whereas this exposure is frequently reported as a cause of allergic respiratory symptoms. This study aimed to assess the frequency of sensitization to aeroallergens by skin prick test (SPT) among workers of the Archives and the Library at Havana University.

**Method:** A descriptive and cross sectional study was performed. It included 55 subjects, 14 workers of the Archives, median age 33.8 (range 18-68 years old), and 41 workers of the Library, median age: 36 (range 21-67 years old). Both groups had female predominance (85.7% and 56.1% respectively). A medical resume and SPT with three domestic mites (*Dermatophagoides pteronyssinus*, *Blomia tropicalis* and *Dermatop[agoides siboney*) and five molds (*Aspergillus*, *Alternaria*, *Cephalotecium*, *Penicillium* and *Cladosporium*) were performed to all subjects.

**Results:** Overall, 69% of subjects showed one or more positive SPT to aeroallegens. The higher sensitization frequencies corresponded to House Dust Mites (*D. pteronyssinus* 50.9%, *D. siboney* 49% and *B. tropicalis* 43.4%), followed by molds *Aspergillus* (20.8%), *Penicillium* and *Cephalotecium* 13.2% each one. The least sensitization value was found to *Alternaria* and *Cladosporium* (9.4%).

**Conclusion:** A significant proportion of subjects working in Archives and the Library are sensitized to common aeroallergens, particularly to House Dust Mites. The frequency of sensitization to HDM is greater than in general population. SPT with Dust mites and molds should be evaluated in workers with occupational exposure.

## 0675 | A case of two allergic patients sensitized to Tenebrio molitor by occupational exposure

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**Background:** Insects are a promising alternative protein source both for human nutrition and in animal breeding, thanks to their good nutritional value and reduced environmental impact. If grown on adequate substrates, insects could provide high quality proteins in comparable amounts to those of meat and fish, but resulting in a

lower $CO_2$ emission, water and feed consumption and limited waste production.

Insects are currently allowed both for human and animal feeding in some EU countries, including Italy and the risk profile related to production and consumption of insects as food and feed, including risk of allergenicity, is currently under evaluation by EFSA. Both food and feed products derived from insects require multiple manipulations by the breeder and/or by the workers who transform the insect into the commercial products, thus the occupational exposure have to be considered too.

The aim of this work is to evaluate the allergenicity of *Tenebrio molitor*, one most used species for animal feeding.

**Method:** *T. molitor* proteins were extracted from intact dried larvae and from flour of dried larvae. The protein extracts were separated in one-dimensional electrophoresis (1-DE) in order to evaluate any variation in protein component and/or any shift in the protein migration profiles caused by processing. Afterwards, immunoblot analysis was performed with the sera of two allergic patients sensitized by occupational exposure and the immune-reactive bands were analyzed by MALDI-TOF/TOF mass spectrometry.

**Results:** Three immune-reactive bands were found: one band at high molecular weight, found only in the intact dried larva sample (band 1), the other two (2a and 2b) at the same low molecular weight in both samples (intact larva and larva flour). The identification showed the presence of one protein in band 1 (the Melanization-related protein belonging to the vitellogenin family) and the same two proteins in band 2a and 2b: the Cockroach allergen-like protein, already known in literature as an allergen in other insect species and the 86 kDa early-staged encapsulation inducing protein, belonging to the hemocyanin family and already known in insects, mites and shellfish as major allergen.

**Conclusion:** According to these results, the larva flour seems to be less immunoreactive than the intact counterpart, probably due to the processing that causes the degradation of protein bands over 50 kDa.

## 0676 | Evaluation of clinical manifestations and the hypersensitivity to occupational allergens among apprentices of culinary school

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**Background:** The high prevalence of allergy in the general population, especially among children and adolescences results in a necessity of constant determination of the risk of work-related diseases. Working in gastronomy is associated with exposure to many factors with an irritating and allergic potential influencing respiratory system. Food products and organic dust are the source of inhaled allergens which may cause sensitization during apprenticeship.

The study aim is a prospective observation of incidence of sensitization to selected environmental and occupational allergens among culinary school apprentices and identification of work-related allergic diseases in this group.

**Method:** The cohort comprised 374 apprentices. They were examined in the first and the second year of education. Questionnaire and allergological tests [(skin prick test) SPT to common and occupational allergens, IgE level evaluation (total and specific for occupational allergens) and pulmonary tests] were performed].

**Results:** The most frequent symptoms reported by examined apprentices were rhinitis (12.8%), conjunctivitis (7%), skin symptoms (6.7%), dyspnea (5.6%) and cough (2.7%). 10 subjects developed nasal symptoms during the second year of education, while in 6 cases the skin symptoms and in 4 subjects conjunctivitis appeared. In 7 cases the work-related symptoms were reported.

The most frequent positive results of SPTs were obtained with *Dermatophagoides pteronyssinus* 24.4%, *Dermatophagoides farinae* 21.6%, grass pollens 18.6%. Positive SPT to rye and barley flour were found in respectively 2.2% and 1.4% apprentices. 4.1% of apprentices had specific IgE to flours.

**Conclusion:** The preliminary results indicate that work-related allergy symptoms and hypersensitivity to occupational allergens are rarely found among culinary school apprentices in the first years of education. The further observation will allow to evaluate the trends in incidence of allergy to occupational allergens, as well as the clinical presentation of allergy in that group.

## 0677 | How multifaceted the clinical presentation and etiology of allergic diseases could be?

Dermendzhiev S[1]; Penchev BT[1]; Krasteva S[2]; Dzhambov A[3]; Dermendzhiev T[4]

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**Introduction:** Allergic diseases in bread production workers are not uncommon. However, the literature has not yet provided a clear answer as to why an individual may suffer a combination of allergic diseases, and what etiological factors and underlying mechanisms have led to their onset? The present case report helps fills this gap in the literature on allergic diseases, whose etiology and combination in a patient may lead to a unique clinical manifestation.

**Key words:** Allergic diseases, occupational exposure, bread production.

## 0678 | Allergy to fly maggots

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**Background:** Fly larvae (maggots), earthworms and crustaceans are different fishing baits used by anglers. We present a 28 years old amateur fisherman, with no personal history of allergy disease, referred to our allergy department with episodes of nasal obstruction, rhinorrhea, dry cough and dyspnoea. The symptoms were controlled with antihistaminic drugs. He developed symptoms immediately after handling fly maggot used as fishing bait. He has been fishing weekly since he was a child but symptoms started three years ago. If he avoided fishing, symptoms did not appear. When he uses *Lumbricus terrestris* or prawn as baits, he doesn't present any allergy problem. He has no allergy symptoms with food or other inhaled allergens.

**Method:** Skin prick tests with our own fly maggot extract and common pneumoallergens were done. Respiratory test with chest x-ray were performed. Total IgE and serum specific IgE to different allergenic sources were measured by EAST (Enzyme AllergoSorbent Test) and SDS-PAGE Immunoblotting was determined.

**Results:** Skin prick tests with common pneumoallergen extracts were negative and positive to *A. simplex*. Skin prick test with fly maggot extract was positive. A baseline spirometry was normal, exhaled nitric oxide was 199 ppb, and his chest x-ray was normal. Total IgE was 511 kU/L. Specific IgE to *A. simplex* extract was 7.33 kU/L, 0.85 kU/L to prawn and fly maggot specific IgE was positive. Specific IgE to *Aspergillus fumigatus*, *Alternaria alternata*, *Acarus siro*, *Ascaris*, Tropomyosin and cockroach were negative (<0.1 kU/L). Immunoblotting with fly maggot extract showed IgE-binding bands with molecular mass of 70, 50, 39, 31, 18.5, 16.5, 13 and 10 kDa.

**Conclusion:** We present a case of allergy to fly maggot in an amateur fisherman with respiratory symptoms and without skin lesions. He also has subclinical sensitization to A. *simplex*. A type I hypersensitivity mechanism has been demonstrated by *in vivo* and *in vitro* studies. Although there are a few cases reported of allergy to fishing baits (earthworms, crustaceans, insect larvae) we recommend that they should be kept in mind when exposure is present.

SUNDAY, 27 MAY 2018
TPS 04
ENVIRONMENTAL INFLAMING ALLERGENS

## 0679 | The short-term effects of particulate matter exposure on asthma-related hospital visits in Korea: Based on the national health insurance data

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**Background:** Particulate matter (PM) is an indicator for air pollution, and may exert harmful effects on subjects with various disease conditions including asthma. Although many epidemiologic studies have shown the associations between PM and risks of emergency room visits and hospitalizations, little have been examined for outpatient visits. The purpose of this study was to investigate the effects of short-term exposure to PM exceeding daily average environmental standards of Korea on asthma-related hospital visits including outpatient visits based on the recent National Health Insurance (NHI) data.

**Method:** This was a population based case-crossover study using the NHI and air pollution data between January 1, 2014 and December 31, 2016. The event day was defined as the day when PM exceeded daily average environmental standard (24-hr event day) or the day when PM exceeded daily average environmental standard for 2 hours (2-hours event day) and the control day was defined as the same day of the week before the event day. Compared to the control days, we evaluated the changes in asthma-related hospital visit from the event days to 5 days after event day.

**Results:** Compared with the control days, the average number of asthma-related hospital visits on the 24-hr and 2-hr event days for $PM_{10}$ and $PM_{2.5}$ were increased by 4.1%, 3.5%, 5.7% and 3.7%, respectively. The ratio of an average number of asthma-related hospital visits increased from the 24-hr event day for $PM_{10}$ (1.09, 95% CI, 1.05-1.12) to 4 days after the event day, peaking on the third day after the event day (1.26, 95% CI, 1.22-1.30). Hospitalization also increased on the third day after the event. Although there was a difference in magnitude, $PM_{2.5}$ exposure showed similar trends when compared with $PM_{10}$ exposure.

**Conclusion:** We found significant association between short-term PM exposure exceeding the current daily average environmental standard and asthma-related hospital visit. These results are expected to contribute to the establishment of appropriate environmental standards and relevant policies for PM.

## 0680 | Effects of air pollution on respiratory system disease admission and health budget

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**Background:** It has been already known that air pollution makes an increase in the admissions to the hospital due to respiratory system diseases. We aimed to investigate the cost of increase in admissions to the hospital to health budget in Erzincan.

**Method:** In 2015-2016, the data of patients who daily applied to the hospital due to respiratory system diseases in Erzincan were taken from Mengücek Gazi Education and Research Hospital IT Department, air pollution measurement data from the web site of Ministry of Environment and Urban Planning Clean Air management and the meteorological data from General Directorate of Meteorology. Risk analyses were determined with STATA programme and by calculating with the patient costs taken from Social security Institution, cost analyses were made.

**Results:** In Erzincan, in 2015-2016, totally 78.793 patients (56.5% female, 43.5% male) were applied to the emergency service and polyclinics of Mengücek Gazi Education and Research Hospital because of respiratory system diseases. It was obtained that the most frequent diagnosis was upper respiratory system infection diagnosis with 29.4%, and the most patients were between the age group of 15-34 and 45-64 years.

A correlation was obtained between declared PM10 for Erzincan, one of the parameters of air pollution, and patients admissions to the hospital in 2015 and 2016. In two years period in Erzincan, the average concentration of PM10 was obtained as 67.46 ± 31.38 μg/$m^3$ in index of air pollution. The number of days which PM10 was over 150 μg/$m^3$ were 52 days, and in 122 days it was over 100 μg/$m^3$.

In 2 years period, the admissions to the hospital due to respiratory system diseases, totally 566 (25 of male, 315 female) patients correlated with the increase in air pollution. In two years period the percentage of increase risk was calculated as 0.72%. Considering in terms of age groups, the most increase risk of admission to the hospital were in 35-44 age groups (2.49%), and in terms of diagnosis Acute Bronchitis (2.46%). While in male patients the risk of

admission to the hospital (in PM10 per μg/m$^3$ increase) was 0.73% (between 0% and 1.67%), in female patients this was 0.71% (between 0% and 2.04%).

**Conclusion:** Increase in air pollution has raised the admissions to the hospital due to respiratory system diseases at the rate of 0.72% and in two year period with SGK prices the direct cost on health budget was calculated 52.642 TL(11.6982 EUR).

## 0681 | Environmental factors and allergic diseases in children

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**Background:** Environmental factors play an important role for the development and manifestation of allergic conditions in genetically predisposed subjects. Early life exposure to the environmental factors and aeroallergens has a strong impact on the development of allergic airway diseases.

Allergic diseases in children are a major cause of morbidity in children. Although there is a genetic predisposition, it is the exposure to environmental allergens, and infections that will determine the sensitization to different dietary and inhalant allergens.

**Method:** The study was done in children from West Georgia randomly and on based of questionnaire of representative cohort. (2014-2016). The cohort was 1500 children, 1-16 years old, risk factors were studied by way of interviewing, clinical-laboratory dates. For assessing the risk factors, was used 'case control' method. The statistical processing of material was done with computer program sps/sv12. Inclusion criteria for enrolment were: collectors of dust, gender, existence of moisture and mold consuming of Tabasco, atopic dermatitis and seasonality.

**Results:** The groups, which we have studied, prevalence of acute respiratory viral infection was 61%, bronchitis −29.3%, allergic rhinitis 33.9%, atopic dermatitis 9.1%, food allergy 5.4%. The reliability was high ($P < 0.05$) in families with bronchial asthma compared with healthy population. Bronchial asthma was detected in 5.7% of population. The hereditary load of allergic diseases in patients with bronchial asthma was 9.7% and in healthy cohort it was 5.7% ($P < 0.001$).

**Conclusion:** Based on the results, we can conclude that, ecological factors and genetic predisposition significantly influences on prevalence of sensibilisation of house dust mite, molds and formation of bronchial asthma.

As the genetic and environmental factors that act on an immune system are better elucidated and their roles established, the implementation of more enduring preventive efforts will be developed. However, at present, the best approach to the child at high risk for the development of allergies is to institute dietary and environmental control measures early to decrease sensitization, and to recognize and appropriately treat the evolving signs and symptoms of allergic disease.

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## 0682 | Effect of air pollution on bronchial asthma in West Georgia

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**Background:** The study aimed to establish the correlation between the concentration of phadiatop, total IgE levels in the blood in patients with diagnostic bronchial asthma and the concentration of specific air pollutants in terms of annual calendar of flowering plants in West Georgia.

**Method:** In the study were involved 45 patients (among them 24 males and 21 females) of different ages, with diagnostic bronchial asthma who for allegro- specific diagnostics applied from January to April, 2017. The study included the following stages of allegro-diagnostics: I step—allergo diagnostic using modern automated system - "Immuno CAP 100", II step - Monitoring of aeropollutants concentration by using aeropolinometer "Burkard Trap".

**Results:** The analysis of the laboratory results showed that the studied patients had high titers of total IgE, which amounted to an average of 273 (N 33-90), while the average concentration of phadiatop was 96 (N < 70), respectively. In the patients with bronchial asthma of a specific positivity of specific IgE to the weeds (Wx2)—ambrosia, plantain, clasp/tarragon, atriplex—in 25 (55%) on average; tree dust (Tx9) - alder, lactarius piperatus, nuts, oak, willow - 16 (35%); and cereals (Gx1) - festuca pratensis, lolium temulentum, timoti grass, poa - 8 (17%); Mx2 -Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Candida albicans, Alternaria alternate- 11 (24%) was revealed, only in 6 (13%) patients we cannot established the allergy specific IgE. From January to April 2017, there were revealed a high concentration of aeropollutants, by high allergenization and widespread; especially high concentrations were found in alder, birch tree and common hazel, while from aeropollutants of low allergenization poplar, elm, willow and plane tree were distinguished.

**Conclusion:** High degree correlation between the above-mentioned markers proves its clinical importance/value with respect to bronchial asthma.

The publication was financially supported by the Ministry of Education and Science of the Russian Federation (The Agreement №02.A03.21.0008).

## 0683 | Incidence of IgE-mediated respiratory sensitization by two dominant avenue trees of Kolkata megacity

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**Background:** Plantation of road-side avenue trees has become a major part of the urbanization programme in Kolkata metropolis of India for megacity beautification and environmental management. Due to evergreen habits, Gulmohor (*Delonix regia*) and Chhatim (*Alstonia scholaris*) are frequently selected for plantation programme to generate green belts. However, an increasing incidence of seasonal pollinosis was observed among the inhabitants living in close vicinity to these trees suggesting a possible link between the airborne pollen load and the concomitant respiratory hazards. This prompted us to investigate the allergens in the pollen of these two dominant avenue trees.

**Method:** Aerobiological surveys were conducted at multiple sites of Kolkata for a period of two years using seven-day volumetric Burkard sampler to record the pollen concentration in the outdoor ambient air. Clinical data and residual blood of pollinosis patients were collected from a public hospital. Allergens were detected in the pollen proteome fractionated in 2D gel by IgE-serology. The major IgE-reactive proteins were partially purified by ammonium sulphate fractionation followed by ion-exchange chromatography. The allergenic activity of the fractions was tested by histamine release assay.

**Results:** A clear correlation was observed between the pollinosis related morbidity and the aeropollen load especially during the peak flowering period of these two trees. About 41% and 52% of the patients displayed positive SPT response and IgE-reactivity using pollen extracts of Gulmohor and Chhatim respectively. Immunoproteomic analyses revealed the presence of 7-8 IgE-reactive components in the 2D pollen proteome of these species. Hierarchical cluster analysis with patient immunoblot data identified a 31 kDa and a 25 kDa protein as major allergens of Gulmohor and Chhatim respectively. The purified fractions containing each of these two major allergens induced histamine release from granulocytes within a range between 42 and 77%.

**Conclusion:** Our study demonstrates an alarming situation of pollen-related respiratory hazards by dominant avenue trees and gives significant message to the metropolitan development authorities to be more careful about the plantation programme to avoid the unnecessary load of pollen biopollutants. Further characterization of these allergens will help to design immunotherapeutic strategies for pollinosis management.

## 0684 | Formaldehyde reduces the expression of structural components and cell adhesion molecules in differentiated human epidermal keratinocytes

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**Background:** Formaldehyde (HCHO) is one of the most ubiquitous airborne indoor chemical pollutants that influence the symptoms of atopic dermatitis (AD). However, the underlying mechanisms associated with effects of airborne HCHO exposure on the skin lesions of AD have not been fully elucidated. In this study, we investigated whether HCHO exposure affect the expression of structural components (filaggrin, involucrin, and loricrin), cell adhesion molecules (desmoglein and desmocollin) as well as thymic stromal lymphopoietin (TSLP) in the AD-like epidermal keratinocytes.

**Method:** Immortalized human keratinocyte cell line (HaCaT) and primary normal human epidermal keratinocytes (NHEKs) were differentiated with calcium chloride for 1 and 3 days, respectively. Following the differentiation, the cells were treated with IL-4 (100 ng/mL), IL-13 (100 ng/mL), and/or HCHO (4 × 10^-4%) for 2 hours. The mRNA expression of *FLG*, *IVL*, *LOR*, *DSG1*, *DSG3*, *DSC1*, *DSC3*, as well as *TSLP* was analyzed using quantitative real-time PCR.

**Results:** HCHO exposure decreased the mRNA expressions of structural components (*FLG*, *IVL*, and *LOR*) and cell adhesion molecules (*DSG1*, *DSG3*, *DSC1*, and *DSC3*) in a short-period time of exposure (2 hours). We also found that HCHO exposure significantly enhanced IL-4- and/or IL-13-induced TSLP production in NHEKs as well as HaCaT. Interestingly, exposure to HCHO alone is enough to increase the TSLP mRNA expression in both cells.

**Conclusion:** Our results suggest that HCHO exposure might synergistically damage the skin barrier function with IL-4 and IL-13 by increasing TSLP expression and decreasing structural components as well as cell adhesion molecules.

## 0685 | Skin prick test reactivity to aeroallergens in adult allergy clinic in a tertiary hospital: a 12-year retrospective study

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**Background:** The global prevalence of allergic rhinitis, asthma, and atopic dermatitis has risen significantly over the last two decades. Allergic sensitization to aeroallergen is a major risk factor in developing the allergic disease. The prevalence of aeroallergen sensitization varies in different regions and countries.

**Method:** A cross-sectional, retrospective study. The data were collected from medical records and database of the result of skin prick test of patients who had the allergic symptoms or chronic urticaria in adult allergy clinic, Ramathibodi hospital from January 2004 to December 2015.

**Results:** A total of 1516 of patients (female 1.118 (73.7%)) were enrolled. The mean ages of participants were 41.34 years (±16.5 SD). 58% of patients were diagnosed with allergic rhinitis, 19.7%, 3.2% and 9.2% with asthma, atopic dermatitis, and chronic urticaria respectively. In the chronic urticaria group, 57.4% underwent the positive skin prick test to common aeroallergens. Mites were responsible for the most common inhaled allergen sensitization in this study as 50.1% of *Dermatophagoides pteronyssinus*, 32% of *Dermatophagoides farinae* and 31.5% of house dust. Cockroach was the second most common aeroallergen sensitization as 32.3% followed by grass pollen, Bermuda (21.1%) and Timothy (13.6%). The animal dander, cat and dog, occupied 12.9 and 10% respectively.

**Conclusion:** Mites were the most common cause of aeroallergen sensitization in all patients followed by cockroach, grass pollen, and animal dander. However, Bermuda sensitization has increased significantly in the last six years.

| | |
|---|---|
| Gender (%) | Female (73.7) |
| Mean age (years) | 41.34 ± 16.499 |
| **Prevalence of aeroallergen sensitization by skin prick test (%)** | |
| Dermatophagoides Pteronyssinus | 50.1 |
| Dermatophagoides farinae | 32 |
| House dust | 31.5 |
| Cockroach | 32.3 |
| Bermuda | 21.1 |
| Timothy | 13.6 |
| Cat | 12.9 |
| Dog | 10 |
| **Underlying disease, (%) (total n = 1516)** | |
| Allergic rhinitis | 879 (58) |
| Asthma | 299 (19.7) |
| Chronic urticaria | 140 (9.2) |
| Atopic dermatitis | 49 (3.2) |
| Allergic conjunctivitis | 49 (3.2) |
| Chronic rhinosinusitis | 44 (2.9) |
| Obstructive sleep apnea | 30 (2) |
| Major depressive disorder | 28 (1.8) |
| History of NSAIDs allergy | 62 (4.1) |

## 0685A | Sublingual allergen immunotherapy for tree-pollen-induced respiratory allergies: a multicentre, observational study of clinical practice in France

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**Background:** Tree pollen is a prevalent trigger for respiratory allergies such as allergic rhinoconjunctivitis (AR) and asthma (A). Sublingual immunotherapy (SLIT) is a treatment option for patients suffering from those. However, not all eligible patients are offered this option by their physician. The aim of the study was to describe allergists' main reasons for prescribing (or not) SLIT with tree pollen extracts.

**Method:** In the winter of 2015, we performed a non-interventional, observational study of patients consulting allergists in France for an indication of tree-pollen-induced allergic disease. The main inclusion criteria were≥5 y.o; tree pollen allergy with clinically relevant symptoms, confirmed by skin prick test or serum IgE assay; eligibility for tree pollen SLIT; and the provision of written, informed consent. The main reasons for prescribing SLIT, the patients' clinical, diagnostic and immunological profiles, the referral route were recorded.

**Results:** 75 allergists were included and recruited a total of 442 patients, 434 of whom were analyzed (mean ± standard deviation (range) age: 27.2 ± 15.8 (5–71). The symptom prevalence was 97.2% for AR, 32.7% for A, 32.3% for food allergy and 8.5% for skin allergy. The clinically relevant tree pollen sensitization were: Betulaceae (n = 279), Oleaceae (n = 175), Cupressaceae (n = 94), Fagaceae (n = 62) and Platanaceae (n = 17). A total of 189 patients consulted the allergist directly, whereas 209 were referred by another physician. Following their consultation with an allergist, 372 patients (88.8%) were given a prescription for tree pollen SLIT. The allergists' 3 most frequently reported patient-related reasons for prescribing tree pollen SLIT were the patient's symptom profile (79.6%), the symptom severity (66.9%), and allergy's impact on the patient's everyday life (52.7%). The 3 main reasons for not prescribing tree pollen SLIT were insufficiently severe allergic disease (34.0%), polyallergy (31.9%), and the need for more time to see whether symptom treatment would be enough to achieve disease control (31.9%).

**Conclusion:** Almost 90% of the study population received a prescription for tree pollen SLIT (generally for a 3 years of pre- and co-seasonal treatment). The prescribing allergists emphasized SLIT's good efficacy/safety ratio in patients with moderate-to-severe disease.

## 0686 | Relationship between pollinosis and ltp sensitization in the southeast of Spain

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**Background:** The pollinosis and the LTP sensitization can be different according to the geographic zone, due to the influence of environment factors and the diversity of vegetables species.

The objective of this research was to know if the number and type of pollen, to which the patients were sensitized have an influence or not on food allergy.

**Method:** 170 patients have been consecutively included, 82 (48.24%) women and 88 (51.76%) men with pollinosis and skin prick-test positive to peach LTP extract (ALK-Abelló). Mean age of 75.29% of the patients was 30 years old (range 5 to 59 years old).

For the study, they were divided into two groups:

Group A: 41 patients without food allergy

Group B: 129 patients with allergy to any vegetable food

**Results:** In group A, 34.1% of patients were sensitized to 1 or 2 pollens and 65.9% to 3 or more pollens.

In group B, 26.4% of patients were sensitized to 1 or 2 pollens and 73.6% to 3 or more pollens.

In relation with the types of pollens, in group A, 33 (80.5%) of patients were sensitized to Olea europaea pollen, 21 (51.2%) to grass pollen, 21 (51.2%) to Chenopodium album, 20 (48.8%) to Artemisia, 20 (48.8%) to Salsola kali, 16 (39.0%) to Salsola oppositifolia and 13 (31.7%) to Platanus acerifolia.

In group B, 101 (78.3%) patients were sensitized to Olea europaea pollen, 74 (57.4%) to Artemisia, 73 (56.6%) to Chenopodium album, 71 (55.0%) to Salsola kali, 68 (52.7%) to Salsola oppositifolia, 56 (43.4%) to Platanus acerifolia and 55 (42.6%) to grass pollen.

**Conclusion:** No differences were observed in the number of pollens to which the patients were sensitized in the two groups studied.

A major number of patients sensitized to Salsola oppositifolia were found in the group with vegetable food allergy; while the number of patients sensitized to grass pollen was higher in the group of patients without food allergy.

## 0688 | Air pollution increase the risk of atopic dermatitis

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**Background:** The aim of this study is to investigate the effect of air pollution in atopic dermatitis (AD) in children.

**Method:** A cross-sectional study of elementary school children (Seongnam Atopy Project 2017, n = 620) were performed. A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to survey children of 11 elementary schools from Seongnam, Korea. Eczema Area and Severity Index (EASI) score and transepidermal water loss (TEWL) were performed by pediatric allergic specialists, blood eosinophil count and skin prick tests (SPTs) were also measured.

**Results:** Children living within 200 m of a four-lane motorway had high upper tertile level of s-phenylmercapturic acid (aOR, 1.70; 95% CI, 1.02-2.85, $P = 0.043$). Children with increased level of s-phenylmercapturic acid had increased TEWL at cheek (B 16.898, SE 0.524, $P = 0.035$), lower leg (B 15.356, SE 0.651, $P = 0.035$).

**Conclusion:** There was relationship between air pollution and AD in children in this study.

## 0689 | The identification of IgE binding proteins in non-biting midges (Cricotopus bicinctus), potentially potent producers of allergens around the river

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**Background:** Chironomids are widely and abundantly distributed in the vicinity of ponds and rivers as well as artificial dammed pool for irrigations. Chironomid larvae are known to contain hemoglobin, which have been described as a major allergen, and the adults that have no hemoglobin also have been reported to contain allergens. The aim of this study was to identify and characterize possible IgE binding proteins in adults of *Cricotopus bicinctus*, a popular species in Korea.

**Method:** Sera from individuals living near the river, having positive IgE to *C. bicinctus* extract, were used for immunoblotting. *C. bicinctus* extracts were separated by 1-dimensional electrophoresis, and IgE-reactive proteins were analyzed by nano-LC-MS analysis.

**Results:** The IgE-positive rate and IgE level of *C. bicinctus* antigen were higher in residents near the river than those who live far the river. Serum samples with high IgE level to *C. bicinctus* extract by ELISA were collected from residents in living around the river. The presence of about 42 kDa and 60 kDa protein homologues to the actin protein isoform and putative ATP synthase subunit alpha were identified in an extract from *C. bicinctus*, respectively, and sequence coverage was determined using inclusion lists for tandem mass spectrometry based on homologous sequences.

**Conclusion:** Two IgE binding proteins were identified in *C. bicinctus* extract showing sequence similarity with actin and putative ATP synthase subunit alpha, respectively. These IgE-binding proteins will be useful for further studies or clinical applications.

SUNDAY, 27 MAY 2018
TPS 05
LABORATORY TESTS AND BIOMARKERS IN ALLERGY DIAGNOSIS

## 0690 | Comparison of the two multiplex arrays in the diagnosis of patients with allergy

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**Background:** Diagnosis of type I allergy is based on the medical history, provocation testing and in vitro diagnostic tests. Currently, molecular allergy diagnostics are using in clinical routine and many allergenic molecules are available for in-vitro specific immunoglobulin E testing which can be performed on singleplex or multiplex measurement platforms. Multiplex arrays-based testing performed with a small amount of serum sample enables clinicians to determine specific-IgE (sIgE) antibodies against multiple recombinants or purified natural allergen components. To compare the multiplex testsystems ImmunoCAP ISAC (Thermo Fisher Scientific, Sweden) and the multiplex ALEX Allergy Explorer (Macro Array Diagnostics, Austria) platform on sIgE to grass pollen (Phl p1, Phl p5), tree pollen (Bet v1), house dust mites (Der p1, Der p2), cat (Fel d1) and weed (Art v1) allergens in allergic patients.

**Method:** Serum samples from 200 patients were analyzed for specific IgE to allergenic molecules included in the ISAC panel and the ALEX panel. The results for the multiplex assays were analyzed.

**Results:** Comparison of allergenic components by ISAC and Alex arrays revealed the following correlation coefficients: 0.94 (Bet v 1), 0.94 (Phl p 1), 0.93 (Phl p 5), 0.94 (Der p 1), 0.92 (Der p 2), 0.91 (Fel d 1), and 0.61 (Art v 1).

**Conclusion:** A good correlation of presently used methods to detect serum sIgE was observed. Multiplex testing of allergen-specific IgE can be the method of choice for a prospective component-resolved diagnosis of type I allergy, and the basis for the design and monitoring of a patient-tailored specific therapy.

## 0691 | The INA (Individual Native Allergy diagnostics) - animal detector

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**Background:** Cats and dogs are the most common allergen source for allergy against animal epithelia. We used the INA test to investigate the allergen sources of rare animal allergens like rabbit (RB), guinea pig (G), rat (R), iguana (I) and horse (H).

**Method:** The test consists of an INA stick, a plastic stick with a reactive surface to bind proteins/allergens covalently. For sampling, either the stick was placed into a cup of urine for 2 minutes (3 × R, 1 × G, 1 × RB, 1 × I), or the animal licked the stick (hazard-free, 3 × H). Specific IgE measurement was performed with 250 µL sera from allergic patient (P), non-allergic patient (N) using the ELISA procedure. All incubations were done at 37 °C (incubator). Washing was performed for 1 minutes under running tap water. (i) P and N sera were pipetted into separate test vials (TV) 1 a+b, one INA stick placed into each vial, incubated for 1 hour and washed. (ii) 250 mL conjugate were pipetted into separate TV 2 a+b, incubated for 1 hour with the INA sticks and washed. (iii) 250 µL substrate were pipetted into separate TV 3 a+b, incubated for 25 minutes with the INA sticks, which were afterwards removed from the solution and dried for 20 minutes at room temperature. The colour response was compared to a colour chart (class 0 - 6, calibrated against WHO IgE reference). To avoid unspecific reactions all measurements were performed in parallel with N serum, requiring INA class 0/1.

**Results:** For RB, R, G (INA class 3 - 6) and I (patient developed asthma when cleaning the terrarium; INA class 3) urine was determined as allergen source. Saliva (INA class 6) has been detected as allergen source of the horse.

**Conclusion:** INA is a simple and easy to handle method to detect allergen sources in animals. The investigation provided a hint to what kind of source material should be used for the manufacturing of respective allergen extracts.

## 0692 | New IVD test for specific IgE measurement in sera of grass and/or birch pollen allergic patients

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**Background:** Atopic patients often have multiple sensitizations. The objective of the present investigation was to analyze the sensitization pattern of grass pollen (GP) or birch pollen (BP) allergic patients using the new IVD test CLUSTO-Scan® neo (CSneo, versions Inhalation A and B).

**Method:** CSneo consists of an allergy strap containing 16 cavities with different allergens (Inhalation A: 10 single allergens plus 4 allergen mixes, Inhalation B: 14 single allergens), negative and positive control. Sera from 9 allergic patients (GP or BP) were analyzed with 25 single allergens from Inhalation A + B, plus alder. All incubations were performed at 37 °C, washing for 1 minutes under tap water. 50 µL serum were pipetted into each cavity, incubated for 1 hour, washed and dried. 50 µL conjugate were added to each cavity, incubated for 1 hour, washed and dried. 50 µL substrate were added,

incubated for 25 minutes, washed, dried and stored for 10 minutes at 15-25°C. The reaction field colours were compared to a colour chart (calibrated against WHO IgE reference) resulting in CSneo classes (CL) 0 - 6.

**Results:** Altogether, 225 single measurements were performed, out of these on average 81.8% (max 100%, minutes 68.0%) showed sensitizations with CL≥2 (clinical cut off), including the cross reactive ones like alder and hazel pollen as well as house dust mites (*Dermatophagoides pteronyssinus* / *Dermatophagoides farinae*), Latex and *Ficus benjamina*. In many cases for *Aspergillus fumigatus* and ash pollen a CL 0 was measured.

**Conclusion:** CSneo is a new useful tool for quick and easy in-vitro screening of patients' sera. Investigation with CSneo can be extended with further allergens, e. g. food allergens or mites, including the components Der p 1 and Der p 2. In case of multiple sensitization, a clinical relevant allergy should be verified by exclusion of CCD relation and by anamnesis and/or provocation tests. The results should be considered for planning any specific immunotherapy for GP or BP allergic patients.

## 0693 | Comparison of three different methods for determination of the titer of specific IgE

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**Background:** Numerous *in vitro* diagnostic methods for determining the titer of specific IgE (sIgE) antibodies are commercially available. Large discrepancies in sIgE level determined with the test systems of the four main suppliers for the important allergen sources bee venom, wasp venom and birch pollen have been reported (Wojtalewicz et *al*., 2017).

**Method:** The goal of the present study was to compare three different methods for determination of specific IgE titers for various allergen sources including mites, animal dander, nuts, grass pollen, tree pollen, weed pollen and molds.

**Results:** Five different human sera were screened for specific IgE level against 29 different allergen sources using test methods of three different suppliers.

The sensitivity of the three different methods can be arranged in the ascending order manufacturer A < manufacturer C < manufacturer B. With the test of manufacturer A, 45% of the measurements were below the detection limit (0.35 kU/L), with the test of manufacturer C, 16% of the measurements were below the detection limit, whereas the test of manufacturer B leads to values below the detection limit in 10% of the cases. In terms of variation coefficient, the test system of manufacturer C had the best performance. Test systems of manufacturers A and B exhibited comparable variation coefficients, which were considerably higher than that of manufacturer C.

**Conclusion:** Based on these test results, only the test of supplier C is recommendable for determination of levels of specific IgE for diagnostics of allergic patients. With the test of manufacturer A, elevated levels of specific IgE antibodies for many allergens cannot be detected due to the poor sensitivity of the test system. The test system of supplier B exhibits a good sensitivity but the coefficient of variation is rather high for a diagnostic test. This drawback could be circumvented by multiple determination of one test parameter. Although this is an advisable strategy in general, the routine in diagnostic laboratories is incompatible with this approach, since throughput would decrease while costs would increase.

This study is another good example for the need of the implementation of a characterized standard material with known values of sIgE, as demanded by Wojtalewicz *et al*.

## 0694 | Evaluation of interference substances with NOVEOS total IgE assay

Bata S; Cruz-Campos A; Braddock B; Kim C; Pierson D; Tran J; Garibay J; Slater K; Martino M; Le P; Bryant S; Wang A; Rodems K

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**Background:** Assay interference occurs when the presence of a substance causes a falsely elevated or low analyte concentration in an assay system. Interfering substances can include endogenous substances present in human serum specimens, or exogenous substances such as medications. In this study we evaluated the effect of various substances on the measurement of Total IgE using a novel immunoassay system, NOVEOS™. The endogenous interfering substances examined were: hemoglobin, bilirubin and triglyceride and the exogenous substances examined were: biotin, ranitidine, diphenhydramine, and methylprednisolone. In addition cross reactivity of the NOVEOS Total IgE assay to endogenous IgA, IgG, IgM, and IgD was also evaluated.

**Method:** The NOVEOS system is a fully automated immunoassay platform to quantify Total IgE concentrations in human serum. It utilizes magnetic microparticles which are coupled on-board with an allergenic capture reagent, and incubated with the patient sample and an anti-human IgE enzyme conjugate. After a final wash the resulting complex is incubated with the enzyme substrate, and chemiluminescent signal is generated, the magnitude of which is proportional to the concentration of IgE in the patient sample. Interference and cross-reactivity testing was evaluated in accordance with CLSI guideline EP7-A2.

**Results:** The endogenous (hemoglobin up to 200 mg/dL, conjugated bilirubin up to 20 mg/dL, unconjugated bilirubin up to 40 mg/dL, triglyceride up to 3000 mg/dL) and exogenous (biotin up to 5.5 mg/dL, diphenhydramine up to 19.6 mmol/L, methylprednisolone up to 0.84 mmol/L and ranitidine up to 19.1 mmol/L) interfering substances show minimum bias with the NOVEOS Total IgE assay. IgA, IgG,

IgM, and IgD do not appear to cross react when used at 0.5 mg/mL, 6.2 mg/mL, 0.6 mg/mL, and 38.6 mg/mL, respectively, with the NOVEOS Total IgE Assay.

**Conclusion:** NOVEOS immunoassay analyzer is capable of quantifying the Total IgE concentration of a sample with minimal risk of interference from the aforementioned substances.

## 0695 | Performance evaluation of the NOVEOS allergen specific IgE assay

Wang A; Cruz-Campos A; Braddpcl B; Kim C; Pierson D; Tran J; Grande Garibay JC; Slater K; Martino M; Le P; Bata S; Bryant S

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**Background:** Accurate determination of IgE concentration is important in the diagnosis and management of patients with established or suspected allergic disease. The primary objective of this study is to demonstrate the analytical performance of the Allergen Specific IgE (sIgE) assay on the NOVEOS immunoassay analyzer, an automated, high throughput instrument developed by Hycor Biomedical.

**Method:** The NOVEOS Allergen Specific IgE assay employs magnetic, streptavidin coated microparticles which are incubated with a biotinylated allergenic capture reagent, patient sample and monoclonal anti-human IgE antibody:horseradish peroxidase conjugate. After a final wash the resulting complex is incubated with enzyme substrate and a chemiluminescent signal is generated, the magnitude of which is proportional to the concentration of IgE in the patient sample.

Three candidate allergens manufactured using FDA standardized extracts were used for the studies: D001 (*Dermatophagoides pteronyssinus*), E001 (Cat dander) and G006 (Timothy grass). Method comparison of NOVEOS sIgE to a commercially available device was carried out in accordance with CLSI EP9-A3, the diagnostic accuracy was assessed in accordance with CLSI EP24, and assay linearity was assessed in accordance with CLSI I/LA20-A3.

**Results:** The overall comparison between the NOVEOS sIgE and a reference method yield good correlation as well as positive and negative agreement between the methods. Clinical sensitivity for each allergen, confirmed either by oral food challenge or skin prick test, demonstrated high concordance across all allergens in this study. Linearity for samples spanning the assay range for the 3 allergens tested showed strong linearity across the assay range (0.25-100 kU/L).

**Conclusion:** The NOVEOS sIgE assay has demonstrated accurate results to a reference device, and to clinical status, with linear results across the assay range.

## 0696 | Analytical performance of the NOVEOS allergen-specific IgE assay: Precision and detection limit studies

Evans D; Cruz-Campos A; Braddock B; Kim C; Dunn C; Pierson D; Tran J; Garibay J; Slater K; Martino M; Aranas N; Le P; Nayak P; Bata S; Bryant S; Wang A; Rodems K

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**Background:** Many allergic disorders are mediated by IgE class immunoglobulins. Allergen-specific IgE determinations are valuable tools for the diagnosis and management of allergy, and identifying the allergen(s) to which an individual is sensitive.

The NOVEOS™ Allergen-Specific IgE assay is a novel method for the quantitative determination of IgE of known allergen specificity in human serum samples; it is to be used with the NOVEOS immunoassay analyzer, a fully automated platform for allergy testing.

**Method:** The NOVEOS Specific IgE assay employs magnetic microparticles which are coupled on-board with an allergenic capture reagent, and incubated with the patient sample and an anti-human IgE enzyme conjugate. After a final wash the resulting complex is incubated with the enzyme substrate, and a chemiluminescent signal is generated, the magnitude of which is proportional to the concentration of IgE in the patient sample.

The concentration of allergen-specific IgE is interpolated from a standard curve which is traceable to the World Health Organization (WHO) reference reagent serum Immunoglobulin E (IgE) 11/234.

**Results:** Precision, Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined for the NOVEOS sIgE assay in accordance with current CLSI EP05-A3 and EP17-A2. Three candidate allergens manufactured using FDA standardized extracts were used for the studies: D001 (*Dermatophagoides pteronyssinus*), E001 (Cat dander) and G006 (Timothy grass).

**Conclusion:** The NOVEOS Allergen-Specific IgE assay demonstrates strong analytical performance when used with the NOVEOS automated analyzer for the quantitation of allergen-specific IgE in human serum samples.

## 0697 | Basophil activation test in clinical and research use: Requirement for standardization and external quality assurance

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**Background:** The Basophil Activation Test (BAT) has become a popular in vitro test for IgE mediated allergy diagnosis. National authorities in the EU require external Quality Assurance (EQA) by an

agency independent of test suppliers as integral part of modern diagnostic laboratories to meet ISO 15189:2012, 15189:2013 and 9001:2015. The lack of EQA for BAT limits its implementation in allergy diagnosis, and limits cross-institute academic research studies. Therefore, standardization and EQA tools to make the procedure readily feasible for clinical laboratories are urgently required.

**Method:** We conducted an online survey among European laboratories performing BAT (n = 57) in 2017, addressing test conditions used and the needs for EQA.

**Results:** High diversity of test conditions and protocols were observed. Various thresholds for positive control (ranging from 5% to 15% of activation rate) as well as 6 different thresholds for negative control (ranging from 1% to 5% of activation rate) were reported. 7 different activation times (5-30 minutes) were used prior to readout and 6 different markers or marker combinations were used to identify basophil populations. The activation marker used in the test was limited to CD63 or CD203c. Importantly, 62% of the laboratories reported usage of in-house allergen preparations highlighting the importance and need for multicenter validation. Most laboratories wished to register for an EQA scheme (80% of Academic, 89% of Clinical and all Private Research Laboratories).

**Conclusion:** EQA for BAT is in high demand to introduce BAT in routine allergy diagnostics. Standardization of the BAT protocol and analysis is essential for setting the grounds for EQA activities as well as controlled multicenter research studies. We have launched a BAT-EQA Task Force initiative aiming at creating publicly available standard operating protocols (SOPs) and reference materials for the test to enhance the usage and accuracy of BAT both in clinical and research settings. A Steering Committee rooted in EAACI will be formed to maintain clinical relevance of EQA.

## 0698 | A scalable streamlined whole blood basophil activation test utilizing automated sample preparation and dry antibody panels In 96 well plate format

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**Background:** The characterization of allergic conditions is complex and involves multiple methods, both *in vitro* and *in vivo*. Basophil activation testing (BAT), as a functional *ex vivo* flow cytometry assay provides additional value to allergy researchers as it grants further mechanistic insight beyond the quantitation of specific IgE and IgG4, skin prick tests and oral food challenges. This unique value of BAT in clinical research, however, is compromised by the cumbersome workflow inherent to current protocols, consequently intricate to automate. To overcome these limitations the combined use of a) the 96 well plate format b) antibody panel coating on the wells' bottom c) the Biomek automation platform d) a no-wash preparation protocol was evaluated.

**Method:** CD203c and CD63 expression on basophils were monitored upon exposure of whole blood samples (<24 hours) to anti-IgE and/or allergenic extracts. Staining was conducted on exposed samples using dry room temperature stable antibody panels (DURA Innovations format) coated in 96 well plates, eliminating all antibody pipetting steps from the workflow. Red blood cells were lysed and data was acquired (without further wash steps) on a CytoFlex flow cytometer (Beckman Coulter). Staining and lysing were automated using a Biomek (Beckman Coulter).

**Results:** The described no-wash preparation protocol, already established for manual preparation mode in tubes, could be transferred completely to the Biomek automation platform in 96 well plate format. Red blood cell lysing efficiency, staining characteristics in negative or positive control and specifically activated samples were comparable to manual expert preparation in 12x75 mm tubes.

**Conclusion:** It is demonstrated here that the previously reported dry reagent based procedure (DURA Innovation format) for BAT can be transposed to the 96 well plate format and automated on the Biomek platform when sample volume reduction, throughput increase or unattended sample preparation is required. The availability of streamlined and rigorous protocols for BAT using either manual mode/low throughput or automated mode/medium-high throughput, is an important prerequisite for multi-site mechanistic studies of allergy, allowing for de-centralized as well as efficient centralized sample processing.



## 0699 | The clinical utility of basophil activation markers in the diagnosis of pollen allergy

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**Background:** There are numerous markers of basophil activation and degranulation used in the basophil activation test. This study assessed the clinical utility of various basophil activation and degranulation markers in the diagnosis of IgE-mediated pollen allergy.

**Method:** 36 patients allergic to timothy grass pollen (Phl p 1, n = 14, Phl p 5, n = 17, Phl p 6, n = 5) as well as 41 nonallergic donors were investigated. Allergy diagnosis was based on skin tests, specific IgE assays, and clinical history. Basophils was gated as $CD123^{hi}HLA\text{-}DR^{neg}$ cells. Upregulation of CD63, CD11b, CD13, CD69, CD107a, CD164 and CD300a on stimulated basophils was examined. ROC-analysis was performed to determine the cut-off points.

| | CD11b | CD13 | CD63 | CD69 | CD107a | CD164 | CD203c | CD300a |
|---|---|---|---|---|---|---|---|---|
| Cut-off point | 1.4 | 1.4 | 1.6 | 1.4 | 1.5 | 1.4 | 1.4 | 1.4 |
| Sensitivity | 88.9 | 83.4 | 88.6 | 55.6 | 88.9 | 44.4 | 100 | 77.8 |
| Specificity | 100 | 85.1 | 100 | 88.9 | 94.5 | 77.8 | 87.5 | 100 |

**Results:** BAT results for 77 subjects (36 allergic and 41 nonallergic) were analyzed. Two allergic patients with unresponsive basophils under positive control anti-Fc epsilon RI were eliminated from data analysis. No differences in spontaneous expression of molecules were found between allergic and nonallergic subjects. The results of sensitivity and specificity values are presented in the table. The most optimal values of sensitivity and specificity of basophil markers were chosen depending on cut-off point higher than 1.4.

**Conclusion:** The greatest clinical utility for diagnosis of the IgE-mediated allergy was found for basophil degranulation markers CD63 and CD107a and basophil activation marker CD203c. The molecules CD13, CD11b, CD164, CD69 and CD300a were less effective for diagnosis due to low sensitivity and specificity.

## 0702 | Histamine- release test in angioedema patients without urticaria—A retrospective cohort study of 404 patients

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**Background:** A subset of patients with angioedema (AE) and urticaria has histamine releasing autoantibodies. The histamine release test (HR-test) has been used as a tool in chronic urticaria to define the autoimmune subgroup and may possibly guide the clinician to a more effective therapy like omalizumab and cyclosporine. The prevalence of positive histamine releasing autoantibodies in monosymptomatic AE is sparsely described in the literature. The purpose of the study was to report the prevalence of positive histamine releasing autoantibodies in a cohort of patients with recurrent AE without urticaria and compare it with previously published data.

**Method:** We performed a retrospective cohort study of 612 AE patients seen at the Department of Dermatology, Odense University Hospital, between 1995 and 2013.

**Results:** Of 404 patients having a HR-test performed results were available in 399 cases. The results showed that 17.3% had positive HR-tests in the subgroup of patients with AE and urticaria and 4.3% positive HR-tests in the subgroup of patients with AE only. There was a statistically significant difference between the two groups ($P$ = .00002).

**Conclusion:** The HR-test was significantly less likely to be positive, if a patient suffered from monosymptomatic AE than in AE patients with concomitant urticaria. This could signify a higher likelihood of treatment response to antihistamine and other anti-allergic medication in the latter group.

Table 1. Patients with angioedema (AE) +/− urticaria tested with a HR-test

| | |
|---|---|
| Total number of patients | 404 with HR-test |
| Males | 171 |
| Females | 233 |
| M:F-ratio | 0.73 |
| Age, mean, median, [range], years | 50.16, 51.39 [range 2.1-85.1 years] |
| Ethnicity | |
| Caucasian | 393 |
| Middle eastern | 3 |
| Black race | 1 |
| Asian | 5 |
| Other | 1 |
| Current tobacco use, n | |
| Yes | 70 |
| No | 188 |
| Unknown | 146 |
| Positive family history of AE, n | 31 |
| Number of HR-tests, total | 404 |
| Positive | 39 (9.7%) |
| Negative | 360 (89.1%) |
| Unknown result | 5 (0.5%) |
| Comorbidities | |
| Diabetes mellitus | 32 |
| Hypertension | 115 |
| Ischemic heart disease | 24 |
| Heart failure | 7 |
| Atopic dermatitis | 21 |
| Allergic rhinitis | 56 |
| Asthma | 42 |
| Other respiratory disease | 4 |
| Follow-up time, mean; [range], weeks | 66.4; [0 - 675.1 weeks] |
| Reported effect of antihistamines, n | 270 |
| Reported effect of corticosteroids, n | 165 |
| Hospitalized due AE, n, (%) | 138 (34.2%) |
| ER visits due to AE, n, (%) | 144 (35.6%) |

n = number of patients

## 0703 | Nasal provocation testing for detection of house dust mite sensitisation with solutions prepared by dissolving the SQ house dust mite sublingual immunotherapy tablet

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**Background:** Clinical efficacy and tolerability of the fast-dissolving SQ® house dust mite (HDM) SLIT-tablet in the treatment of allergic asthma and rhinitis is well established. In unclear cases nasal provocation tests (NPT) are suggested by the current German guideline. Confirmation of the clinical relevance of a HDM sensitization based on skin prick test (SPT) and/or specific IgE just by clinical history can be difficult in some cases. The aim of this study was to investigate the feasibility of NPT by using solutions of the dissolved SQ® HDM SLIT-tablet. This allows to use the exact allergens for NPT that might later be used for treatment.

**Method:** NPT was applied in 36 patients with positive SPT and specific IgE results to HDM to confirm their clinical history. Stock solution (0.36 SQ-HDM/0.15 mL puff) for NPT was prepared by dissolving one SQ® HDM SLIT-tablet (ALK, Denmark; 12 SQ-HDM) in a vial containing 5 mL 0.9% NaCl solution (gently shaken 10 times). A lower concentration of HDM allergens (0.014 SQ-HDM/0.15 mL-puff) was prepared by adding 0.2 mL stock solution to 5 mL 0.9% NaCl solution; 0.9% NaCl solution was used as negative control. NPT was applied by spraying a 0.15 mL-puff of negative control, 0.014 SQ-HDM and, if negative, 0.36 SQ-HDM into one nostril. It was evaluated after 20 minutes by Linder Score Scale (0–2 sneezes: 0, 3-4: 1, ≥5: 3 points; itchiness of nose, palate, ear: 1 point each; rhinorrhea, nasal obstruction (no, mild, moderate, severe): 0-3 points; ocular symptoms: 1 point) with ≥5 points as positive result (maximum score: 13).

**Results:** NPT with solutions of dissolved SQ® HDM SLIT-tablet was positive in 32 of 36 patients tested. Negative results were obtained in 4 patients in which also the clinical history was not strongly supportive for HDM allergy. Negative controls resulted in 0 score points in 26 patients, 1 point (itchy nose) in 9 patients and 2 points (nasal secretion) in 1 patient. In 9 of 36 (25%) patients tested the result was positive with 0.014 SQ-HDM, and in 27 (75%) patients with 0.36 SQ-HDM.

**Conclusion:** A NPT using a solution of dissolved SQ® HDM SLIT-tablet appears feasible and was in good agreement with the clinical history. These preliminary results should be confirmed by a randomised clinical trial.

## 0704 | Impairment of pulmonary functions in children during nasal allergen provocation tests with house dust mites

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**Introduction:** Sensitization to house dust mites are very common in children with allergic diseases. However, to assess the clinical relevance for asthma and/or allergic rhinitis symptoms, e.g. before starting an immunotherapy, nasal allergen provocation tests can be performed. A symptom score including nasal and conjunctival symptoms, along with respiratory symptoms is established to evaluate the test result.

**Case 1:** A 7 year old girl with perennial allergic rhinoconjunctivitis and sensitization against house dust mite, pollen, mold and animal dander was admitted to our outpatient department. She had no history of asthma. Initial lung functions were within normal limits. 10 minutes after nasal provocation test with Dermatophagoides pteronyssinus she developed slight nasal secretion and itching of the ears and after 20 minutes sneezing and itching of the eyes. The symptom score after 10 and 20 minutes was 2 respectively, representing a negative result. She had no dyspnea, however the lung function test revealed a decrease in $FEV_1$ of 17% (330 mL). Including this distant symptom the score was 4 and the overall test result was positive.

**Case 2:** A 13 year old boy with asthma and allergic rhinitis with sensitization against house dust mite, mould and cat dander was admitted to our outpatient department. He complained about frequent nasal obstruction in the morning and in dusty environment. Initial lung function tests were normal. 10 minutes after nasal provocation test with Dermatophagoides pteronyssinus he developed slight nasal secretion, a feeling of moderate nasal obstruction and dyspnoea. The symptom score after 10 minutes was 3, representing a positive result. Repeated lung function test showed a decrease of FEV 1 of 22% or 790 mL respectively.

**Conclusion:** The awareness of respiratory distress symptoms and the perception of dyspnea may be impaired in children. Lung function tests can help to objectively identify pulmonary symptoms in patients who undergo nasal allergen provocation tests.

## 0705 | The identification of the mediators for specific and nonspecific upper respiratory tract hypersensitivity diagnosis by the provocative tests

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**Background:** Pathogenetic mechanisms of allergy are polymorphic. They include IgE-dependent and IgE-independent, allergen-specific granulocyte-mediated and lymphocytic reactions, as well as non-specific hypersensitivity, which are realized through a variety of mediators: histamine, tryptase, etc.

Allergen bucal challenge mimics the natural situation and is useful for understanding the mechanisms of allergic airway inflammation and airway hyperresponsiveness (AHR).Saliva used as a non-invasive readily available bio-sample for diagnosis instead of blood. Biomarkers in saliva are associated with the pathogenesis and clinical outcome of allergic diseases

**Method:** Aim: to examine mediators for AHR with buccal(mucosal) challenge tests. We examined 14 patients with allergic asthma(the history, positive skin prick test, serum specific IgE) and 12 healthy volunteers. Saliva were collected. Then, both groups were subjected to buccal(mucosal) allergen challenge by a water-salt solution of the mite allergen *Dermatophagoides pteronyssinus*. Saliva was recollected in 30 minutes and 24 hours after the provocation. The level of myeloperoxidase, elastase, tryptase in saliva were determined by the ELISA. That provocative test did not cause clinical symptoms development or reduction in nasal bronchial patency in any patient.

**Results:** In patients with allergopathology, an initially increased level of myeloperoxidase and tryptase in 30 minutes after the provocation, elastase increased in 24 hours (Table 1).

Tryptase in saliva after 30 minutes increased till 0.07 (0.04; 0.19) (Me, pg/mL (LQ;UQ)), $P = 0.0006$. Increased tryptase is presence of increased cellular inflammation, e.g. mast cells. Its IgE-dependent hypersensitivity, because there was the correlation between the elevated level of tryptase and positive prick tests.

Elevated levels of myeloperoxidase and elastase in saliva may be the criteria for the neutrophil hypersensitivity and IgE-independent reactions.

In healthy volunteers this increase was not observed.

**Conclusion:** The identification of tryptase, myeloperoxidase, elastase can be used for diagnosis of types of AHR. Tryptase is a mediator of early (immediate) response to allergen.

Increased myeloperoxidase and elastase indicates the involvement of the eosinophils and neutrophils in the oral mucous membrane in the allergic process. These mediators have additional roles in the late phase response. Elevated levels of myeloperoxidase and elastase in saliva may be the criteria for the neutrophil hypersensitivity.

Table 1 Change level (%) of mediators in 30 minutes and 24 hours after provocation., Me(LQ;UQ)

| | Tryptase(%) in 30 min | Myeloperoxidase (%) in 30 min | Elastase (%) in 24 hour |
|---|---|---|---|
| Patients with allergopathology, n = 14 | 0.93 (0.5, 2.4) * | 6.5 (0, 29)** | 14 (0, 26.76) *** |
| Healthy volunteers, n = 12 | 0 (0, 0) | 0 (0, 0) | 0 (0, 7.28) |

*$P = 0.002$; **$P = 0.008$; ***$P = 0.038$.

## 0706 | The importance of laboratory methods of diagnostics in respiratory allergy

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**Background:** The purpose: to study the spectrum of specific immunoglobulins of class E at various clinical manifestations of respiratory allergy (allergic rhinitis, allergic bronchitis, atopic bronchial asthma).

**Method:** 165 patients from 5-23 years old were examined. To determine specific IgE antibodies, RIDA qLine Allergy panels (Germany) with the list of allergens adapted for Uzbekistan (Uzbekistan panel №1, №2, №3, №4) were used. Each panel allows quantifying sIgE to 20 allergens.

**Results:** Presence of household allergy in the content of sIgE to Derm. Pteronyssinus, Derm. Farinae is found in 30.6% of patients. Epidermal allergy is defined in 35.2% of patients, most often (70.5%) was detected sIg E to the epidermis of the cat. Allergy to pollen of wood (birch, oak, maple, hazel) - is established in 36.1%, to a mixture of weed grasses it is revealed in 38, 5% of patients, to pollen of Artemisia - was noted in 44.5% of patients. Food allergy was found in children 5-8 years old, immunological intolerance of peanuts, legumes, eggs, carrots, potatoes, wheat flour was more often detected. Food polyvalent sensitization to several products was detected in 48% of patients under the age of 7 years. The total prevalence of fungal sensitization among the surveyed was 65.7%. Sensitization to Alternaria alternata was detected in 56.5% of patients. Polyvalent fungal sensitization to several types of fungus has been established in more than half of the patients examined.

**Conclusion:** Safe and acute in vitro methods allow to conduct early etiological diagnosis of allergy, which contributes to the effectiveness of therapy; the detection of polyvalent sensitization dictates the need for molecular diagnostics to single allergens, which has a higher prognostic level and the clinical significance of predicting the appropriateness and effectiveness of allergen-specific therapy; laboratory diagnostics of the allergy allows to reveal sensitization at the

subclinical level, which increases early diagnosis and identify persons with a predisposition to allergy; the establishment of causal allergens, allows the development of individual treatment and prevention programs.

## 0707 | How to use serum level of tryptase for assessing operational risks of anaphylaxis

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**Introduction:** Mastocytosis is a rare disease which is characterized by aberrant proliferation of mast cells in tissues. The mastocytosis can have different types of clinical manifestation. Mastocytosis is a huge problem for anesthesiology. Mast cells can be activated by any physical stimuli in time of operation which can led to anaphylaxis and death.

**Objectives:** A 62- y/o woman was admitted with diagnosis neoplasm of colon. After examination diagnosis was adjusted to adenocarcinoma of cecum. She mentioned unclear history of mastocytosis, which was diagnosed in Russia 40 years ago. She has avoided of any surgical manipulation until now and never experienced attacks. Past medical history is remarkable for drug hyper reaction after aspirin and folic acid. Preoperational tests and analysis are non-remarkable and after allergological consult was measured serum level of tryptase in rest—34.1ug/L.

**Result:** The patient was given preoperative dexamethasone 4 mg IV, for 3 days. She was injected 8 mg IV dexamethasone before the induction of anesthesia. Induction of general anesthesia was done with inhalational anesthetic (Sevoflurane 5-8 vol%), myorelaxation - with pipecuronium bromide - 0.07 mg/kg, analgesia - with fentanyl 0.005%-3 μg/kg. Maintenance of anesthesia was done with sevoflurane (2.5 vol %), pipecuronium bromide (0.02 mg/kg), fentanyl 0.005% (as needed). Antibacterial therapy was done with cefuroxime. After successful hemicolectomy dexamethasone was given for 3 more days—4 mg IV daily.

**Conclusion:** The level of serum tryptase can be predictive in time of surgical interventions. Even high index of tryptase is not a contraindication for surgical manipulation, if preoperative premedication was done.

SUNDAY, 27 MAY 2018

TPS 06

DIFFERENT ASPECTS OF ATOPIC DERMATITIS AND CONTACT DERMATITIS

## 0708 | Russian mothers of allergic children: Worries and beliefs

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**Background:** Eczema and food allergy have been considered as a major burden, significantly effecting the quality of life of millions of people. Organisations and patient support groups are constantly attempting to improve awareness of allergic diseases among parents. Despite joint efforts, misperception of allergic conditions and associated worries are prevalent, which is particularly worrisome in developing countries. In this study we were aiming to investigate common worries and perceptions among Russian-speaking mothers of children with allergic disease residing in Eastern Europe and EU.

**Method:** We approached social network society of Russian-speaking mothers of allergic children. An online survey was designed and published online at the society webpage. Information on respondents' demographics, common worries and beliefs regarding food allergy and eczema and their trust in physician recommendations was collected.

**Results:** 776 women responded to the survey questionnaire. Respondents were residing in Eastern European countries (EECs) (Russia, Ukraine and Belarus) (n = 644) and European Union (EU) (n = 132). Most of the women (67%) were older than 30 years of age and having a child with eczema, food allergy or both.

A third of all respondents, believe that eczema is always caused by food allergy/intolerance. 45% of women suggest that food allergen should always be found and excluded to get rid of eczema and 35% of all respondents believe that woman breastfeeding baby with eczema should follow a strict restrictive diet. Half of our respondents admit that they are scared to introduce new foods into their child diet, this pattern is seen more often in EECs than in the EU ($P < 0.01$).

82% of the EU mothers trust physicians in what they say about eczema and/or food allergy, which is significantly different ($P < 0.01$) from EECs (49%). 67% of women from EECs reported acquisition of a fundamentally distinct recommendations from physicians on management of eczema and/or food allergy, which is significantly ($P < 0.01$) more often than in EU (34%).

**Conclusion:** Many mothers still have beliefs, which may negatively impact their children health. There is also a lack of trust in physician recommendations, which may be partially explained by mixed message from doctors, especially in EECs. These findings highlight a need in special educational programmes, particularly among mothers residing in EECs. Social network groups may represent a plausible way to deliver education to a modern generation of mothers.

## 0709 | Bacterial colonization and antibiotic resistance in patients with atopic dermatitis

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**Background:** The altered epidermal integrity and leakage of subjects with atopic dermatitis (AD) offer favourable conditions for bacterial skin colonization, which in turn is a predisposing factor for disease exacerbation. Staphylococcus (S.) aureus is considered a leading pathogen maintaining the chronicity of the disorder. The development of antibiotic resistant strains further limits the options for effective treatment. The goal of our study was: 1) to determine *S. aureus* colonization in skin lesions 2) to compare it to colonization of the nose of patients with AD (children and adolescents), and 3) to specify the antibiotic susceptibility of the isolated strains.

**Method:** Twenty-two patients (mean age 8.4 years) with AD were recruited in the study after obtaining informed consent from their guardian. The severity of AD was assessed by SCORAD index. Swabs were taken from overt lesions of the skin and from nasal cavity following a standardized protocol. Standard microbial cultivation techniques for bacterial growth and for determination of antibiotic susceptibility of *S. aureus* were applied.

**Results:** *S. aureus* was isolated in 64% of the studied patients. Bacterial colonization of the skin and in the nose were found in 46%, and colonization of the skin alone in 18% of the patients. The median SCORAD score were slightly greater in those colonized with *S. aureus*. Antibiotic resistance was documented to penicillin—79%, to oxacillin—8%, to cefoxitin—8%, and to tetracycline—28% of the cultures. All strains were susceptible to clindamycin, vancomycin and fusidic acid.

**Conclusion:** These results demonstrate that colonization of the skin lesions with *S. aureus* in pediatric patients with AD is more prevalent in comparison with the nasal bacterial carriage. So far no antimicrobial resistance of *S. aureus* against fusidic acid was found, which we believe is a favorable circumstance provided this drug is widely used for empiric treatment of skin staphylococcal infections.

## 0710 | Treatment strategy of different immunopathogenetic phenotypes of atopic dermatitis

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**Background:** The study considers advantages of differential approach to the treatment of children (Ch) with different immunopathogenetic phenotypes (IPGP) of atopic dermatitis (AD).

**Method:** 300 Ch with moderate course of AD in the exacerbation phase and 30 healthy Ch aged 3-17 were examined. The patients underwent general clinical (CA), immunoallergological (IAA) assessments aimed at detection of clinical and laboratory signs of allergen-induced inflammation. House dust mite allergens (HDMA) were used as a cause-significant allergen. CA was aimed at collection of allergic anamnesis and evaluation of severity of clinical symptoms according to SCORAD scale.

**Results:** It has been found that patients with non-IgE-mediated type of AD was not sensitization to IgE to HDMA and was observed a decline in macrophage-phagocytic component of immune system (MPCIS). It was shown, that the IgE-mediated phenotype includes 3 forms of AD: allergic form; mixed form (in combination with allergic rhinitis, asthma); immunocompromised form (ICF). Allergic and mixed have a proven sensitivity to non-eliminated HDMA, which promoted allergization and provoked the development of symptoms in the course of AD, and in Ch with ICF of AD a decrease in parameters of MPCIS. On the basis of immune system disorders (ISD), has been developed a different complex of immunotherapy (CIT).

**Conclusion:** The developed algorithm of examination and diagnosis of AD patients allows the choice of an adequate CIT in accordance with IPGF based on ISD. Implementation of individual treatment allowed to reduce the risk of developing severe and chronic AD and to improve the quality of life of patients.

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## 0711 | Experience with omalizumab in the treatment of severe atopic dermatitis

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**Background:** Omalizumab is a humanized monoclonal anti-IgE antibody that interrupts the allergic cascade which suggests that it can be effective in the treatment of several allergic conditions, including atopic dermatitis (AD). A number of studies have been published on the usefulness of omalizumab in the treatment of atopic dermatitis, and the results have been variable. We describe the follow-up of 6 patients with severe AD and high levels of total IgE successfully treated with Omalizumab.

**Method:** A retrospective analysis was performed to assess the efficacy of Omalizumab in 6 patients (5 male, 1 female; 21-year-old average) with severe AD, associated with other allergic disorders such as asthma and allergic rhinitis and IgE high levels ranged from 755 to 5264 IU/mL, not responding to conventional therapies. They were evaluated for SCORAD index and daily/rescue medication before and during treatment. Omalizumab was administrated subcutaneously, dose adjustment according to weight and the number of infusions was variable (8- 49).

**Results:** Before treatment all patients were medicated with anti-H1 antihistamine, topical and oral steroids and UV therapy. 4 patients were also medicated with cyclosporine and 1 of them was also medicated with mycophenolate mofetil with no response.

All patients reported a decrease in pruritus and an improvement *of* their atopic dermatitis and in quality of life. Those patients who also had asthma achieved good control of their respiratory symptoms and daily/rescue medication decreased in both dose and number of drugs. Systemic steroids were stopped with no relapse of symptoms. SCORAD index was average at the beginning 72 and after treatment 29. The patients did not experienced adverse side effects.

**Conclusion:** In conclusion, this study indicates that Omalizumab is a safe and effective alternative in the treatment of severe atopic dermatitis refractory to other systemic therapies in allergic patients which decreases serum IgE level, scoring atopic dermatitis, as well as clinical manifestations.

This monoclonal anti-IgE antibody is a major therapeutic advance as it open the door to the management of atopic dermatitis using systemic immunomodulating therapies.

## 0712 | Localized staphylococcal scalded skin syndrome in children with atopic dermatitis

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**Background:** Staphylococcal scalded skin syndrome (SSSS) in both localized and generalized form is caused by exfoliative toxin from *S. aureus*. Exfoliative toxins are serine proteases that cleave desmoglein-1, which induce an epidermal desquamation at the level of the stratum spinosum/granulosum. The association of localized SSSS and atopic dermatitis(AD) has not previously been reported, but SSSS were frequently reported less than 5 years old children with AD. We analyzed SSSS with underlying AD or not.

**Method:** We collected SSSS cases at single institution for 10 years and classified into localized and generalized forms by medical records and pictures. Localized form was defined by negative Nikolski sign and involved less than 30% of body surface area, generalized form was positive Nikolski sign and over 30%. Preceding diseases were

separated by respiratory, gastrointestinal, skin infection and unknown. Throat and skin culture were done in all subjects.

**Results:** There were 124 subjects, and 60 boys. Average age was 2.8 years old (4 days to 8 years old). AD were 31. Subtypes were 59 generalized and 65 localized. *S. aureus* were cultivated 47 in throat, 87 in skin lesion.

With AD, 29/31 were localized compared to 36/88 without AD. Localized SSSS risk was 20.944 in AD, which was statistically significant. ($P$ = 0.000)

*S. aureus* growth in skin culture were 53/65 in localized form compared to 30/54 in generalized. Odds ratio was 3.533, which was statistically significant. ($P$ = 0.002)

With AD, preceding causes were impetigo (41.9%), respiratory (35.5%), and unknown (19.4%), but

Respiratory (48.4%), impetigo (22.6%), and unknown (22.6%) in children without AD.

**Conclusion:** Localized SSSS occurred in children with AD, often began with impetigo. *S. aureus* were cultivated more and frequently in AD group. Localized SSSS may be the form of secondary skin infection in children with AD.

## 0713 | Food sensitization results in children with food-triggered atopic dermatitis

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**Background:** Atopic dermatitis (AD) is a chronic, recurrent and pruritic inflammatory skin disorder. In recent years, there is an increase in the frequency of food allergies in patients with moderate-to-severe disease who are younger than 5 years of age.

**Method:** The study was a retrospective evaluation of AD patients who attended follow-up at the Pediatric Allergy and Immunology Department of the University of Health Sciences, Ankara Pediatrics Hematology and Oncology Research and Training Hospital. Among these patients, those who had positive skin prick test to food and positive serum-specific IgE levels were included in the study.

**Results:** A total of 273 patients were found to have food allergies along with atopic dermatitis. Median age at diagnosis was 3 months (interquartile range: 1-6) and 73.6% of patients were male. When the results of skin prick test to food and serum-specific IgE results were analyzed, we found that 76.3% egg, 18.3% milk, 13.5% egg and milk, 5.8% wheat, 3.6% peanut, 1.8% fish sensitivity. None of the patients had sensitivity to soy bean.

**Conclusion:** In the current study, we determined the source of sensitivity in AD patients with food allergies. Our findings indicated that a large portion of our patients were male, sensitivity to eggs was more frequent than other sources, and none of the patients had soya sensitivity.

## 0714 | Associations between antibacterial chemicals, eczema and body mass index

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**Background:** Antibacterial chemicals like parabens and triclosan have been associated with allergic disease in children. Parabens are also suspected to affect metabolic functions, possibly due to their weak endocrine disrupting properties. Furthermore, a possible link has been suggested for eczema and adiposity, and thus, how body burden of chemical exposures affect both of these outcomes are of interest. We aimed to describe the association between exposure to parabens and eczema and body mass index (BMI) in an adult population in Norway.

**Method:** Urine biomarkers of butyl-, ethyl-, methyl- and propyl-parabens were quantified by mass-spectrometry in 496 adult participants (median age=29 years) from the RHINESSA study in Bergen, Norway. Linear regression models adjusted for gender, age and BMI (for eczema outcomes) and with clustering for siblings, were applied to model possible association between specific gravity standardized urine biomarker concentrations of parabens with BMI and eczema.

**Results:** Propyl- (PPB) and methyl-parabens (MPB) were detected in 95% of the urine samples; ethyl (EPB) in 62% and butyl (BPB) in 38% of the samples. In women, EPB and BPB were detectable in 73% and 61%, respectively. Participants with current eczema (15%) had lower level of several parabens compared to those without eczema (BPB for both genders; EPB in women only and sum of all parabens in men only). Body burden of EPB (geometric mean (GM)) was 6.7 μg/L in women with current eczema compared to 22.3 μg/L in women without eczema ($P$ = 0.03). Body burden of parabens (MPB and EPB) were inversely associated with obesity (BMI>30, (11.4%)), as compared to normal range BMI (BMI=18.5-25 (56.4%)) in both men and women. The concentration of MPB for obese women was GM=2213 μg/L compared to 11503 μg/L in women with normal range BMI. For men, the GM for MPB was 35.3 μg/L in obese compared to 134.4 μg/L in normal weight men ($P$ = 0.03).

**Conclusion:** Person with eczema or obesity had lower paraben levels in urine. We speculate that these chemicals might be stored in adipose tissue, and therefore excreted in urine in lower levels among the obese. Eczema and obesity was not strongly associated in the current study.

## 0715 | Results of late patch test readings with dental screening materials in 75 adult patients

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**Background:** Studies on dermatitis patients have shown that additional positive patch test reactions can be found after day 3. The objective was to analyse frequency of positive patch test reactions on day 7 in patients tested with our dental patch test screening series.

**Method:** We retrospectively analysed medical records of 75 patients who were patch-tested with our dental screening series of 23 substances. Adverse reactions to dental materials were suspected based on subjective complaints in the oral cavity and/or objective conditions of the oral mucosa. Square plastic chambers on hypoallergenic tape were used. Patch tests were applied to the upper back and removed by the patient after 48 hours. Readings were performed 3 and 7 days after application (D3 and D7). Results were evaluated according to the International Contact Dermatitis Research Group guidelines. Positive patch test reactions fulfilled the criteria of at least a one plus (+) reaction on D3 and/or D7. The term »contact allergy« is usually used for such reactions. We prefer the term »contact sensitization«. Clinical relevance of positive reactions to dental materials was not systematically assessed in this analysis.

**Results:** A total of 53 contact sensitizations were confirmed in 25 (33.3%) out of 75 tested patients. The highest frequency of contact sensitization was found with nickel (in 11 out of 75 tested patients), balsam of Peru (11/75), palladium (6/75), amalgam (5/75) and carvone (3/75).

Fifteen (28.3%) out of 53 positive reactions (confirmed sensitizations) to substances in our dental series were demonstrated on D7 only and they were found in 12 (48.0%) out of 25 patients with positive reactions. Three patients had two concomitant positive reactions on D7 only. The number of positive reactions on D7 only was the highest for nickel (4/15) and balsam of Peru (3/15), followed by ethylene glycol dimethacrylate, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, ammoniated mercury, palladium, amalgam, cobalt and colophony (1/15, respectively).

**Conclusion:** We report a high frequency of positive reactions on D7 that were not seen on D3. This finding demonstrates the importance of an additional late patch test reading in patients with suspected contact allergy to dental materials.

## 0716 | Skin patterns of Nickel contact dermatitis evaluated by means of optical coherence tomography

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**Background:** Nickel contact allergy remains a major health issue in especially female pediatric and adult population. Not everyone with nickel sensitization develops a visible contact allergy; it was hypothesized that clinically undetectable skin changes could be displayed through non-invasive diagnostic techniques such as optical coherence tomography (OCT).

**Method:** We analyzed the skin reaction of 5 women (mean age 52 years) with positive patch test to Nickel and 13 women (mean age 51 years) with known Nickel allergy presenting subjective and objective symptoms like itching, erythema or dryness immediately after 2 hours of handwriting with both Nickel releasing and not Nickel releasing pens. The subjects were part of the study "compatibility of writing instruments with Nickel containing components in individuals with nickel allergy " (2016). For each patient, clinical, OCT and dermoscopy images of affected skin and a healthy control area were taken. In absence of clinical evidence like erythema, the affected area was selected based on the patients' indication.

**Results:** OCT could show in all patients a combination of features on the positive patch test area: increased entrance signal and increased epidermal thickness compared to healthy areas, acute spongiosis seen as larger intercellular spaces between keratinocytes and microvesiculation, papillary dermis edema visible as lower dermal reflectivity and vasodilatation seen as increased number and size of dark hyporeflective vessels. Those changes were visible in all grades of responses; one case showed microvesicles, seen as coalescing dark round spaces in the epidermis among keratinocytes with cellular infiltrate.

Concerning patients with symptoms after writing, mild spongiosis and vasodilatation could be identified in 4 of 13; these features alone were only detectable in the thinner interdigital spaces and not in the thicker palmar skin. Moreover, they can also be present in mechanical irritation and atopic skin. None of the patients had eczema-like reactions such as hyperkeratosis and parakeratosis. There was no significant correlation between symptoms, detected changes and use of Nickel releasing pens.

**Conclusion:** Skin changes in acute allergic contact dermatitis can be displayed through in-vivo optical coherence tomography. In this pilot study, we found mild subclinical OCT features after exposure to Nickel releasing writing instruments in only few patients with known Nickel allergy. Larger case-series are needed to better characterize the topic.

## 0717 | Case report: Irritant contact dermatitis induced by capsaicin cream 0.025%

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**Case report:** We report a case of a 76-year-old female patient (a retired health-care provider) diagnosed with acute irritant contact dermatitis, characterized by erythemato-vesicular lesions, associated with burning sensation on right knee, induced by topical application of 0.025% capsaicin cream twice daily. She applied the cream continuously for two weeks, under occlusion, for knee pain.

Skin patch test to incriminated cream was negative.

Usual lab investigations were within normal limits.

Discontinuation of application of capsaicin cream, antihistamines twice daily orally administered and a potent steroid cream were followed by complete resolution of the lesions.

Current topical treatments, out of medical prescription but intensely promoted, for knee pain include topical nonsteroidal anti-inflammatory drugs, capsaicin, salicylates, herbal remedies and hot or cold therapy.

This type of medication is preferred by many patients, especially elderly; efficacy, safety and risk of adverse reactions should be underlined and clearly explained to the patients.

## 0718 | Frequency of contact allergy in psoriasis

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**Background:** Psoriasis is a chronic inflammatory skin disease. Its etiopathogenesis is not exactly known. It is believed that the disease occurs in people with genetic tendency with the effect of a triggering factor. In some studies it is observed that contact dermatitis in psoriasis is increased with respect to normal population. For this reason it is proposed that allergen materials could trigger psoriasis. In this study it is aimed to determine contact allergy frequency in psoriasis cases using patch test.

**Method:** 80 psoriasis cases and 50 control people are taken for the study. Erythrodermic and pustular psoriasis cases are not included in the study. PASI values are evaluated. Cases who have not taken phototherapy, systemic and topical treatment for the last one month are included in the study. European standard series is applied to cases: 2 days left closed, the first was performed when opened, the second was performed 48 hours after reading. Patch test results and PASI values are assessed statistically.

**Results:** 62 of the cases were plaque, 5 of them were guttate, 10 of them were palmoplantar and 3 of them were inverse type. More positivity rate is observed in psoriasis cases (26.25%) than control (12%). The positively responsed materials with respect to decreasing number of patients are found as follows: Nickel sulphate (16.25%), thimerosal (7.5%), peru balsam(5%), p-phenylenediamine(2.5%), colophony(2.5%), n-isopropyl-n-fenil-4-fenilendiamin(2.5%), mercaptobenzothiazole(2.5%), benzocaine(2.5%), Most frequently plaque type and following guttate type positive responses are observed in evaluations with respect to clinical types. No statistical significance is found between patch test results and PASI values in psoriasis cases.

**Conclusion:** Patients with psoriasis should be carefully evaluated. Sometimes some materials may trigger psoriasis.

## 0719 | A case report of a patient allergic to red tattoos

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**Background:** Tattoos have become very popular in our society in the last decades, particularly among younger generations. Tattoo-related complications usually include acute and delayed inflammatory reactions.

The composition of the pigments that professional tattooists use are varied inorganic salts of metals or organic vegetable pigments. Red tattoos, especially those that contain mercury, are the most common cause of late reactions.

**Method:** 35 year-old male patient with no previous allergy history known, who gets a tattoo on his right leg and develops within months, cutaneous erythema and pruritus on the same location as the tattoo.

TRUE TEST ® for skin allergy patch epicutaneous testing is performed.

**Results:** 48 and 96 hours reading: showed positiveness for mercury ++, with no late positive reactions after that.

**Conclusion:** As allergists we should be familiar with the different types of tattoos available, and know the possible cutaneous complications that each of these decorative techniques can present.

It is our responsibility to be able to diagnose any complications at an early stage, establish the most appropriate treatment and, if possible, prevent them by informing the possible users.

## 0720 | Allergic contact dermatitis as a cause of chronic external otitis

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**Background:** Within otorhinolaryngological pathology chronic eczematous otitis externa is one of the most common, usually treated with topical medication successfully; however, there are cases in which the poor response to treatment, or the recurrence thereof, may be due to causes secondary to the medication itself, as observed in cases of allergic contact dermatitis caused by these drugs.

**Case Report:** We present a 68-year-old male patient without relevant pathological antecedents or known allergies, who consulted the otorhinolaryngology service of our center for otorrhea of 15 days of evolution, bilateral external otitis is diagnosed and a topical otological combination is recommended (beclomethasone dipropionate 0.025% and clioquinol 1%, excipient: macrogol) with improvement. However, during the following 3 years the patient presents exacerbations and remissions of the condition, with negative or inconclusive microbiological studies. During all that time he was using the prior topical treatment and other combination treatments of topical antibiotics, corticosteroids and local antiseptics. More aggressive causes of external otitis such as malignant external otitis were ruled out.

During the third year of follow-up, a clear relationship of exacerbations was observed with the use of the first combination of topical drugs, so it was decided to investigate allergic sensitization.

**Material and Methods:** We perform patch tests using True Test®, standard spanish series (GEIDAC - Spanish group for investigation of contact allergy dermatitis), topical corticosteroid battery, antiseptic, as well as topical medications used by the patient.

**Results:** From the first reading on day two, positivity was observed for: Mixture of quinolines ++ patient's otological combination ++ and Chlorquinaldol ++; being confirmed in the reading at day four.

Eczematous external chronic otitis is diagnosed with allergic sensitization to quinolines (clioquinol, chlorquinaldol).

**Conclusion:** We conclude that in the case of chronic external otitis, allergic contact dermatitis should also be investigated as a possible cause, and it is important to perform epicutaneous tests with the patient's own products to evaluate non-common or hidden allergens that may be relevant to their current pathology.

## 0721 | Contact allergy to chromium: Case report of total hip replacement implant failure

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**Introduction:** Cutaneous and systemic hypersensitivity reactions to implanted metals are uncommon, challenging to evaluate and treat and can lead to implant failure. Implant failure has a significant impact on patient's quality of life and a diagnosis of hypersensitivity is important to prevent further re-exposure.

**Case Report:** We present the case of a 64-year-old woman who underwent total right-hip replacement. Days after the surgery, she developed pain at the site of the implant (with no other apparent signs or symptoms), which increased gradually during the following 10 months. At this time, imaging studies revealed loosening of the femoral stem. She underwent a new replacement surgery and during the post-op she developed an intense local inflammatory reaction of the surgical wound, without fever, and which improved under anti-inflammatory therapy. After the surgery, she re-initiated pain at the site of the implant. Imaging studies revealed loosening of the femoral stem and a PET scan showed hyperfixation at the site of the femoral stem component of the prosthesis, suggesting aseptic displacement.

The patient was referred to Immunoallergology and Dermatology Departments for evaluation. Patch tests (Chemotechnique Diagnostics) with Portuguese standard series, metal series and acrylate series showed a positive reaction for chromium at day 4 and 7. Evaluation showed presence of chromium solely on the femoral stem portion of the prosthesis (27-29%).

**Conclusion:** Following arthroplasty, the persistence or early reappearance of inflammatory symptoms should raise suspicions for hypersensitivity. These patients should be promptly evaluated to prevent new surgeries and placement of implants with the relevant components. However, hypersensitivity is a diagnosis of exclusion and non-allergic causes should be excluded in advance.

## 0722 | Allergic contact dermatitis with topical bacitracin

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**Case report:** Allergic contact dermatitis (ACD) is a delayed-type hypersensitivity reaction to materials that come in contact with the skin. Metals, preservatives, perfumes and topical antibiotics are the

most common causes of ACD. It is important to distinguish local findings of infection from ACD caused by topical antibiotic treatments. Here we present a patient with ACD with topical use of bacitracin and neomycin combination therapy due to recurrent blepharitis.

An 11-year-old male patient presented with the complaints of itching, redness, swelling of the eyelids and facial edema. He had used various topical ophthalmic antibiotherapy and eye shampoo for 7 years due to recurrent blepharitis. Five days ago, due to the redness of the eyelids, burning sensation in the eye, itching of the eyes; he was examined by an ophthalmologist. The eyelids and eyelashes were scaly and dry. The patient was treated with warm water soaked cloth dressing, mechanical eyelash cleaning and topical antibiotherapy (neomycin-simple combination therapy). After the second day of treatment, the patient's topical ophthalmic antibiotherapy was discontinued due to an augmentation of the redness in the eyelids, scaling and swelling of the eyes and edema of the face. The patient was treated with topical dexamethasone and olopatadine. He had purple plaques with a sharp line of demarcation over erythematous and edematous skin of the both lower eyelids. Two days after the cessation of the patient's topical antibiotic treatment, the edema on the face regressed. Within ten days edema and purpuric plaques in the eyelids of the patient regressed completely. During the follow-up period, dryness, itching and desquamation continued on the eyelids for 2-3 weeks. Six weeks later, the patch test was performed with a diagnosis of sensitivity against bacitracin.

Allergic contact dermatitis of the eyes due to topical antibiotics should be distinguished from local infection of the eyes and the other eyes diseases. Allergic contact dermatitis usually presents with papules and vesicles over the erythematous inflamed edematous skin. But as seen in our case report it is rarely presented with purpuric plaques. Patch testing should be performed to detect the responsible antigen.

## 0723 | Contact allergy after exposure to ivy (Hedera Helix L)

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**Background:** Contact allergy after exposure to ivy (*Hedera helix L.*). Danielle Boehmer, Andreas B Weins, Maria Uretzki, Bernadette Eberlein, Tilo Biedermann, Ulf Darsow

We report a case of a patch-test diagnosed contact allergy after contact with the commonly occurring plant *Hedera helix* (ivy), which is not related to poison ivy (commonly causes contact dermatitis). A 60-year-old male patient presented with multiple painful blisters and skin erosions on the lower arms at our outpatient clinic after having trimmed his ivy. Ivy (*Hedera helix L)* can cause irritative and allergic contact dermatitis. Case reports are rare due to a lack of a diagnostic standard of contact allergy after ivy exposure

**Method:** After the skin lesions had healed we performed a patch test with ivy in alcohol (0.1%), native celery and native carrot (1:10 dilutions in petrolatum).

**Results:** The results showed a two-fold positive reaction for ivy (*Hedera helix L.*) and celery after 72 hours. A control group (n = 4) showed no positive results.

**Conclusion:** The most potent sensitizer is Falcarinol (heptadeca-1,9 (Z)-diene-4,6-diyne-3-ol), which is the main allergen and main irritating substance of *Hedera helix L*. It can be found in the plant all-year-round. It can also be detected in the family of the Apiaceae (such as carrots, celery, coriander).

As ivy is commonly toxic, a negative patch test in the control group suggests the diagnosis of a contact allergy after *Hedera helix L*. exposition. Once the patient avoided contact with the plant and after topical therapy no new skin lesions appeared.

Cutaneous skin reactions after contact with ivy (*Hedera helix L.)* are more common in our daily clinical routine, but are often not diagnosed as there is no standardised patch test containing this substance. Our case report emphasizes that for correct clinical diagnosis of various plant-derived skin reactions Hedera helix L. should be added to the plant substances in patch-testing panels at the suggested 0.1% concentration.

## 0724 | Marjolin's ulcer: a rare, aggressive skin cancer misdiagnosed as irritant contact eczema

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**Background:** Malignant degeneration in burn scars is estimated to be 1-2% of patients, so an aggressive form of squamous cell carcinoma is caught, even for long periods of time, under different other diagnosis.

Many cases are delayed in establishing a correct diagnosis and optimal medical care, despite of the high risk of metastases and poor prognosis.

**Case report:** We present a case of a 62-year-old female patient, who underwent, three decades prior to present consultation, long hospitalization and intensive treatment care for third degree burns covering more than 50% of her body surface, especially upper limbs and chest.

She admitted the presence of the lesion many months previously, for which she sought medical advice. A diagnosis of irritant contact dermatitis was followed by long term administration of topical

potent steroid treatment associated with systemic antihistamines, but with no improvement.

On dermatological examination a small, well delineated, eczema-like plaque was noticed on a digital finger, as a new finding striking with her old burn scars. She denied any symptoms and was in good health condition. A 4 mm punch biopsy was performed and histological report established the diagnosis of squamous cell carcinoma. The patient was transferred to Oncology Department for further investigation and treatment.

**Conclusion:** Early diagnosis and prompt surgical therapy are recommended to all patients with chronic wounds and scars who develop malignant transformation.

*Written informed consent for the publication of potentially identifiable personal details of patient (gender, age, illness, location) was obtained.

**In relation to this presentation, I declare that there are no conflicts of interest.

## 0725 | A case report of angioedema caused by chickpea water application in an adolescent with acnes

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**Introduction:** The incidence of contact sensitization among adolescent has been increasing. Nickel is one of the important causes of allergic contact dermatitis (ACD) in this age group. Increased exposure to nickel and deterioration of the skin barrier are among the important risk factors in children. The gold standard for diagnosis is skin patch test. We report here an adolescent patient who has allergic sensitization to nickel and cobalt.

**Case:** A 17-year-old female patient admitted in our clinic with a complaint of edema on her face. The patient had applied chickpea water to her face at least once a day for one week because of her acnes. Her medical history revealed that she had experienced similar edema on her face after applications of clay mask one year ago. She was diagnosed with cellulitis and she had been treated with antibiotics for five days. On her physical examination, angioedema was observed on her face, especially on the glabellar region. Eosinophilia was not found on her laboratory data. C-reactive protein (CRP), C4 and C1 esterase inhibitor protein levels were also normal. The skin prick test was performed with aeroallergens, chickpea, lentil, bean and nuts, and no reaction had been observed. The patch test was performed with 'Thin-Layer-Rapid-Use-Epicutaneous' (T.R.U.E) test and chickpea. The patient had positive reactions to nickel and cobalt. Detailed questioning disclosed that the patient was preparing the chickpea water in a metal pot.

**Result:** Chickpea water and clay mask contain varying amounts of nickel. It was thought that the edema of the patient is due to nickel allergic contact sensitization. An increased exposure to nickel and cobalt raises the frequency of sensitization. Nickel allergy can cause different clinics ranging from localized lesions to systemic reactions. We want to emphasize that a detailed medical history and the patch test would enable clinicians to demonstrate hidden allergens and then make a correct diagnosis.

## 0726 | Pre-menstrual dermatitis: Case report

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**Case report:** Autoimmune progesterone dermatitis is a condition of hypersensitivity to progestogens. It is not an easy diagnosis given the variety of clinical presentations it may have, ranging from eczema, urticaria, erythema multiforme, folliculitis, to angioedema or even anaphylaxis. Manifestations are cyclical, occurring when the levels of progesterone are higher, this is, at the luteal phase of the menstrual cycle, and disappear during menses, with the physiological decrease of the hormone. It can also be triggered by exposure to exogenous progestins. We report the case of a 49-year-old woman with a cyclical erythematous and violaceous rash related to the menstrual period. The symptoms typically began 4-6 days before the onset of menses and ended 1-2 days before. The diagnosis was based in the clinical history and intradermal skin tests: skin prick testing with levonorgestrel and medroxyprogesterone were negative, but the intradermal skin test with medroxyprogesterone was positive at a concentration of 50 mg/mL. We performed intradermal testing with the same concentration in three other women with no symptoms to exclude an irritative reaction, which were negative. Autoimmune progesterone dermatitis is, perhaps, not so rare, but rather poorly recognized and reported, and thus, underdiagnosed. Clinicians should be aware and include always this condition in the differential diagnosis, especially in cases of atypical or intractable skin eruptions.

SUNDAY, 27 MAY 2018

TPS 07

TYPES OF ANGIOEDEMA AND URTICARIA DIFFERENTIAL DIAGNOSIS

## 0727 | When it's not just chronic urticaria - Recognizing and diagnosing Schnitzler's syndrome

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**Case report:** A 46 year old male was referred to a community allergy clinic for assessment of chronic urticaria (CU). Allergy assessments for foods, inhalant and inducible physical triggers revealed no association. An autoimmune workup followed, with treatment consisting of standard dose antihistamines (H1 and H2). Blood work revealed a persistently low hemoglobin with low-normal Ferritin. Hematology consulted and followed attempted iron replacement to no avail. Skin biopsy revealed neutrophilic rich urticaria with the presence of eosinophils. Serum protein electrophoresis (SPEP) revealed a monoclonal gammopathy with elevated IgM, felt to be of undetermined significance (MGUS). C-Reactive Protein (CRP) was consistently elevated (183, 256) in conjunction with anemia. Rheumatology consulted and cleared of any evidence of vasculitis. Hematology considered the anemia to be of chronic disease linked to CU.

The CU was resistant to treatment including high dose antihistamines, cyclosporine, omalizumab (up to 450 mg), tacrolimus, and dapsone. Prednisone bursts were often required. With time, a marked neutrophilia presented with worsening anemia. Patient incurred a 10 kg weight loss. Hematology was re-consulted for consideration of a bone marrow to rule our malignancy. A skeletal survey identified abnormal bone remodeling and sclerotic changes. As the result of worsening presentation, the patient's case was reviewed for the possibility of an auto-inflammatory condition. A formal diagnosis of Schnitzler's Syndrome was made based on Lipsker criteria of chronic urticarial rash, MGUS, bony abnormalities, neutrophil infiltration on skin biopsy, and exceedingly high C-Reactive Protein. Documentation of recurrent fevers was lacking. Patient was started on anti-IL-1 therapy, anakinra, with immediate improvement, within 24 hours. Within days, patient had complete resolution of all symptoms, most notably the long-standing urticaria, with regained weight and normalization of anemia. Patient has remained stable on daily dosing of 100 mg anakinra SQ for the last 2 months.

**Discussion:** In CU that is difficult to control, the above patient's early serum abnormalities of elevated CRP++, positive SPEP should highlight the need to investigate for auto-inflammatory causes such as Schnitzler's syndrome. Directed treatment, i.e. anti-IL-1 is most effective in prompt resolution of symptoms.

## 0728 | Chronic urticaria after coronary stent placement: Is there a causative relationship?

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**Introduction:** Hypersensitivity reactions to metals such as nickel, cobalt and chromium are well known. Implantation of a metal containing medical device to a sensitized patient may cause adverse reactions including systemic contact dermatitis. However the outcome of coronary stent placements in metal allergic patients is not sufficiently clarified. In some patients in-stent restenosis because of metal hypersensitivity has been proposed. Here we describe a patient with chronic urticaria which arose after a coronary stent placement.

**Case:** A 53 year old male, working as an electrical technician, applied to our outpatient clinic for his treatment-resistant chronic urticaria. His complaints emerged shortly after a coronary stent placement on his posterior descending coronary artery 2 years before. Since then he had emergency visits average four times a month because of urticaria attacks frequently accompanied by chest tightness and face edema despite of using anti-histaminic tablets four times per day. He was under anti-hypertensive treatment concomitantly. He stated that he reacted to metals for a long time, the most prominent examples being dermatitis to belt buckles or metallic watch bands. He had a smoking habit of 2 packs per day for 40 years. Physical examination was normal, all routine biochemical tests were within normal limits and the autolog serum skin test was negative. However, skin patch testing with metals displayed Grade 3 positivity for cobalt chloride and nickel sulfate. His cardiological records confirmed that his coronary stent was *cobalt-chromium everolimus eluting stent*. His situation was discussed with his cardiologist and the stent removal was not considered as a treatment option because it was considered to be too risky. Accordingly, omalizumab was initiated.

**Conclusion:** Although a causal relationship between metal allergy and triggering of urticaria after coronary stent placement can not be proven, this patient suggests that metal allergy must be questioned before implantations of medical devices and if necessary skin patch testing should be performed.

## 0729 | Bradykinin mechanism is the main responsible for death by asphyxiating angioedema in France

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**Background:** Isolated head and neck angioedema (AE) can be mediated by bradykinin (Bk) or histamin (Hi). The objective of our study was to determine which etiology was most frequent in cases of death by asphyxiating AE in France.

**Method:** We sought all cases of death by isolated asphyxiating AE reported in France between 2000 and 2014 via death certificates and/or the national pharmacovigilance database.

**Results:** The overall mortality by asphyxiating AE for all causes was 0.36 / million inhabitants. The death rate of BkAE per million inhabitants was 0.14 and lethality of 0.27 per thousand patients per year. The death rate of HiAE per million inhabitants was 0.09 and lethality of 0.006 per thousand patients per year. We found a 45 times higher risk of death in case of BkAE than HiAE.

**Conclusion:** Consequently, particularly severe episodes must be initially considered as bradykinin mediated and quickly reassess any first-line treatment that is inappropriate.

## 0730 | Acquired angioedema: The common symptom of four different diseases

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**Background:** Acquired angioedema with C1-INH deficiency (C1-INH-AAE) should be considered when patients present with isolated angioedema without urticaria in the fourth decade of life or later without a family history of angioedema. A quantitative and functional C1-INH deficiency with negative family history and low C1q is required to diagnose C1-INH-AAE. We report four patients presenting as acquired angioedema diagnosed with different underlying diseases.

Case 1: 70 year old male applied to our hospital due to recurrent abdominal pain. Laboratory findings showed anemia, thrombocytopenia, hypocomplementemia [C4:6.2 mg/dl (10-40), C1q:12 mg/L (70-350), C1 esterase inhibitor (INH):12.6 mg/dl(21-39), C1 inhibitor function: 6.4% (70-130)]. Abdominal computerized tomography(CT) showed left colonic wall thickening and splenomegaly. Bone marrow aspiration biopsy resulted in splenic marginal zone lymphoma.

Case 2: 48 year old female had abdominal pain attacks for 10 years, facial and extremity edema for 2 years in her medical history. Laboratory findings showed hypocomplementemia (C1q:34 mg/L, C4: <4 mg/dL, C1 INH:5.8 mg/dL, C1 INH function: 3.3%). Retroperitoneal, mesenteric, mediastinal lymphadenopathy were detected in CT. Bone marrow aspiration biopsy resulted in small lymphocytic lymphoma.

Case 3: 49 year old female applied to hospital due to dyspnea and stridor. Her neck CT showed laryngeal edema of the throat. Laboratory findings showed elevated blood protein level 10.7 gr/dL(6.4-8.3), hypergammaglobulinemia, hypocomplementemia (C4:<4 mg/dL, C1q:70 mg/L). Serum protein electrophoresis showed monoclonal gammopathy. Bone marrow aspiration biopsy resulted in multiple myeloma.

Case 4: 56 year old female had recurrent extremity edema for 3 years, and laryngeal edema and abdominal edema once. Thoracal and abdominal CT were normal. Other etiological assessments resulted in normal ranges. Laboratory findings showed hypocomplementemia (C4:<4 mg/dL, C1 INH: 5.28 mg/dL, C1q:8 mg/L). She was diagnosed as idiopathic acquired angioedema.

**Discussion:** All patients diagnosed with C1-INH-AAE should be evaluated for underlying B-cell lymphoproliferative disorders and autoimmune diseases at the time of diagnosis. Treatment focuses on symptom control with therapies that regulate bradykinin activity (C1-INH concentrate, icatibant, ecallantide, tranexamic acid, and androgens) and treatment of any underlying conditions.

Consent: Written informed consent was taken from the patients.

Table -Clinical and laboratory findings of the patients diagnosed with acquired angioedema.

| Case | Age | Sex | Localisation of edema attacks | C4 (10-40 mg/dl) | C1-INH (21-39 mg/dl) | C1-INH (70-130%) | C1q (70-350 mg/L) | Serum protein electrophoresis | Diagnose |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 48 | F | Abdominal and face edema | <4 | 5.8 | 3.3 | 34 | Minimally monoclonal spike in gamma region | Small lymphocytic lymphoma |
| 2 | 49 | F | Laryngeal edema | <4 | 27.6 | 101 | 70 | IgG-kappa monoclonal gammopathy | Multiple myeloma |
| 3 | 70 | M | Abdominal, uvula, and neck edema | 6.2 | 12.6 | 36.4 | 12 | Nonspecific hypogammaglobulinemia | Splenic marginal zone lymphoma |
| 4 | 56 | F | Face, extremity, laryngeal, and abdominal edema | <4 | 5.28 | 8.5 | 8 | Normal serum protein electrophoresis | Idiopathic |

## 0731 | Hereditary Angioedema (HAE), still a fatal illness despite C1-INH substitution

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**Background:** We report a 35 years-old man undergoing chronic hemodialysis three times a week while waiting for the second kidney transplantation. After some time, he developed nausea, palpitations, hypotension, dyspnea, cough, abdominal discomfort, eyelid-, lip- and tongue swelling after every hemodialysis and was presented for allergy diagnosis.

**Method:** As all materials used for hemodialysis were skin prick tested negatively and -if available- for specific IgE determination with negative results, the patient was then evaluated for Hereditary Angioedema (HAE) and was diagnosed positively in 2004. Mother and sister did not appear for HAE evaluation but were symptom-free until then.

**Results:** A prophylactic treatment with danocrine was started with symptom attenuation. In 2006, tranexamic acid was added to the treatment and the patient was symptom-free after dialysis for a while. Three months later, he developed hand swelling and was treated with C1-INH (C1-inhibitor) for the first time. In the following, he was substituted at least once a month or as needed with C1-INH. Due to attack worsening in 2007, he got C1-INH substitution every Friday after dialysis. He additionally was instructed in stress-avoidance techniques and got psychological support.

In November 2007, after hemodialysis he developed fever, dyspnea, cough, hematemesis regardless of treatment with C1-INH and was transferred to intensive care unit where he died of respiratory and heart failure.

**Conclusion:** For sure, this was before the era of the new treatments for HAE and the patient suffered from additional serious diseases but can we still be sure that he would have survived with today's possibilities?

## 0732 | The physician and hereditary angioedema friend or foe: 62-year diagnostic delay and iatrogenic procedures

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**Case report:** We present the case of a 72-year-old man who suffered recurrent abdominal pain since age of eight, leading to 3 unnecessary emergency surgical interventions and 5 endoscopies before hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE) was diagnosed at the age of 70. Rare subcutaneous swellings were considered allergic reactions preventing proper diagnosis. Family history, positive for recurrent abdominal pain and swellings was totally neglected until diagnosis of C1-INH-HAE type I was established through appearance of severe oro-facial symptoms in the propositus' grandson. The diagnosis was suggested by the boy's mother, directed by educational materials available in the international HAE patients' association website (www.haei.org). This report highlights and emphasizes the importance of accurately evaluated personal and family history to suspect condition that are scarcely known to the majority of physicians.

**Highlights:** Diagnostic delay in HAE and iatrogenic procedures are an underestimated problem, hiding undefined consequences, possibly destructing an entire lifetime. Correct, publically available information provided by patients' associations raise awareness about the disease and could put the milestone of establishing correct diagnosis.

## 0733 | Diagnostic role of epicutaneous in patients Consultings for angioedema in the facial region

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**Background:** In the protocol for the study of patients who consult for recurrent acute angioedema with facial involvement, the contactant battery is included (epicutaneous test). We review the results in our patients with facial angioedema to evaluate the contactants to which these patients present sensitization, some of them coexisting with contact dermatitis clinic.

**Method:** We reviewed the patients referred to the clinic for recurrent acute angioedema with facial involvement and to whom a standard battery epicutaneous test was requested. In all these patients, other habitual triggers included in the diagnostic protocol (food, medications, autoimmune diseases, bradyinergic AEA/complement deficit …) were ruled out.

**Results:** 14 revised patients of which: men 2 / women 12, with an average age of 40.5 years (25-71 years). The epicutaneous tests were positive in 9 patients: of which 9 were women, the contactant involved nickel sulfate in 6 patients, mixture of cainas 1, cobalt 1, thiomersal 1, balsam of Peru 1 and metals 1. In two patients there was a double sensitization (to nickel and cobalt sulfate and another nickel sulfate and mixture of cainas). Of the 9 patients with positive results, only 4 reported in addition to the episodes of angioedema, coexistence of eczema plaques. Avoidance measures are recommended with the positive contactant, the evolution being very favorable in 5 patients (there have not been any new episodes of angioedema although one of them is under daily treatment with oral antihistaminic) and the remaining 4 are pending review after measures of avoidance.

**Conclusion:** It seems to be profitable to continue including in the diagnostic battery of patients who consult for AEA with facial affectation, study of epicutaneous with standard battery. It is a small sample, but the data correlate with what has been published, being more frequent the sensitization to contactants in women and the contactant more frequently involved nickel sulphate.

## 0734 | Ace inhibitor- related angioedema—the value of history taking

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**Background:** Angioedema is a well-recognized side effect of angiotensin-converting enzyme (ACE) inhibitor therapy. Although it occurs in <1% of the patients who take these drugs, it seems to be responsible for 40% of the episodes of angioedema. This entity is underdiagnosed and failure to recognize it leads to recurrence of episodes, with an impact on morbidity and increased risk of serious reactions.
Our objective is to analyze the clinical, therapeutic and orientation approach of patients diagnosed with ACE inhibitor—related angioedema, evaluated at the outpatient consultation (OA) of Immunoallergology (IA).

**Method:** A 3-year retrospective study was performed by analyzing the clinical files of all patients diagnosed with angioedema observed in OA of IA. The following variables were analyzed: gender; age; clinical data; evaluation in emergency department (ED); therapy in the episode; evolution and orientation. The Chi-square test was used to study the association between categorical variables: ''established therapy''/''disease evolution'' and ''place of reference''/''withdrawal of ACE inhibitor''.

**Results:** Review of 62 cases of patients referred for angioedema. Only in 29% the final diagnosis was ''ACE inhibitor-related angioedema''. The mean age of the patients was 63.7 years and 67% were male. The location of angioedema occurred in the tongue in 33% and in the remaining sites (lip, hemiface, tongue and hemiface, tongue and lip) appeared in the same frequency, 17%. None of the patients had airway obstruction. During the episode of angioedema, 22% of patients were not referred to ED and the therapeutic approach was done with antihistamines in 75%. In patients who were referred to ED (78%), antihistamines and corticosteroids medications were administered in 85%. Regarding the evolution, it was verified that the duration of the episode was independent of the established therapy ($P > 0.05$). Regarding the place of reference, 60% of the patients were referred form Hospital (EC or ED) and, in these, the ACE inhibitor was suspended in 73%. In patients referred from General Practitioners (40%), in none of them the ACE inhibitor had been withdrawal.

**Conclusion:** A causal association between the use of ACE inhibitors and the episode of angioedema becomes crucial, since drug withdrawal is indicated. A reference for AI OA should be weighed. Therapy with antihistamines and corticosteroids has no proven efficacy.

## 0735 | Clinical characteristics and geographical distribution of a cohort of patients with Hereditary Angioedema (HAE) seen by physicians belonging to the HAE scientific committee of the AAAeIC

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**Introduction:** Hereditary Angioedema is an infrequent, genetic, immunological disease. It is characterized by the C1-inhibitor plasma protein deficit (C1-INH-HAE Type 1), or by the presence of a dysfunctional protein (C1-INH-HAE Type II), besides there is another type the HAE with Normal C1-inhibitor (nC1-INH-HAE). Clinically presents recurring episodes of subcutaneous or sub -mucosal angioedema being a life-threatening disease.

**Objectives:** To asses patients with HAE, type, family history, geographical distribution, demographic characteristics, clinics and treatment, onset age, diagnoses age and its delay.

**Materials and Methods:** An Excel spreadsheet was created as an instrument for data collection. They were completed by their authors. Statistical analysis was performed.

**Results:** 169 patients casuistry; 160 C1-INH-HAE: 158 Type I, 2 Type II and 9 nC1-INH-HAE. Female was 59%, and male 41%. Symptoms beginning average: 19 years old. Diagnoses age: 29 years old. 87% had family history. There were 12 novo mutations. 30% of professionals do not have a local laboratory for diagnoses. 78% of patients has had crisis in the last year. Sites mostly affected are: Limbs, face, lips, tongue and gastrointestinal tract. 48% of crises are treated at home. 7.2% has been hospitalized in the last year. Crises are mostly treated with subcutaneous Icatibant and intravenous C1 inhibitor concentrate.

**Conclusion:** This casuistry shows that the distribution of different types of HAE, its clinical characteristics and delay in diagnoses is similar to the international reports.

## 0736 | Prophylactic therapy with BCX7353 improves anxiety and stress in hereditary angioedema with C1- inhibitor deficiency (C1-INH-HAE) patients

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**Background:** Patients with C1-INH-HAE frequently suffer from anxiety and stress. The impact of prophylactic treatment on anxiety and stress in C1-INH-HAE patients is largely unknown. Here, we analyzed data from the ApeX-1 study, a phase II study that investigated the effects of the oral kallikrein inhibitor BCX7353.

**Method:** C1-INH-HAE patients with a history of at least 2 HAE attacks per month were randomized to receive four different doses (350, 250, 125, 62.5 mg) of BCX7353 or placebo for 28 days. The depression anxiety stress scale (DASS) was administered at Baseline and at Day 29. The DASS consists of three self-reported scales designed to measure the negative emotional states of anxiety and stress. Subjects used a 4-point severity/frequency scale to rate the extent to which they have experienced each state.

**Results:** Baseline DASS total scores as well as anxiety and stress domain mean (SD) scores for the 125 mg treatment arm (N = 13) were 20.9 (23.7), 5.0 (5.9), and 8.9 (9.1) points respectively. Placebo scores were generally similar or slightly lower at baseline than for the 125 mg treatment arm. The DASS questionnaire data showed statistically significant improvements in total score vs. placebo at day 29 (−11.4 points, 95% CI [−21.3, −1.4], $P = 0.025$) and in the domains anxiety (−2.9 points, 95% CI [−5.7, −0.02]) and stress (−5.5 points 95% CI [−9.8, −1.2]) in the 125 mg dose group.

**Conclusion:** Treatment with 125 mg BCX7353 for 28 days reduced anxiety and stress in C1-INH-HAE patients.

## 0737 | Hereditary Angioedema Rapid Triage Tool (HAE-RT): Translating research into clinical practice

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**Background:** HAE patients (both diagnosed and undiagnosed) commonly present to the emergency department (ED). Presenting symptoms (swelling and pain) may be wrongly attributed to common allergic and gastrointestinal conditions resulting in major delays in diagnosis and treatment. No published tools currently exist for HAE screening and management in undiagnosed disease. The overall goal of the study was to develop a HAE-RT tool for ED settings.

**Method:** A two-phase mixed methods approach was used to develop the HAE-RT Tool including: Phase 1: Delphi study [HAE specialists (N = 9) and National Patient Advocacy Group Members (N = 3)] was conducted to reach consensus (80% agreement) on predictor variables to include in the Tool. Phase 2: Retrospective chart review was conducted to assess the predictive findings of the decided variables. A convenient patient sample presenting with angioedema (with and without HAE) between January 2012—January 2017 were included in the study.

**Results:** Nine of 12 invited experts (75%) participated in the Delphi study. Of 8 HAE-specific predictive variables, 4 reached consensuses including: (i) recurrent angioedema; (ii) absence of urticaria; (iii) recurrent abdominal pain/swelling; (iv) lack of response to allergic therapy. The retrospective study included 85 patients (N = 46 with HAE; N = 39 non-HAE; overall 72% female). HAE patients were significantly more likely to have a family history of HAE (72% vs 0%; $P < 0.0001$); previous recurrent angioedema (96%; $P < 0.009$); present with no hives (91%; $P < 0.036$); previous recurrent abdominal pain (80%; $P < 0.0001$); and 2% responded to allergy treatments ($P < 0.0001$). A regression analysis categorized observed frequencies (actual patient outcomes from chart review) versus predicted (by model); plotted on a 2 by 2 table and calculated the sensitivity and specificity of the HAE-RT which resulted in one hundred percent for both.

**Conclusion:** Our study demonstrated that expert involvement led to the identification and prioritization of variables that when included an HAE-RT tool, were associated with a high level of sensitivity and specificity when applied to known patients. The next step is to observe the effect of the HAE-RT tool on patient care in the ED.

## 0738 | Assessment of 105 patients with angiotensin converting enzyme-inhibitor induced angioedema eva

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**Background:** The objective of this study was to asses a cohort of 105 consecutive patients with angiotensin converting enzyme-inhibitor induced angioedema with regard to demographics, risk factors, family history of angioedema, hospitalization, airway management, outcome, and use of diagnostic codes used for the condition.

**Method:** This was a retrospective cohort study of 105 patients with angiotensin converting enzyme-inhibitor induced angioedema in the period 1995-2014.

**Results:** The cohort consisted of 67 females and 38 males (F :M ratio 1.8), with a mean age of 63 [range 26-86] years. Female gender was associated with a significantly higher risk of angiotensin converting enzyme-inhibitor induced angioedema. 6.7% had a positive family history of angioedema. Diabetes seemed to be a protective factor with regard to angioedema. 95% experienced angioedema of the head and neck. 4.7% needed intubation or tracheostomy. 74 admissions took place during the study period with a total of 143 days spent in the hospital. The diagnosis codes most often used for this condition were "DT783 Quincke's oedema" and "DT78.4 Allergy unspecified". Complement C1 inhibitor was normal in all tested patients.

**Conclusion:** Female gender predisposes to angiotensin converting enzyme-inhibitor induced angioedema, whereas diabetes seems to be a protective factor.

| **Hospitalization data** | |
|---|---|
| Patients assessed at Emergency Department | 48 |
| Patients admitted to a hospital | 55 |
| Number of admissions, total | 74 |
| **Number of admissions** | |
| 1 | 39 patients |
| 2 | 7 patients |
| 3 | 2 patients |
| 4 | 4 patients |
| Unknown number | 3 patients |
| Days of admission, total | 143 |
| Days of admission, mean, [range] | 2.9 [1-35] |
| **Department of initial admission** | |
| Internal Medicine | 40 |
| Otorhinolaryngology | 19 |
| Emergency Department | 6 |
| Intensive Care Unit | 2 |
| Dermatology and Allergy | 2 |
| Unknown | 5 |
| **Diagnostics codes in Emergency Department** | |
| DT78.3 Quincke's edema | 56.3% |
| DT78.4 Allergy unspecified | 33.3% |
| DT88.6 Anaphylactic shock | 2.0% |
| Miscellaneous | 8.4% |
| Diagnostic codes in other departments | |
| DT78.3 Quincke's edema | 59.6% |
| DT78.4 Allergy unspecified | 15.9% |
| DT88.6 Anaphylactic shock | 2.1% |
| Miscellaneous | 18.1% |
| Unknown | 4.3% |

## 0739 | Preliminary study - Pulmonary and cardiovascular symptoms in patients with mastocytosis

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**Background:** Mastocytosis is a group of rare diseases characterized by excessive growth of mast cells in skin, bone marrow, liver, spleen, lymph nodes. Signs and symptoms result mostly from mast cells mediators and mast cells organ infiltration. Pulmonary and cardiovascular localization of mastocytosis is extremely rare and in most instances have not been substantiated with pathologic confirmation.

**Method:** Evaluation of cardiovascular manifestation included morphology, serum level of troponin T, electrocardiography (ECG) and echocardiography. Evaluation of pulmonary manifestation included spirometry, diffusing capacity of the lung for carbon monoxide (DLCO) and evaluation for mastocytosis included bone marrow biopsy and serum total tryptase measurements.

**Results:** In the study there were 55 patients - 35 women and 20 men between 21 and 71 years old (the average age was 45). There were 7 (12.73%) patients with MPCM, 4 (7.28%) with BMM, 42 (76.36%) with ISM and 2 (3.64%) with SSM. The average level of serum tryptase was 45.1 μg/L (6.9-270). Troponin levels was within the normal range in all patients. One patient had lowered the ejection fraction (EFLV=23%). No one patient had restriction. The average value of a forced lung capacity was 3.33 L (104%) and a total

lung capacity was 5.79 L (98%). And impaired DLCO (under 80% of predicted value) had 18 patients (32.7%).

4 patients (7.3%) were treated due to asthma, but dyspnea was presented among 23 patients (41.8%). Chest pain have been reported in 12 patients (21.8%). 14 (25.5%) patients were treated due to hypertension, 8 (14.5%)—diabetes mellitus and prediabetes, 6 (10.9%)—arrhythmias.

**Conclusion:** All patients with systemic mastocytosis should be systematically evaluated for the presence of bronchial hyperresponsiveness. Troponin level measurement can be useful in determining the risk of heart disease but requires further research.

## 0740 | Mastocytosis in the skin: a Russian center case series

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**Background:** More than 95% of adult patients with mastocytosis in the skin (MIS) suffer from a systemic mastocytosis (SM), whereas indolent systemic mastocytosis (ISM) is the most common form. Here, we describe a case series of twelve MIS patients seen at our Department over a 3-year period and report how many of these patients have SM.

**Method:** All patients were pre-diagnosed with MIS and underwent bone marrow investigation. The SM diagnosis was established according to WHO criteria: detection of clusters of mast cells (MCs), atypical and/or CD25/CD2-positive MCs in bone marrow; KIT D816V mutation; serum tryptase level more than 20 ng/mL. Further examination included biochemical and hematologic evaluation, abdominal ultrasound, X-ray assessment of bone mineral density and gastrointestinal mucosal biopsies if diarrhea and weight loss were present. All patients were treated in accordance with clinical guidelines.

**Results:** All patients were males (n = 3) and females (n = 9) aged 29 or older (mean: 47 years). Clinically, all patients presented with widespread red-brown maculopapular lesions up to 0.5 cm in diameter. The mean age at onset of the disease was 34 years (range: 18-55 years). Cutaneous mastocytosis (CM), smoldering SM, aggressive SM and ISM were diagnosed in 17% (n = 2), 25% (n = 3), 25% (n = 3) and 33% (n = 4) of patients, respectively. SM but not CM patients had pruritus and other mast cell mediator-related symptoms. Second generation antihistamines were effective in reducing itching in two of four SM patients. Four patients reported complete pruritus remission and/or reduction in the number of lesions during or at the end of the PUVA therapy.

**Conclusion:** The results of our study correlate with literature data and prove that most adult patients with MIS have SM. There are many mediator-related symptoms characteristic of SM, including, but not limited to, pruritus, nausea and vomiting, diarrhea, bone pain and neuropsychiatric disturbances. PUVA is an effective and well tolerated second line treatment option for the cutaneous symptoms in mastocytosis especially in patients with refractory disease or esthetically unpleasant lesions.

## 0741 | Hereditary angioedema type 1 experience in KwaZulu-Natal, South Africa. (Late Breaking Abstract)

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**Background:** Hereditary angioedema type 1 (HAE1) is a rare autosomal dominant genetic disorder secondary to a mutation of a gene that codifies for the synthesis of the enzyme C1 esterase inhibitor (C1INH). HAE1 was identified for the first time in KwaZulu-Natal among members of a Zulu family in Rural Northern KwaZulu Natal by E. Moran et al in 2008. We studied this family to review the genetic burden over 4 contiguous generations, to identify the

Table 1. Clinical and laboratory screening data

| Patient, age, gender | Clinical data past year (2017) | C1INH (21-39 mg/dL) | C3 (0.90-1.80 g/L) | C4 (0.10-0.40 g/L) |
|---|---|---|---|---|
| DM1, 28 F | Face and extremities | 7.4 L | 1.23 N | 0.03 L |
| DM2, 7 M | Face and extremities | 5.5 L | 1.23 N | 0.04 L |
| DM3, 12 F | Neck and extremities | 3.0 L | 1.08 N | 0.01 L |
| DM4, 10 F | Face and extremities | 5.6 L | 1.10 N | 0.07 L |
| DM5, 14 F | Face and extremities | 5.7 L | 0.85 L | 0.03 L |
| DM6, 8 F | Extremities | <2.8 L | 1.44 N | 0.00 L |
| DM7, 2 F | Face and extremities | 5.0 L | 0.82 L | 0.03 L |
| DM8, 6 M | Neck and extremities | Unavailable | 1.17 N | 0.01 L |
| DM9, 9 F | Neck and extremities. | 4.3 L | 1.29 N | 0.02 L |
| DM10, 11 M | Face and extremities | 4.9 L | Unavailable | 0.03 L |
| DM11, 10 F | Face and extremities | 7.8 L | 1.32 N | 0.01 L |
| DM12, 17 M | Face, Extremities and Larynx | 7.8 L | 1.26 N | 0.02 L |
| DM13, 22 M | Face and extremities | 5.6 L | 1.04 N | 0.09 L |

*Abbreviations*: C1INH (C1 ESTERASE INHIBITOR).

Table 2. Questionnaire results

The socio-economic burden secondary to HAE1 (10 participants/5 identical questions each)

| QUESTIONS | ANSWERS ON AVERAGE |
|---|---|
| Question 1 (0-5 POINTS) | 3 |
| Question 2 (0-3 points) | 2 |
| Question 3 (0-3 points) | 1 |
| Question 4 (0-3 points) | 1 |
| Question 5 (0-1 point) | 1 |
| TOTAL | 8 |

Interpretation: Total of 15 points

Category 1 (Mildly affected) :<5 points

Category 2 (Moderately affected) : 5-10 points

Category 3 (Severely affected) :>10 points

common phenotypical manifestations of acute HAE1 episodes in this region, to review therapeutic challenges in a rural setting in comparison with world standards, and lastly to evaluate the socio-economic burden inflicted by the disease.

**Method:** A sample of 13 individuals from a total of 28. The exclusion criteria was the inability to attend booked appointments more than 3 times in 1 year (2017). The following methods were used: An interview to formulate a family tree identifying affected individuals in 4 contiguous generations, and review of the acute presentations in the past year (2017). A questionnaire to obtain the relevant HAE1 associated socio-economic burdens. A chart review to identify the therapeutic strategies in this region. C1INH levels, and Complement C4 to confirm the diagnosis.

**Results:** Polygamy as a local culture was found to be an important factor that perpetuated the genetic burden of the disease. C1INH and C4 levels confirmed HAE1 in all participants individually. Clinical features during acute attacks included swelling of extremities (100%), facial swelling (69%), neck swelling (23%), and laryngeal swelling (8%). Therapeutic strategies for acute attacks included Fresh Frozen Plasma or Fresh Dried Plasma. Danazol was used for prophylaxis. HAE1 has had a significant negative impact upon the socio-economic status of the affected individuals.

**Conclusion:** HAE1 is a newly identified disorder in the broad spectrum of Allergy Medicine in KwaZulu-Natal. The diagnosis is simple to confirm but requires an initial high index of suspicion, and therapeutic management still poses a challenge in this region due to lack of resources. Genetic counselling is of paramount importance during intervention since polygamy forms part of most cultures in this region. A support strategy is highly recommended in order to help alleviate the socio-economic burden posed by the disease in this region.

SUNDAY, 27 MAY 2018
TPS 08
DIFFERENT ASPECTS OF ALLERGIC SYMPTOMS

## 0743 | The effect of modification of inhaler spacer's visual user guide on the correct use of the inhaler spacer

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**Background:** Generally, metered dose inhaler medication is prescribed in patients under six years of age with asthma. Even if the inhaler spacer training is given, parents can forget to use it after they stop treatment. For this reason, it is important that the visual user guide that should be simple and understandable and should be placed on the inhaler spacer. Our aim in this study was to determine the effect of modifying the visual user guide on the inhaler spacer for the correct usage skill.

**Method:** A total of 172 medical faculty senior year students were included to study on a voluntary basis. Students are divided into two groups. One group was given visual user guide that has not been modified, and a visual user guide on which we have modified to the other group (Figure 1). Then they were asked to show how to use the inhaler spacer.

**Results:** The mean age of the volunteers was 25.3 ± 126 years and 104 (60.5%) were male. There were 82 students in the group without modification of the visual user guide and 90 students in the other group with modified the visual user guide. Sixty-four per cent of the modified user guide group showed correct use of the inhaler spacer, while 15% of the unmodified group showed correct use ($P = 0.001$). The group that given modified visual user guide was more successful in all of the display steps of the inhaler spacer.

| Variables | pMDI spacer (n = 82) | Modified pMDI spacer (N = 90) | *P*-value |
|---|---|---|---|
| Shaking MDI and removing cap*, n (%) | 45 (54.9) | 89 (98.9) | |
| Connect MDI to spacer* | 62 (75.6) | 86 (95.6) | <0.001 |
| Holding MDI upright | 44 (53.7) | 84 (93.3) | <0.001 |
| Place mouthpiece between teeth and lips or place facemask* | 57 (69.5) | 89 (98.9) | <0.001 |
| Activation of the MDI only once* | 60 (73.2) | 88 (97.8) | <0.001 |
| Take 5-6 deep and slow breaths* | 28 (%34.1) | 88 (97.8) | <0.001 |
| Wait for at least 30 seconds before next actuation* | – | 90 (100) | <0.001 |
| Rinse the mouth after the use of a steroid inhaler | – | 90 (100) | |

**Conclusion:** Modification of the currently available visual user guide of inhaler spacer in our country will increase the correct usage rate.

## 0744 | Pulmonary function in boys with Duchenne Muscular Dystrophy

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**Background:** Duchenne muscular dystrophy (DMD) is an X-linked disorder. The mutations (dystrophin gene) leading to progressive muscle degeneration. One of the most important consequences of DMD is progressive weakness of respiratory muscles resulting in respiratory failure, which in turn often determines the length of survival of patients. The aim of this study was to assess pulmonary function in children with DMD and identify factors affecting it.

**Method:** We evaluated 56 boys (mean age 10.7 ± 3.5 year) with DMD. Data about weight, height, BMI z scores, steroid therapy (GC), ambulatory status were collected. The spirometry (Jaeger) were made in all subjects. The statistical analysis was done using program Statistica vs 10.0.

**Results:** Mean FEV1, FVC, FEV1/FVC z-score were 1.8 (1.1-3.9), 1.7 (0.9-3.7), 0.9 (0.8-0.9), respectively. Restriction had 31 (57.4%) and obturation 3(5.3%) patients. FEV1 ($P < 0.001$, $r^2 = 0.37$) and FVC ($P = 0.001$, $r^2 = 0.38$) decreased with age (%PV and z-score). GC (35 patients; 63.6%) had significant influence on FEV1 ($P = 0.025$) and FVC ($P = 0.003$), it reduced degree of FEV1 and FVC decrease with age. Ambulatory vs non-ambulatory patients (30/25) had higher FEV1, FVC z scores (−1.02 +/− 0.56 vs 3.18 + /-0.76; $P < 0.001$ and −1.28 +/−0.59 vs −3.65 +/−0.9; $P < 0.001$, respectively. Ambulatory status transitional period fell between 10.1 a 13.3 years of age; mean age of ambulatory patients was 8.29 +/− 0.87 years vs 13.47 +/− 0.96 yesrs of non-ambulatory ($P < 0.001$).

**Conclusion:** In our study we confirmed decreasing pulmonary function with age in DMD patients, and positive effect of steroid therapy.

## 0745 | Lung infection, in particular with cytomegalovirus (CMV) is a risk factor for impairment of lung diffusion capacity in the survivors of childhood haematologic malignancies

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**Background:** Children who were treated for leukemia are known to have developed long term impairment of lung function. The reasons that complication are only partially known. The aim of this study was to asses pulmonary function in children treated due to leukaemia in the past, and indentify risk factors and clinical manifestations for the impairment of pulmonary function test (PFT).

**Method:** 74 survivors of childhood leukaemia: 46 treated with chemotherapy (HSCT-), 28 with chemotherapy and haematopoietic stem cell transplantation (HSCT+), 42 healthy subjects (control group CG) were evaluated. Spirometry and Diffusion Limit of Carbon Monoxide (DLCO) tests were performed in all subjects.

**Results:** The mean values of FEV1, FVC, FEV1/FVC were not significantly different in survivors vs CG. 47(66%) patients had reduced DLCO, 10(14%) restrictive, 5(7%) obstructive pattern. The mean values of the DLCO were lower in survivors than in CG ($P < 0.03$), and in the HSCT+than in the HSCT- group ($P < 0.05$). The pulmonary infection increased the risk of diffusion impairment OR 5.1 CI (1.16-22.9) $P = 0.019$. DLCO was reduced in patients after CMV pneumonia ($P < 0.001$). The main symptom of impaired lung diffusion was poor tolerance of exercise ($P < 0.005$).

**Conclusion:** The lower DLCO is the most frequent abnormality in childhood leukemic survivors. HSCT and pulmonary infection (in particular CMV pneumonia) is a strong risk factor for impairment of DLCO in children. Clinical manifestation of DLCO impairment is poor exercise tolerance. A screening for respiratory abnormalities in survivors following treatment for childhood haematologic malignancies, seems to be of significant importance.

## 0746 | Phenotyping allergic respiratory diseases: An unsupervised classification using latent class analysis

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**Background:** The aims of this study were to identify distinct classes (phenotypes) of adults with allergic respiratory diseases, using an unsupervised method, and to examine their associations with inflammatory biomarkers, and allergic sensitization.

**Method:** Analysis of all adult participants (n = 728) in the Portuguese nationwide and cross-sectional study ICAR (Control and Burden of Asthma and Rhinitis-PTDC/SAU-SAP/119192/2010). The structured medical interview included data on respiratory symptoms, healthcare usage, and current medication. Measurements of blood eosinophils (B-Eos), serum IgE, fractional exhaled nitric oxide (FeNO) and skin prick test were performed (testing 6 groups of allergens: mites, dog and cat epitheliums, tree, grass and weed pollens mixtures and molds). Latent class analysis (LCA) was applied using 16 different clinical variables on upper/lower airways symptoms and activity limitations/impairment. Associations of LCA classes with biomarkers and sensitization were examined by multinomial logistic regression, adjusted for co-variables.

**Results:** A four-class model was obtained: Class 1—"Upper & lower airways symptoms with limitations" (UA&LAwL) (n = 110;15%), Class 2-"Upper airways symptoms with impairment" (UAwI) (n = 135;19%), Class 3-"Upper symptoms without impairment" (UAsI) (n = 240;33%), and Class 4-"No/minimal symptoms" (n = 241;33%). Higher values of B-Eos, IgE, FeNO, and number of sensitizations were strong and positively associated with UA&LAwL, when comparing to any other class. Distribution of the number of allergen groups in all sample and stratified by LCA classes is presented in table 1. Being sensitized to ≥3

allergen groups was significantly associated to UAwI (aOR[95% CI]:2.1[1.3-3.6]), compared to UAsI.

**Conclusion:** With an unsupervised cluster analysis, we identified four phenotypes of allergic respiratory diseases in the Portuguese general population, that are similar to clinical diagnosis. Being polysensitized to a high number of allergen groups was associated with multimorbidity (UA&LAwL) and severity (UAwI versus UAsI), warranting further investigation. Moreover, the number of allergen sensitization groups may help differentiate between upper airways disease phenotypes.

| | No sensitization | 1-2 sensitizing allergen groups | ≥3 sensitizing allergen groups |
|---|---|---|---|
| UA&LAwL, n (%) | 16 (14) | 28 (26) | 66 (60) |
| UAwI, n (%) | 46 (34) | 24 (18) | 65 (48) |
| UAsI, n (%) | 95 (40) | 74 (31) | 69 (29) |
| No/minimal symptoms, n (%) | 134 (56) | 54 (23) | 51 (21) |
| Total, n (%) | 291 (40) | 180 (25) | 251 (35) |

## 0747 | Knowledge of pharmacists about allergic rhinitis and its impact on asthma guidelines (aria guidelines): a comparative Brazilian/Paraguayan pilot survey

Urrutia-Pereira M[1]; Bittencourt R[1]; Fernandez C[2]; Cruz AA[3]; Simon L[1]; Rinelli P[1]; Solé D[4]

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**Background:** Allergic Rhinitis (AR) is one of the most common chronic diseases, and frequently not recognized by patients who do not seek medical attention. Pharmacists are generally the first to attend these patients. Allergic Rhinitis and its Impact on Asthma (ARIA) establishes evidence-based standards of best practice for the management of patients with AR and their comorbidities.

**Objective:** To evaluate and compare the level of knowledge about AR and recommendations of ARIA guidelines among pharmacists in Brazil (BR) and Paraguay (PY).

**Method:** 205 pharmacists (BR:78, PR:127) answered the self-applicable online questionnaire, (*ARIA One Airways questionnaires* * questions about personal and professional data and knowledge about AR, and ARIA guidelines) using the *Google Forms* tool.

**Results:** 80.8% of BR and 49% of PY were women, median age was 32 years, 35% BR and 52% PY reported having more than four years of training. Although they recognized the main symptoms of AR, 26% BR and 100% PY never asked whether the patient had a medical diagnosis of AR; 20.5% BR and 100.0% PY did not ask whether the symptoms occurred when close to animals or allergens; 55% BR and 76% of PY did not ask if the patient had a medical diagnosis of asthma; 59% BR and 70% PY did not ask if rhinitis worsens asthma symptoms and 51.3% BR and 84.3% PY did not ask whether symptoms of rhinitis interfere with their daily activities. Regarding treatment, 34.6% BR and 26.8% PY pharmacist still recommend first-generation antihistamines, 59% BR and 52% PY use nasal topical corticosteroids.

94.9% BR and 60.6% PY would refer the patient to a specialist but 85% BR and 100% PY are unaware of the ARIA Guidelines.

**Conclusion:** Although pharmacists are the first professionals sought by the AR patient for symptom relief their level of knowledge about AR and ARIA Guidelines is very low and do not follow best clinical recommendations. Training of these professional would allow the most appropriate advice for the patients they attend.

## 0748 | Knowledge of primary care physicians about allergic rhinitis and its impact on asthma (aria guidelines): a comparative Brazilian/Paraguayan/Uruguayan pilot survey

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**Background:** Allergic Rhinitis (AR) is a high prevalence chronic disease, which starts in childhood and persists throughout life. It limits work productivity and causes absenteeism at school. *Allergic Rhinitis and its Impact on Asthma (ARIA)** establishes evidence-based standards of best practice for the management of patients with AR and its comorbidities.

**Objective:** To evaluate and compare the level of knowledge about AR and recommendations of ARIA guide among Primary Care Physicians (PCP) in Brazil (BR), Paraguay (PY) and Uruguay (UY).

**Method:** 336 PCP (BR: 109, PY: 127, UY: 100) answered the self-applicable online questionnaire (*ARIA One Airways questionnaires)* with questions about personal and professional data and knowledge about AR, and the ARIA guideline using the *Google Forms tool*.

**Results:** There was a predominance of female (BR: 73%, PY 50.4%, UY: 70%) median age 31 years old, 124/235 worked in the community and 75/127 in the emergency departments, 34% of the BR had more than 10 years of education, 67% from PY had between 1 and 5 years, and 82% from UY had been graduated for less than 1 year. BR/UY recognize the main symptoms of AR, however 67% of those from Uy *do not ask*: if the patient has physician diagnosis of AR, 72% present shortness of breath, and 93% a medical diagnosis of asthma, 94% if rhinitis worsens asthma symptoms and 90% if symptoms of rhinitis interfere with the patient's daily activities. The prescribed treatment varied a lot, the intranasal corticosteroid use rate was: BD: 78%, PD: 92% and UD: 54%.

100% of doctors in PY, 73.4% in BR and 78% of UY never refer the patient to the specialist. 22.9% of PCD of BR, 62% of PY and 6.0% of UY are aware of ARIA guideline.

**Conclusion:** Although AR is largely attended by PCP, recognition of symptoms and their impact on asthma, as well as the knowledge about ARIA Guide is low and treatment is not always prescribed according to best practice. Allergy education programs, with an emphasis on AR and ARIA guide, need to be directed to PCP in LA for the better assistance of AR patients.

## 0749 | Assessing knowledge of allergic rhinitis among final year medical and pharmacy students in Croatia—Curriculum change necessity?

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**Background:** Allergic rhinitis (AR) is a global health problem, with a prevalence of 22.7% in the European Union, and is associated with impaired work productivity, numerous co-existing medical conditions and thus has a major socio-economic impact. For patients suffering from AR general practitioners and community pharmacists are usually the first contact and source of information. This study assessed the current knowledge of AR general characteristics and treatment approach among final year medical and pharmacy students. The primary aim was to determine if there is a necessity for additional education targeted to future medical doctors, community pharmacists, or both.

**Method:** Data were collected from September 2017 to November 2017 through an online questionnaire via snowball method. Participation was voluntary and anonymous. Final year students from all of the Croatian Schools of Medicine and Pharmacy were included (N = 201). The two factor structured questionnaire was formed by the authors regarding the topics mentioned. T-test was used for statistical analysis.

**Results:** The global results were formed as composites of (1) AR general characteristics, (2) AR treatment approach, and (3) the participants' overall knowledge. Of the 201 respondents, 143 (71.1%) were female and 58 (28.9%) were male ($P < .0001$). Medical students had a median score of 6 of 10 correct answers on (1), 4 of 10 on (2), and 10 of 20 on (3), whereas pharmacy students had median score of 7 of 10 correct answers on (1), 4 of 10 on (2), and 10 of 20 on (3). There were no significant differences in knowledge between two student groups.

**Conclusion:** The results indicate an inadequate level of knowledge of AR in both groups, especially regarding the therapy approach. Since general practitioners and community pharmacists have a major role in providing treatment to patients suffering from AR, it is important to develop advanced knowledge on this topic during medical and pharmacy degree courses. Despite a relatively small study population, it would be advisable to introduce change by improving the core curriculum regarding AR with more emphasis on treatment, but additional research on this topic is necessary.

## 0750 | Understanding the reasons behind medication self-selection by people with allergic rhinitis in community pharmacy

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**Background:** People with allergic rhinitis symptoms frequently self-select over-the-counter medications from community pharmacies without seeking advice from a health care professional. This increases the incidence of complications due to delayed diagnosis and suboptimal treatment. This study aims to (i) compare the demographics, clinical characteristics and medication selected, between pharmacy customers who choose to self-select and those who interacted with a pharmacist when purchasing medication for allergic rhinitis symptoms, and (ii) identify the key factors associated with allergic rhinitis patients' medication self-selection behaviour.

**Method:** A cross-sectional observational study was conducted in a convenience sample of community pharmacies from the Sydney metropolitan area. Data were collected using a researcher administered questionnaire that included: demographics, pattern of allergic rhinitis symptoms, their impact on quality of life, factors triggering allergic rhinitis symptoms and medication(s) selected. Logistic regression was used to identify key factors associated with participants' medication self-selection behaviour.

**Results:** Of the 296 recruited participants, 202 were identified with allergic rhinitis, of which 67.8% were female, 54.5% were aged more than 40 years old, 64.9% had a diagnosis of allergic rhinitis, and 69.3% self-selected medication(s). Significant differences were noted in allergic rhinitis symptoms, impact of allergic rhinitis on quality of life and medication(s) selected between participants who chose to self-select and those who interacted with a pharmacist. Participants who experienced moderate-severe wheeze were 4 times more likely to self-select allergic rhinitis medication(s), and those who had allergic rhinitis symptoms impacting on their quality of life were 0.4 times less likely to self-select allergic rhinitis medication(s).

**Conclusion:** There is a high incidence of self-selection of over-the-counter treatments for allergic rhinitis symptoms in community pharmacy, with the majority of allergic rhinitis sufferers failing to seek pharmacist advice. This research identified predictors of medication self-selection behaviour in community pharmacy among people with allergic rhinitis, which can inform the design of tools/strategies and targeted interventions, aimed at improving pharmacist engagement and future practice in optimising allergic rhinitis management.

## 0751 | Assessment of impact of ARIA guideline implementation vs routine care on rhinitis related quality of life in a primary care setting in Ireland

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**Background:** Allergic rhinitis is a common condition that is predominantly managed in primary care. The incidence of allergic rhinitis is increasing. It is frequently under diagnosed, misdiagnosed and mistreated. It has a significant impact on patients' health related quality of life and represents a huge cost both to healthcare systems and society. The aim of this study was to implement appropriate guidelines regarding the management of allergic rhinitis in primary care and evaluate the effect on patients' health related quality of life.

**Method:** Patients with a history of allergic rhinitis were selected from three general practice bases in West Cork, Ireland and quality of life of patients was assessed initially in year one and followed up one year later in a general practice setting using the standardised Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines and appropriate prescribing were implemented during this year and patient education and structured follow up was arranged in the intervention group. This was compared with the control group who received usual care.

**Results:** 93 valid responses were received, 34 from the control group and 59 from the intervention group. The study demonstrated a statistically significant difference in quality of life in the intervention group. In the adult intervention group the quality of life score decreased between 2015 and 2016 representing an improvement in their quality of life, ($t = 4.13$; df=56; $P < 0.01$). The difference in the score between the control and intervention groups in 2016 was also statistically significant.($t = 6.11$; df=54; $P < 0.01$). The numbers in the adolescent groups and paediatric group also demonstrated an improvement in quality of life but the sample size was too small to demonstrate a statistically significant difference.

**Conclusion:** As the majority of patients rely on their general practitioners for treatment and diagnosis of allergic rhinitis, primary care represents an important area to target in the management of allergic rhinitis to improve patients' quality of life. The implementation of guidelines has been shown to improve patients' quality of life. This study demonstrates this care can be delivered in a primary care setting with an improvement in patients quality of life but substantial investment in education and resources available to primary care physicians is needed.

## 0752 | The predictive value of allergy tests in the diagnosis of peanut allergy in adults

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**Background:** Adults presenting with either new-onset symptoms attributed to peanuts or with early-onset peanut allergy, often wish to know whether they should continue to avoid peanuts. Clinical history and standard tests may be sufficient to provide an answer, but for many the tests are inconclusive and an oral food challenge is required. This review was undertaken to determine the most accurate tests.

**Method:** This case note review evaluated the results from adult patients with reported allergic reactions to peanuts. All subjects had a clinical history taken, underwent allergy diagnostic tests and an open oral food challenge (OFC) to peanuts. The diagnostic tests included skin prick tests (SPT) and/or specific IgE tests (SIgE) and/or component-resolved diagnostic (CRD) tests to the peanut allergens Ara h 1, 2 and 8.

**Results:** Results are presented for 41 patients (24 female, mean age 27 years, range 17-53), 90% or more of whom had results for SPT, Ara h 1, Ara h 2 and Ara h 8, and 71% SIgE results. Eleven patients (27%) had their OFC classed as positive; of these, 91% had concordant positive SPT, 80% concordant positive SIgE and 55% concordant positive Ara h 2 and Ara h 8, but none were positive to Ara h 1. Of the 31 patients with negative tests, none had a positive Ara h 1, 7% a positive Ara h 2, 41% a positive SPT, 43% a positive SIgE and 45% a positive Ara h 8. The test with the best sensitivity (91%), negative Likelihood Ratio (LR) (0.15), and Negative Predictive Value (NPV) (94%) was peanut SPT. However Ara h 2 had the best specificity (93%), positive LR (7.6) and positive predictive value (PPV) (75%), with an overall top accuracy of 82%.

**Conclusion:** These data suggests that peanut SPT and Ara h 2 provide the most accurate prediction of the outcome of oral food challenge in adults. Should components not be available, then SPT would be the test of choice being more accurate in all aspects than SIgE. Combining SPT and SIgE improves the sensitivity and negative predictive value of SPT alone. However, the best combination is SPT and Ara h 2, which increases the overall accuracy to 87%. Further studies are needed before it can be determined whether peanut diagnostic tests can replace the oral food challenge in adult patients.

## 0753 | Food allergy or intolerance: Characterization of fructose intolerance (FI) in an allergy clinic

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**Background:** Patients with "IBS-like" symptoms, such as recurrent abdominal pain (RAP), bloating and altered stools are often referred for allergy investigation. Carbohydrate Fructose Intolerance (FI) is a common, yet under-recognized cause of the above symptoms, confirmed by breath test (BT). Characterization of the above chronic gastrointestinal (GI) symptoms was assessed post-BT to determine patterns of identification.

**Method:** Retrospective chart review was carried out in a community allergy clinic. Patients with RAP, bloating and altered stools who underwent BT were characterized by age, gender and atopic status. A separate study to assess patients' outcome post-dietary counselling was carried out to determine impact on symptom management.

**Results:** Thirty-four patients were assessed for FI from January 2014 to December 2017. Female gender predominated (31/34, 91%) with an average age of 31 years at presentation. Results of FI were positive in 15/34 (44%), borderline in 2/34 (6%) and negative in 17/34 (50%). The average age of patients with a positive, borderline and negative tests were 30, 20 and 34, respectively. Of the patients who tested positive for FI, 5 (33.3%) had comorbid inhalant allergies alone, 1 (6.7%) had comorbid (unrelated) food allergies alone, 2 (13.3%) had inhalant and food (unrelated) allergies, and 7 (46.7%) were non-atopic. Of the patients who tested negative for FI, 7 (41.1%) had comorbid inhalant allergies alone, 0 (0%) had comorbid (unrelated) food allergies alone, 1 (5.9%) had inhalant and food (unrelated) allergies, and 9 (53.0%) were non-atopic.

**Conclusion:** Patients investigated for carbohydrate intolerance with RAP, bloating and altered stools were predominantly female (91%). FI was confirmed in half. Atopic status did not help differentiate between the FI positive or negative groups. Results of a FODMAP elimination diet are separately reported.

## 0754 | Benefits of a low fructose/FODMAP diet in suspected fructose intolerance: Follow up and natural history

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**Background:** Fructose intolerance (FI) is characterized by recurrent abdominal pain, bloating and altered stools, diagnosed by way of breath test (BT), and managed with dietary fructose/FODMAP restriction. FODMAPs are a group of carbohydrates found in both natural and processed foods. Dietary changes were characterized post-BT to determine impact on symptom management.

**Method:** Retrospective chart review was carried out in a community allergy clinic. Patients who underwent a BT for suspected FI were contacted by phone and email to complete an online survey on their response to dietary intervention (provided through counselling) and symptom management.

**Results:** The chart review identified 34 patients who underwent BT for suspected FI from January 2014 to December 2017. Seventeen of 34 patients were confirmed to have FI. Seventeen of 34 patients completed the online survey. The remainder of the data will report strictly on the 17 patients who completed the online survey. Twelve of 17 (71%) patients had confirmed FI and 5/17 (29%) had a negative BT for FI. Fifteen of 17 (88%) reported an improvement in GI symptoms. Of the 12 patients with confirmed FI, 11 reported symptom improvement. Six of 17 patients reported strict fructose avoidance, 6/17 reported partial fructose avoidance, and 5/17 chose not to avoid fructose. Eleven of 12 (92%) patients who strictly or partially avoided fructose reported GI symptom improvement. Two of 17 patients implemented a low FODMAP diet, 5/17 partially implemented a low FODMAP diet, and 10/17 chose not to implement a low FODMAP diet. Of the patients who implemented a low FODMAP diet, 1 had a positive BT and 1 had a negative BT. Both patients reported symptom improvement. Of the 5 patients who partially implemented a low FODMAP diet, 5 had a positive BT and 5 reported symptom improvement. Of the 5 patients with a negative BT, 4 (80%) had improvement in symptoms independent of dietary restrictions. One of the 5 implemented a low FODMAP diet and reported symptom improvement.

**Conclusion:** Post-BT, 88% of patients reported symptom improvement. Patients who implemented fructose or FODMAP avoidance reported symptom improvement. One patient who tested negative for FI reported symptom improvement with a low FODMAP diet. Patients suspected as being fructose intolerant may benefit from a fructose restriction or FODMAP diet, while awaiting BT confirmation. This form of dietary intervention may assist and shorten the natural history of non-specific chronic GI symptoms.

## 0755 | The Great Allergy Delusion: Inappropriate referrals to a UK paediatric tertiary allergy clinic demonstrate lack of allergy education and knowledge in primary care

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**Background:** Up to 8% of children have a food allergy. Allergy has become an explanation for all manner of nebulous symptoms and self-diagnosis is common. Sham allergy tests are easily available giving incorrect results and resulting in unnecessary, potentially harmful

parentally-imposed dietary exclusions. There are 100 million allergy-related Google searches per year. The rising prevalence of perceived allergic disease has led to an increase in health service utilisation, including increased referrals to secondary care. Clinic waiting lists are long and children with severe food allergies have to wait longer than necessary to be seen

**Method:** UK paediatric tertiary allergy clinic referrals were prospectively reviewed over three months. Five inappropriate referrals deemed most reflective of poor knowledge in Primary Care were selected as case summaries to highlight this gap in knowledge.

**Results:** 1: Schoolchild referred for investigation of allergic cause for a red, watery eye after splashing juice in her eye whilst cutting a kiwi, despite having a co-existent dendritic ulcer.

2: Schoolchild referred for peanut allergy testing after inhaling a peanut and developing wheeze, with all respiratory symptoms resolving following peanut removal.

3: Young child referred for peanut allergy testing after developing a rash on leg following skin contact with faeces 24 hours after ingestion of peanut butter.

4: Teenage boy referred for investigation of likely peanut allergy despite eating peanut butter and tree nuts almost every day. The family were concerned he was allergic to peanut butter.

5: Toddler referred for milk allergy investigation after developing urticaria lasting 24 hours 15 minutes after drinking a bottle of milk. The child had consumed cow's milk formula since birth, and continued to consume milk daily for a further five months following the episode of urticaria.

**Conclusion:** Provision of allergy services in the UK is poor and lack of investment in allergy services has led to suboptimal recognition and management of food allergy in primary care. Allergy education provision for primary care practitioners is inadequate and fails to empower healthcare professionals to discern between allergy requiring full investigation and management, parentally-diagnosed allergy or symptoms which clearly have no association with allergy. Progress to improve primary care training for allergy needs to be optimised to prevent further unnecessary referrals and lengthening clinic waiting lists.

## 0756 | Content and development of the Allergy App

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**Background:** In case of allergic reactions to food or insect venom, quick and adequate treatment, based on clear instruction for use of emergency medication and calling for help, is necessary. However, daily practice shows that patients do not use the prescribed emergency medication because they are afraid to use the epinephrine auto- injector or they do not know how to use it. Information and instruction offered by a reliable app could be a useful aid. We aim to develop an app for adult patients and children older than 12 years with allergy to food or insect venom, which offers a step-wise approach to support patients, their relatives or acquaintances in case of an allergic reaction.

**Method:** First, the content of the app, including a step-wise approach to treat the allergic reaction has been determined, based on literature, a survey about needs of patients and on consultations of healthcare professionals. Subsequently, a web-based prototype has been developed with an adult profile and children profile. The content and flow of this prototype was tested by the project group, as well as by selected healthcare professionals and patients and improved according to the test results. Next, the revised prototype was submitted to representatives of patient and professional organizations for final approval. Currently the procedure for CE approval is ongoing. Finally, the app will be built and offered to the market for iOS and Android.

**Results:** A web-based prototype of the Allergy App is available with two profiles: adult and older children. The app is useful for patients with a doctor's diagnosed allergy to food or insect venom, who received emergency medication and instructions to use prescribed medication in case of an allergic reaction. Based on severity of complaints, the user is informed about the steps to treat the allergic reaction. In case of a moderate to severe reaction, the patient is advised to use an epinephrine auto-injector, to call the emergency number and, if prescribed, to use medication such as antihistamines, prednisone or inhaler. Besides that, the app provides links to websites of expertise centres and patient organisations and includes instructions how to use the epinephrine auto-injector.

**Conclusion:** The Allergy App will help patients, their relatives or acquaintances to adequately treat an allergic reaction to food or insect venom. Involving patients and professionals in the development of the app will contribute to its acceptability and usability.

## 0757 | Electronic documentation of drug allergies in a tertiary hospital in Singapore: are we relying too much on it?

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**Background:** Singapore has 26 hospitals shared between public and private healthcare system. Its healthcare system, ranked #6 in the world by WHO in 2010 serves a multi-racial population of 5.2 million of which 9% are above 65 years old. Drug allergy alert cards (Medik Awas) were started in 1970s by Singapore Medical Association to improve patient safety. Work on computerisation of drug

allergy and medical alerts started in the 80s, a precursor to today's Critical Medical Information System (CMIS). CMIS serves as a platform across all public hospitals in Singapore. It promotes uniform reporting of drug allergy and notification of adverse drug events to the Health Science Authority.

Yet, we found that there is a lack of awareness of one's own drug allergies.

**Method:** All patients admitted to ward 73 (general medicine ward) at Singapore General Hospital from 17 July to 31 Oct 2017 were screen for any previously documented drug allergies. Consenting patients who had previously documented drug allergies on CMIS were interviewed to document their demographics, education level, current medications, knowledge of their own drug allergies and possession of a drug medication alert card. The answers were then compared with their electronic documentation of drug allergies for accuracy.

**Results:** We interviewed 192 patients aged 20–94 with documented drug allergies during the recruitment period. 74% had secondary school education or higher. The majority (76%) spoke English and (58.5%) Mandarin. Almost half had medical problems and are on long term medications (mean 5.17 medications); hypertension and diabetes being the top two common diseases. 48% of the patients could accurately relay their drug allergies; antibiotics and analgesia being the most labelled. Only 24% had a drug allergy alert card while the rest both rely on the hospital's electronic documentation and/or their caregivers to record and relay their allergies to future prescribers. About 21% received prescription from multiple healthcare sites in both the public and private healthcare system.

**Conclusion:** We found patients' knowledge of their own drug allergies dismal. The CMIS electronic documentation provided a false sense of security. Unfortunately, the CMIS platform is not available to all private hospitals, increasing the risk of mis-prescription due to the lack of information. Unless this is made available nationally, patients with drug allergies should be given some written documentation, either a letter or Medik Awas.

## 0758 | Allergies in rural regions in Bavaria: How frequent are they and how are they treated?

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**Background:** Allergies are common and can have a significant impact on the daily lives of affected persons. Especially in rural areas where allergists are scarce, allergies might not always be treated appropriately. The aim of this study was to determine the prevalence of allergies in a rural Bavarian region and to find out how the allergies are treated.

**Method:** For this cross-sectional study, participants were recruited in the waiting rooms of local doctors in the rural Bavarian Forest region of Southern Germany (Q1/2017). A paper questionnaire was handed out to the participants, asking for allergies (pollen, animal hair, bee and wasp venom, drugs, food, house dust mites, contact allergies and other allergies) and how or rather by whom (e.g. general practitioner, specialist, self-treatment) these allergies are treated.

**Results:** 718 participants with a mean age of 50.61 years (SD=15.15) and 59% women were included in this study. 38.2% indicated to have at least one allergy, including pollen allergy most frequently (17.4%). Women had significantly more often at least one allergy than men (RR= 1.552; CI [1.243;1.937]) and for almost all examined allergies a significant higher risk of disease. Younger age groups indicated more often to have at least one allergy (18-29y.= 46.3%; 30-44y.= 43.6%; 45-64y.= 39.3%; ≥65 = 22.3%). Regarding occupational groups, indoor workers (RR=1.224; CI [.972;1.542]), farmers (RR=1.409; CI [.814;2.440]) and unemployed persons (RR=1.392; CI [.833;2.327]) seemed to be affected particularly, while outdoor workers (RR=.764; CI [.506;1.151]) seemed to be affected less. Participants indicated most frequently that their allergy was treated by a general practitioner (37.5%), except of the 18-29-year-old young adults who indicated "no treatment" most frequently (28.2%).

**Conclusion:** There is a high self-reported prevalence of allergies in the examined rural Bavarian region, that increases with decreasing age and is significantly higher among women. Moreover, the data on the absence of an appropriated treatment for allergies is alarming. Therefore, medical care needs to be improved in rural regions to lower the burden of allergies.

## 0759 | The prevalence of the burnout syndrome among medical professionals involved in allergology education programmes

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**Background:** Increasing demands in health care put a significant pressure on medical professionals. Work overload and stress frequently lead to burnout syndrome, which can be categorised as an emotional exhaustion(EE), depersonalization (DP) and reduced sense of personal accomplishment (RPA). This research aimed to explore the burnout syndrome among a spectrum of medical specialists involved in allergology education programmes.

**Method:** The research conducted in 2016–2017 included 259 respondents: 86% students, 4.6% junior specialists; 4.6% clinical allergologists, 3.9% lecturers / clinical academics. Burnout was assessed with Maslach Burnout Inventory - total scores for EE (Low ≤15, Moderate 16-24, High ≥25), DP (Low ≤5, Moderate 6-9, High

≥10) and RPA (Low ≥0-11, Moderate 12-18, High 19-48) subscales were calculated and analyzed.

**Results:** On average students demonstrated: moderate/high EE scores (24-26); moderate/high DP scores (9-12) and moderate RPA scores (17); higher RPA scores were common (41.4%) among junior students, which is also linked with their levels of engagement, and lower (28%) among senior students.

Junior specialist (starting specialization) had very low scores in all 3 subscales and expressed a very high motivation in their course and new profession.

Clinical allergologists with significant experience demonstrated moderate / high EE scores (22-26); low DP (1-5) and RPA (below 10) scores. High EE scores associated with pressures of service were compensated by a substantial loyalty to their profession and positive assessment of the outcomes of their work.

Clinical academics demonstrated the highest level of EE scores (29 + among 70 + % of the group) with low to moderate DP and RPA scores, the latter being associated with a loyalty to their profession. It was also possible to identify a correlation between engagement in research activities and lower RPA scores.

**Conclusion:** Burnout is a complex and multifaceted phenomena, which requires further investigation. However, this research identified that students and junior specialists involved in allergology and clinical immunology programmes with higher levels of engagement and motivation to acquire new specialist knowledge had lower levels of EE, while loyalty to the profession and positive assessment of the outcomes of clinical and research work allows to compensate high levels of EE among experienced practitioners and clinical academics and to reduce burnout effects overall.

## 0760 | APPEAL (Allergy to Peanuts ImPacting Emotions And Life): the first pan-European study to evaluate the psychosocial burden of living with peanut allergy

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**Background:** Peanut allergy, one of the most common and rapidly growing food allergies, is most frequently a lifelong condition. Current management is limited to avoidance and symptomatic treatment of allergic reactions when accidental exposures occur. Peanut allergy can affect the quality of life (QoL) of individuals and also that of parents/caregivers and family members. APPEAL was designed to assess the impact of peanut allergy on QoL in peanut-allergic individuals and their parents/caregivers and families.

**Method:** The first, quantitative part of APPEAL is described here and consisted of a pan-European, cross-sectional online survey of approximately 30 minutes in length. The study was conducted in the UK, Republic of Ireland, France, Spain, Germany, Italy, the Netherlands and Denmark. Over 1800 participants were recruited via patient advocacy groups or directly through a specialist survey recruitment panel. Ethics committee approval was obtained and all participants provided their informed consent. Eligible participants were: (1) parents or caregivers of a child/adult with peanut allergy; (2) parents or caregivers responding as a proxy for a child aged under 18; (3) adults. All allergic subjects had self-reported diagnosed peanut allergy.

After several screening questions, eligible participants answered a set of clinical questions about their (or their child's) allergies and other conditions, details on the peanut allergy diagnosis, contact with healthcare professionals, worst allergic reaction to date and use of emergency medicine.

Depending on whether they were an allergic adult, a parent responding on behalf of the child, or a parent/caregiver recounting their own experience, they then answered specific questions on restrictions on life choices, coping strategies and the impact of peanut allergy on feelings and emotions of families, friends and other people. Sociodemographic questions completed the questionnaire.

**Results:** The results of the survey are being summarized using descriptive statistics and the data are being analysed on a pan-European level, by country, and according to the participant's perspective (parent, caregiver or individual).

**Conclusion:** This comprehensive, pan-European online survey has been specifically designed to uncover the psychosocial burden and effect on QoL of peanut allergy in terms of individuals' lives and those of their families.

SUNDAY, 27 MAY 2018
TPS 09
PEDIATRIC FOOD ALLERGY

## 0761 | Sensitizing characteristics of cow's milk and major components in young children with allergic diseases in Guangdong Province

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**Background:** Cow's milk is the main food of young children. It is also the main sensitized food. The purpose of this study is to explore the sensitizing characteristics of cow's milk and major components in young children with allergic diseases in Guangdong Province.

**Method:** This is a retrospective study. 301 children age below 12 years old were collected from the First Affiliated Hospital of Guangzhou Medical University from December 2014 to September 2016, who have detected cow's milk sIgE and finished the questionnaire. We screened 103 cow's milk sIgE positive cases from Guangdong Province to detect the components sIgE of cow's milk, including Alpha lactalbumin (ALA), beta lactalbumin (BLG) and casein (CAS).

**Results:** The average age of 103 cases is 2.0 (1.4.3.0) years. 68.93% (71/103) children have allergic airway diseases,64.08% children have a family history of allergies.Two or more kinds of cow's milk components sIgE positive children accounted for 84.47%. The average level of CM-sIgE is 3.40(1.46, 5.75) kUA/L. The average levels of cow's milk components sIgE are:ALA-sIgE 1.91(0.66, 5.24) kUA/L, BLG-sIgE1.81(0.77, 4.19)kUA/L, CAS-sIgE0.62(0.27, 1.32)kUA/L. The level of CM-sIgE is higher than ALA-sIgE, BLG-sIgE and CAS-sIgE($z = -2.439$, $P = 0.015$;$z = -3.228$, $P = 0.001$;$z = -8.726$, $P < 0.001$; respectively). The level of BLG-sIgE have the highest correlation with CM-sIgE ($r = 0.834$, $P < 0.001$), follow by ALA-sIgE ($r = 0.817$, $P < 0.001$), the lowest is the CAS-sIgE ($r = 0.550$, $P < 0.001$).

**Conclusion:** ALA and BLG are the major sensitized components of cow's milk sensitized children with allergic diseases in Guangdong Province. Most of the children were sensitized to two or more kinds of cow's milk components. The levels of ALA-sIgE and BLG-sIgE are highly correlated with CM-sIgE.

## 0763 | The evaluation of children with cow's milk allergy: Single center experience

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**Background:** Cow's milk protein allergy (CMPA) is the most common food allergy in early childhood. CMPA impacts up to 2-3% of infants. We aimed to evaluate the outcome of our clinical experience on children with CMPA.

**Method:** We examined patients who were diagnosed with cow's milk (CM) allergy in Health Sciences Univercity Dr Sami Ulus Maternity and Children Training and Research Hospital, Department of Pediatric Allergy-Immunology, between January 2014 and February 2016. The demographic and laboratory characteristics of the patients were evaluated retrospectively from hospital medical records.

**Results:** 246 pediatric patients were included in the study. 65.9% (n = 162) were male. The median age of onset of symptoms (interquartile range) was 4 months (2-6).The median age (interquartile range) of diagnosis was 6 months (4-7). Initial reactions associated with CMPA were observed in 95.8% of patients before 12 months old. Patients' diagnoses were atopic dermatitis (39%), urticaria-angioedema (24%), anaphylaxis (12.2%), proctocolitis (10.2%), atopic dermatitis and urticaria (8.9%), food protein induced enterocolitis (4.9%) and eosinophilic esophagitis (0.4%). The patients' skin prick tests results made by CM standardized allergen and CM itself were different from each other. 29.7% of the skin prick tests made with the CM itself were negative, while 53.5% of the skin prick tests made with the CM antigen were negative. There were multiple food allergies in 142 patients (57.7%), the most common non-dairy food allergy was hen's egg. There were no significant difference in the CM tolerance status between patients with single food and multiple food allergies (p: 0.437).15.9% of the patients had accompanying asthma. There was no difference in CM tolerance between patients with asthma and those without asthma (p: 0.299). 46.7% of the patients had a family history of allergic disease. Those patients with family history of allergic disease had lower CM tolerance rates than those without family history (p: 0.008).

**Conclusion:** As a significant part of CMPA occurs at an early age, questioning the infant's nutrition story in the routine examination leads to early diagnosis. The results of skin prick tests performed for the diagnosis; the CM itself showed a higher positivity than the CM standardized antigen. The family history of atopy has negatively affected the prognosis in CMPA.

## 0764 | Evaluation of prognosis in patients with cow's milk allergy

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**Background:** Cow's milk allergy is the most common food allergy in children. The purpose of this study is to investigate the tolerance building processes and the factors influencing tolerance building based on socio-demographic and clinical features, lab and diagnostic test findings (skin-prick test, specific IgE level) pertaining to patients diagnosed with cow milk allergy.

**Method:** The study involved 147 patients, who are two years old (and above), diagnosed with cow milk allergy and are observed for at least six months in our hospital. Socio-demographic features of the patients, their symptoms, symptom-start ages, age of diagnosis, clinical findings at diagnosis and during observation were recorded in data collection questionnaires.

**Results:** The samples were 91 (61.9%) boys. The average symptom-start age was observed to be 5 months (1- 36), average diagnosis age 6 months (1- 54) and average age of final check 36 months (13-193). When symptoms at entry were observed, 85.7% of the patients had dermal system, 25.2% gastrointestinal system, respiratory system disorders, and 15% were detected to have developed anaphylaxis. Among the patients diagnosed with cow milk allergy, 31.3% showed food reaction to nutrients with IgE agents, 51.7% to mixed types, and 17% to nutrients with non-IgE agents. It was also observed that, in the end of 30.4 ± 19.8-month observations, sensitivity to cow milk was observed to continue in 34 (23.1%) of our patients. When tolerance improvement rates among the patients were compared, anaphylaxis ($P < 0.001$) during entry were observed to be influential in continued allergic state. 5 (3.4%) patients were able to consume yoghurt, 10 (6.8%) patients could consume dairy products and 19 (12.9%) patients could not consume dairy products.

**Conclusion:** In the end of our investigation, it was observed that 57 (50.5%) of the 113 patients developed cow milk tolerance before the age of 2. When the factors enabling the continuation of sensitivity in cow milk allergy were investigated, anaphylaxis during entry, entry specific IgE and pasteurized milk antigen as well as high skin-prick test results were detected to be significant.

## 0765 | Initial lower threshold was a risk factor of severe adverse reaction during oral immunotherapy for cow's milk anaphylaxis

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**Background:** Previous studies indicated that oral immunotherapy (OIT) accidentally induced severe adverse reactions during the therapy. The purpose of this study is to clarify risk factors of severe adverse reaction during OIT in cow's milk (CM)-anaphylactic children.

**Method:** One hundred thirteen CM anaphylactic patients, who had undergone OIT between August 2009 and March 2013 at Sagamihara National Hospital, were included in this study. In our OIT protocol, a combination of initial rush OIT followed by slowly building up to full dose (200 mL/day CM) at home. The patients, who had taken maintenance doses without any symptoms at least for 3 months, underwent oral food challenge after 2 weeks' CM complete avoidance to confirm sustained unresponsiveness. We analyzed the risk factors of patients who had severe adverse reactions during 3-year follow up of OIT.

**Results:** Before OIT, median age was 5.7 years old, median threshold to induce initial reaction was 2.1 mL, to induce anaphylaxis was 14.6 mL of CM and median milk specific IgE was 56.4 kU/L. Twenty-seven subjects (24%) dropped out from the protocol, 69 subjects (61%) could achieve 200 mL of CM during rush OIT, and 30 subjects (27%) were confirmed as sustained unresponsiveness by the oral food challenge within 3 years. The rate of patients experienced severe adverse reactions was 27% (30/113) at home and rate of intramuscular adrenaline usage was 18% (20/113) at home. Of 69 patients who achieved 200 mL of CM, 25% experienced severe adverse reaction. The cumulative rate of severe adverse reaction was 37% (11/30) within 1 year and 67% (20/30) within 2 years after starting OIT, respectively. In the patients who had severe adverse reactions, threshold to induce initial reaction were significantly lower than those of other patients. Other factors were not significant

**Conclusion:** In CM- OIT targeting full dose for CM-anaphylaxis, lower threshold of immediate allergic reaction prior to the therapy was a risk factor to induce severe adverse reaction during OIT.

## 0766 | Investigation of heat and matrix effect on milk proteins' allergenicity and the development of hypoallergenic food products

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**Background:** Cow's milk allergy is one of the most common food allergies during childhood. It has been shown that high heat can

reduce some milk proteins' allergenicity (ß-lactoglobulin). In this project we aimed to investigate the effect of heat and matrix on different milk protein fractions through Maillard reaction and eventually develop hypoallergenic food products that have milk protein with low reaction risk.

**Method:** Milk cake matrix is prepared in different flour/sugar (F/S) ratio (2F/1S, 1F/1S, 0.5F/1S) and baked 30 minutes at 180°C. Proteins that cake contains are separated using SDS PAGE and stained with coomassie blue to check total protein. In parallel specific proteins are detected by western blotting using pooled sera from patients with milk specific IgE>60kU/L for incubation

**Results:** In normal milk cake recipe (2F/1S) ß-lactoglobulin bands are disappeared but casein bands did not differ in size. In order to investigate the matrix effect F/S ratio is changed and it is found that when this ratio decreases, with the affect of heat and maillard reaction, milk casein bands' intensities also decrease in SDS gel coomassie staining. In western blot experiments it is also shown that milk specific IgE bound weakly to casein bands in low F/S ratio cake (0.5F/1S) whereas in cakes that have high F/S (2F/1S) ratio it bound significantly higher.

**Conclusion:** Heat and matrix effect cause disruptions in milk casein and ß-lactoglobulin proteins' structure and lower the milk specific IgE bindings to milk proteins in low F/S ratio cake through Maillard reaction.

## 0767 | Extensively hydrolyzed formulas for the management of cow's milk protein allergy in infants: is extensive hydrolysis sufficient to guarantee success?

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**Background:** There are currently no aligned definitions to characterise extensively hydrolysed formulas (eHFs) despite the fact that most eHFs are intended for the same purpose: to be well tolerated by most infants with cow's milk protein allergy (CMPA). Recent publications have drawn attention to the chemical heterogeneity of eHFs and surprisingly only a few eHFs have been proven in clinical trials to be efficient in terms of allergy and growth.

**Method:** To better understand the range of eHFs, we aimed to analyse samples of commercially available eHFs from 11 countries and various manufacturers, with a focus on suitability for CMPA management.

Samples were de-identified and coded for the analyses. Molecular weight (MW) distribution of hydrolysates and residual proteins and peptide profiling were assessed with SDS-PAGE gel and size exclusion-high-performance liquid chromatography (SE-HPLC), as they reflect both the design of the formula and the quality management applied during production. Osmolarity, nitrogen fractions, lactose content, total and free amino acids, β-lactoglobulin, and casein content were quantified and β-lactoglobulin residual allergenicity was assessed.

**Results:** Peptide MW distribution displayed significant variation, with the percentage of peptides with MW >1.2 kDa varying from 1% to 36%. MW distribution was shown to be positively correlated with β-lactoglobulin specific *in vitro* degranulation.

Twenty % of samples had non-measurable β-lactoglobulin content (smaller than or at the limit of quantification (LoQ): 0.010 mg/kg); however, 80% of samples had β-lactoglobulin content greater than the LoQ, with high variability from 0.020 to 36 mg/kg. Surprisingly, even in samples featuring a high degree of hydrolysis, significant levels of residual β-lactoglobulin were quantified.

**Conclusion:** Lack of consensus over the definition of 'extensively hydrolysed' is reflected in the wide range of degree of hydrolysis in commercially available eHFs, and can result in products that are mislabelled as 'extensively hydrolysed' and may be high-risk or even unsuitable for the management of CMPA. Results of these analyses also highlight that degree of hydrolysis alone is not sensitive enough to characterise eHFs, and that whilst a high degree of hydrolysis is desirable, further quality control measures are essential to ensure clinically safe and suitable products. Actionable guidelines to better define hypoallergenic formulas based on extensively hydrolysed milk proteins are warranted.

## 0768 | Effect of baked milk on accelerating cow's milk tolerance: a clinical trial

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**Background:** Assessing the effect of baked milk products on accelerating unheated milk tolerance in patients with cow's milk allergy.

**Method:** A randomized clinical trial was done on 84 patients (6 months-3 years old) divided randomly to case and control groups matched for age and sex. Baked milk in form of muffin for 6 months followed by baked cheese in form of pizza for next 6 months was given to the patients in case group. Skin prick test and serum IgE (sIgE) levels (ImmunoCAP) of milk, casein and beta-lactoglobulin were measured before and after the study. The ones having milk sIgE less than 3 kU/L and being asymptomatic during the study underwent oral food challenge test for evaluating unheated milk tolerance.

**Results:** It was shown that 88.1% (37/42) of the patients in case group and 66.7% (28/42) in control group developed milk tolerance at the end of the study (*P*-value: 0.018). The positive results of skin prick test by milk extract and ImmunoCAP levels showed significant decrease in case group at the end of the study. Assessing the effects

of initial ImmunoCAP results on developing unheated milk tolerance demonstrated no significant association.

**Conclusion:** Introducing baked milk products in diet of patients with milk allergy can accelerate unheated milk tolerance in these patients. SIgE levels of milk, casein and beta-lactoglobulin were not predictable factors in cows milk tolerance.

## 0769 | International survey identifies educational needs around the management of infants with cow's milk allergy and lactose intolerance

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**Background:** Problems in recognising cow's milk allergy (CMA) and lactose intolerance (LI) in infancy may lead to a delayed or incorrect diagnosis, as well as inappropriate dietary interventions.

**Method:** Between January and November 2017, a survey was conducted online in China, India, Singapore, Thailand, Mexico, Kuwait, United Kingdom, Australia, and paper-based in the Philippines. The survey consisted of 12 multiple-choice questions on CMA and LI in infants aged under 12 months, two case scenarios (non-IgE CMA and anaphylaxis) and 10 questions on educational needs (Likert scale 1-5). Data on the type of medical practitioner and clinical setting were collected. Responses were summarised as percentages and categorised by country.

**Results:** 1663 responses were received from general practitioners (22.2%), paediatricians (39.7%), paediatric allergists (6.9%), paediatric gastroenterologists (11.2%) and other specialities (20.0%). There were significant misconceptions about the clinical importance of primary LI in infancy. While primary LI rarely manifests before 3 years of age, 73.7% of participants felt it was a significant clinical problem in the first year of life. Regarding secondary LI, 44% of respondents recommended lactose restriction for viral gastroenteritis, and 36% for cow's milk protein-induced enteropathy. While the management of IgE CMA was relatively well understood, there were greater knowledge gaps for non-IgE CMA. 59% of practitioners appropriately identified extensively hydrolysed formula (EHF) as first-line treatment of CMA in formula-fed infants. However, the distinction between lactose-free and lactose-containing EHF appeared to be an area of uncertainty. In India, 34.4% used soy-based formulas as first-line treatment for IgE CMA. Contrary to guidelines, use of partially hydrolysed formula in the management of infants with IgE CMA was reported by 10.6% of respondents. Only 23.6% correctly prescribed amino acid-based formula for the case scenario on CMA anaphylaxis. 62% of participants felt proficient in the management of CMA, and 61% were confident to be able to distinguish CMA from LI. Regarding educational needs, 82% of participants expressed an interest in further education on CMA management in infancy.

**Conclusion:** The management of CMA and LI in infants still poses clinical dilemmas. Targeted educational campaigns are required to provide further training on these conditions in order to promote evidence-based clinical practice.

## 0770 | Patch testing during unexplained long lasting symptoms in a general paediatric setting

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**Background:** The aetiology of persisting digestive or respiratory symptoms, poor growing pattern or eczema is often difficult to identify in an outpatient general paediatric setting.

Symptoms were digestive in 51 children (38 gastroesophageal reflux, 11 constipation, 1 chronic diarrhea, 1 abdominal pain), poor growth in 18, asthma in 16, laryngitis in 2, eczema in 13. Nine children were suspected of previous cow's milk allergy.

**Method:** 78 children, aged 2.8 ± 2.24 years (4 months-11 years) were prospectively assessed between September and December 2017 using patch testing (Finn Chambers® equipped with native foods except for egg white, cod and nuts (Stallergènes extracts®)).Specific IgE measurements (RAST®) had been previously performed in 50 and were negative in 25 (ALATOP n = 2, Trophatop and Phadiatop n = 21, Trophatop n = 2). Trophatop positivity levels were usually low, with IgE<1 KU in 22 patients and exhibited high levels in only 3 patients (eggs: 5 KU, arah2 > 10 KU, Fx2: 1.65 KU).

**Results:** Patch tests were positive in 62 (79.5%) and negative in others. Positivity to milk was seen in 29 patients (37.2%), to soy in 41 (52.6%), to egg white in 7/72 (9.7%), to wheat in 12/66 (18%), to potatoes 6/48 (12.5%), to corn (maize) in 3/38 (7.9%), to rice in 1/2, and to peanut in 3/37 (8.1%).

Patients were requested to withdraw the suspected food(s) from their diets during a 4 months period. Preliminary follow-up data show the improvement of one or more symptom in 19/20 patients (gastroesophageal reflux in 10, appetite in 5, stool consistency in 1, respiratory symptoms in 10, pain in 3, eczema in 1).

**Conclusion:** Patch tests are informative, easy to use tools in order to identify potential causes of common lasting symptoms in children with negative or weak RAST results and introduce beneficial changes in the daily diet. Longer follow-up is necessary in order to refine and assess the benefit of such strategy.

## 0771 | Agreement of specific ige values by the immunocap and the immulite 3 g allergy systems

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**Background:** The ImmunoCAP® specific IgE (ImmunoCAP) and the IMMULITE® 2000 3gAllergy™ (3gAllergy) are the major quantitative specific IgE (sIgE) systems often utilized at clinical practice. Since the two systems give different predictive values, the results may not correspond well. However, we recently reported good agreement in the diagnosis of egg allergy.

**Method:** Residual serum samples that specific IgE to milk, casein, wheat, ω5-gliadin, peanut, sesame, shrimp, crab, Dermatophagoides pteronyssinus (Der p), dog, cat and Japanese cedar pollen (JCP) had been measured by ImmunoCAP were collected. Specific IgE to corresponding allergens with 3gAllergy was then measured. Agreement of logarithmically transformed specific IgE values by the 2 methods were tested with linear regression. The samples that gave discrepant results were examined for clinical symptoms and OFC results.

**Results:** Goodness of fit in linear regression yielded $R^2 > 0.9$ in milk, casein, peanut, wheat, ω5-gliadin, Der p and JCP tests. High $R^2 > 0.95$ was found in casein, Der p and JCP. R square for crab, shrimp, cat, dog and sesame was relatively low around 0.8. Discrepant results were found mainly in low value range of sIgE, not in high value range, with no association of allergen-induced symptoms.

**Conclusion:** Good agreement of ImmunoCAP and 3gAllergy specific IgE values to common allergen was found. Discrepant results may arise from allergen source and warrant further clinical validation.

## 0772 | Common dietetic questions in the food allergy clinic: what do families need to know?

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**Background:** Currently in the US, 1 in 13 children suffer from food allergies. At present, there is no cure and strict avoidance of the relevant foods is the only way to prevent allergic reactions. Elimination diets put infants and children at risk for nutritional deficiencies and impaired growth. We examined the role of the registered dietitian (RD) in advising patients and families of food allergic children.

**Method:** A retrospective review of clinical notes was performed for the first 13 consecutive children who required a dietetic consultation in a dedicated food allergy clinic. We examined common questions from parents that were addressed by the dietician during the consultation.

**Results:** Patients were aged 10 months - 9 years (median: 16 months) and were diagnosed with the following food allergies: Cow's milk: 69.2%, Egg: 62%, Tree Nut: 54%, Peanut: 39%, Wheat: 31%, Soy: 31%, Fruit/Vegetable: 15%, Legume: 8%, Fish: 8%, Sesame: 8%.

The most common questions for the dietitian included: ways to meet nutritional needs following a prescribed allergen-restricted diet (31%), meeting vitamin D and calcium requirements on a milk protein-free diet (23%), suitable oral supplements and recommended serving sizes (14%), appropriate order of solid foods introduction in food protein-induced enterocolitis syndrome (FPIES) (14%), cautionary food ingredient statements (7%), baked milk protein introduction (7%), cross-reactivity risk of milk protein with soy (7%) and cross-reactivity of nuts in retail bakeries (7%).

**Conclusion:** Parents of children with food allergies have multiple questions with regards to nutrition. Dietetic input in the food allergy clinic addresses important issues for children and families including successful avoidance of allergen-containing foods while ensuring optimal nutrition, decreased exposure to high-risk situations and avoidance of allergen cross-contamination.

## 0773 | Multicenter prospective study of a stepwise single dose oral food challenge of egg

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**Background:** Oral food challenges (OFCs) are necessary for allergy management. We previously reported that a low-dose OFC can avoid complete elimination, even if patients react to higher doses of causative foods. Nevertheless, this approach has only been validated in a retrospective single-center trial. We have previously reported that the median time for initial symptom onset is 50 minutes for egg OFC using a single exposure. Therefore, this study aimed to confirm the safety and effectiveness of a stepwise single-dose OFC in a multicenter, prospective study.

**Method:** A stepwise OFC for egg using a low- and medium-dose OFC was administered to diagnose food allergy or confirm tolerance acquisition safely at 4 hospitals and 3 pediatric clinics between 2016 May and 2017 September. Of 250 egg-allergic patients who experienced a prior immediate reaction to exposure enrolled. We initially performed low-dose OFC for egg (protein dose: 250 mg). Patients who tolerated the low-dose OFC received the medium-dose OFC for egg (protein dose: 769 mg) within 12 months later.

**Results:** The median age of patients was 1.6 years. Of 250 egg-allergic patients, 25 (10%) experienced egg-induced anaphylaxis. The median serum specific immunoglobulin E (sIgE) to egg white and ovomucoid were 14 and 8 kUA/L, respectively. Of these, 200 (80%) passed the low-dose OFC. Among 114 patients who underwent a medium-dose OFC, 106 (93%) passed the OFC. Among 50 patients

who showed a positive reaction to low-dose OFC, only 1 patient (2%) showed a severe reaction: barking cough immediately improved with adrenaline inhalation. Among 8 patients with a positive reaction to medium-dose OFC, none had a severe reaction. The median times to symptom onset were 60 and 50 minutes following low-dose and medium-dose OFC, respectively. Patients in the three groups, divided according to threshold doses, differed significantly in sIgE levels against egg white and ovomucoid.

**Conclusion:** This multicenter prospective study confirmed that stepwise single-dose OFC to egg will help to clarify the severity of egg allergy, and will contribute to improved food allergy management. The stepwise OFC can determine whether patients with allergy to egg can safely consume egg-containing foods at low or medium doses. Single-exposure OFC is relatively safe and easy to monitor for symptom.

## 0774 | The effectiveness and the safety of tiny dose oral immunotherapy for children with food allergy

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**Background:** Recently, evidence has shown that oral immunotherapy (OIT) can be successful in desensitizing patients against food allergies. However, sometimes patients have an adverse reaction during OIT since safe and the most effective dose of food protein was not previously determined. The aim of this study was to identify the safer and more effective way of OIT for children with egg or milk allergy.

**Method:** The study design was a retrospective cohort study extracting data from the electronic chart of children older than 4 years who visited our out-patient clinic for egg or milk allergy and who underwent an oral food challenge test (OFC) twice within 24 months between November 2013 and December 2017. The patients were divided into five groups according to their treatment schedule, which consisted of those who: a) Started from 1/10 of the first OFC reaction threshold and maintained 1/10 till the end of OIT; b) Started from 1/100 of the threshold and maintained 1/10; c) Started from 1/10 000 of the threshold and maintained 1/10, d); Conventional slow OIT (started from just below the first OFC reaction and increased 1.2-1.5 times every few weeks); or e) Continued elimination. We determined the presence or absence of an increase in threshold reacted to the allergen, any adverse events during OIT, and food-specific IgE reduction.

**Results:** The number of participants was 217 and their median age was 6 years. The number of patients in groups a, b, c, d, and e was 17, 51, 33, 95, and 21, respectively. The percentage of patients in groups a, b and c showing an increase in reaction threshold to the allergen was higher than that in group e ($P < 0.05$), and that in group b was higher than that in group d ($P < 0.001$). The number (percentage) for group a, b, c, d, and e was 12 (70.6%), 43 (84.3%), 23 (69.7%), 54 (56.9%), and 5 (23.8%), respectively. There was a significant difference in the frequency of adverse events during OIT between group a-c and d, which was as follows: 5 (29.4%), 9 (17.6%), 8 (24.2%), and 67 (70.5%), for the respective groups ($P < 0.0001$). There was no significant difference in the percentage of patients showing a decrease in food-specific IgE in each group.

**Conclusion:** The regimen starting from 1/100 of the OFC reaction threshold and maintaining the dose at 1/10 was safer and more effective for increasing the threshold reacted to the allergen than the 'conventional slow OIT' regimen. Elimination continuation was not effective for increasing the threshold reacted to the allergen.

## 0775 | Clinical features and prognosis in pediatric patients with legumes allergy

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**Background:** Legumes are a commonly consumed food group within the Mediterranean region, Middle East, Asia, and Turkey. Allergic reactions to legumes are seen frequently but there is a lack of studies on allergic reactions to legumes. In this study, we aimed to gain knowledge about frequency of legumes allergy, its clinical manifestations, cross food allergies and prognosis.

**Method:** In our study, we evaluated the patients who were followed up with legumes allergy from 2010 to 2017, their clinical features, laboratory findings and prognosis at University of Health Sciences, Ankara Child Health And Diseases, Hematology, Oncology Training Research Hospital.

**Results:** In this study, 37 patients were evaluated. The median (min-max) age of the patients were 7 (2.1-15.5) years and 78.3% (n = 29) were male. Twenty one (56.8%) patients had peanut allergy, 16 (43.2%) patients had lentil, 13 (35.1%) chickpea, 6 (16.2%) pea, 5 (13.5%) beans, 2 (5.4%) broad bean, 1 (2.7%) kidney bean allergy. Thirteen (35.1%) patients were allergic to more than one legumes. 13 patients who had multiple legumes allergy, of them 10 (%77) had lentil and chickpea allergy, 6 (46%) had lentil and pea allergy, 4 (31%) patients had lentil and peanut allergy together. 32 (86.4%) patients had an allergy to at least one non-legumes food. In 37 legumes allergic patients, we identified 64 allergic reactions.

Legumes allergy was presented in different clinical features; urticaria and angioedema in 32 (50%) patients, anaphylaxis in 23 (35.9%) patients, atopic dermatitis in 5 (7.8%) patients, eosinophilic esophagitis in 3 (7.8%) patients and as food-related enterocolitis in 1 (1.5%) patient. Thirteen (35.1%) of the patients had asthma, 9 (24.3%) had allergic rhinitis. Fourteen (58.3%) of the 24 patients with single legume allergy showed improvement. The patients who developed tolerance, of these 7 (29.1%) had peanut allergy, 4 (16.6%) had lentil allergy and 3 (12.5%) had chickpea allergy. Two of 13 patients with multiple legumes allergies, it developed tolerance to all the legumes they are allergic.

**Conclusion:** Peanut and lentils were the most frequent legumes that displayed allergic reactions in our study. In these patients the rate of allergy to non-legumes food is high. In patients who were allergic to single legumes, the symptoms were ameliorated in 58.3%.

## 0776 | A potent food allergen: Cashew allergy

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**Background:** The prevalence of tree nuts is increasing recently. The increase in the consumption of nuts and the changes of eating and cooking habits is responsible for this rapid increase. Cashew nut is a potent allergen that can cause severe reactions. In children cashew allergy is a rapidly increasing nutritional allergy that has not been focused on sufficiently in the literature. We aimed to investigate the clinical presentation and clinical course of cashew nut allergy in children. We want to draw attention to the childhood cashew nut allergy.

**Method:** Between 01.01.2016 and 01.10.2017, at the Pediatric Immunology Allergy department of Health Sciences Univercity Dr Sami Ulus Maternity and Children Training and Research Hospital, 516 pediatric patients diagnosed as food allergy were evaluated retrospectively from the medical files. Among those patients, cashew sensitization was detected in 17 of them.

**Results:** The demographic and clinical characteristics of children with cashew nut sensitization are shown on the table 1. Clinical reaction was observed with 76% of 17 patients with cashew-nut sensitization. In five of them the reaction was anaphylaxis. All of the patients had multiple food allergies. 59% of the patients had food allergies (cow's milk, hen's egg) out of tree nut allergy.

**Conclusion:** Cashew nut is a potent allergen and can cause quite severe reactions. Avoidance of pistachio nut and other related allergens should be advised to patients after allergologic investigation. In the majority of the patients, presence of atopic dermatitis with food allergy is noteworthy. Therefore, it would be useful to investigate these patients for cashew and other tree nut allergy before they present with a serious clinical reaction.

**Table -** Demographic and clinical characteristics of children with cashew nut sensitization:

| | |
|---|---|
| Total | 17 |
| Gender | |
| Male | 11 (64.7%) |
| Female | 6 (35.3%) |
| Mean age (month) | 37 (min-max 11-66) |
| Clinical Symptoms after cashew nut intake | |
| Never eaten | 4 (23.5%) |
| Skin (Urticaria, angioedema, redness, itchiness, atopic dermatitis exacerbation) | 13 (76.4%) |
| Respiratory symptoms (cough, wheeze, shortness of breath) | 3 (17.6%) |
| Gastrointestinal symptoms (Nausea, vomiting, diarrhea) | 4 (23.5%) |
| Atopic disease | |
| Atopic dermatitis | 14 (82.3%) |
| Anaphylaxis | 9 (52.9%) |
| Asthma | 5 (29.4%) |
| Sensitization of other tree nut | |
| Pistachio nut | 14 (82.3%) |
| Walnut | 9 (52.9%) |
| Hazelnut | 9 (52.9%) |
| Almond | 5 (29.4%) |
| Peanut | 5 (29.4%) |
| Mean Total IgE (ku/L) | 309 (min-max 16-2150) |
| Mean tryptase level (μg/L) | 6.7 (min-max 3.8-10.9) |

## 0777 | Fermented soybeans (japanese natto) induced late-onset anaphylaxis in a fisherwoman: a case report

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**Introduction:** Although Japanese fermented soybeans (Natto) allergy is rare, it might trigger late-onset anaphylaxis. Previously, anaphylaxis cases related to jellyfish sting have been reported. Here, we report a case of Natto late-onset anaphylaxis presumably associated with a jellyfish sting.

**Case report:** A 57-year-old fisherwoman with a medical history of an unknown type of anaphylaxis visited our hospital. In the past, she had been brought to the emergency department several times when she ate meals after 1-7 hours because of abdominal pain, diarrhea, vomiting, general itchy rash, and sometimes shock. She reported incidences of anaphylaxis after eating Natto, pork, crustaceans, wheat,

and jellyfish sting. Serum allergen-specific IgE test was negative; skin prick test was positive for Natto and pork. We performed an oral food challenge with Natto, pork, crustaceans, and wheat, and she developed a general itchy rash after 7 hours of eating Natto. H1-blocker was administered and she recovered soon. However, the general itchy rash relapsed after 4 hours. Hence, we intramuscularly injected epinephrine, H1-blocker, and steroids; then, her symptoms did not relapse. Based on these findings, we inferred that anaphylaxis caused by Natto could be associated with a jellyfish sting.

**Discussion:** Although association between Japanese fermented soybeans (Natto) allergy and jellyfish sting has been previously reported, its anaphylaxis is a rare event. In this case, we suggest that anaphylaxis was caused by Natto allergy, which was perhaps related to jellyfish sting. Hence, further investigation is essential to elucidate the association between fermented soybeans allergy and jellyfish sting.

## 0779 | Non-celiac gluten sensitivity: A case report

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**Introduction:** Non-celiac gluten sensitivity (NCGS) is a syndrome characterized by intestinal and extra intestinal symptoms related to the ingestion of gluten-containing food, in subjects that are not affected by either celiac disease (CD) or wheat allergy (WA).Once the gluten-containing foodstuff is removed from the diet, the patients will have relief of their symptoms.

**Case:** A 6-year-old girl was referred by his General Practitioner with history of occasional constipation and abdominal pain (especially after main meals and defecation), short stature and low weight. The growth indices were proper for her age till she was 5. Then after there was a stunting. She had short stature and low weight. Despite different types of supplementation, there was no improvement in growth indices, so she was referred to a pediatric endocrinologist for GH therapy. Primary investigations and anti-TTG, IgA, anti-EMA all were normal. After a consultation with a pediatric gastroenterologist, a genetic study of HLADQ2 and 8 were done because of the highly suspicion of celiac disease. The results were also negative. At last she was referred to immunology-allergy clinic for evaluation of probable food allergy. IgE level was checked and a prick test was performed which they were not indicative of any suggestive food allergy. Because of the history of the abdominal pain and constipation which was more prominent after meals, negative results of genetic study, SPT to wheat, and serologic markers, a gluten free diet was suggested for her with the suspicious of non celiac gluten sensitivity.

A significant improvement in her symptoms was noticed within 2 weeks of starting gluten free diet. She has 2Kg of weight gain and height improved from 116 cm to 120 cm in 4 months. She continued to improve on a GFD and when seen in the follow-up clinic 6 months later reported complete resolution of symptoms and another 2 cm and 1 Kg gain in her height and weight.

**Conclusion:** Non-celiac gluten sensitivity syndrome is a diagnosis made by excluding celiac disease and wheat allergy. It should be taken into consideration especially in patients who have the suspicious symptoms of celiac without supporting lab data, and also negative SPT to wheat.

## 0780 | Interpretation of specific IgE and component testing in hazelnut allergy, case presentation

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**Background:** A 16 year old male, who had avoided all nuts as a result of having experienced an allergic reaction to a nut product in early childhood, was reassessed for his nut allergy status. Results showed that he may have out grown some of these. He successfully completed various mixed nut food challenges. The only nut we did not include was hazelnut, as results suggested that he may still be allergic to hazelnut.

Results were as follow: Skin prick test result of 4 mm, using a commercial extract, specific IgE to hazelnut of 26 kUa/L on 2 successive occasions, with component results of Cor a 9 of 0.65 and Cor a 14 of 0.89

The young man in question along with his parents were keen to proceed, so with some hesitation we proceeded to a hazelnut oral provocation challenge, having very carefully explained the risks of undertaking such a challenge.

He successfully completed the challenge and experienced no allergic symptoms and is now able to have hazelnuts in his everyday diet.

**Discussion:** This young man wanted to confirm if indeed he was allergic to hazelnuts. Not being hazelnut allergic would mean that he would be no longer allergic to any nut and would not have to take precautions prior eating products.

Positive results to both Cor a 9 and Cor a 14, hazelnut storage proteins are associated with the patient possibly experiencing systemic reactions, at a higher risk of experiencing anaphylaxis it they were to ingest hazelnut. These facts in conjunction with his specific IgE to hazelnut would have prevented us from proceeding to challenge was it not for this young man's persistence that he wanted to proceed to challenge despite the risks.

**Conclusion:** Appearances are deceptive, as this case demonstrates; allergen-specific IgE and component testing can only predict the probability of an allergic reaction, the final test in the diagnostic process is the oral provocation challenge.

The patient and his family were happy for me to share the above with other health care professionals.

SUNDAY, 27 MAY 2018
TPS 10
CLINICAL ASPECTS ON DRUG HYPERSENSITIVITY

## 0781 | Unusual cutaneous adverse reaction to omalizumab in acu

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**Background:** Acquired cold urticaria (ACU) is a chronic physical urticaria and is associated with wheals of the skin (with or without angioedema) in response to exposure to cold temperature. Patients with ACU are potentially at risk of severe systemic anaphylactic shock—like reactions after immersion in cold water.

Treatment of ACU relies largely on non-sedating antihistamines and epinephrine in response to systemic shock. ACU lesions and symptoms are often challenging to control with antihistamines, even at high doses, sometimes being insufficient for the control of the disease, requiring the use of Omalizumab.

**Method:** We present the case of a female of 29 years old diagnosed of ACU with poor control of the symptoms at maximum doses of antihistamines. We decided to associate Omalizumab treatment.

The patient had a good control of the symptoms with Omalizumab at dose of 300 mg/4 weeks, but in the 6th month she presented an erythematous, raised and pruritic lesion in the area of injection together with localized abdominal edema at 12 hours of the administration, with two weeks of evolution without symptomatic treatment. We decided to discontinue Omalizumab alter a second episode with half doses.

**Results:** We performed a skin biopsy of the lesion and epicutaneous tests with the drug. Immediate hypersensitivity tests were not taking due to the impossibility of stopping antihistamines.

Skin biopsy showed a perivascular lymphocytic inflammation of the superficial and deep dermis with frequent presence of perivascular and interstitial eosinophils, suggestive of a hypersensitivity reaction.

The epicutaneous tests with Omalizumab direct and in 5% vaselin with readings at 48, 72 and 96 hours were negative.

**Conclusion:** We present an immunologic cutaneous adverse reaction due to the subcutaneous administration of Omalizumab. The result of the biopsy is reporting as immune reaction of delayed hypersensitivity. Until now, and after reviewing the literature, is the first case found after Omalizumab administration.

## 0782 | Unusual presentation of a serum sickness-like reaction due to sulfonamides

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**Background:** Serum sickness-like reactions (SSLRs) are uncommon adverse reactions to a variety of drugs (antibiotics in most cases), characterized by clinical features resembling serum sickness (mainly fever, rash and arthralgias) with a typical delayed onset (one to three weeks after drug exposure). No specific laboratory findings/allergy tests are available for the diagnosis of SSLR, that is therefore clinically-based. Although rarely reported, trimethoprim-sulfamethoxazole (TMP/SMX) may induce a SSLR.

METHODS: We report 54-year-old woman treated with TMP/SMX for a recently diagnosed pulmonary nocardiosis who developed SSLR. Written informed consent was obtained from the patient.

RESULTS: Nine months before presentation at our clinic, the patient had been hospitalized and treated with imipenem and TMP/SMX for pulmonary nocardiosis. Once discharged, she had been prescribed oral TMP/SMX alone, according to antimicrobial susceptibility. At our first evaluation, the patient presented with fever, macular erythematous non-pruritic (vasculitic-like) skin lesions on the upper limbs, polyarthralgia and bilateral ankle arthritis. TMP/SMX was transiently stopped. After four days, there was a dramatic improvement, with resolution of all signs and symptoms. She was tentatively diagnosed with a viral infection and thus TMP/SMX was started again. However, after three days, the symptoms (fever, arthritis and skin lesions) recurred. Laboratory investigations showed increased levels of inflammatory markers. Complete blood count with differential, serum creatinine, urinary sediment, liver enzymes, rheumatoid factor, antinuclear antibody, C3, C4, immune complexes, serology for Rickettsia, Borrelia and Coxiella were all negative. Hence, TMP/SMX was stopped again and cutaneous lesions, fever and arthritis resolved spontaneously in five days.

CONCLUSION: Given the clinical course and the resolution after the withdrawal of TMP/SMX, we diagnosed a SSLR due to sulfonamides. To the best of our knowledge, this is the first case of SSLR occurring after a nine-month therapy with TMP/SMX and allergists/immunologists should be aware of the possibility of such a reaction even after months.

## 0783 | Unusual clinical manifestation of laryngeal edema in a case of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

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**Case report:** * We received written informed consent for publication of these clinical details and/or clinical images included in my abstract was obtained from the patient.

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a severe adverse cutaneous reaction that usually appears 2-6 weeks after treatment with the causative drug. This syndrome is characterized by severe dermal rash, fever, eosinophilia, and internal organ involvement, and clinically, diffuse maculopapular eruption, exfoliative dermatitis, and facial edema are often observed.

We performed blood tests and laryngeal fiberscopy for the diagnosis of the patient. Intradermal test with delayed reading and patch test were performed 2 months after the end of treatment.

A 53-year-old man had begun treatment with carbamazepine for epilepsy. After 4 weeks of treatment, he observed skin rash with pruritus on both lower extremities, and after 6 weeks, his skin lesions had begun to spread over his whole body, and he complained of several new symptoms, including hoarseness, dyspnea at rest, and dysphagia. An examination revealed maculopapular rash, facial edema, and bilateral cervical lymphadenopathy. Laryngeal fiberscopy revealed both arytenoid and epiglottic swelling. Laboratory studies revealed eosinophil counts of 2100 /μL and increase in alanine aminotransferase level to 65 U/L. A diagnosis of DRESS syndrome was definite according to the RegiSCAR group criteria. Carbamazepine, the suspected culprit drug, was withdrawn, and systemic corticosteroid was initiated. The patient experienced rapid improvements in hoarseness, dyspnea, and dysphagia. After 5 days of treatment, laryngeal fiberscopy revealed complete resolution of both arytenoid and epiglottic swelling.

To the best of our knowledge, our case is the first reported case of DRESS syndrome to manifest with laryngeal edema.

Figure 1.

## 0784 | A case of bortezomib (velcade) induced Stevens-Johnson syndrome

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**Case report:** Bortezomib (Velcade®), a targeted therapy works by blocking the action of proteasomes in side cells, is commonly used to treat newly diagnosed as well as relapsed/refractory myeloma. Bortezomib has been reported to have gastrointestinal symptoms, peripheral neuropathy, neuropathic pain and thrombocytopenia as its most common side-effects. Although several cases of skin lesion caused by bortezomib have been reported, severe cutaneous adverse reaction (SCAR) such as Stevens-Johnson syndrome (SJS) is very rare. We here report a case of bortezomib induced SJS.

A 71-year-old female patient, who was diagnosed with multiple myeloma, received bortezomib and melphalan /dexamethasone therapy. After the 4th dose of bortezomib, she presented with fever and maculopapular skin rashes spreading from face to the trunk. Erosive lesions in the oral mucosa and corneal ulceration with conjuntival injection were observed. She was diagnosed as SJS. The symptoms of SJS improved after bortezomib was discontinued and systemic steroids and intravenous immunoglobulin were administered. Drug patch test was performed, the result was positive in bortezomib.

This is the first case report of bortezomib induced SJS in this country, which was diagnosed by a patch test. Although the SCAR by bortezomib is generally considered very rare, we suggest that clinicians be aware of potential adverse reactions, including SJS.

## 0786 | Fixed drug eruption due to fluconazole

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**Background:** Fixed drug eruption (FDE) is a distinctive drug-induced dermatosis with a characteristic recurrence at the same sites of the skin or mucous membrane, after repeated administrations of the causative drug. It accounts for about 11%-30% of all adverse drug reactions.

**Case report:** We report the case of a healthy 46-year-old woman with history of red erythematous macules in both hands, one hour after taking a fluconazole (150 mg) tab for a vaginal candidiasis. It faded spontaneously. She didn't recall if she had ever taken that medicine, but denied known drug allergies. Although FDE is primarily a clinical diagnosis, we conducted an oral challenge test with fluconazole (150 mg). Two hours after intake of the drug the patient started complaints of pain and erythema in both hands and the challenge was stopped. Two days after the challenge, she developed red painful erythematous macules on the same sites of the first episode. Due to the specificity of the challenge, local patch testing was not performed.

**Conclusion:** FDE is considered a form of delayed type hypersensitivity, mediated by CD8 + T cells. The lesions recur in the same spot, usually within 30 minutes to 12 hours post-drug exposure. Typical locations for the lesions include the genitals, face, hands and feet. Intermittent drug administration is more likely to cause sensitization than continuous administration. Nowadays the association between fluconazole and FDE is growing, as every year new cases are reported. Cross reactivity has been documented with structurally related triazoles, such as itraconazole. Physicians should be aware of

this possibility so that occurrences may be readily diagnosed and future recurrences avoided.

## 0787 | Atypical presentation of nsaid intolerance: Fixed drug urticaria

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**Introduction:** The classic form of a fixed drug eruption is one or more anular or oval erythematous patches as a result of systemic exposure to a drug. These skin lesions normally resolve with hyperpigmentation and may recur in the same location with re-exposure to the drug.

Other types of fixed drug eruptions have been described, being fixed drug urticaria a rare form of presentation. (1,2)

**Case Report:** In the last 2 years, a 48 year old woman has developed more than 15 episodes of a wheal in the right supraciliary region 5 minutes after taking 600 mg of oral Ibuprofen. The symptoms resolved in less than 6 hours without treatment and without leaving residual lesion.

After the last episode, she refers good tolerance to 1 g of oral Paracetamol. She denies local traumas.

She also refers mild spring rhinoconjunctivitis well controlled with antihistamine, and sneezing with house dust.

Physical exploration: No hyperpigmented lesion. Darier`s sign: negative.

**Material and Methods:** Skin test (prick) for standard aeroallergens were done.

Single Blind Oral Challenge Test with Acetylsalicylic acid, Meloxicam and Celecoxib were also performed.

**Results:** Skin test (prick) for standard aeroallergens were positive for pollens and house dust mites.

Single Blind Oral Challenge Test with Aspirin: 50 minutes after 125 mg, she developed the same wheal in right supraciliary region, as described with ibuprofen, that resolved without leaving residual lesion in 20 minutes with oral Cetirizin 10 mg.

Single Blind Oral Challenge Test with Meloxicam and Celecoxib showed negative results.

**Conclusion:** To our knowledge, we present the first case of fixed drug urticaria due to intolerance to nonsteroidal anti-inflammatory drugs (NSAIDs).

This case report could resemble a local form of NSAIDS-induced urticarial/angioedema (NIUA), attending to EAACI classification of hypersensitivity reactions to NSAIDs (3).

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Sharma VK; Dhar S et al. Drug Related Involvement of Specific Sites Fixed Eruptions: A Statistical Evaluation. The Journal of Dermatology 1996; 23: 530-534.

## 0788 | Ornidazole-induced fixed drug eruption: Is there a cross-reaction with Metronidazole?

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**Introduction:** Fixed drug eruptions (FDEs) are rare drug reactions which are characterized by lesions recurring typically in the same regions of skin and mucosa as a result of repetitive intake of the causal drugs. A cross-reaction may be observed between structurally similar drugs. In general, in case of development of a FDE against a drug, it is thought that other structurally similar drugs from the same pharmacological group should be avoided. In this case report, a case that developed FDE due to ornidazole, a drug belonging to the azole group, but could tolerate metronidazole will be discussed.

**Case report:** 47 year-old female patient. She admitted to our clinic with oval rashes healing with dark spots in right thumb, left forearm, left thigh and gluteal regions 4-5 hours after concomitant intake of first doses of drugs containing ornidazole and fluconazole. The patient underwent to skin patch test for metronidazole, ornidazole and fluconazole. A positivity for ornidazole was determined. Skin patch tests for metronidazole and fluconazole were negative. Oral provocation tests performed thereupon for metronidazole and fluconazole were determined to be negative. Usage of ornidazole was restricted.

**Discussion:** It should be remembered that ornidazole, which is used commonly in protozoal and anaerobic bacterial infections, may be a cause of FDE. There may be cases that do not exhibit a cross-reactivity with other drugs from azole group.

## 0790 | Enteropathy related to angiotensin II receptor antagonist losartan: Case study

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**Background:** On August 2012 Rubio-Tapia et al reported an association of olmesartan therapy with an unexplained enteropathy symptomatically resembling celiac disease or sprue. Olmesartan is an Angiotensin II Receptor Antagonist (ARA II) widely used in high blood pressure, heart disease and diabetics. On July 2013 the Food Drug Administration (FDA) approved label changes to include

intestinal problems, Severe Spruelike Enteropathy (SSE) linked to blood pressure medicine olmesartan.

Losartan was the first ARA II commercialized in 1995 and it seems to produce similar Adverse Drug Reactions (ADR) that olmesartan.

**Method:** Design: Case series of enteropathy associated with losartan. Scope: Allergy Service, Hospital Central de la Defensa, Madrid. Period: May 2015-Jan 2018: Main variables assessed: demographic and clinical variables, diagnostic criteria, treatment, evolution, causal relationship between drug and enteropathy according to the modified Karch Lasagna algorithm.

The patients have given written informed consent for publication.

**Results:** Two female patients 81/77 years, diagnosed of hypertension, treated for three/ten years with losartan 100 mg/day. After starting treatment they refer chronic diarrhea and two/four years ago worsening diarrhea, abdominal pain and weight loss. The patients were treated at the emergency service for episodes of watery, nonbloody diarrhea associated with abdominal bloating. The patients failed conservative management including gluten-free diet, oral antibiotic and corticosteroid. Additionally to diarrheal syndrome, both patients showed other ADR like hoarseness and cough.

Allergologic study: immediate and delayed prick test and specific IgE were negative for food.

Colonoscopy with colonic biopsies revealed evidence of microscopic colitis in both cases.

Treatment: Losartan withdrawal, achieving complete remission in four/two weeks.

**Conclusion:** The allergist should keep in mind this possible and rare ADR in patients treated with losartan (ARA II) showing enteropathy, as discontinuing losartan may lead to clinical improvement.

These enteropathy cases are very similar to SSE described in 2012 related to olmesartan.

## 0792 | Erythema multiforme-like dermatitis to isoniazid in a patient with psoriasis

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**Case report:** Isoniazid (INH) associated drug reactions are rarely reported, and skin rashes are accepted as minor side effects with no need to stop the drug. Herein, a patient with psoriasis who developed dermatitis due to INH, but had to withdraw was presented.

A 37-year-old-M patient had psoriasis vulgaris for 15 years, and had been using methotrexate at intervals of 4 years. Despite the addition of phototherapy, he underwent a new treatment with biological agent (antitumor-necrosis-factor; anti-TNF), since the disease control was insufficient. Before anti-TNF, preventive treatment against latent tuberculosis (TB) activation was indicated with positivity in tuberculin skin test (20 mm). He was given INH 300 mg/day, and at the 20th day of treatment, desquamation, erythema, and subsequent exfoliation developed in his hands and foots dorsum. INH was withdrawn. In order to distinguish the lesions from psoriasis attack, skin biopsy was performed and reported as erythema multiforme-like dermatitis with no relation to psoriasis. The lesions were completely improved at 3 weeks of topical steroids, and INH was re-initiated at the same dose. A week after the initiation of the drug, skin lesions similar to previous reoccurred with more severity and progression from distal to proximal extremities. Cell counts, renal and hepatic function tests, and hepatitis markers in blood were in normal limits. Skin lesions were retracted after 4 weeks of topical steroids, and withdrawal of INH. There was positivity in skin patch test with INH at 72 hours. Finally, for TB prevention an alternative drug rifampicin (10 mg/kg/day) was given, and the patient successfully completed with no adverse event. His psoriasis lesions were improved with anti-TNF which was started after 1 month of TB prevention with rifampicin.

In these days which the use of biologic agents is increasingly widespread, INH use will be more prevalent than the past. Even tough, it is effective and safe in most of the patients, its adverse event dermatitis may be a reason to withdraw in patients with dermatological diseases. In this case, diagnostic drug allergy evaluation should be performed to optimize the second-line treatment of TB infection, in addition to early withdrawal of the culprit drugs.

## 0793 | Post-radiotherapy multiforme erythema, a case report

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**Background:** Around 50% of cancer patients will receive radiotherapy (ionizing radiations) as a treatment, either as a single therapy or as an adjuvant to chemotherapy and surgery.

Several side effects have been described due to radiotherapy, of which we can mention Erythema Multiforme and Stevens Johnson Syndrome, but in lower prevalence.

Erythema Multiforme can be described as an acute skin condition and may be present within a wide spectrum of severity. Erythema multiforme minor represents a localized eruption of the skin with minimal or no mucosal involvement. The papules evolve into pathognomonic target or iris lesions that appear within a 72-hour period and begin on the extremities (see the following image). Lesions remain in a fixed location for at least 7 days and then begin to heal.

It is considered to be a type IV hypersensitivity reaction associated with certain infections, medications, and other various triggers

Precipitating factors and complex interactions may trigger the appearance of signs and symptoms. These include especially recurrent herpes simplex virus (HSV), Epstein-Barr virus (EBV), histoplasmosis, alcohol, systemic diseases and immunological factors.

**Method:** 69-year-old male diagnosed with Prostate Adenocarcinoma who underwent transurethral resection and was taking Trinomia (Ramipril, Atorvastatin, Acetyl-salicylic Acid)

After his 8th RTE external radiotherapy session, he presented erythematous maculo-papular lesions in the suprapubic area with some vesicles. Therefore, withdrawal of treatment was decided and the performance of a skin biopsy.

15 days later, regarding the improvement of the lesions, RTE was continued, presenting incipient exacerbations of the lesions but it allowed us to end the cycle of treatment.

**Results:** *Skin biopsy results (Anatomical Pathology)*: basal keratinocytes, which blur the dermoepidermal interface, with lymphocyte exocytosis at this level, associated with isolated images of spongiosis. The dermis shows a superficial perivascular lymphocytic inflammatory infiltrate of moderate intensity. Compatible with erythema multiforme.

**Conclusion:** Radiotherapy is a technique of increasing use, so it is important to recognize the associated cutaneous lesions that appear less frequently and are sometimes underdiagnosed.

Diagnosis is both clinic and pathological and is usually late in most cases so it is vital to take into account this skin disease complication in order to be properly managed.

## 0794 | Potential allergic and adverse reaction in some complementary and alternative medicine (CAM) from China

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**Background:** Complementary and alternative medicine (CAM) including Chinese herbal medicine is usually considered to be without any allergic and adverse reaction.

**Method:** Visits were made to pharmacies in Hong Kong and Luoyang, China and a martial art monastery/temple in Dengfeng, China. Some CAM were found to have ingredients with potential allergic and adverse reaction.

**Results:** Three CAM, one from Hong Kong (1), one from Shaolin martial art monastery/temple in Dengfeng (2) and one from Luoyang (3), China were found to contain Chinese herbal medicine with potential allergic and adverse reaction.

(1) Cordyceps Ling-Zhi Complex

Ingredients: Cordyceps sinensis "caterpillar fungus", Tremella fuciformis "snow fungus", Ganoderma lucidum (Ling-Zhi) "Reishi mushroom" and others

Function: anti-cancer, boost immunue system, improve liver, lung & kidney function, increase blood circulation, detoxification, enhance sleep

Potential adverse reaction: April 2016, China State Food and Drug Adminstration (CFDA) issued stop order on a prominent supplier of caterpillar fungus products due to excessive level of arsenic

(2) Shaolin Shujin huoluo health paste

Ingredients: myrrh, safflower, pseudo-ginseng, frankincense and others

Function: Ease neck, shoulder, back and knee pain and other discomfortable symptoms caused by wind cold dampness evil and strain, to promote health

Potential allergic reaction: Myrrh may cause allergic contact dermatitis

(3) Extra Strong Heart Saving Pill

Ingredients: Radix Salviae Miltiorrhizae, Astragalus Extract, Organic Ginseng and others

Function: improve heart function, strengthen cardiac vitality, relieve tiredness, increase alertness

Potential adverse reaction: Radix Salviae Miltiorrhizae has bleeding-tendency.

**Conclusion:** Potential allergic and adverse reaction are noted in three CAM including allergic contact dermatitis, bleeding tendency and presence of arsenic.

Careful examination of the ingredients of CAM is important.

Health authority warning should be respected.

## 0795 | Multiple antihistamines can induce urticaria in NECD

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**Case report:** Antihistamines (AHs) are major therapeutic agents used in treatment of many allergic diseases although they can rarely cause allergic symptoms. Here, we present 2 rare cases who experienced flare up of urticarial symptoms due to both AHs and nonsteroidal anti-inflammatory drugs (NSAID) on different occasions.

**Case 1:** A 42-year old female patient referred to us due to a history of recurrent urticaria exacerbated by AHs or chemically different NSAIDs in 30 minutes. Her urticarial attacks were due to drugs or sometimes spontaneous and resolved with corticosteroids (CS). Skin prick tests (SPT) with pheniramine, cetirizine, desloratadine and fexofenadine and intradermal tests with pheniramine (the only injectable AH) were negative. The single blind placebo controlled oral provocation test (SBPCOPT) with pheniramine, cetirizine, and fexofenadine as well as with aspirin and metamizole were all positive, respectively. She was tolerating paracetamol and meloxicam. Any

leading cause for her urticarial attacks other than AHs and NSAIDs was not detected: She was diagnosed as NECD and prescribed CS to use in urticarial attacks.

**Case 2:** A 27-year old woman with a 6-year history of chronic urticaria exacerbated with NSAIDs and AHs in 8-10 hours but responded to CSs, was consulted with us for management. SPT and patch tests with pheniramine, fexofenadine, rupatadine, cetirizine, hydroxyzine and desloratadine were negative. SBPCOPT with pheniramine, fexofenadine and aspirin were positive. She could tolerate paracetamol. The routine work-up of chronic urticaria did not point to any causative disturbances and since she needed frequent CS treatment for urticaria, omalizumab treatment (300 mg per month) was started.

**Conclusion:** NECD is a newly described clinical entity. This report is describing patients who could experience flare up of urticaria both with AHs or NSAIDs on different occasions. Physicians should keep in mind that AHs can induce or exacerbate urticaria.

## 0796 | Fluconazole related fix drug eruption and Stevens Johnson Syndrome and anaphylaxis

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**Case report:** Fixed drug eruption (FDE) is cutaneous drug reaction that occurs same location when re-exposure with culprit drug. Rare severe reaction of FDE is generalized bullous variants, share clinical features with Stevens Johnson syndrome. However there is not any report in English literature about recurrent FDE and anaphylaxis afterwards. In this case report we present fluconazole related FDE, Stevens Johnson Syndrome and anaphylaxis.

30 years old female patient who has ulcers in oral mucosa and purple, itchy lesions on her right hand palmar area, little finger, index finger, on her left hand palmar area, pollex finger. In her history, she has relapsing vaginal yeast and she hasn't any hypersensitivity reaction with fluconazole before 1 month ago she started to take fluconazole because of vaginal candidiasis. After using fluconazole she started to itch from described areas and dark red - purple eruptions appeared. She was prescribed oral methylprednisolone and topical pomade which included corticosteroid for four days but she didn't aware of fluconazole related drug reaction. Lastly four days ago she took fluconazole and metronidazole for severe vaginal yeast. 12 hours later pruritus, same eruption appear on the same area, lip and tongue angioedema than she had dyspnea, dizziness, hypotension, arrhythmia and consciousness. She had admitted to the emergency department and performed adrenalin. After a day bullae and ulcers came into existence in her oral mucosa.

In her blood analysis there was mild increase in white blood cell count (13.300 /$mm^3$), eosinophil count was normal (300 /$mm^3$), biochemistry parameters were in normal limits, CRP and sedimentation rate were in normal limits, total IgE was 439 IU/L.

Flucanazole allergy was diagnosed by her history, and prescribed systemic steroid and topical antiseptic solutions for oral lesions. Then all lesions recovered. Drug allergy information card was given to the patient.

Fluconazole is a rare cause of severe cutaneous adverse drug reactions. It is important that aware of cutaneous drug reactions otherwise re-exposure to culprit drug may result in severe systemic reactions.

## 0797 | Maculopapular drug eruption in late period after desensitization with isoniazid

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**Introduction:** Tuberculosis is a disease that most commonly affects the lungs, which is transmitted by the respiratory tract and drugs are the most important factor in the treatment. Non-resistant tuberculosis infection is usually treated with HRZE. In rare cases, a hypersensitivity reaction may develop against one or more of the drugs during treatment.

**Case:** A 37-year-old female patient was diagnosed with culture-positive pulmonary tuberculosis and HREZ treatment was started by the related department. Seven days later she referred to the policlinic with edema and itchy erythematous lesions which are common in her extremities, which developed after 6 hours of taking her medication.

Liver and kidney function tests and eosinophil count were normal. Drug eruption was considered with current physical examination findings. The treatment was interrupted, short time systemic corticosteroids and antihistamine treatment started. Desensitization planned. There was no feature in the prick and patch tests with drugs. Desensitization was performed with isoniazid, no reaction was observed during the procedure. Six hours after the procedure, the patient applied to the emergency department with painful edema and pruritic erythematous lesions in the extremities. Desensitization procedures with rifampicin, ethambutol, pyrazinamide were performed without any problems after the lesions were regressed. isoniazid was withdrawn from the treatment protocol.

**Outcome:** We would like to present on this case that drug eruption may develop in the form of maculopapular rash after desensitization.

SUNDAY, 27 MAY 2018
TPS 11
CLINICAL ASPECTS OF ENT AND OCULAR ALLERGY

## 0799 | Allergic rhinitis patients with concomitant sinusitis are more sensitized to allergens compared to distinct atopic rhinitis and less colonized to bacteria

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**Background:** The integrated airway allergic diseases often present as comorbidities in atopic patients. Allergic rhinitis (AR) and Chronic rhinosinusitis (CRS) have a significant impact on quality of life. In some cases, CRS may appear as a complication of atopic rhinitis although frequently regarded as coexisting disease. The authors aimed to investigate a possible correlation between atopic sensitization, evidence of microbe colonization and functional bias among subjects with upper respiratory symptoms implying allergy.

**Method:** A total of 151 subjects, hospitalized for allergic-like symptoms from upper respiratory tract were analyzed. Skin prick tests, spirometry and nasal microbiology were performed. Patient`s diagnoses were classified as: Allergic Rhinitis, Allergic Rhinitis with concomitant Sinusitis (AR+ S) and Chronic Rhinosinusitis.

**Results:** Ninety patients (59.6%) were with AR; 39 of them (25.8%) were defined as: AR and concomitant sinusitis. As CRS were identified 66.2% of all patients (n = 100). Sensitized to pollens were 80% of AR patients, while 67.8% had positive skin prick test for perennial allergens. In AR+ S group 79.5% showed pollen allergens (grass and tree), House Dust Mite (HDM) and fungal sensitization (perennial allergens) ($P = 0.04$). AR patients had 15.6% positive microbiology test while only 12.8% from AR+ S group showed bacteria colonization. Eighty four from all investigated who were positive to tree had explicit data for nasal bacterial carriage also ($P = 0.03$). AR subjects presented with obstructive type of spirometry in 1.1%. None of AR+S group showed spirometry disturbances. Fifty eight from studied patients presented with fungal sensitization; 40 of them (69%) were positive to HDM while 18 (31%) were negative ($P = 0.03$). In HDM positive group (55%) 59 (71.1%) subjects were presented with pollen sensitization ($P = 0.02$).

**Conclusion:** Compared to AR patients those with concomitant sinusitis are sensitized to more allergens.

AR patients showed more colonization with pathogenic microorganisms than AR+S group.

Therefore being genetically predisposed to atopy AR patients are prone to higher frequency of sinusitis. Spirometric parameters showed not significant differences in all studied groups.

Obtained data leave a number of issues to resolve.

## 0800 | Histopathology of ethmoid mucosa versus nasal polyp on diagnosing eosinophilic rhinosinusitis

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**Background:** Eosinophilic chronic rhinosinusitis (ECRS) is one subtype of chronic rhinosinusitis (CRS) presenting with tissue eosinophilia, comorbidities, and high rate of relapse. While researchers assess polyp for diagnosing ECRS, others assess ethmoid mucosa. There is no consensus regarding the appropriate site of tissue for evaluation. This study aims to compare ethmoid mucosa and nasal polyp regarding density of tissue eosinophil and its sensitivity, specificity, and correlation with clinical characteristics for diagnosing ECRS.

**Method:** Patients with CRS with polyps scheduled for endoscopic sinus surgery were enrolled. Specimens were collected from polyp apex, polyp pedicle and ethmoid mucosa. Tissue eosinophil from these three sites in the same patient were compared. Using eosinophilic mucin as a reference, sensitivity, and specificity of each site for diagnosing ECRS was assessed. Correlations between tissue eosinophilia (defined as greater than 10/ HPF) and clinical characteristics of ECRS including asthma, serum eosinophilia, and eosinophilic mucin were analyzed using each site of specimens.

**Results:** Thirty patients with CRS with polyps were enrolled. Polyp apex, polyp pedicle and ethmoid mucosa gave similar results regarding tissue eosinophilia in 16 patients (53.3%). Eleven (36.7%) patients were ECRS (having tissue eosinophilia at all sites) and five (16.6%) were non ECRS (no tissue eosinophilia at any sites). Median tissue eosinophil was significantly greater in polyp apex (84, IQR: 34-194) and polyp pedicle (96, IQR: 80-320) than ethmoid mucosa (21, IQR: 10-220), $P = 0.04$. Sensitivity of polyp apex, polyp pedicle and ethmoid mucosa for diagnosing ECRS were 100%, 60% and 80% respectively. Specificity were 36%, 40% and 48% respectively. Correlations between tissue eosinophilia and asthma were significant when assessing ethmoid mucosa ($P = 0.04$), and polyp pedicle ($P = 0.05$) but not polyp apex ($P = 0.21$). Correlations with serum eosinophilia, and eosinophilic mucin were not significant ($P > 0.05$) when assessing any specimens.

**Conclusion:** Assessing various sites of specimens reported different results. Density of tissue eosinophil was greater in nasal polyp than ethmoid mucosa. Polyp apex had greater sensitivity for diagnosing ECRS than others. Specificity was poor at any site. Polyp pedicle and ethmoid mucosa better revealed a correlation with asthma than polyp apex.

## 0801 | Obstructive sleep apnea syndrome may be a poor prognostic factor in allergic rhinitis: A mini-review and hypothesis

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**Background:** Obstructive sleep apnea syndrome (OSAS) is a common disease with an incidence as high as 75% among those with a body mass index exceeding 40 kg/m$^2$. OSAS patients experience intermittent episodes of partial or complete closure of the upper airway during sleep, which lead to intermittent periods of hypoxia in the patient's tissues. Previous research has shown that OSAS can contribute to hypertension, insulin resistance, diabetes, dyslipidemia, and even cancer. Intermittent hypoxia can be viewed as prolonged continuous hypoxia interrupted by recovery of the normal oxygen supply. Allergic rhinitis (AR) is a nasal inflammatory disease with an increasing prevalence that is mediated by T-helper type 2 cells together with mast cells and eosinophils, as well as a number of inflammatory cytokines and chemokines. Specifically, hypoxia-inducible factor HIF-1α expression has been linked to AR. We hypothesized that OSAS may affect the prognosis of AR patients.

**Method:** A literature search on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) was performed using the following key words: "Obstructive sleep apnea syndrome"; "allergy rhinitis"; "hypoxia"; "intermittent hypoxia"; "fluctuating hypoxia"; "cyclic hypoxia"; and "HIF-1α"

**Results:** OSAS may affect the prognosis of AR patients based on the following evidence: 1) AR is thought to be a cause of OSAS.
2) Exposure to hypoxia could mediate immune activation in AR and affect the response to treatment.
3) HIF-1α expression may be a risk factor for AR.
4) Intermittent hypoxia can induce robust expression of HIF-1α.

**Conclusion:** First, improvement of ventilation during sleep represents an efficient strategy for treating AR. Therefore, continuous positive airway pressure or nasal surgery to resolve a nasal obstruction could be added to AR treatment. Finally, medications that target HIF-1α, such as digoxin, can be tested as adjuvant therapy.

## 0803 | Acupuncture therapy of olfactory dysfunction in allergic rhinitis

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**Background:** The aims of this study were to recommend as an adjuvant therapy for neuropathy. To investigate the efficacy and safety of traditional Chinese acupuncture therapy of olfactory dysfunction in allergic rhinitis patients and to compare the results with the impact observed in an observation group.

**Method:** Forty patients diagnosed with allergic rhinitis and olfactory dysfunction were recruited in current study in the Group 1 and 2. Patients of Group 1 were administered with no treatment and patients administered with the traditional Chinese acupuncture therapy were incorporated into the Group 2. Before the treatment, all of them underwent T&T olfactory testing, nasal sinus computer tomography scanning and visual analog scale (VAS; 0-100), and repeated the assessment after four-week treatment.

**Results:** Improved total T&T olfactory testing scoring averages and VAS Scoring averages was observed in eleven patients treated with traditional Chinese acupuncture compared with four patients in the observation group. No side effect was found. No significant differences in olfaction recovery were found according to age, gender, or duration of disease between the two groups.

**Conclusion:** The primary outcomes suggest the efficacy and safety of the traditional Chinese acupuncture therapy in treatment of olfactory dysfunction of allergic rhinitis patients.

## 0805 | Analysis of therapeutic effect of endoscopic sinus surgery on chronic sinusitis in geriatric patients

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**Background:** To investigate the therapeutic effect of endoscope sinus surgery on chronic sinusitis in geriatric patients.

**Method:** A total of 68 geriatric patients with chronic sinusitis underwent surgery in our hospital from Jun. 2016 to Sep. 2017 were divided into observation group (n = 34) and control group (n = 34). The observation group underwent nasal endoscopic sinus surgery and the control group underwent external approach surgery, and the therapeutic effect of the two groups were investigated.

**Results:** The total effective rate was 94% in observation group and 74% in control group, the total effective rate of observation group is significantly higher than control group ($P < 0.05$). The recurrence rate was 3% in observation group and 24% in control group, the recurrence rate of observation group is significantly lower than control group ($P < 0.05$). Complication occurrence rate of observation group was 6% which is significantly lower than control group 24% ($P < 0.05$).

**Conclusion:** The therapeutic effects of endoscopic sinus surgery on chronic sinusitis in geriatric patients are better than conventional external approach surgery which is worth clinical application.

## 0809 | Nasal obstruction - beyond rhinitis

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**Background:** The most common causes of nasal obstruction are rhinitis, chronic rhinosinusitis, upper respiratory viral infections and structural/mechanical abnormalities.

Case report: The authors present a case of a 41 years old woman, sent to our consultation due to nasal obstruction. The patient had complaints of frontal headache and bilateral nasal obstruction since April of 2015, with more severe obstruction during the day, accompanied by persistent posterior nasal secretions and anosmia. She denied previous symptoms, personal or family history of allergic disease or use of daily medication. She performed skin prick tests to common airborn allergens, mites and fungus, all negative. The patient was medicated with nasal budesonide 64 ug bid, deflazacort 30 mg (short course) without clinical improvement. Due to chronic, refractory symptoms, further investigation was performed. Perinasal CT- scan showed: normal pharynx, no inflammatory abnormalities of the sinus cavities; osteoma on the right side of the ethmoidal bone with dense matrix, well defined limitations with 10 mm of axial diameter. Left septal deviation with bone spur, compressing the inferior nasal concha, thus reducing nasal permeability. After this incidental finding, the patient was sent to the otorhinolaryngology consult and awaits clinical evaluation.

Conclusions: Paranasal sinus osteoma is a benign tumor, with slow growth, occurring most commonly in frontal (71.8%), ethmoid (16.9%), maxillary (6.4%) and sphenoid (4.9%) sinuses. Osteomas are commonly observed in third to fourth decades of life. Small osteoma of paranasal sinuses are often asymptomatic and discovered incidentally on neuroimaging (3% of cases). Its' size can range in 2 mm - 30 mm diameter, resulting in clinical symptoms (localized headache, sinusitis, frontal mucocele, anosmia, cerebrospinal fluid rhinorrhea). Surgery is indicated in this case due to persistent headache. It is essential to investigate all differential diagnosis in patients with chronic relapsing symptoms, as these cases may need surgical treatment.

## 0810 | Validating an electronic tool for monitoring symptoms and treatments for children with Vernal Kerato-conjunctivitis

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**Background:** Vernal Keratoconjunctivitis (VKC) is a severe allergic eye disease predominantly affecting pre-pubescent males. Treatment typically involves supportive management with topical antihistamines, mast cell stabilisers and the suppression of inflammation with steroids and / or calcineurin inhibitors. Recently, omalizumab has been reported to be beneficial. There is no universally accepted method at present to systematically gather temporal data on signs, symptoms and health related quality of life (QoL) following clinical interventions. An Italian-language validated QoL score (QUICK) specific for VKC has been previously published. This has not been validated for use in English.

**Method:** The existing Italian-language paper-based for VKC symptom tracker (QUICK) was co-adapted to a digital version of VKC-QUICK—"eQUICK" with input from 9 children with VKC and 12 healthy young individuals from our Trust's Youth Forum. Steps included -

Phase 1: translation to English of the Italian VKC-Quick questionnaire with symbolic pictures to aid responses from pre literate children or for those who do not use English as their first language.

Phase 2: piloted/refined paper based tool with VKC affected children and their parents attending the eye/allergy clinic in the hospital.

Phase 3: the feedback helped devise an electronic platform (eQUICK) with images. Our Information and Technology Department assisted in relevant graphic design of images.

eQUICK can run on iOS or Android enabled mobile devices and desktops allowing reporting by patients in between clinic visits. Responses from these electronic questionnaires upload to a secure online database and integrated with the hospital's existing patient record system. Clinicians access an internal admin application to view patient responses in conjunction with treatments prescribed and relevant parameters collected at the clinic visit/s. This allows progress monitoring and advice on alteration in management if needed.

**Results:** (descriptive).

**Conclusion:** The eQUICK app is user-friendly even for VKC patients with sub-optimal reading ability. Home use between clinic appointments allows responsive temporal data gathering of QoL, symptoms, medication scores and impact of medical interventions. eQUICK may be used in future as a research tool in gathering outcome data following interventions for VKC.

*This project received ethics approval (15/SC/0421) and received an innovation grant from Manchester University Hospitals NHS Foundation Trust.*

## 0811 | 2% Ectoine eye drops in prevention of vernal kerato-conjunctivitis relapses

Allegri P[1]; Ciurlo C[1]; Buzzanca C[2]; Rissotto R[3]
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**Background:** Vernal Kerato-Conjunctivitis (VKC) is one of the most severe ocular allergic forms characterized by seasonal (sometimes perennial) recurrences of ocular surface inflammation (giant tarsal conjunctival papillae and/or limbal inflammatory Trantas nodules). Ectoine, a substance deriving from halophilic micro-organisms, is a strong water structure forming solute exerting cell protective antiinflammatory and antiallergic properties.

**Method:** Purpose of our study was to assess the efficacy of the preventive administration of 2% Ectoine eye-drops (3 times a day for 6 months) to shorten the duration of VKC relapses (which begin, in our country, very early in Spring and usually end in October), or to mitigate the attacks, which are only controlled by topical corticosteroids or cyclosporine resulting in an important burden of side-effects.

In this retrospective study, we included 192 children of both sexes (148 males and 44 females), under the age of 10 years (mean age 7.8 years), affected by VKC from more than 3 years/seasons and treated for more than 4 months during a year, with cyclosporine eye-drops.

These patients underwent, from February to September 2017, the additional-to-the-usual protocol treatment with 2% Ectoine eye-drops.

**Results:** 8% of the included subjects astonishingly had no relapse of VKC, 38% needed topical CS or CYC treatment but it was started 2 months later compared to previous years, 29% needed the topical drugs 3 months later and 25% had a similar to previous years course (no Ectoine efficacy).

The treatment was well tolerated and only 1 child had to stop it because of local allergy to the eye-drops.

**Conclusion:** The preventive administration of 2% Ectoine eye-drops was able to stabilize and to delay VKC attacks in more than 50% of the selected patients showing the importance of anti-inflammatory and anti-allergic properties of this product.

## 0812 | Pertinence of extraocular allergy tests compared to conjunctival provocation test in presumed allergic conjunctivitis

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Hopital Bichat et Fondation A de Rothschild, Paris, France

**Background:** Aim:To evaluate the correlation between systemic allergy tests (prick tests and specific seric IgE levels) and conjunctival provocation test (CPT).

**Method:** We retrospectively studied the files of 65 patients, 20 males and 45 women, mean age 33.6 year (6 to 74 years) suffering from presumed ocular allergy. Skin prick tests and CPT were performed in all cases, whereas specific seric IgE level assessment was done in selected cases.

**Results:** Systemic tests and CPT were concordant in 68% of cases (44/65) and discordant in 32%. Among the patients with positive extraocular allergy testing, ocular allergy to the candidate antigens was ruled out by the CPT in 42% (16/36) of cases. On the opposite, ocular allergy was proven by CPT in 21% of patients with negative systemic allergy testings. Overall, agreement between extra ocular and ocular tests measured by Cohen's Kappa coefficient was poor (K = 0.36).

Medical history of rhinitis was not a factor predicting for a better correlation between general and ocular tests (K = 0.35) : CPT was negative in 42% (9/21) of patients with positive systemic testings and rhinitis.

**Conclusion:** The rate of discordance between extraocular and ocular tests is high, meaning that the eye can often be immunologically isolated. CPT is the gold standard for testing ocular allergy.

## 0813 | Is there a correlation among different forms of ocular allergies and serum levels of Vitamin D?

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**Background:** Among Vitamin D actions, a reduction in inflammation was recently recognized and some experimental trials showed that Vit. D supplementation modulates Th2 immune response by inducing T regulatory cells in allergic conjunctivitis. Recent literature reports showed that low vitamin.

D levels are related with worsening of seasonal allergic conjunctivitis (SAC) and vernal kerato-conjunctivitis (VKC).

**Method:** We retrospectively investigated the levels of plasma 25 hydroxy-vitamin D compared to normal values in 187 children (143 males and 44 females, mean age 7.3 ± 1.4 years) followed in our tertiary referral center who were affected by different forms of allergies; 62 children suffered from SAC, 74 from VKC and 51 from Atopic Kerato-Conjunctivitis (AKC).

Following international criteria we considered normal levels of vitamin D the levels between 50 nmol/L (20 ng/mL) and 125 nmol/L (50 ng/mL), a potential deficiency between 30 nmol/L and 50 nmol/L and a severe deficiency less than 30 nmol/L.

**Results:** 58.8% (30 children) of AKC group patients presented vitamin D low levels, among them 18 children showed a potential deficiency and 12 a severe deficiency.

24.3% (18 subjects) of VKC patients suffered a deficiency in vitamin D which was mild in 13 and severe in 5 patients.
40.3% (25 children) of SAC group showed a deficiency in vitamin D which was potential in 17 and severe in 8 subjects.

**Conclusion:** Our study shows that in different forms of allergic conjunctivitis many children are suffering a Vit. D deficiency and it can be supposed that a correlation between the severity of the allergic form and the level of vit. D deficiency exists.
We recommend allergists and ophthalmologists to check Vit. D levels in children suffering from allergic conjunctivitis because its deficiency is very common and many are unaware of it; in case of a vit. D insufficiency it is fundamental to give a vit. D suitable-to-the-case supplementation.

## 0814 | Epidemiology and risk factors for allergic conjunctivitis in adolescents

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**Background:** The ISAAC study (International Study of Asthma and Allergies in Childhood), assessed epidemiological data on the prevalence, severity and risk factors of allergic diseases, but it did not address to the epidemiology of allergic conjunctivitis.

**Method:** ISAAC written questionnaire added by specific allergic conjunctivitis questions previously validated (main instrument) was filled by adolescents 13-14y/o from Curitiba, Brazil. A representative group was submitted to skin prick tests (SPT) with a panel of regional aeroallergens and answered a supplementary questionnaire on family history, immunization status, infectious diseases, environmental conditions and diet.

**Results:** Four thousand, five hundred and twenty adolescents fulfilled the main instrument and the prevalence of asthma was 17.5%, medical diagnosis of asthma 13.2%, rhinitis 34.7%, rhinoconjunctivitis 20.1%, medical diagnosis of rhinitis 51.1%, atopic eczema 5.9%, medical diagnosis of eczema 13.2% and allergic conjunctivitis 15.5%. Four hundred seventy two were submitted to SPT, 121 (25.6%) had allergic rhinoconjunctivitis (ARC) and 232 (49.1%) had conjunctivitis. Thirty eight (32.2%) of ARC patients had asthma versus 13.1% in the non-ARC group ($P$ = 0.0003) and 17.3% had eczema versus 5.1% in the non-ARC group ($P$ = 0.0001). Male gender was a protection factor for ARC (OR= 0.42 95% CI 0.24 to 0.72). Boys with positive SPT to the mite *Blomia tropicalis* had OR= 5.1 (95% CI 1.43 to 18.24) for ARC. Subjects who were polysensitized had OR= 2.3 (95% CI 1.11 to 4.81) for ARC.

**Conclusion:** Allergic conjunctivitis is a prevalent medical condition in Curitiba. Boys had less ARC, except if sensitized to Blomia tropicalis.

## 0815 | Is the associated treatment with intranasal corticosteroids useful in the management of vernal kerato-conjunctivitis acute episodes?

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**Background:** Recent studies showed that the use of intranasal corticosteroids (INCS) relieves ocular allergic symptoms in acute and perennial forms.
Purpose of our study was to retrospectively assess the effect of the adjunctive treatment of INCS in seasonal forms of VKC associated with rhinitis.

**Method:** 83 children (57 males and 26 females, mean age 7.3 ± 5 months) affected by VKC and allergic rhinitis from more than 2 years were treated with mometasone furoate nasal spray 1 spray bid × 2 weeks in a month, for 3 consecutive months as a co-seasonal treatment at the beginning of eye allergic symptoms.
Other systemic or topical treatments did not vary compared to the previous 2 years.

**Results:** A quick questionnaire administered to children and their care-givers showed that nasal symptoms regressed after a mean period of 9.2 days from their beginning but, impressively, in more than 30% of them, these patients did not show a VKC typical relapse along the 3 months of mometasone treatment, moreover the following summer period was milder in subjective ocular symptoms in more than 25% of the patients.

**Conclusion:** Our experience pointed out that INCS adjunctive treatment was positively associated with a regression of eye and nose symptoms in children suffering from VKC, confirming previous literature data which concern milder forms (seasonal allergic conjunctivitis or allergic rhino-conjunctivitis) compared to the severe forms (like VKC) we analyzed in our work. One of the involved mechanisms of action can be the alleged effect on the reduction of substance P in tears; it is supposed to reflect the neuropeptides levels in ocular tissues.

## 0816 | Patient response to MP-AzeFlu in an allergen exposure chamber

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**Background:** Many patients with allergic rhinitis (AR) take multiple drugs to achieve symptom control, and medication efficacy and

onset of action (OOA) timing may impact treatment adherence. MP-AzeFlu, intranasal azelastine hydrochloride (AZE) and fluticasone propionate (FP) in a single device, has proven to have greater efficacy and faster OOA than a combination of oral loratadine and intranasal FP (LORA/INFP), but the clinical relevance for patients is unclear. This single-center (Ontario, Canada), randomized, double-blind, double-dummy, three-period crossover trial examined by which extent MP-AzeFlu provides clinically relevant symptom improvements according to different efficacy parameters.

**Method:** AR symptoms were induced in asymptomatic, ragweed-sensitive patients via ragweed pollen challenge in an environmental exposure chamber. Patients received a single dose of MP-AzeFlu, LORA/INFP, or placebo and were monitored for 4 hours. Symptoms were assessed using total nasal symptom score (TNSS) and total ocular symptom score. Responder analyses included the number of patients to achieve relevant response (RR) to therapy (30% or 50% reduction in TNSS), time to RR (ie, first time point at which RR was reached), and minimal clinically important difference (MCID) in OOA.

**Results:** Of the 82 patients in the full analysis set, 78 completed all treatments. Compared with LORA/INFP and placebo, ≥10% of subjects who received MP-AzeFlu achieved RR at the 5 minutes time point. Similarly, a significantly higher rate of change in the hazard ratio for both 30% RR and 50% RR was seen with MP-AzeFlu vs LORA/INFP ($P < 0.05$) or placebo ($P < 0.05$), while no difference in this regard could be seen between LORA/INFP and placebo. The median time to response of 50% symptom reduction was reached with MP-AzeFlu at about 30 minutes and with LORA/INFP and placebo at about 150-180 min. The difference in TNSS score points observed at 5 minutes after dosing between MP-AzeFlu and placebo (0.47) as well as between MP-AzeFlu and LORA/INFP (0.72) corresponded to a MCID.

**Conclusion:** MP-AzeFlu provides clinically relevant improvements in AR symptoms that are greater in magnitude and more rapid than LORA/INFP or placebo. MP-AzeFlu may be a preferable drug choice in patients who desire an early onset of symptom improvement.

## 0817 | Safety and reproducibility of nasal allergen provocation test

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**Background:** Nasal allergen provocation test (NAPT) is a standardized diagnostic tool indicated in the diagnosis of allergic rhinitis, to design and monitoring allergen immunotherapy, and to study the pathophysiology of airway allergy. Unfortunately, until now very few studies have evaluated its reproducibility and safety.

In this study we wanted to analyse the safety and reproducibility of NAPT in a large group of rhinitis patients and healthy controls.

**Method:** Retrospective study of all NAPT carried out in our Allergy Unit until December 2017. A bilateral saline challenge followed by a bilateral NAPT were performed in symptoms-free individuals. The response was assessed by nasal-ocular symptoms and acoustic rhinometry. All subjects signed a written informed consent.

The safety of NAPT was checked by the occurrence of extra-nasal/ocular reactions (ENOR), severe adverse events (SAE), and use of rescue medication (RM). ENOR was assessed by clinical symptoms, physical examination, cardiopulmonary auscultation, spirometry, and oxygen saturation. The reproducibility of NAPT was tested by comparison of the results in 2 or more sessions with≥1-month interval.

**Results:** We analysed 11256 NAPT carried out in 6160 subjects (32% male and 68% female) studied in our Allergy Unit from September 2005 to December 2017. A low rate of ENOR (0.04%), and use of RM (0.04%) was detected: 4 patients had mild-moderate uvula oedema, and 1 pharynx pruritus. Three patients required oral antihistamines, and 1 oral antihistamine+corticosteroid. No bronchospasm or SAE occurred. A high reproducibility of the NAPT was obtained (coefficient of correlation of 99.61%).

**Conclusion:** Nasal allergen provocation test has demonstrated to be a very safety and high reproducible diagnostic test that can be used in the clinical practice.

## 0818 | Efficacy of MP-AzeFlu versus fluticasone propionate and azelastine in patients with allergic rhinitis and nasal hyperreactivity: A post hoc analysis from three clinical trials

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**Background:** Nasal hyperreactivity (NHR) is self-reported by a majority of patients with allergic rhinitis (AR) and is likely mediated by neural-immune interactions. The combination of fluticasone propionate (FP) and azelastine (AZE) hydrochloride administered in a single spray (MP-AzeFlu) has been shown to be superior to FP or AZE alone in patients with seasonal AR (SAR). We hypothesize MP-AzeFlu may reduce neuro-immune mediators in AR with NHR. In a post hoc analysis of three pivotal studies of MP-AzeFlu, we analyzed the efficacy of MP-AzeFlu, FP, and AZE in patients with AR with and without nonallergic triggers.

**Method:** In three randomized, double-blind, controlled trials, patients with SAR were randomized 1:1:1:1 to MP-AzeFlu, FP, AZE,

or placebo (PBO). Patients self-reported sensitivity to nonallergic triggers. Change from baseline in total nasal symptom score (TNSS) and treatment differences between active agents and PBO were calculated.

**Results:** Across 3412 patients in three studies, mean age was 36.3 years and mean age at AR symptom onset was 15.6 years. Overall, 89% reported ≥1 nonallergic trigger, which included sudden temperature/humidity change (72%), tobacco smoke (61%), perfumes/fragrances (57%), incense/candles (38%), and cleaning products (38%). Change from baseline in TNSS for patients with AR and nonallergic triggers was greater with MP-AzeFlu than with FP or AZE (Table), and patients with nonallergic triggers improved slightly less than patients without nonallergic triggers in both the MP-AzeFlu and FP groups.

**Conclusion:** MP-AzeFlu is more effective than FP or AZE alone in reducing nasal symptoms among patients with AR and nonallergic triggers. This finding is consistent with recent studies showing improvement in NHR in AR with MP-AzeFlu vs PBO and reinforces MP-AzeFlu as preferred therapy for patients with AR and nonallergic triggers.

| | No Nonallergic Triggers (n = 366) | ≥1 Nonallergic Trigger (n = 3056) |
|---|---|---|
| MP-AzeFlu | 3.53 (0.22) | 2.33 (0.22) |
| Fluticasone propionate | 2.73 (0.33) | 1.51 (0.20) |
| Azelastine | 1.32 (0.26) | 1.39 (0.20) |

SE, standard error.

## 0819 | Serum osteopontin levels in children with allergic conjunctivitis

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**Background:** The pathogenesis of allergic conjunctival diseases (ACD) is not fully understood. Osteopontin (OPN) is a protein expressed during the inflammatory processes related to Th2 lymphocyte activity. It was demonstrated in previous studies that OPN plays role in asthma and response to venom immunotherapy. As far as we know, there is no other study regarding serum OPN levels in school-age patients with allergic conjunctivitis. In this study, we investigated the serum OPN levels in school-age children with simple allergic conjunctivitis.

**Method:** Patients aged between 6-16 years who were admitted to Bagcılar Training and Research Hospital Pediatric Ophthalmology outpatient clinic and were diagnosed with allergic conjunctivitis were included in the study. The children in the same age range who were admitted to the healthy child outpatient clinic of our hospital and had no symptoms of an allergic disease were included in the control group. The complete blood count parameters and osteopontin levels of the patients were studied.

**Results:** The average age of the patients with allergic conjunctivitis was 10.68 ± 3.07 years, 64.2% of them were female, and all patients had mite sensitivity. No statistically significant difference was observed between the osteopontin levels of the patients ($P > 0.05$). No correlation was found between the IgE levels and eosinophil count and OPN levels ($P > 0.05$).

**Conclusion:** We think there is a need for larger scale studies including patients with chronic and severe symptoms in which clinical symptoms and more parameters are evaluated to clarify the pathophysiological role of OPN in allergic conjunctival diseases.

SUNDAY, 27 MAY 2018
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## 0820 | The major birch pollen allergen Bet v 1a displays reduced allergenic potential with retinoic acid in the pocket

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**Background:** Bet v 1a represents the most typical allergen prototype. Its isoform Bet v 1d, however, is a hypoallergen despite of being structurally homologous. We hypothesized that the ligand-binding capacity of these lipocalin-like molecules could discriminate their level of allergenicity. We investigated thus whether the active vitamin A metabolite retinoic acid (RA) can bind to both isoforms, and how this affects their allergenicity *in vitro*.

**Method:** Binding of RA was determined by *in silico* docking analyses and ANS assay. Sera and PBMCs from BP-allergic donors were used to determine IgE (ELISA), ß-hexosaminidase release (RBL-cells) and cytokine production (ELISA) after stimulation with the "empty" birch pollen allergens (*apo*-Bet v 1a/d) or isoforms loaded with RA (*holo*-Bet v 1a/d).

**Results:** *In silico* calculations predicted a high affinity energy of RA to both isoforms, with an estimated dissociation constant of 0.364 μM. *In vitro* RA was able to dose-dependently displace ANS from both isoforms to a similar extent. In ELISA Bet v 1a loaded with RA (*holo*-Bet v 1a) showed significantly reduced binding of serum IgE compared to "empty" *apo*-Bet v 1a. In agreement, *holo*-Bet v 1a produced significantly less mediator release from RBL cells. In contrast, both *apo*- and *holo*- Bet v 1d displayed much lower IgE binding/crosslinking capacity. PBMCs from birch pollen allergic donors produced significantly less IFN-γ, IL-10 and IL-13 when stimulated with *holo*-Bet v 1a in comparison to high Th1/Th2 levels induced by *apo*-Bet v 1a.

**Conclusion:** Loading of RA into the intramolecular pocket of Bet v 1a reduces its IgE-binding and IgE-crosslinking potential together with its Th1/Th2 inducing abilities *in vitro*. Our data may have implications for improving the safety of birch pollen allergen immunotherapy.

## 0821 | IgE-Bet v 1 oligomer complexes are more efficiently presented to specific T cells via CD23 mediated FAP than IgE-Bet v 1 monomer complexes

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**Background:** CD23 is the low affinity receptor for IgE and belongs to the C-type lectin receptor family. CD23 is mainly expressed on B cells and is known to mediate facilitated antigen presentation (FAP). FAP is initiated by the binding of IgE-antigen complexes to CD23. Those complexes are endocytosed and processed, leading to the display of antigen peptides onto MHC II molecules and subsequent activation of specific T cells. IgE-antigen complexes have been shown to trigger specific T cell activation by CD23-mediated facilitated antigen presentation at 100-10000 lower concentrations than antigen alone. The density of CD23 has been shown to correlate with IgE-antigen uptake and specific T cell activation. Our aim is to study how different IgE-Bet v 1 complexes affect CD23-mediated FAP.

**Method:** Epstein Barr virus transformed human B cells (EBV B cells), expressing high levels of CD23 on their surface, were incubated with different concentrations and ratios of complexes consisting of chimeric Bip 1 IgE, which is specific for Bet v 1, and recombinant Bet v 1 in monomeric or oligomeric form. Primed EBV B cells were co-incubated with human Jurkat T cells expressing a specific TCR for the major peptide of Bet v 1 (142-153) and a luciferase reporter gene under the control of IL2 promotor. The release of luciferase indicated specific T cell activation.

**Results:** Equimolar concentrations of CB1 IgE-oligomer Bet v 1 complexes induced higher specific T cell activation when compared to CB1 IgE-Bet v 1 monomer complexes. Likewise 25 to 125 fold lower concentrations of CB1 IgE-Bet v 1 oligomer complexes were sufficient to induce specific T cell activation in comparison to CB1 IgE-Bet v 1 monomer complexes. Blocking of CD23 using anti-CD23 completely inhibited specific T cell activation triggered by IgE-Bet v 1 complexes, regardless of their composition.

**Conclusion:** IgE-Bet v 1 oligomer complexes trigger specific T cell activation more efficiently than IgE-Bet v 1 monomer complexes. The uptake of IgE-Bet v 1 complexes is solely mediated by CD23.

## 0822 | Sensitisation to cross-reactive carbohydrate determinants obscures true atopy, but shows no evidence of protection against allergy-related disease, in urban and rural Uganda

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**Background:** In low-income countries (LICs), assessment of phenotypes, prevalence and risk factors for allergy-related diseases (ARDs) using allergen-specific IgE may be complicated by environmental exposures such as helminths. These exposures may also induce cross-reactive carbohydrate-specific IgE profiles that could inhibit allergic effector responses. We sought to elucidate the molecular basis of IgE sensitisation among individuals in Uganda, using a component-resolved approach to IgE measurement.

**Method:** We employed the ISAC® allergen microarray to assess plasma IgE reactivity to 112 purified natural and recombinant allergen components in participants of three studies: a trial of intensive versus standard anthelminthic treatment in the rural helminth-endemic Lake Victoria islands (n = 126), a parallel urban survey of allergy outcomes in a lower helminth exposure community (n = 60) and a study on asthma risk factors in children from the urban setting and from nearby rural schools (n = 100). Data on sensitisation to crude allergen extracts were obtained by skin prick testing (SPT) with cockroach and house dust mites (HDM), and by ImmunoCAP IgE testing (cockroach, HDM, and peanut).

**Results:** The rural setting was characterised by high prevalence (≥34%) of sensitisation to crude extracts (ImmunoCAP IgE>0.35 kU/L) but low sensitisation to the major, established, allergenic components on the microarray (≤2%, IgE>0.30 ISU). However, sensitisation to cross-reactive carbohydrate determinant (CCD)-bearing components and venoms was more common in rural (up to 14%) versus urban (up to 8%) individuals, and was associated with helminth infection. Urban individuals mounted higher responses to allergenic components of dust mites but responses to other components were similar between the two settings. Sensitisation to allergenic components was higher among asthmatics and SPT+ children but CCD sensitisation profiles were similar between asthmatics and non-asthmatics, and between SPT+ and SPT- school children.

**Conclusion:** We show that, in LICs, IgE to crude allergen extracts (detected in standard ImmunoCAP assays) reflects sensitisation to a myriad of environmental exposures (absent in more developed countries), such as CCDs expressed by helminths, and may not accurately define ARD phenotypes in this setting. However, our data does not seem to indicate that CCD-specific IgE detected by ISAC® microarray protects against ARDs.

## 0824 | Fel d 1-specific human ige monoclonal antibodies with natural heavy and light chain pairing

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**Background:** Structural analysis of allergenic epitopes using complexes of allergen with antibodies requires monoclonal antibodies, but IgE is naturally polyclonal. The aim was to isolate human IgE monoclonal antibodies with natural pairing of heavy and light chain from patients allergic to cat for subsequent antigenic studies.

**Method:** Hybridomas expressing human IgE were obtained from electrical cytofusion of cultured human B cells from peripheral blood of three different allergic patients and a human myeloma cell line. The relative epitope specificity of the IgE mAbs expressed by these hybridomas was assessed by performing two-site ELISA using different combinations of IgE and/or murine IgG currently used to measure Fel d 1 levels (coating mAb 6F9 and detection biotinylated-mAb 3E4).

**Results:** Four hybridomas expressing high affinity Fel d 1-specific IgE were selected by screening with purified natural Fel d 1. The mAb IgE were 6A1 and 1B7—both from the same patient but with different sequences-, mAb 11A12 and mAb 15H7. The four mAb IgE bound to at least three different epitopes on the Fel d 1 surface. One epitope was for mAb 11A12 and the other two seemed to be in close proximity to the binding sites of the murine mAbs. ELISA results suggest that IgE mAb 6A1 overlaps with both IgG mAbs, while IgE mAbs 1B7 and 15H7, and IgG mAb 3E4 seemed to bind to an overlapping site. The area where most antibodies bound could be an immunodominant region of Fel d 1.

**Conclusion:** Four anti-Fel d 1 human IgE monoclonal antibodies with natural pairing of heavy and light chains were isolated by human hybridoma technology. These antibodies will facilitate structural analysis of antigenic determinants for the future design of hypoallergens for immunotherapy.

## 0825 | Polcalcin: calcium-binding requirement for allergenicity and cross-reactivity

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**Background:** Polcalcins constitute a family of calcium-binding plant allergens. They contain EF-hand motifs and their allergenicity is associated with the calcium-bound form of the protein, hence, they need the presence of calcium to be recognized by IgE. They have been identified in pollen from diverse plant families where they are

considered minor allergens. Due to their sequence homology and conserved structure, they show a high cross-reactivity. The objectives were to study the IgE/IgG binding properties of polcalcin in relation to the calcium ions, and the IgE cross-reactivity between purified polcalcin from *Olea europea* (Ole e 3) and two recombinant polcalcins (rPhl p 7 and rBet v 4).

**Method:** Ole e 3 was purified by immune-affinity chromatography using polyclonal antibodies anti-rChe a 3. Serum samples were obtained from 6 patients allergic to grasses recruited at Hospital de Guadalajara (Spain), all of them positive to Phl p 7 with sIgE values ranging from 12.1 to 92.6 kU/L. Equal volumes of all sera were used to prepare a pool. Calcium binding assay was performed either by addition or not, or depletion of $Ca^{2+}$. Ole e 3 was incubated with 0.1 mM $CaCl_2$ or with 1 mM EGTA pH 7.5 ($Ca^{2+}$ chelator agent) at the same time as the antibody in immunoblot or ELISA assays with the pool of sera or with anti-Che a 3 polyclonal antibody. Cross-reactivity assay was performed by ImmunoCAP inhibition. Aliquots of the pool of sera were previously incubated with amounts of Ole e 3 ranging from 0.02 to 12.5 ng. The same dilution of the pool of sera without Ole e 3 was used as a control. After 2 hours of incubation, sIgE (kU/L) binding to rBet v 4 or rPhl p 7 was determined.

**Results:** A 9 kDa protein was purified from the *O. europea* extract and identified by LC/MS-MS as Ole e 3. In the calcium binding assay there were no differences between the samples with or without $Ca^{2+}$. However, the addition of EGTA to the reaction completely inhibited the binding of the polyclonal antibody by immunoblot and also produced a 32.3% reduction of IgE binding by ELISA. In the cross-reactivity assay, a 50% inhibition of IgE binding was obtained with 2.8 ng of Ole e 3 for rBet v 4 and 3.9 ng for rPhl p 7. The maximum rate of achieved inhibition was 68.6% for rBet v 4 and 61.6% for rPhl p 7.

**Conclusion:** Native purified Ole e 3 contains the $Ca^{2+}$ necessary to bind to the specific antibodies and the depletion of $Ca^{2+}$ inhibited this binding.

High cross-reactivity of Ole e 3 with rPhl p 7 and rBet v 4 was demonstrated.

## 0826 | Effect of Glutathione-S-transferase pi on the cysteine protease activity of the house dust mite allergen Der p 1

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**Background:** Environmental proteases have been proposed to be involved in the pathogenesis of allergic disorders via different mechanisms, such as the disruption of epithelial tight junctions, the cleavage of surface proteins, the activation of damage and pathogen-associated molecular patterns receptors, and the alteration of redox status. Der p 1 from house dust mite is one of the most clinically relevant indoor allergens worldwide, which exhibits cysteine protease activity and has been linked to allergenic rhinitis and asthma. However, it is unknown whether the host microenvironment could regulate Der p 1 activity once it reaches the mucosal surface. Glutathione-S-transferase pi (GSTpi) is an anti-oxidant and detoxification enzyme. GSTpi is the predominant GST in human lung epithelial cells, where it is expressed in high levels. Polymorphic variants of GSTpi have been associated to various inflammatory lung disorders such as allergic asthma. More recently, GSTpi has been identified as a redox regulator through protein S-glutathionylation, a post-translational modification where glutathione (GSH) is conjugated to cysteine residues.

**Method:** This work aimed at determining if GSTpi affects the cysteine-protease activity of Der p 1, compared to GSTmu -a different GST isoform- by using different *in vitro* approaches.

**Results:** We found that GSTpi increased Der p 1-activity, but not GSTmu.

**Conclusion:** Our results suggested a potential role of GSTpi in upregulating the protease activity of Der p 1 allergen. However, the clinical implications of these findings in allergic airway diseases needs for further investigations.

## 0827 | Cari p 1, a novel polygalacturonase allergen from papaya acting as respiratory and food sensitizer

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**Background:** Papaya was globally reported to elicit IgE-mediated hypersensitivity. Certain papaya sensitive patients with food allergic symptoms were found to experience recurrent respiratory distresses at peak flowering period of papaya even after quitting the consumption of papaya fruits.

**Method:** The immunoreactive protein present both in pollen and fruit proteome was detected by IgE-serology and identified by mass spectrometry. One such allergen, designated as Cari p 1 was cloned, and purified as recombinant protein. The IgE-reactivity of rCari p 1 was examined by immunoblot using patient sera. The allergenic activity of rCari p 1 was evaluated by histamine release assay from IgE-sensitized granulocytes. The aggregation and folding pattern of rCari p 1 was assessed by size exclusion chromatography and circular dichroism spectroscopy respectively. The presence of Cari p 1 in papaya fruit was searched by IgG-immunoblot using allergen-specific rabbit antisera. A mouse model of papaya allergy was established to study the role of rCari p 1in eliciting respiratory and food hypersensitivity.

**Results:** A 55 kDa IgE reactive protein commonly present in pollen and fruit proteome of papaya was identified as endopolygalacturonase. Recombinant Cari p 1 remained monomer and the CD-spectra revealed predominantly β-sheet characters. The melting curve of the allergen showed partial refolding from a fully denatured state indicating the possible presence of conformational IgE-epitopes in addition to the linear IgE-epitopes of food allergens. 7 out of 7 papaya allergic patients displayed IgE reactivity to rCari p 1. rCari p 1 at 1 μg/mL, induced histamine release from challenged granulocytes within a range of 30% to 72% (i.e. 50 ± 9.2%; n = 4 patients). Expression of Cari p 1 was detected in the peel and pulp tissues of papaya fruits at two edible stages of fruit maturation. In mouse model, rCari p 1 exhibited a comparable level of eosinophil infiltration and goblet cell hyperplasia in lung and duodenum histology.

**Conclusion:** Cari p 1 the first major allergen reported from papaya with a dual role in respiratory sensitization via pollen inhalation and sensitization of gut mucosa via fruit consumption. The recombinant allergen can be used as marker allergen for molecular diagnosis and immunotherapeutic management of papaya allergy.

## 0828 | Developing Bla g 1 as a vehicle to test the influence of lipids in allergic sensitization

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**Background:** Lipids can be potent stimulators of the immune system, and their role in allergy is highly investigated and debated. Since many allergens bind lipids, one question that arises is the relative importance of the lipids versus the lipid-allergen complex in eliciting the immune response. Also of interest is an evaluation of the importance of the allergen-lipid complex. In our characterization of the structure of the cockroach allergen Bla g 1, we discovered that it could promiscuously bind a variety of lipids in a large central cavity. This suggested that Bla g 1 could be used as a prototypical allergen and lipid delivery vehicle to test in various models of sensitization.

**Method:** CD spectroscopy. NMR spectroscopy. Molecular modeling.

**Results:** We have developed an HPLC procedure to strip the phospholipids derived from the *E. coli*-based expression system, and reconstitute the allergen with a variety of lipids. Using CD spectroscopy and NMR, we have verified that the protein conformation is highly similar in the presence and absence of lipids. Temperature dependent CD spectroscopy revealed that unloaded Bla g 1 is the least stable, and the melting temperature increased with increasing fatty acid chain length up to C20. Similar CD melting experiments revealed that Bla g 1 could bind lipoteichoic acid (LTA) from Gram positive bacteria, but did not interact with lipopolysaccharide (LPS) from Gram negative bacteria. Molecular modeling studies have suggested that the stoichiometry of phospholipid binding is likely 4 phospholipids per Bla g 1 and give insight as to the different binding characteristics that would allow Bla g 1 to bind LTA but exclude LPS.

**Conclusion:** These biophysical studies will allow the design of Bla g 1-lipid systems to test a variety of sensitization models.

## 0829 | Sal k 7, a new allergen from Salsola kali

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**Background:** The polcalcin from *Salsola kali* was identified and sequenced (GenBank KT254655) and the recombinant protein was characterized as a minor allergen with a prevalence of 40% of patients with a SPT positive to *S. kali*. The objective of this study was to purify the polcalcin from *S. kali* pollen and to include the allergen in the website for the systematic allergen nomenclature (www.allergen.org).

**Method:** The native polcalcin from *S. kali* (nPSk) has been purified from pollen after a first step of protein extraction and then diverse chromatographic steps: a size exclusion chromatography to remove particles minor than 5 kDa, an ionic exchange chromatography, a hydrophobic interaction chromatography and a final step of size exclusion chromatography to obtain the purified sample of polcalcin. The purity of the nPSk has been determined by SDS-PAGE and the binding capacity to a specific polcalcin antibody from rabbit serum was tested by immunoblot. The specific antibody had previously been obtained by immunization with the recombinant polcalcin from *S. kali*. The allergenicity of the nPSk has been assayed by immunoblot with a pool of sera of patients sensitized to *S. kali*. The identity of the purified nPSk has been analyzed by peptide footprint in HPLC-MS/MS after digestion with trypsin. All the information about the polcalcin from *S. kali* was sent to WHO/IUIS Allergen Nomenclature Sub-Committee.

**Results:** The nPSk showed a high purity in SDS-PAGE with a molecular weight of approximately 9 kDa and this purified protein reacted with the specific polcalcin antibody from rabbit serum. The IgE binding capacity of the nPSk was confirmed by immunoblot using a pool of sera from patients sensitized to *S. kali*. The analysis of peptide footprint confirmed that the purified protein is a polcalcin. The WHO/IUIS Allergen Nomenclature Sub-committee included the polcalcin from *S. kali* in the website for the systematic allergen nomenclature as a new minor allergen named Sal k 7.

**Conclusion:** The polcalcin from *S. kali* has been purified from pollen and tested for its IgE binding. It is included in the website for the systematic allergen nomenclature as the new allergen Sal k 7.

## 0830 | Allergenicity resulting from functional mimicry of a Lipocalin 2

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**Background:** Alt a 1 protein is the major allergen from the fungus *Alternaria alternata* and responsible for chronic asthma, yet little is known about its physiological role and immunological activity. Our main purpose was to investigate the mechanism through which Alt a 1 induces an allergic response in bronchial epithelium.

**Method:** Although Alt a 1 has a unique topology, we studied the structural relationship by *in silico* procedures consisting of three distinct structural alignment methods in order to understand its nature. The immunological properties of the allergen were investigated by using monocyte cell line THP1 and human peripheral blood mononuclear cells.

**Results:** Its crystal structure has been recently reported and claimed to be exclusively in fungi without equivalent in the Protein Data Bank. Data obtained *in silico* show that this allergen shows some structural relationships with a number of other β-barrel proteins such as human lipocalin 2 (LCN2). Besides, our experimental data demonstrate that Alt a 1 is also able to interact with LCN2, human lipocalin. In this way, the results obtained from several immunological assays showed that Alt a 1 is able to produce a response of the immune system through different immune innate receptor pathway inducing the Th2 cytokines.

**Conclusion:** Results reported here are significantly relevant for elucidating the molecular mechanisms that lead to allergic sensitization to Alt a 1. Our findings help elucidate the molecular events that lead to the immune response to Alt a 1 and can be also of interest for the development of new immunotherapeutic strategies.

## 0831 | Cypress pollen/peach associated syndrome: Clinical exploration and in-depth biological characterization of a patient reactive to both species

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**Background:** Increasing evidence of cross reactivity syndromes between pollen grains and fruits, with immediate or delayed reactions, has been reported. While some syndromes such as the birch pollen/apple syndrome are well documented, some other such as the cypress pollen/peach syndrome remain to be understood. For the latter, significant progress has recently been made with the discovery of a new allergen family, the gibberellin regulated proteins (GRPs), which has been shown to be responsible for the observed cross reactivity *i.e.* Pru p 7 and BP14 (1, 2) for the peach and the cypress pollen respectively. GRPs are small cationic proteins with anti-microbial properties and have been shown to be over produced in response to a stress. Herein, the case of a patient, born and raised in the south of France but currently living in Paris, has been studied. This patient has been suffering since childhood from allergic rhinoconjunctivitis to cypress pollen and from some oral symptoms to peach and other fruits (including pomegranate).

**Method:** In addition to the clinical exploration and cutaneous tests, a very thorough biological characterization of the patient samples has been performed through various specific IgE quantitation techniques, western blotting after one and two-dimensional gel electrophoresis and flow cytometry based basophil activation testing (BAT).

**Results:** Specific IgEs to cypress pollen, birch pollen, peach, orange and apple have been found. PR10 allergenic proteins are recognized by IgEs but no LTPs. The presence of specific IgEs to cypress pollen BP14, peach peamaclein (Pru p 7) and a cationic 14 kDa protein from pomegranate has been shown through western blotting after gel electrophoresis separation of the protein extracts. The use of BAT finally enabled to demonstrate that the basophils of this patient were, *ex vivo*, strongly activated with protein extracted from orange and cypress pollen and also with purified proteins such as BP14 and Pru p 7.

**Conclusion:** These results unambiguously show that the cypress pollen GRP, BP14, is clinically relevant, similarly to its homologous protein in peach, Pru p 7. It can be proposed that these two allergens are at the basis of the observed cross-reactivity syndrome. The search for new cross-reactive allergenic GRPs in pollen, fruits or vegetables may enable to better understand other pollen/food associated syndromes that still remain unexplained.

**References:** 1. Sénéchal et al. *JACI* 2017.
2. Sénéchal et al. *Rev Fr Allergol* 2018.

## 0832 | Comparison of the immunological response produced by rPhl p 1 and rPhl p 5a

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**Background:** Nine allergens of *Phleum pratense* have been described until now (IUIS database) and classified into groups based on their function and cross-reactivity. Group 1 and 5 allergens are considered the most immunodominant, due both to their greater IgE-binding capacity and the number of patients IgE-reactive to them. Previously published studies have estimated that group 1 is recognized by almost 95% of grass pollen-allergic patients, and group 5 by 80%. However, until now a comparative of the ability of these allergens to provoke an immune response has not been performed. The objective was to study the immunogenicity of the major allergens Phl p 1 and Phl p 5, by analyzing the ability of the recombinant forms (rPhl p 1 and rPhl p 5a) to induce a humoral immune response.

**Method:** Five mice were immunized with the same amount of each recombinant protein: rPhl p 1 and rPhl p 5a (Indoor Biotechnologies) (60 μg plus two boosters of 30 μg). The specific IgG antibodies produced by each mouse were tested against the recombinant proteins by direct ELISA and the title of each of them was determined by optical density (O.D.). Additionally, the recognition of both allergens in native and depigmented-polymerized (Dpg-Pol) extracts of *P. pratense* was studied by direct ELISA using these generated antibodies.

**Results:** Preimmune sera were negative. All mice produced antibodies against the corresponding recombinant protein. The immune response (sIgG) was statistically significant higher in mice immunized with rPhl p 5 than in those immunized with rPhl p 1; it was needed 8 times more rPhl p 1 serum than rPhl p 5a serum to obtain the same O.D. values. The difference in responses was higher in the group of mice immunized with rPhl p 1 than with rPhl p 5a.

Differences in the recognition of Phl p1 and Phl p 5 in native and depigmented-polymerized extracts of *Phleum pratense* was also observed. It was necessary 8 times more rPhl p 1 serum to produce the same signal than rPhl p 5a serum in native extract and it was necessary 4 times more rPhl p 1 serum to produce the same signal than rPhl p 5a serum in Dpg-Pol extract.

**Conclusion:** rPhl p 5a is more immunogenic than rPhl p 1, which was also probed with native and Dpg-Pol extracts.

## 0833 | Delayed glioblastoma progression by repeated nasal instillations of house dust mite extract in a mouse model

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**Background:** Glioblastoma (GBM) is an incurable primary malignant brain tumour with a median life span of less than 15 months despite multimodal treatments. Therefore, there is a serious need for the development of innovative medications. Several epidemiological studies underlined an inverse correlation between pre-existing IgE-mediated allergy and GBM risk, where having such an allergy decreased the odds of developing GBM by 20 to 40%. We aim to delineate the intrinsic immuno-biological and molecular mechanisms that can be responsible for these correlations, based on the hypothesis that allergies may promote a state of increased immuno-surveillance in the brain through the presence of immunological factors such as immunoglobulins, cytokines and cells involved in Th2-driven allergic reactions. We consider that as the major immune cell type of the brain, microglia should be implicated in this beneficial association and may favour the elimination of the nascent tumour in brain parenchyma in an allergic context.

**Method:** We implemented a long term allergic airway inflammation by repeated nasal instillation of house dust mite (HDM) extract in a syngeneic orthotropic mouse model of GBM. We followed animal survival and the tumour growth by MRI. In addition, we purified microglia from allergic *vs* non-allergic mice in order to assess their cytotoxic function against the GBM cell line *ex vivo* and their secretory capacities. Finally, we investigated immunoglobulin reactivity against GBM antigens in the context of allergic reactions by reverse phase protein array (RPPA).

**Results:** We demonstrated an increase of the animal survival that was correlated with a delayed tumour engraftment and a reduced tumour growth. These phenotypes were associated with functional modification of microglia from sensitized mice. Indeed, these microglia showed a rise in the production of IL-6 and TNF-a as well as an increase in cytotoxic functions against a GBM cell line *ex vivo*. In parallel, we observed an increase in serum IgG1 reactivity against GBM antigens in mice sensitized with HDM compared to control mice.

**Conclusion:** These findings implicate microglia as a potential player favouring the anti-GBM effect conferred by the allergy state. Future investigations should delineate the molecular pathways and events by which the Th2-driven allergic reactions protect against GBM development, focusing on microglia in our murine model with the aim of developing more effective treatments in patients.

SUNDAY, 27 MAY 2018

TPS 13

COMMON PRIMARY IMMUNODEFICIENCIES AND MALIGNANT DISEASES

## 0834 | Safety and immunogenicity of post exposure rabies vaccination in children with primary immunodeficiency

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**Background:** Rabies is a serious public health problem since it is fatal. Intravenous immunoglobulin (IVIG) does not provide protective rabies antibody levels. This puts patients with primary immunodeficiency disorders (PID) at risk when expose to rabies. Our study aimed to evaluate the immunogenicity, dynamic antibody responses and safety of rabies vaccine in PID patients.

**Method:** We evaluated antibody response to rabies vaccine in PID patients, compared to age and sex-matched controls. All subjects received five doses standard intramuscular regimen of rabies vaccine and 2 booster doses three days apart at one year later. Serum rabies neutralizing antibody titers were measured at day 0,14,28,90,180,360,367 and 374 after vaccination. An acceptable protective lever is>0.5 IU/mL.

**Results:** Thirteen PID patients and 13 healthy children were included. Median age of patients and controls were 7.8 (2.2-20.8) and 8 (2.6-20.2) years respectively. Baseline rabies neutralizing antibody in patients was lower than protective levels. After immunization, the titers were significantly lower in patients than controls at all time points. Seventy percent of PID patients (9/13), except X-linked agammaglobulinemia and common variable immunodeficiency disorders (CVID), could produce rabies neutralizing antibody higher than the protective level at day 14 and 28. At day 180 all controls retained protective levels while the titers declined to less than 0.5 IU/mL in 60% of PID patients (5/12). Only 3 patients with combined immune deficiency disorders could maintain protective antibody levels at one year. Half of the patients who received booster dose were able to produce adequate antibody response. Serious side effects were not reported in both groups.

**Conclusion:** Five doses regimen of rabies virus vaccination is safe and able to induce rabies specific antibody in most PID patients. However, less than half of the patients can maintain protective antibody levels. A follow up titer and booster dose is important to ensure long lasting protection.

## 0835 | The evaluation of prognosis in pediatric patients with common variable immunodeficiency

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**Background:** Common Variable Immunodeficiency (CVID); is a primary immunodeficiency which has different clinical and immunologic phenotypes, characterized by hypogammaglobulinemia, recurrent sinopulmonary infections and impaired antibody response towards vaccines and pathogens. The majority of cases are sporadic, but from 5% to 25% of patients have a family history. Following up these patients may develop morbidities such as lymphoid malignancies, autoimmune diseases, granulomatous diseases. The aim of our study is to evaluate the prognosis of patients with CVID.

**Method:** In our study, CVID-diagnosed patients' age, gender, duration of follow-up, parental consanguinity, family history of immunodeficiency, morbidity (such as malignancy, autoimmune disease), and mortality were recorded from the files of the patients.

**Results:** Forty-six patients with CVID were evaluated in our study. The median (Interquartile range-IQR) age of the patients were 15.7 (9.77-21.12) years, and 56.5% (n = 26) were female. The duration of following up was median (IQR: 5.25 (3.37-11.25) years. 41.3% of patients (n = 19) had parental consanguinity. The follow-up period of the patients was median (IQR): 5.25 (3.37-11.25) years. Parental consanguinity was present in 41.3% (n = 19) of the patients. 13% of the patients (n = 6) had immunodeficiency in the family. In the follow-up of the patients 34.7% (n = 16) had autoimmune disease, 41.3% (n = 19) had lung pathology, 8.7% (n = 4) had chronic inflammatory bowel disease, 21.7% (n = 10) had allergic disease, 13% (n = 6) had malignant diseases. The number of patients who developed mortality was 4 (8.7%).

**Conclusion:** As seen in our study, various morbidities and mortality can be developed in CVID-diagnosed patients. Therefore, it is important that patients are closely monitored and regularly evaluated in terms of autoimmune disease and malignancy development.

## 0836 | A mild thrombocyte number decrease is frequent in common variable immunodeficiency

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**Background:** Common variable immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by decreased IgG, IgA and variable IgM levels accompanied with impaired antibody response after specific antigen challenge. Besides a proneness to bacterial infections a variety of non-infectious complications appear in patients with CVID, including autoimmune disorders. Although severe decrease in thrombocyte count in patients with CVID is supposed to be of autoimmune origin, little is known about frequency of mild thrombocytopenia in these patients. On the contrary non-infectious complications are less common in patients with X-linked agammaglobulinemia (XLA). The goal of this study was to determine frequency and severity of decreases in thrombocyte numbers in patients with CVID.

**Method:** We performed a retrospective analysis of medical records of 46 patients with CVID (28 females, 18 males, aged 22-78 years) and 10 patients with XLA (aged 10-50 years) in the follow-up period of 12 years. Blood count was routinely investigated at least every 6 months. All patients were treated with either intravenous or subcutaneous immunoglobulin replacement therapy with minimal duration of 3 years. Fisher's exact test was used for evaluation of statistical significance.

**Results:** In 23 patients (48%) with CVID we recorded at least one temporary platelet count decrease below $150 \times 10^9$/L compared to only 1 patient (10%) with XLA ($P = 0.024$). More importantly in 18 patients (38%) with CVID this decrease was observed in a period longer than 6 months compared to 1 patient (10%) with XLA ($P = 0.077$). In 10 patients (21%) with CVID we recorded at least one temporary platelet count decrease below $100 \times 10^9$/L and only in 3 patients (6.5%) with CVID this decrease was observed in a period longer than 6 months. We did not record any platelet count decrease bellow $100 \times 10^9$/L in patients with XLA however the difference with CVID did not reach statistical significance. No thrombocyte count decrease bellow $50 \times 10^9$/L was observed in either group. None of patients required immunosuppressive treatment for immune thrombocytopenia (ITP).

**Conclusion:** Although the statistical significance was documented only in temporary platelet count decrease below $150 \times 10^9$/L it is obvious that numbers of thrombocytes commonly fluctuate in some patients with CVID. The mechanism leading to these temporary decreases is unclear. Monitoring of complete blood count is a basic follow-up investigation in patients with CVID.

## 0837 | The clinical and immunologic features of patients with Immunoglobulin A deficiency: A tertiary center experience from Turkey

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**Background:** Immunoglobulin A deficiency (IgAD) is the most common predominantly antibody deficiency, with a wide range of presentations from asymptomatic to severe manifestations. We aim to investigate clinical and immunological findings of IgAD patients.

**Method:** Retrospective analysis of the clinical and laboratory records of symptomatic pediatric IgAD patients diagnosed between 2004 and 2017 in our clinic was performed. Based on clinical manifestations of patients and various immune abnormalities associated with IgAD, patients divided into four different groups including minor infectious, allergic, autoimmune and severe phenotype which has severe infections and evolve into common variable immunodeficiency after diagnosis. Each patient group is also divided by age: 4-6 years, 7-13 years and 14-18 years.

**Results:** A total of 54 patients were included in this study. 55.5% (n:30) were boys and 44.6% (n:24) were girls. 68.5% (n:37) of the cases were diagnosed before the age of 7. The dominant manifestation at the time of diagnosis was infectious manifestations. Out of 54 patients, we found 33 (61.1%) patients with allergic diseases, 28 (51.8%) patients with minor infections, 8 (14.8%) patients with autoimmune diseases and 12 (22.2%) patients with severe phenotype. 5 patients had bronchiectasis,2 patients had nervous system infections (meningitis and encephalitis), 2 patients had cyst hydatids in lung and liver and 4 patients progressed to CVID. Regarding the family history, parental consanguinity rate was 16.6% (n:9) and we identified 4 families with multiple cases of PIDs. Allergy clinical phenotype (n:25) and severe forms (n:7) tended to present at early ages (before <7 years old) while minor infections (n:15) and autoimmunity phenotypes (n:6) tended to present at older ages. (after >6 years old).

**Conclusion:** Based on different clinical phenotypes and associated varieties in immunological abnormalities of patients with IgA deficiency, IgAD still presents a challenge for clinicians and researchers. Therefore, classifying them into clinical and immunological phenotypes may help us in appropriate management and treatment as well as in better monitoring for the future complications.

## 0839 | A rare coexistence: Immune Deficiency and Wegener's granulomatosis

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**Introduction:** Wegener's granulomatosis (WG) is a systemic disease that may affect all organs, most frequently the ears, noses, throats, sinuses, lungs and kidneys. It is a rare autoimmune disease, also called granulomatosis with polyangiitis, and characterized by necrotizing granulomatous inflammation in small and medium sized blood vessels. Anti-neutrophil cytoplasmic antibody against to proteinase 3(c-ANCA) is thought to be responsible for autoimmune inflammation. The coexistence of WG and common variable immunodeficiency (CVID) is extremely rare. In this report, we describe a patient with WG and CVID who was treated with immunosuppressive drugs and intravenous immunoglobin concomitantly.

**Case report:** A twenty-four-year-old male patient was referred to our clinic for immunological evaluation due to recurrent infections, fever of unknown origin and neutropenia. The patient had been diagnosed with WG and taking immunosuppressive therapy for three years. He had chronic renal failure due to WG and had also been on peritoneal dialysis for three years. Serum IgG, IgA levels, peripheral blood CD19 + B cell percentage and absolute count of the patients were found to be low according to reference limits. He was diagnosed with CVID after excluding secondary reasons for hypogammaglobulinemia and he started to receive 600 mg/kg intravenous immunoglobulin (IVIG) therapy once in a month. Also, the treatment that consists of mycophenolate mofetil (MMF) and glucocorticoids was continued to decrease c-ANCA levels in serum. He has been accepted as a candidate for kidney transplantation, and prepare for this purpose.

**Discussion:** The management of the patient with CVID and WG may be complicated. It is considerably difficult and needs competency and courage. Moreover, the cases similar to ours, are extremely rare. Therefore, the authors should share their own experiences on CVID and discuss them by comparing the data obtained from other cases.

**Key words:** Wegener's granulomatosis, Immune Deficiency, intravenous immunoglobulin.

## 0840 | Atypical hereditary angioedema?

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**Background:** Hereditary angioedema is a rare autosomal dominant disease. The main clinical feature is angioedema in different localizations.

**Method:** In 43-year old woman with clinical history of recurrent angioedema (including laryngeal attacks) levels of C4, C1INH and C1INH function were examined. Also genetic testing was performed.

**Results:** The levels of C4 and C1INH were repeatedly normal (C4 0.24 - 0.27 g/L, C1INH 0.23- 0.25 g/L), but the C1INH function was reduced in 3 out of 4 results (23-48-92-3%). Decreased results of C1INH function were detected in the presence of the clinical signs of angioedema, however the normal C1INH function was detected in asymptomatic period. Genetic testing showed an unknown mutation for the C1INH gene (mutation cDNA c.248C> G, protein p.Thr83Ser, 3.exon-missense, ref.sequence NM_001032295). The same mutation was found in 3 of 4 family members. One of them has a recurrent abdominal disorder.

**Conclusion:** In our opinion, despite of atypical laboratory results, this patient has atypical hereditary angioedema mediated by C1INH dysfunction.

## 0841 | Evaluation of patients with leukocyte adhesion deficiency, single center experience

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**Background:** Leukocyte adhesion deficiencies (LADs) are a group of three genetic disorders leading to defective leukocyte adhesion to the endothelium and as a consequence decreased leukocyte recruitment and immune defense. LAD-I is caused by mutations in the gene encoding the ß2-integrin CD18 on chromosome 21.LAD-III is a rare primary immunodeficiency syndrome, characterized by homozygous mutations in the KINDLIN-3 gene (official symbol FERMT3). We have aimed to evaluate our patients who were followed up with LAD for the last 15 years, retrospectively.

**Method:** All data of the cases were obtained from the file records of age at diagnosis.

**Results:** Seven patients from separate 6 families were included in the study. Four patients were LAD-III and 3 patients were LAD-I. The female to male rate was 2/5. The age of diagnosis is ranged from 16 days to 4 years. The median umbilical cord detachment was 21 days (7 - 53 days). All patients were the product of consanguineous marriage. Growth pattern was normal in all patients except one. Recurrent severe infections and hepatosplenomegaly were

| | Family 1 | | Family 2 | Family 3 | Family 4 | Family 5 | Family 6 |
|---|---|---|---|---|---|---|---|
| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Patient 7 |
| LAD subgroups | III | III | III | III | I | I | I |
| Parental consanguinity | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Ethnic origin | Turkish | Turkish | Turkish | Turkish | Turkish | Turkish | Arab |
| Age at onset | 1 day | 1 month | 1 day | 1 week | 6 day | 10. day | 1. month |
| Age at diagnosis | 15 months | 1.7 years | 2 months | 7 months | 16. day | 4. years | 4. months |
| Bleeding disorder | Severe | Severe | Severe | Severe | No | No | No |
| Umbilical cord detachment (day) | 20 | 20 | 26 | 7 | 53 | 30 | 21 |
| Neurological defect | Motor retardation | Mild motor retardation | Convulsion, Motor retardation | Seizures, Developmental delay, Motor retardation | No | Mild mental retardation | No |
| **Laboratory data (earliest recorded)** | | | | | | | |
| Hb (g/dl) | 8.70 | 9.90 | 9.90 | 7.30 | 8.7 | 9.4 | 9.7 |
| Plt ($\times 10^9$/L) | 191 | 281 | 115 | 244 | 297 | 366 | 427 |
| WBC ($\times 10^9$/L) | 50.4 | 34.1 | 38.9 | 75.7 | 48 | 55 | 33.7 |
| Ne % (count/mm$^3$) | 40 (20160) | 54 (18414) | 22 (8558) | 44 (33308) | No data | 89.2 (49060) | 42.7 (14390) |
| Ly % (count/mm$^3$) | 50 (25200) | 30 (10230) | 58 (22562) | 46 (34822) | No data | 5 (2750) | 48.8 (16445) |
| Mo % (count/mm$^3$) | 10 (5400) | 12 (4092) | 16 (6224) | 10 (7570) | No data | 5.5 (3025) | 6.4 (2156) |
| HSC transplant | No | No | Yes | No | No | No | No |
| Platelet aggregation response to ADP, epinephrine, and collagen | ND | Decreased | Decreased | Decreased | No data | No data | No data |
| **Lymphocyte subsets %,** | | | | | | | |
| CD3 | 35 | 37 | 53 | 51 | 82 | 76.90 | 61.8 |
| CD19 | 36 | 38 | 16 | 25 | 7 | 13.50 | 30.4 |
| CD4 | 23.5 | 22 | 29 | 21.7 | 56 | 46.60 | 45.4 |
| CD8 | 9.7 | 12 | 22 | 23.2 | 26 | 26 | 14.6 |
| CD16 + Cd56 | 17.2 | 6.5 | 27 | 10.30 | 13.40 | 6.60 | 6.6 |
| **Neutrophil gate (%)** | | | | | | | |
| CD18 | 98.4 | 99.7 | 97.3 | 97.5 | 0.18 | 19.40 | 2.9 |
| CD11a | 99 | 99.8 | 99.5 | 99.9 | 0.3 | 1.80 | 2.8 |
| Genetic defect | Kindlin-3 | Kindlin-3 | Kindlin-3 | Kindlin-3 | ITGB2 | ITGB2 | ITGB2 |
| Outcome | Died at 15 months | Died at 8 months | Died at 7 months | Died at 1.5 years | Died at 8 months | Alive | Alive |
| Cause of death | Massive pulmonary hemorrhage | Pulmonary hemorrhage | Bacterial and fungal sepsis | Massive pulmonary hemorrhage | Meningitis | | |

LAD, Leukocyte adhesion deficiency; HSC, hematopoietic stem cell; ND, non diagnostic.

detected in all patients. However, bleeding tendency and increased bone density were only in LAD-III patients. Five of all patients died due to severe bleeding or infection. Clinical and laboratory data of our LAD patients were summarized in Table 1.

**Conclusion:** Children who have a 'delayed' umbilical cord separation should be evaluated for the possibility of a neutrophil disorder, especially if there are clinical indications of LAD. The diagnosis of LAD requires high index of suspicion in a child with history of delayed umbilical cord separation, repeated infections and marked leukocytosis. Additionally, patients with osteopetrosis and bleeding tendencies should be evaluated for LAD-III.

## 0842 | Registry and biobank establishment of inflammatory bowel disease suspected to primary immunodeficiency diseases for the first time in Iran and as a partner of international campaign

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**Background:** Alterations in intestinal microbes and the immune system are mentioned as the inflammatory bowel diseases (IBD) pathogenesis, suggesting that IBD might be an immunodeficiency rather than an excessive inflammatory reaction. IBD, suspected to primary immunodeficiency diseases (IBDSPID) registry and biobank can support an extensive range of research intended to improve the prevention, diagnosis, and treatment of the illness.

**Methods:** Among 365 IBD patients, 39 were enrolled to our study. The inclusion criteria were:

IBD diagnosis before 5 year of age, resistance to conventional therapy, severe IBD, positive past history for warning signs of primary immunodeficiencies, history of other autoimmune disorders.

DNA, RNA and cDNA were extracted from whole-blood and saved as IIRC biobank and also have been sent for further genetic evaluations to our collaborative research center working on PID and IBD as part of international campaign. Achieved data was computerized using the MySQL Database.

**Results:** The mean age was 32.92 ± 15.90 years old and 51.3% were males. The Ulcerative colitis (79.5%) was the most common type. 50% of patients had severe IBD. Age of onset was more than 17 years old in 65.8% of patients. Resistance to drugs and consanguinity were in 12.9% and 47.4%. 33.3%, 33.3%, 10.3% of patients had history of autoimmunity, allergy, and PID and the family history of IBD, autoimmune disease, allergy, PID and malignancy was in 15.4%, 25.7%, 28.2%, 2.6% and 20.5% respectively. The genetic evaluation of the cases with novel findings is continued.

**Conclusion:** The IBDSPID biobank and registry in our region provides useful data that could be valuable for future genetic and molecular study to find out more about the relation between IBD and PID and increase the awareness about this disease for determination the prevalence, early diagnosis and effective treatment.

## 0845 | The nature of changes in the factors of the innate and adaptive immune response in various variants of the course of hereditary angioedema

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**Background:** The clinical manifestation of the hereditary defect C-1 inhibitor (C1-INH) is shown by the formation of edema due to a violation of the kallikrein-kinin system and the accumulation of bradykinin. At the same time, the C1-INH is a participant of the interaction of innate and adaptive immunity. The purpose of the study is to analyze the functional activity of the immune system of patients with type I of hereditary angioedema (HAE) with according to the frequency of edema formation.

**Method:** 12 patients (38.8 ± 18.6 years, men 6, women 6) with type I HAE were examined. The clinical manifestation of the disease was shown by edema of different localization. According to the frequency of edema within one year, all patients were divided into 2 groups: up to 6 times (6 people) and from 6 to 12 times (6 people). 10 healthy donors were examined as a control. Flow cytofluorometry method was used to study peripheral blood and assess the parameters of innate and adaptive immunity

**Results:** It was found that at a frequency of edema up to 6 times a year there are changes in the T-system of adaptive immunity, which are shown by a decrease in the expression of late activation markers (CD3 + HLADR+ 3.46 ± 0.60%, in control 8.04 ± 0.14%), an increase in the number of CD3 + CD8 + cytotoxic lymphocytes (0.60 ± 0.17x$10^9$/L, in control 0.39 ± 0.01x$10^9$/L) and as an increase in their functional activity (CD8 + Gr+ 0.53 ± 0.02x$10^9$/L, in control 0.16 ± 0.01x$10^9$/L). The nature of disorders of cellular factors of the innate immunity is manifested by decrease in the adaptive resources of neutrophils (KstNBT 1.62 ± 0.13u.e., in control 2.15 ± 0.02u.e.). Patients with HAE with a frequency of edema up to 12 times a year, we observed the disorders of the humoral link of adaptive immunity, which consist in an increase in the number of circulating B lymphocytes (0.27 ± 0.11x$10^9$/L, in control 0.11 ± 0.01x$10^9$/L). In addition, with the strengthening of the HAE clinic, changes in the system of innate immunity progressed very fast and consisted in increasing the amount (CD16 + 0.37 ± 0.05x$10^9$/L, in control 0.21 ± 0.01x$10^9$/L), and functional activity (CD16 + Gr+ 0.32 ± 0.16x$10^9$/L, in control 0.14 ± 0.0210$^9$/L) of natural killer cells

**Conclusion:** Defect C1-INH leads to changes in the functional properties of other factors of innate and adaptive immunity. The criteria associated with the frequency of swelling manifestation are the indicators of functions of effector lymphocytes of the adaptive and innate immune response.

## 0846 | Lymphocyte subpopulations in patients with suspicion of primary immunodeficiency from the Peruvian National Institute of Child Health

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**Background:** Primary immunodeficiencies represent a group of congenital diseases secondary to alterations in the immune response. In Latin America, social and economic problems do not allow the development of specialized laboratories to complete the diagnostic tests that are fundamental for the specific diagnosis of PID, such as flow cytometry, TREC / KREC analysis and mutational genetic analysis. The objective of the present study was to describe the lymphocyte population count by means of flow cytometry in Peruvian patients with clinical suspicion of primary immunodeficiencies having been performed in the first laboratory specialized in the diagnosis of PID in Peru.

**Method:** A review of the records of flow cytometry results of patients with suspected primary immunodeficiencies to which their treating physician indicated the test was made. The determination of subpopulations of lymphocyte cells was established from the results of flow cytometry. A descriptive analysis was performed using SPSS V.20.0.

**Results:** We included 261 children, mostly males (54%), aged between 1 month and 16 years. 37.5% of patients (n = 98/261) showed abnormal absolute results of lymphocyte count for age. We found more patients evaluated in the age group of 2 to 5 years (31.8%), followed by 5-10 years (24.5%), Lymphopenia was found in 15.4% of patients. B lymphocyte deficiency was the most common pattern (37%) followed, in decreasing order, by low CD4, T CD3, TCD8 and NK. Many patients have more than one affected population (12.6%). Some patients were affected in all three series (4.2%). The CD4 / CD8 ratio decreased in 28.7% of the patients.

**Conclusion:** The majority of the children were males between the ages of 1 month and 16 years. 37.5% of patients showed abnormal absolute lymphocyte count for age. B-cell deficiency was the most common pattern followed, in decreasing order, by low CD4, T CD3, TCD8 and NK. Many patients have more than one affected population.

## 0847 | Indicators of the humoral immunity in the mechanical jaundice of benign genesis

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**Background:** Mechanical jaundice (MJ) of benign genesis is a serious condition caused by the appearance of an obstruction for the outflow of bile to the duodenum, as a result of benign diseases of the gastrointestinal tract. The resulting cholestasis, hypertension in the bile ducts, acholia lead to the development of severe functional and morphological changes in the liver and a rapid increase in liver failure. Multiple pathogenetic features of the disease contribute to the development of the dysregulation of many body systems.

Table 1. Sex and lymphocyte subpopulation median according to age group in patients with PID suspicion

| | Age group | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1w-2 m | 3-5 m | 5-8 m | 9-15 m | 15-24 m | 2-5 y | 5-10 y | 10-16 y | Total |
| Sex no. (%) | | | | | | | | | |
| Male | 1 (0.4) | 4 (1.5) | 9 (3.4) | 11 (4.2) | 13 (5) | 49 (18.8) | 35 (13.4) | 19 (7.3) | 141 (54) |
| Female | 2 (0.8) | 5 (1.9) | 13 (5) | 11 (4.2) | 11 (4.2) | 34 (13) | 29 (11.1) | 15 (5.7) | 120 (46) |
| Total | 3 (1.1) | 9 (3.4) | 22 (8.4) | 22 (8.4) | 24 (9.2) | 83 (31.8) | 64 (24.5) | 34 (13) | 261 (100) |
| Lymphocyte subpopulation median | | | | | | | | | |
| T CD3 | 3270 | 3320 | 2756 | 2971 | 2898 | 2449 | 2243 | 1465 | 2482 |
| T CD3 + CD4+ | 1792 | 1934 | 1562 | 1469 | 1491 | 1353 | 1032 | 870 | 1267 |
| T CD3 + CD8+ | 1315 | 1279 | 824 | 1319 | 1049 | 939 | 817 | 666 | 921 |
| CD4/CD8 ratio | 1.74 | 1.5 | 2.15 | 1.29 | 1.51 | 1.35 | 1.23 | 1.42 | 1.4 |
| B CD19+ | 1400 | 1394 | 847 | 1259 | 1048 | 966 | 417 | 229 | 661 |
| NK CD16/56+ | 331 | 386 | 325 | 387 | 411 | 350 | 277 | 223 | 310 |
| Total lymphocytes | 4783 | 5210 | 3647 | 4369 | 4430 | 4145 | 3154 | 2153 | 3720 |
| Total leucocytes | 10 034 | 9895 | 9876 | 9136 | 9329 | 8918 | 8647 | 7004 | 8816 |

PID, primary immunodeficiency; w, week; m, months; y, years.

The aim of the investigation was to study the indices of humoral immunity in patients with benign MJ, depending on the level of bilirubin.

**Method:** 62 patients with MJ and 125 practically healthy volunteers were examined. Patients with a level of bilirubin less than 60 μmol / l - 9, with a bilirubin level of 60-200 μmol / l - 37 and with a bilirubin level of more than 200 μmol / l - 16 patients. The concentration of immunoglobulin classes A, M, E and G in serum was determined by enzyme immunoassay. The statistical significance of the differences was determined using the ranked Mann-Whitney test. The critical level of significance in checking statistical hypotheses was assumed to be $P < 0.05$.

**Results:** In patients with MJ of benign origin with a level of bilirubin in the blood of less than 60 μmol / l, the IgE content was increased and the indicators of IgA, IgM, IgG were decreased, in patients with a level of bilirubin in the blood 60-200 μmol / l the content of IgA, IgM, IgG, IgE was increased, in patients with a level of bilirubin in the blood of more than 200 μmol / l IgG, IgE values were increased and IgA, IgM were lower compared to the control group.

**Conclusion:** Multidirectional changes in the content of immunoglobulins indicate the failure of the humoral immunity in MJ of benign genesis, depending on the level of bilirubinemia.

## 0848 | Peculiarities of chemiluminescent activity of neutrophiles in mechanical jaundice of malignant genesis

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**Background:** Mechanical jaundice of malignant genesis (MJ) is a pathological syndrome consisting of a violation of the outflow of hepatic bile through the bile ducts to the duodenum due to mechanical obstructions of malignant genesis. The prognosis of the disease depends on the severity of MJ, the level of bilirubinemia, hypoproteinemia, complications, infectious and tumor factors. An unfavorable factor is the development of local and systemic inflammation. Neutrophils (NG) are nonspecific phagocytes, the first to eliminate the infectious agents in the affected area.

The purpose of this research was to study the characteristics of the chemiluminescent activity of neutrophils in MJ of malignant genesis, depending on the level of bilirubin.

**Method:** 42 patients with MJ and 125 practically healthy volunteers were examined. Patients with a level of bilirubin less than 60 μmol / l - 5, with a bilirubin level of 60-200 μmol / l - 20 and with a bilirubin level of more than 200 μmol / l - 17 patients. As a method for studying the activity of NG, chemiluminescence analysis of spontaneous and induced production of reactive oxygen species of NG on a biochemiluminescent analyzer CL3606 was used. The time of the curve yield to the maximum of the chemiluminescence intensity (Tmax), the maximum value of the chemiluminescence intensity (Imax), and the area of the chemiluminescence curve (S) were determined. The statistical significance of the differences was determined using the ranked Mann-Whitney test. The critical level of significance in checking statistical hypotheses was assumed to be $P < 0.05$.

**Results:** In the group of patients with MJ of malignant genesis, regardless of the level of bilirubin, the parameters of the time to the maximum of spontaneous and induced emission, the area under the spontaneous and induced luminescence curves and the activation index were increased, the intensity of spontaneous and induced luminescence was reduced in comparison with the control group.

**Conclusion:** The chemiluminescence activity of neutrophils, in particular, and their function, in general, is reduced in all patients with malignant MJ, which confirms the toxicity of bilirubin at any concentration and tumor influence to the cells of the immune system.

## 0849 | Microcrystalline tyrosine (MCT), a promising depot adjuvant for effective T cell responses in virus-like particle-based vaccines in murine melanoma models

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**Background:** Enhancing the immunogenicity of T cell vaccines without compromising their tolerability and safety is an inherent dilemma for vaccine development. The prolonged presence of antigens for effective T cell activation can be achieved by using depot adjuvants such as aluminium hydroxide. However, it is still unclear whether aluminium hydroxide (Alum) adjuvants can effectively stimulate cytotoxic T cell (CTL) responses as research suggests that Alum preferentially induces type 2 immunity, which may not be favorable for induction of CTLs. Microcrystalline tyrosine (MCT) is a depot adjuvant that has been used in licensed products and subject to further clinical development in allergy immunotherapy. Combining MCT with target antigen facilitates the slow release of the antigens while MCT particles are metabolised and cleared from the body. The current project aims to study the efficacy of MCT when combined with virus-like particle (VLP) based vaccines for effective T cell responses in murine melanoma models and to compare its efficacy to the widely used aluminium hydroxide adjuvants.

**Method:** Vaccines were generated using recently described cucumber mosaic virus derived VLPs coupled to the p33 CTL epitope from

LCMV as a model antigen, using bio-orthogonal Cu-free click chemistry. The developed vaccine was formulated with MCT or Alum to test their efficacy at inducing specific T cell response *in vivo* in murine models bearing B16F10 melanoma tumors. The kinetics of drainage of VLPs formulated with MCT adjuvants was also studied using stereomicroscopic imaging.

**Results:** Our results show a superior ability of VLPs formulated with MCT at inducing p33 specific T cell response compared to VLPs formulated with Alum. Frequency of $CD8^+$ IFN-$g^+$ cells were significantly increased when combining the VLP-p33 vaccine with MCT compared to Alum. The stereomicroscopic imaging of the drainage of VLPs when formulated with MCT was significantly delayed when compared to free VLPs, demonstrating a depot effect. Experiments in tumor bearing mice are ongoing.

**Conclusion:** MCT is a promising depot adjuvant which enhances CTL responses in murine models. P33 specific T cell response and the production of IFN-γ were significantly enhanced when formulating VLPs with MCT.

## 0850 | Delay diagnosis of ataxia-telangiectasia in a 13-year-old girl presenting as Cerebral Palsy and Hodgkin lymphoma

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**Methods:** A 13-year-old girl with history of Hodgkin lymphoma from 6 months before consultation was consulted to the allergy and clinical immunology department for tachypnea and cough. She was the third child of consanguineous parents, with 2 healthy siblings. She had a history of recurrent sinusitis and cough from 1 year. She had begun walking from 1 year but her ability in walking regressed from 4 year. Her cognitive function and IQ were normal. Regarding to fever anemia and cervical lymphadenopathy Hodgkin Lymphoma was diagnosed for her by excisional lymph node biopsy. Chemotherapy began for her after diagnosis of lymphoma. Six months after beginning chemotherapy she was consulted regarding to her recurrent cough and tachypnea as a case of cerebral palsy and lymphoma. In physical examination, eyes bulbar telangiectasia were visible. With considering her ability regression in walking, recurrent respiratory infections and her eyes telangiectasia, Ataxia Telangiectasia was suspected for her and laboratory tests for diagnosis confirmation were requested.

**Results:** Complete blood Count was normal. IgA: 11 mg/dl (reference range 42-495 mg/dl), IgG: 397 mg/dl (reference range 503-1719 mg/dl), HBs antibody level 2.7mIU/mL (reference range more than 10 mIU/mL) were less than normal range. Alfa feto protein level 430 μg/L (reference range<10 μg/L) was significantly higher than normal range. Diagnosis of Ataxia Telangiectasia was considered for her and Blood sample was sent for ataxia telangiectasia mutation gene analysis.

**Conclusion:** A careful history tacking and physical examination are key elements in correct diagnosis of diseases. Early diagnosis of A-T can improves their quality of life by Intravenous immunoglobulin replacement therapy, prophylactic antibiotic and Limitation of ionizing radiation.

## 0851 | The role of cytokine regulation in the progress of gastric cancer

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**Background:** The gastric cancer is one of the leading causes of death from cancer. Currently, the mechanisms of the pathogenesis of gastric cancer remain insufficiently studied. Cytokines act as regulators of the main stages of the body's vital activity. Regulation provides proliferation, differentiation and functioning of cells, as well as the direction and nature of the immune response to the introduction of pathogens of infectious and non-infectious genesis. Cytokines, interacting with complementary receptors on the cell surface, activate certain genes, the synthesis of specific proteins that regulate the above processes occurs. The role of cytokines in the tumor progression is ambiguous, despite the fact that on the one hand, they activate the immune response aimed at eliminating the tumor, on the other, they themselves contribute to the progression of the malignant process.

The purpose of this research was to study the features of cytokine regulation in patients with gastric cancer in the late stages of the disease.

**Method:** 50 patients with stomach cancer (III-IV stages) and 60 practically healthy volunteers were examined. Levels of IL-2, IL-4, IL-8, TNF-alpha, gamma-interferon in the blood serum of patients and healthy individuals were determined by enzyme immunoassay using reagent kits produced by Vector-Best. The statistical significance of the differences was determined using the ranked Mann-Whitney test. The critical level of significance in checking statistical hypotheses was assumed to be $P < 0.05$.

**Results:** In patients with gastric cancer, there is an increase in the concentration of IL-2, IL-8, interferon-gamma and IL-4 relative to the control group.

**Conclusion:** The increase in the production of Th1 and Th2 cytokines, indicates the activation of immunity in Th1 and Th2 types in late stage gastric cancer.

## 0852 | Ras-associated autoimmune leukoproliferative disorder (RALD) identified in a child presenting with diagnostic criteria for juvenile myelomonocytic leukemia (JMML)

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**Case report:** Ras-associated autoimmune leukoproliferative disorder (RALD) has been recently classified as a new entity, characterized by hepatosplenomegaly (HSM), lymphadenopathy, autoimmune cytopenias, monocytosis, either normal or marginally increased DNT levels and defective lymphocyte apoptosis upon cytokine withdrawal. RALD, which usually has an indolent course, shares clinical and laboratory findings with neoplastic disorders such as juvenile myelomonocytic leukemia (JMML) and chronic myelomonocytic leukemia (CMML). JMML is an aggressive hematopoietic neoplasm in childhood with a median survival of 1 year for untreated patients. CMML is mainly seen in adults often requiring chemotherapy. Upon molecular assessment, RALD and JMML share common KRAS or NRAS mutations. We present an asymptomatic 4-month-old male with new-onset HSM, leukocytosis (WBC 28 780), with peripheral 2% blasts and 10% monocytes and concomitant severe thrombocytopenia (PLT 29 000). Bone marrow aspirate showed trilinear hematopoiesis with left-shifted myeloid maturation and decreased megakaryocytes and no evidence of leukemia/lymphoma. Flow-cytometry performed on bone marrow only showed 3% blasts. Bone marrow FISH analysis was negative for BCR/ABL1 rearrangement. Microarray resulted positive for a germ-line heterozygous missense mutation: NRAS c.37G>T;pGly13Cys (47%). The patient met all category I criteria for JMML. Based on the percentage of cells with NRAS mutation, this is most likely a germline mutation, in contrast to somatic NRAS mutations (category II) usually seen in JMML and RALD patients. Out of 2016 revised WHO JMML criteria he meets only one of two category III required (increased circulating myeloid precursors). The patient is growing well after one and a half years of follow-up. Due to an overlap of phenotypic clinical presentation of RALD and JMML, genetic testing and interdisciplinary assessment of such patients would be advisable in the light of unfolding research about RALD. Given the significant clinical differences between both diseases and their potential outcomes, further research is needed in order to determine adequate management and long-term follow-up.

SUNDAY, 27 MAY 2018
TPS 14
INNOVATIVE IMMUNOMODULATION STRATEGIES

## 0853 | Dupilumab reduces risk of severe exacerbations and improves FEV1 in patients on both high- and medium dose ICS with uncontrolled, moderate-to-severe asthma from the phase 3 LIBERTY ASTHMA QUEST Study

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**Background:** Dupilumab (DPL), a fully human anti-interleukin (IL)-4-α monoclonal antibody that inhibits IL-4 and IL-13, key drivers of type 2 inflammation, is approved in the EU, USA, and other countries for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). In a double-blind, placebo (PBO)-controlled phase 3 study (NCT02414854), asthmatics aged ≥12 years, without a minimum baseline eosinophil requirement, uncontrolled with medium-to-high-dose inhaled corticosteroids (ICS) plus up to two additional controllers, received add-on DPL 200/300 mg or matched PBO every 2 weeks (q2w) for 52 weeks. For the overall intent-to-treat (ITT) population, both DPL regimens significantly reduced annualized severe exacerbation rates during the 52-week treatment period, improved pre-bronchodilator (BD) forced expiratory volume in 1 second ($FEV_1$) at Week 12, improved asthma symptoms/quality of life measures, and were generally well tolerated. This pre-specified analysis assessed the efficacy of DPL by disease severity determined by baseline ICS dose (high/medium).

**Method:** Annualized severe exacerbation rates during the 52-week treatment period and change from baseline in pre-BD $FEV_1$ (L) at Week 12 were analyzed by baseline ICS dose (high/medium) subgroups.

**Results:** Both DPL q2w doses vs PBO significantly reduced annualized severe exacerbation rates over the 52-week treatment period ($P < 0.01$) and improved pre-BD $FEV_1$ at Week 12 ($P < 0.01$) regardless of baseline ICS dose (Table). Overall, reduction in exacerbation rate and improvement in $FEV_1$ appear similar between high- and medium-dose ICS subgroups. The most frequent adverse event (AE)

| | ICS dose subgroup | PBO (N = 317) | DPL 200 mg q2w (N = 631) | Relative risk/ difference vs PBO (95% CI) | *P* value vs PBO | PBO (N = 321) | DPL 300 mg q2w (N = 633) | Relative risk/ difference vs PBO (95% CI) | *P* value vs PBO |
|---|---|---|---|---|---|---|---|---|---|
| Adjusted annualized severe exacerbation rate over 52 weeks, estimate (95% CI); N | High | 1.040 (0.824, 1.314); 172 | 0.560 (0.455, 0.690); 317 | 0.539 (0.400, 0.725) | <0.0001 | 1.038 (0.818, 1.317); 167 | 0.639 (0.523, 0.780); 323 | 0.615 (0.456, 0.830) | 0.0015 |
| | Medium | 0.697 (0.515, 0.944); 144 | 0.344 (0.267, 0.442); 310 | 0.493 (0.334, 0.727) | 0.0004 | 0.879 (0.667, 1.160); 151 | 0.414 (0.325, 0.527); 303 | 0.471 (0.329, 0.674) | <0.0001 |
| Baseline pre-BD $FEV_1$ (L), mean (SD) | High | 1.74 (0.55) | 1.69 (0.56) | | | 1.65 (0.50) | 1.70 (0.60) | | |
| Change from baseline in pre-BD $FEV_1$ (L) at Week 12, LS mean (SE); N | High | 0.17 (0.03); 167 | 0.31 (0.02); 310 | 0.13 (0.06, 0.21) | 0.0003 | 0.21 (0.03); 162 | 0.33 (0.02); 309 | 0.12 (0.04, 0.19) | 0.0018 |
| Baseline pre-BD $FEV_1$ (L), mean (SD) | Medium | 1.80 (0.67) | 1.88 (0.66) | | | 1.86 (0.62) | 1.87 (0.59) | | |
| Change from baseline in pre-BD $FEV_1$ (L) at Week 12, LS mean (SE); N | Medium | 0.19 (0.03); 139 | 0.34 (0.02); 298 | 0.15 (0.07, 0.23) | 0.0001 | 0.20 (0.03); 148 | 0.34 (0.02); 294 | 0.14 (0.06, 0.22) | 0.0003 |

Sample size for the analysis of annualized severe exacerbation rate and change from baseline in $FEV_1$ (L) at Week 12 are different because some patients withdrew from study before Week 12. A severe asthma exacerbation was defined as deterioration of asthma requiring use of systemic corticosteroids for ≥3 days or asthma-related hospitalization or emergency room visits requiring systemic corticosteroids between first dose and last dose plus 14 days. CI, confidence interval; LS, least-squares; SD, standard deviation; SE, standard error.

occurring at higher frequency in the DPL-treated groups vs PBO was injection-site reactions (15%/18% vs 5%/10%, respectively). Conjunctivitis AEs were similar between DPL and PBO, in contrast to DPL studies in AD.

**Conclusion:** Dupilumab significantly reduced the rate of severe exacerbations, and improved $FEV_1$ regardless of disease severity (as measured by ICS dose at baseline) in patients with moderate-to-severe asthma, and was generally well tolerated.

## 0854 | Dupilumab reduces exacerbations and improves lung function in uncontrolled, moderate-to-severe asthma patients across prior historical exacerbation subgroups in the phase 3 LIBERTY ASTHMA QUEST study

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**Background:** Dupilumab (DPL), a fully human anti-interleukin (IL)-4R-α monoclonal antibody that inhibits IL-4 and IL-13, key drivers of type 2 inflammation, is approved in the EU, USA, and other countries for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). In a double-blind, placebo (PBO)-controlled phase 3 study (NCT02414854), asthmatics aged ≥12 years, without a minimum baseline eosinophil requirement, uncontrolled with medium-to-high-dose inhaled corticosteroids plus up to two additional controllers, received add-on DPL 200/300 mg or matched PBO every 2 weeks (q2w) for 52 weeks. For the overall intent-to-treat population, both DPL regimens significantly reduced annualized severe exacerbation rates during the 52-week treatment period, improved pre-bronchodilator (BD) forced expiratory volume in 1 second ($FEV_1$) at Week 12, improved asthma symptoms/quality of life measures, and were generally well tolerated. This post hoc analysis assessed the efficacy of DPL by the number of exacerbations experienced prior to the study.

**Method:** Annualized severe exacerbation rates during the 52-week treatment period and change from baseline in pre-BD $FEV_1$ (L) at Week 12 were analyzed by subgroups of patients (pts) with ≥1, ≥2, ≥3, or ≥4 exacerbations in the prior year.

**Results:** Both DPL q2w doses vs PBO reduced severe exacerbations over the 52-week treatment period ($P < 0.01$) and improved $FEV_1$ (L) at Week 12 ($P < 0.01$), regardless of prior exacerbation history (Table); greater reductions in severe exacerbations were observed as prior exacerbation history increased. The most frequent adverse event (AE) occurring at higher frequency in the DPL-treated groups vs PBO was injection-site reactions (15%/18% vs 5%/10%, respectively). Conjunctivitis AEs were similar between DPL and PBO, in contrast to DPL studies in AD.

**Conclusion:** Dupilumab significantly reduced severe exacerbations and improved $FEV_1$ regardless of exacerbation history, with generally greater improvements as prior exacerbation history increased, in pts with uncontrolled, moderate-to-severe asthma, and was generally well tolerated.

| | Pts with ≥1 exacerbations | | | | Pts with ≥2 exacerbations | | | | Pts with ≥3 exacerbations | | | | Pts with ≥4 exacerbations | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PBO (N = 317) | DPL 200 mg (N = 631) | PBO (N = 321) | DPL 300 mg (N = 633) | PBO (N = 167) | DPL 200 mg (N = 291) | PBO (N = 177) | DPL 300 mg (N = 303) | PBO (N = 76) | DPL 200 mg (N = 128) | PBO (N = 84) | DPL 300 mg (N = 145) | PBO (N = 37) | DPL 200 mg (N = 64) | PBO (N = 48) | DPL 300 mg (N = 65) |
| Adjusted annualized severe exacerbation rate over 52 weeks, estimate (95% CI); N | 0.871 (0.724, 1.048); 317 | 0.456 (0.389, 0.534); 631 | 0.970 (0.810, 1.160); 321 | 0.524 (0.450, 0.611); 633 | 1.234 (0.991, 1.560); 167 | 0.512 (0.413, 0.634); 291 | 1.274 (1.024, 1.584); 177 | 0.600 (0.489, 0.736); 303 | 1.648 (1.174, 2.312); 76 | 0.625 (0.457, 0.855); 126 | 1.850 (1.360, 2.516); 84 | 0.675 (0.506, 0.901); 145 | 2.563 (1.661, 3.955); 37 | 0.571 (0.372, 0.876); 64 | 2.530 (1.763, 3.632); 48 | 0.999 (0.688, 1.452); 65 |
| Relative risk vs PBO (95% CI); P value vs PBO | | 0.523 (0.413, 0.662); <0.0001 | | 0.540 (0.430, 0.680); <0.0001 | | 0.412 (0.305, 0.557); <0.0001 | | 0.471 (0.353, 0.629); <0.0001 | | 0.379 (0.244, 0.589); <0.0001 | | 0.365 (0.242, 0.551); <0.0001 | | 0.233 (0.124, 0.399); <0.0001 | | 0.395 (0.238, 0.654); 0.0004 |
| Baseline pre-BD $FEV_1$ (L), mean (SD) | 1.76 (0.61) | 1.78 (0.62) | 1.75 (0.57) | 1.78 (0.60) | 1.74 (0.55) | 1.76 (0.64) | 1.69 (0.53) | 1.73 (0.59) | 1.71 (0.52) | 1.69 (0.64) | 1.64 (0.48) | 1.66 (0.57) | 1.69 (0.53) | 1.71 (0.58) | 1.62 (0.47) | 1.59 (0.56) |
| Change from baseline in pre-BD $FEV_1$ (L) at Week 12, LS mean (SE); N | 0.18 (0.02);307 | 0.32 (0.02);611 | 0.21 (0.02); 313 | 0.34 (0.02); 610 | 0.17 (0.03); 160 | 0.34 (0.02); 285 | 0.22 (0.03); 174 | 0.39 (0.02); 292 | 0.17 (0.05); 73 | 0.33 (0.04); 125 | 0.18 (0.04); 82 | 0.40 (0.03);140 | 0.20 (0.07); 35 | 0.32 (0.05); 63 | 0.15 (0.06); 47 | 0.40 (0.05); 62 |
| Difference vs PBO (95% CI); P value vs PBO | | 0.14 (0.08, 0.19); <0.0001 | | 0.13 (0.08, 0.18); <0.0001 | | 0.17 (0.09, 0.24); <0.0001 | | 0.17 (0.10, 0.24); <0.0001 | | 0.16 (0.05, 0.27); 0.0042 | | 0.22 (0.12, 0.33) <0.0001 | | 0.12 (–0.03, 0.28); 0.1240 | | 0.25 (0.11, 0.39); 0.0008 |

For inclusion in the study, all patients were required to have ≥1 severe asthma exacerbation in the prior year. PBO-treated pts with greater numbers of prior exacerbations had greater numbers of exacerbations during the treatment period. A severe asthma exacerbation was defined as deterioration of asthma requiring use of systemic corticosteroids for ≥3 days or asthma-related hospitalization or emergency-room visits requiring systemic corticosteroids between first dose and last dose plus 14 days. Sample size for the analysis of annualized severe exacerbation rate and change from baseline in $FEV_1$ (L) at Week 12 are different because some patients withdrew from study before Week 12. CI, confidence interval; LS, least-squares; SD, standard deviation; SE, standard error.

## 0855 | Dependence of transfection activity on PEG length

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**Background:** The molecular weight of the PEG molecules exerts a large influence on properties of the polymer coating. It was found that the optimal values of the PEG molecular mass are in the range from 1000 to 4000 Da. Too short PEG molecules can not provide a significant increase in the circulation time of particles in the bloodstream, which is the main goal of pegylation method. On the other hand, too large molecules of PEG (with a molecular weight of 5000 Da or more) sterically interfere the interaction of liposomes with the target cell, penetration into the cell and further release from the endosomes. $PEG_{2000}$ is thought to be the most suitable substance for prolonged liposomes creation.

**Method:** Liposomes were prepared from thin lipid layer of lipopeptides and PEG derivatives. Particles size distribution was defined by means of photon-correlation spectroscopy. Transfection activity was detected with luciferase assay.

**Results:** Liposomes based on lipodipeptide $OrnGlu(C_{16}H_{33})_2$ and lipotripeptide $OrnOrnGlu(C_{16}H_{33})_2$ were obtained. Each type of liposomes was modified by addition 5% (by mass) of $PEG_{2000}$ (37-46 units in length) or $PEG_{3400}$ (68-77 units in length) derivative during thin lipid bilayer preparation step. The photon-correlation spectroscopy data showed that PEG addition does not affected the size of liposome particles significantly regardless of the PEG units' amount. It was found, that all pegylated liposomes possess lower transfection activity than non-modified ones. However, liposomes containing long PEG derivatives on their surface tend to have bigger decline of transfection efficiency. $PEG_{2000}$ conjunction leads to decrease in activity only 2-3 times, while the $PEG_{3400}$ addition decreasing the activity index more than 5 times.

**Conclusion:** Thus, it was confirmed that 2000 Da is an optimal molecular mass to form sterically stabilized liposomes, which would not influence the gene drug transfection too much.

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## 0856 | Successful treatment of refractory anaphylaxis using omalizumab in monoclonal mast cell activation syndrome

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**Case report:** In 2008, a then 43 year old man developed sudden onset of vision loss, flushing, and diarrhea. He proceeded to the emergency room where hypotension (BP 70/30) was documented, and attributed to a vasovagal event. His symptoms resolved following treatment with IV fluids. Subsequently, he had several episodes of flushing, chest pain, and tachycardia, which resolved spontaneously. In 2013, he was admitted to hospital after sudden onset of visual changes, flushing, diarrhea, hypotension and acute renal failure, all presumed to be secondary to myocardial infarction. In 2014 he developed urticaria and was assessed for mastocytosis. Urinary leukotrienes were found to be elevated though his baseline serum tryptase was normal. Examination of bone marrow revealed a clonal population of spindle shaped mast cells, which were KIT D816V mutated establishing the diagnosis of MMAS.

Despite treatment with Cetirizine, Ranitidine, Hydroxyzine, Montelukast, and acetylsalicylic acid (ASA) the patient continued to experience urticaria on a daily basis, in addition to episodes of anaphylaxis. Upon initiation of treatment with Omalizumab there were no further episodes of anaphylaxis and a significant reduction in urticaria. Cetirizine, Hydroxyzine and Montelukast were discontinued. We attempted to increase the interval between injections to 5 and then 6 weeks, but this resulted in recurrence of episodes of flushing, diarrhea and hypotension. Maintained on Omalizumab 300 mg every 4 weeks, the patient has remained asymptomatic.

Owing to the rarity of these conditions, there is a paucity of evidence examining effective treatment for mast cell activation disorders, including MMAS. Treatment recommendations are typically individualized for patients depending on the affected organ systems and severity of symptoms. These may include H1 and H2 blockers, montelukast, ASA and corticosteroids. In a recently published cohort of 13 patients with systemic mastocytosis, 11 reported improvement in their symptoms following treatment with Omalizumab, with no severe adverse reactions observed.

Omalizumab should be considered as a treatment option in patients with mast cell activation disorders, particularly those who are recalcitrant to other therapies. Given the rarity of these disorders, collaboration and communication are essential in optimizing management of these challenging patients.

## 0857 | Patient-centred care focusing on biologicals in urticaria patients and possible barriers in a non-hospital setting

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**Background:** In Germany, approximately 800.000 people suffer from chronic spontaneous urticaria (CSU). According to the current German guideline, biologicals can be used for treating refractory forms of this disease. Studies targeting the patient-centred care of individuals suffering from this often serve dermatologic disease in a non-hospital environment and possible barriers in the use of biologicals are extremely rare.

**Method:** In order to analyse the current patient-centred care with respect to guideline-compliant use of medication and possible barriers, all Bavarian office based dermatologists (n = 499) received a questionnaire within the framework of a non-interventional cross-sectional study. They were selected using the database of the KVB (Kassenärztliche Vereinigung Bayerns) and supplemented using the webpages of the selected physicians. The KVB is an institution listing all physicians who are allowed to treat patients who are part of the statutory health insurance in Bavaria.

**Results:** Of the contacted dermatologists, 136 participated (53 women, 83 men; mean age 53.2 ± 8.5) which results in a response rate of 27.3%. The guideline compliant prescription rate of biologicals in patients with CSU was 6.9%. The most prevalent barriers in the prescription were the high cost of the treatment (64.7%), low reimbursement for doctors (62.5%) and the fear of a recourse claim (52.9%). However, a lack of evidence or an insufficient efficiency were not considered as a barrier by most of the physicians (86.0% and 83.1%). Age and working years spent in a dermatological hospital were major significant influencing factors on the perception of barriers.

**Conclusion:** Doctors' clinical education and external factors have a substantial influence on their perception of barriers on guideline compliant prescription of modern therapy in CSU. Considering these factors in future trainings could lead to an optimisation of patient-centred care.

## 0858 | Management of eosinophilic colitis with the use of Anti- IgE monoclonal antibody

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**Case report:** Eosinophil associated gastrointestinal disorders (EGIDs) including eosinophilic colitis are commonly associated with atopy. Aeroallergen sensitization may accompany food allergy in these patients. A case with eosinophilic colitis responsive to anti-IgE monoclonal antibody (Omalizumab) treatment is presented.

An eleven-year-old boy had bloody diarrhea lasting nearly one month in autumn for last 3 years. This year diarrhea lasted more than 3 months. Colonoscopic biopsy revealed lymphoplasmacytic inflammatory cells including eosinophils leading to a diagnosis of ulcerative colitis. Corticosteroid and mesalazine treatment was started with a good clinical response. Recurrence of diarrhea during corticosteroid dose reduction suggested corticosteroid dependent ulcerative colitis. Eosinophilic/allergic colitis was an alternative diagnosis when seasonal recurrence, lack of weight loss, eosinophils in biopsy and high serum IgE level were considered. Colonoscopy done after cessation of therapy for one month, revealed exudative ulcerous lesions, lacerations, loss of haustration compatible with colitis (inflammatory/allergic?). Presence of significant mucosa associated lymphoid tissue in biopsy supported any inflammatory, reactive process.

He had recurrent bronchiolitis until age six and allergic rhinitis in spring for three years. Total IgE and mix aeroallergen specific IgE were high (518 IU/mL, 56.1 kUA/L), absolute eosinophil count was normal (210/mm3). Food skin prick and patch tests were negative. He had positive skin reactions with dermatophagoides, grass and olea pollens (induration diameter: 9, 10, 6 mm, respectively). Pulmonary function test was normal.

He was considered as eosinophilic/allergic colitis and Omalizumab was started according to manufacturer's dosing table (300 mg/2 weeks). Rectal bleeding decreased after first dose and ceased after the second dose. Early colonoscopy examination after 3rd month of therapy showed that exudations disappeared and haustrations became evident. Microscopy revealed mild nonspecific colitis.

Few patients with eosinophilic colitis improved with Omalizumab were reported before. IgE-mediated processes are responsible from eosinophilic inflammation in EGIDs, making Anti-IgE therapy as a promising treatment option.

## 0859 | Design of liposomal carriers modified by glycoconjugates for liver cell delivery of nucleic acids

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**Background:** Gene therapy is a highly developing direction of research. The main problem of its implementation is the complexity of delivery of pharmaceutical nucleic acids to the target cells. To overcome this problem, various carriers, including liposomes, are

used. The surface of liposomal nanoparticles can be modified to increase the selectivity of intracellular delivery. It is well known that asialoglycoprotein receptors of hepatocytes have a strong affinity to galactose carbohydrate. Therefore, the aim of this study was to assess the effect of the modification of the liposome surface by glycoconjugates on the selectivity of intracellular transport of nucleic acids into the liver cells.

**Method:** Liposomes based on OrnOrnGlu($C_{16}$)$_2$ were chosen previously as the effective nucleic acid delivery system. We modified liposomes with novel lactose-based derivatives. Every of four glycoconjugates was added to OrnOrnGlu($C_{16}$)$_2$ in an amount of 5, 10 and 15%. As a result, 12 variants of modified liposomes were obtained. To determine the cytotoxicity, an MTT test was used. Using luciferase test, the selectivity of penetration was evaluated on nonspecific 293T (human embryonic kidney) and specific HepG2 (human liver cells) cell lines.

**Results:** Modified liposomal compositions OrnOrnGlu($C_{16}$)$_2$-4 + Lac$C_{16}$ (5%) and OrnOrnGlu($C_{16}$)$_2$-4 + LacGGG16 (15%) had the lowest cytotoxicity similar to that for unmodified OrnOrnGlu($C_{16}$)$_2$. The $IC_{50}$, calculated based on the data of MTT test, was 0.14 and 0.26, vs. 0.16 mg/mL, respectively. OrnOrnGlu($C_{16}$)$_2$-4 + LacGGG16 (15%) showed a 1.5-fold increase in transfection activity on the nonspecific 293T cells, compared to unmodified OrnOrnGlu($C_{16}$)$_2$, whereas the modification of OrnOrnGlu($C_{16}$)$_2$-4 + LacC16 (5%) resulted in a 6-fold decrease in transfection activity. However, the ability of these variants to penetrate the specific liver HepG2 cell was significantly higher by 15 and 25 times, respectively, than for unmodified OrnOrnGlu($C_{16}$)$_2$.

**Conclusion:** It was shown that the modification of the surface of liposomes by glycoconjugates increases their ability to penetrate to hepatocytes and reduces the cytotoxicity. These ways of modification of liposomal carriers could be a promising approach for target delivery of pharmaceutical nucleic acids to the liver. Supported by the RFBR grant No. 17-04-01080.

## 0861 | A new potent microbicide composition based on soluble butanol fractions of humic derivatives

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**Background:** Soluble butanol fractions of humic derivatives (SBFHD) are substances obtained by multi-step hydrolysis of natural lignin. The objective of this study was to assess the anti-HIV activity of SBFHD and their potential as a microbicide.

**Method:** The evaluation of anti-HIV efficacy of SBFHD was performed using HIV-1 BaL (R5) and different cell targets (PBMC, MDM, DC, Caco-2, and HEC-1A). It was also evaluated in a TZM-bl assay. The level of virus replication was detected by p24 HIV-1 antigen (intracellular and/or released) ELISA. Cytotoxicity was determined using the MTT assay.

**Results:** The greatest inhibitory effect of SBFHD was observed in MDM infected with HIV-1 Bal: 90% and 50% suppression of HIV replication was achieved at concentrations of 1.5 μg/mL and 0.4 μg/mL, respectively. The activity in PBMC and DC was less pronounced (the respective IC90 values were 5.8 μg/mL and 19.7 μg/mL). Studies in endometrial HEC-1A cells demonstrated that SBFHD suppressed CD4-independent entry of HIV-1 ($10^3$ $TCID_{50}$/mL) by 33%, 54%, and 98%, respectively, at 1, 10, and 100 μg/mL. The effect was also observed after increasing the dose of the virus. At $10^4$ $TCID_{50}$/mL, SBFHD suppressed HIV infection by 45% (10 μg/mL) and 97% (100 μg/mL). The cytotoxicity of SBFHD in this system was low. Similar results were obtained with colorectal Caco-2 cells. SBFHD exhibited no spermicidal activity at concentrations of up to 3 mg/mL. Combining within a single microbicide two agents that target distinct steps of HIV life cycle will maximize its efficacy (via synergistic effects and/or interference with multiple stages of the transmission). We therefore explored the synergistic potential of combinations of SBFHD and AZT, the classical nucleoside RT inhibitor. In these experiments, 50% suppression of HIV infection was reached at concentrations of SBFHD and AZT, which were significantly lower than the respective IC50 values of each component (determined in parallel experiments). The synergistic effect was most pronounced for the combination of 0.1 μg/mL SBFHD (which is 60 times less than the IC50) and 0.16 nM AZT (which is 45 times less than its IC50).

**Conclusion:** The low cytotoxicity and high anti-HIV activity of SBFHD indicate that these substances hold significant promise as a safe and efficacious vaginal and rectal microbicide. The ability of SBFHD to exert synergistic effects in combinations with RT inhibitors is viewed as an added benefit suggesting potential for further development as a combination microbicide.

## 0862 | Studies on anti-allergy effect of glucomannan extract from porang (Amorphophallus oncophyllus) tuber

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**Background:** Glucomannan found in porang *(Amorphophallus oncophyllus)*, an Indonesian local tuber is mainly composed of mannose and glucose. Glucomannan has health benefits as dietary fiber, prebiotic, anti-inflammatory, and immune-modulatory. In this study, the anti-allergy potential of porang glucomannan (PNG) was investigated through its suppressive effect on degranulation by mast cell *in vitro*

and passive cutaneous anaphylaxis (PCA) reaction model mice *in vivo*.

**Method:** The suppressive effect of PNG on the IgE-mediated degranulation response in Rat basophilic Leukemia RBL-2H3 cells was evaluated by measuring the release of β–hexosaminidase. Effect of PNG on the elevation of $Ca^{2+}$ concentration induced by antigen was evaluated to reveal the mode of inhibition effect of PNG. The effect of PNG on PCA reaction in mice was examined to determine the *in vivo* effect of PNG.

**Results:** PNG suppressed the degranulation of RBL-2H3 by inhibiting the elevation of intracellular $Ca^{2+}$ concentration induced by antigen without cytotoxicity. Oral administration of PNG suppressed PCA reaction in mice.

**Conclusion:** These findings suggest that glucomannan extracted from porang tuber has anti-allergy activity via the suppression of mast cell degranulation *in vitro* and *in vivo*.

## 0863 | Effects of 3 different mushrooms, ganoderma lucidum, lentinula edodes and boletus edulis on T cell and dendritic cell function

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**Background:** *Ganoderma Lucidum* (Reishi) and *Lentinula Edodes* (Shiitake) are well known mushrooms used in the traditional medicine for centuries. *Boletus edulis* is the most commonly distributed mushroom in Belarus and Eastern Europe. The aim of the investigation was to compare the effects of Reishi, Shiitake and Boletus mushrooms on dendritic cell (DC) and T-cell immunophenotype.

**Method:** Reishi, Shiitake and Boletus mushroom extracts (0.5% w/v final concentration in the culture media) were used. Monocyte-derived DC (n = 6) and T-cells (n = 9) isolated from human whole blood were stimulated for 24 hours with mushroom extracts. PMA was used as positive control and PSB as negative control (C). Expression of CD69 and HLA-DR by T-cells and CD80, CD205, CD206 and HLA-DR by DC were assayed by flow cytometry.

**Results:** Aqueous extracts of all the studied mushrooms increased the expression of CD69 by human blood T-cells (C–2.7(2.1-3.5)%,; PMA—23.2(51.1-42.0)%; Boletus—8.5(6.8-10.0)%; Reishi—12.2(7.0-19.3) %; Shiitake—5.7(3.9-9.6)%; $P < 0.02$ for all), while the expression of the HLA-DR remained intact. Reishi and Boletus extracts induced 2.5-fold increase of the CD205 expression by DC, while the changes in the expression of CD206 were statistically insignificant. CD80 expression was increased after the co-culture with Reishi, Shiitake and Boletus mushrooms (C — 5.6(1.4—9.2)%; PMA — 60.5 (27.2—70.9)%; Reishi — 12.7(6.5-19.9)%; Shiitake — 9.6(4.3—15.5)%; Boletus — 16.6 (14.0-24.0)%).

**Conclusion:** All 3 mushrooms had a significant effect on the CD80 and CD205 expression by the DC and CD69 by the T-cells. The effects of all the mushrooms studied on the immune cell immunophenotype was similar, indicating the Boletus mushrooms could be a source for new immunomodulatory drugs.

## 0864 | The influence of acute professional stress on the immune system

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**Background:** Factors of professional stress of emergency situations contributes the formation of severe comorbid pathology and is a unique model for studying homeostatic changes at different stages of the formation of post-stress disorders. Aim: to study the state of the innate and adaptive components of immunity in military man in the acute phase of stress during 4 weeks after staying in countries with a hot climate.

**Method:** the study included 38 men (mean age 34 ± 5.9 years) before and immediately after staying in countries with a hot climate. Immune status was assessed by expression of CD 3 + , CD 4 + , CD 16 + , CD 19 + , CD 4 + CD25 + Foxp3, content granzyme in T-cytotoxic lymphocytes, NK cells in immunofluorescence test on a flow cytofluorometry Cytomics FC 500 (Beckman Coulter, USA) using appropriate monoclonal antibodies, the levels of serum immunoglobulins by radial immunodiffusion in gel by Mancini.

**Results:** The development of lymphopenia observed In the first week of observation. This was accompanied by a decrease in the number CD3 + lymphocytes expressing the markers of late activation (CD3 + HLADR+ 4.8 ± 1.09x$10^9$/л и 3.2 ± 2.04x$10^9$/л). Revealed significant decrease of CD4 + CD25 + Foxp3 + regulatory cells in the first week after returning from the area of adverse climatic conditions, as well as a significant sustained decrease in the number CD3 + CD8 + HLADR+($P < 0.05$). Change of the effector link of innate immunity was determined in significant reliable decrease in relative (CD16 + 13.2 ± 2% and 4.6 ± 2.1%, respectively, $P < 0.05$) and absolute (CD16 + 0.3 ± 0.02 x109/L and 0.1 ± 0.03%, respectively, $P < 0.05$) in the number of a population of natural killer cells in the first week of observation. In the context of acute stress marked a significant increase in relative and absolute numbers of B lymphocytes (8 ± 1.16% (0.15 ± 0.04 × 109/L) before a trip to countries with a hot climate and 19 ± 3.1% (0.4 ± 0.07 × 109/L) in the first week after returning, $P < 0.05$). The activity is the production of antibodies was not changed.

**Conclusion:** the formation of the acute phase of stress in servicemen involved in military training accompanied by severe immune dysfunction, requiring dynamic monitoring and personalized therapy.

## 0868 | Efficacy of autologous serum therapy in patients with chronic idiopathic urticaria compared to control group assessed by dermatological life quality index(DLQI) questionnaire (Late Breaking Abstract)

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**Background:** Chronic idiopathic urticaria(CIU) is a skin disorder defined by frequent occurrence of erythematous, itchy wheals that lasts for six weeks or more. CIU lesions can severely impact patients' lives through itching, disturbances in sleep and work/school-related daily activities. Patients with CIU have worse health-related quality of life than those with psoriasis or atopic dermatitis. The EAACI/GA2LEN/EDF/WAO Guideline suggests the second generation of antihistamines as the first line of treatment in CIU patients. Considering the ineffectiveness of antihistamines in a major group of CIU patients, the side effects and high costs of the next line treatments, searches for new treatments in CIU patients can improve their life qualities. Recent studies have shown that autologous serum therapy (AST) which is the intramuscular injection of patients own serum, is a promising therapy with a substantial efficiency on CIU patients. In this study we aim to assess the efficacy of AST on chronic urticaria patients by DLQI questionnaire.

**Method:** This was a single-blind randomized clinical trial which evaluated the efficacy of autologous serum therapy compared to oral antihistamines in patients with CIU. 49 CIU patients received the AST. Every session 5 cc of each patient's blood was centrifuged at the speed of 2000 rpm for 10 minutes and 2.5 cc of the serum was injected intramuscular into the patient's deltoid muscle weekly for 9 weeks. The control group consisted of 51 CIU patients took 10 mg of Cetirizine daily for 9 weeks. Patients answered the DLQI questionnaire at the first session of treatment as baseline and 7 weeks after the last session(week 16) as response to treatment.

**Results:** The mean baseline score of DLQI for AST group was 18.51 and the score of week 16 was 2.22 which shows a substantial improve in the patients' quality of life. The mean baseline score of the control group was 16.78 and the mean score of week 16 was 14.43. The results show a significant decrease in the of score in AST group compared to control group ($P$ = 0.0001).

**Conclusion:** This study shows that the patients receiving the AST had better results with DLQI questionnaire compared to the group receiving antihistamine which means the AST group had major improvement in life quality compared to the group taking the first line of treatment. This shows the efficacy of AST as a new and low-cost treatment in patients not responding to antihistamines and as potential substitute for next line treatments such as omalizumab.

SUNDAY, 27 MAY 2018
TPS 15
IMMUNOTHERAPY: VACCINES AND EFFICACY

## 0869 | Costs and resource use in allergic rhinitis

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**Background:** Allergic rhinitis (AR) and allergic asthma are chronic diseases characterised by inflammation of the upper and lower airways in response to allergens such as pollen. Both diseases are typically managed with symptom-relieving pharmacotherapy, which does not treat the cause of the disease. Allergy immunotherapy (AIT) treats the underlying disease, but is only available to individuals who are unable to adequately manage their symptoms using pharmacotherapy. This study aimed to generate estimates of actual healthcare costs and resource use for patients with AR and patients with asthma, prescribed and not prescribed AIT.

**Method:** Anonymised data for all German National Health Insurance beneficiaries insured by the AOK PLUS (Saxony) from January 2005 to December 2014 (*N* = 1 739 440) were retrieved. For cohorts of patients with prevalent AR (prescribed AIT: *n* = 17 289; not prescribed AIT: *n* = 57 353) and asthma (prescribed AIT: *n* = 3460; not prescribed AIT: *n* = 30 902), mean annual costs of pharmaceutical treatments (2005, 2010, 2014) and inpatient costs (2010 and 2014) were calculated, including and excluding the cost of AIT. Patient groups were not mutually exclusive.

**Results:** In all years, mean annual costs of pharmaceuticals were lower in AR patients who had been prescribed AIT (2005: €467; 2010: €523; 2014: €543) than those who had not (2005: €487; 2010: €656; 2014: €714). The same was true for asthma patients (prescribed AIT, 2005: €704; 2010: €927; 2014: €848; not prescribed AIT, 2005: €1080; 2010: €1250; 2014: €1133). When the AIT pharmaceutical costs themselves were subtracted, this difference was more pronounced, with the lowest mean costs of non-AIT pharmaceuticals at €47 for patients with AR and €470 for patients with asthma (AR prescribed AIT, 2005: €47; 2010: €336; 2014: €348; asthma prescribed AIT, 2005: €470; 2010: €696; 2014: €615).

In AR patients, inpatient costs were ~40% lower in patients prescribed AIT (2010: €457; 2014: €587) than those not (2010: €803; 2014: €956). In asthma patients, inpatient costs were over 50% lower in patients prescribed AIT (2010: €624; 2014: €726) compared with those not prescribed AIT (2010: €1407; 2014: €1497).

**Conclusion:** Pharmacotherapeutic and inpatient costs for patients with prevalent AR and asthma were lower in those prescribed AIT than in those not prescribed AIT in all years, both with and without including the cost of AIT itself. This indicates that treatment with AIT is associated with lower cost burden for health services.

## 0870 | Safety of a 3-week allergen immunotherapy course with grass pollen peptides: A randomised double-blind placebo-controlled trial

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**Background:** Immunotherapy with peptides rather than conventional whole allergens is being developed to improve the benefit/risk balance of subcutaneous immunotherapy (SCIT). Lolium perenne peptides (LPP) demonstrated reduced allergenicity following ex-vivo analyses, allowing higher doses to be given over a shorter period to improve treatment adherence and compliance. Such treatment resulted in significant reduction in symptoms and rescue medication intake during the grass pollen season. Here we report the safety of LPP immunotherapy in adults.

**Method:** The safety of LPP was assessed in a RDBPC trial. Local and systemic (SR) adverse reactions were assessed in 545 patients with hay fever after 8 subcutaneous injections of placebo (n = 178) or 170 μg LPP (n = 367) administered with increasing doses for 4 visits over 3 weeks by trained allergists.

**Results:** Local reactions at the injection site were reported in 28.5% (105/368) of patients after LPP and 2.8% (5/177) after placebo injection. Most local reactions (93.7%) were reported as mild; none as severe or serious. None of the injections resulted, within 30 minutes, into a wheal diameter exceeding 5 cm. Mostly mild and WAO grade 1 early (≤ 30 min) SR were observed in 10.5% of LPP-treated patients and in 2.3% of placebo patients. Three LPP patients (<1%), all with a medical history of asthma, experienced a serious early SR that adequately resolved with rescue medication, allowing patients to return home the same day: one WAO grade 2 (bronchospasm), one grade 3 (throat swelling) and one grade 4 (blood pressure drop) event. No serious SR occurred after patients had left the investigational site (>30' after last injection). Most reported systemic symptoms after LPP injection included: rhinitis (4.6%), dyspnea (2.2%), urticaria (1.6%), pruritus and rhinorrhea (1.4%).

**Conclusion:** LPP immunotherapy was well tolerated and, overall, safe. Local reactions were limited in size, and serious systemic reactions were uncommon (<1%), occurred within 30 minutes after injection (still in the allergist's practice), and were rapidly controlled with adequate rescue medication.

## 0871 | Skin response and clinical tolerance of an allergoid from Alternaria alternata

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**Background:** A new allergoid from *Alternaria alternata* was characterized to determine its reduced allergenicity *in vitro*. The objective of this study was to determine the skin response to the allergoid and to evaluate the clinical tolerance of the immunotherapy with the allergoid product using a rush schedule.

**Method:** To assess the skin response (SR) two groups of patients were included: group 1 with patients sensitized to *A. alternata* and with respiratory disease caused by this mold; group 2 (control) with patients sensitized to others allergens and non-atopic patients. The SR was determined by SPT using three concentrations of the allergoid: P1 (lowest concentration), P2 (four times higher than P1) and P3 (estimated to obtain a wheal area similar to histamine 10 mg/mL). In SPT was also used a native extract of *A. alternata* (N) and histamine 10 mg/mL (H). All products were tested in duplicate in all patients and the SR was evaluated by comparing the median of the wheal area produced by different products. To evaluate the clinical tolerance to immunotherapy the patients of group 1 were treated with the allergoid product using a rush schedule consisting in a dose of 0.2 + 0.3 mL the first day and 0.5 mL after one month (maintenance dose). The clinical tolerance was determined as the percentage of adverse reactions (AR) to the treatment and the classification of AR was established according to EAACI.

**Results:** The number of patients included to evaluate the SR was 46 (group 1: 25; group 2: 21, 16 atopic and 5 non-atopic) with an average age of 34.8 (range 16-74). The SPT data from group 1 were expressed as median and interquartile range of wheal area ($mm^2$): H: 19.58 (15.3-25.2); N: 22.71 (11.1-33.1); P1: 0.99 (0-5.7); P2: 6.44 (0-12.5); P3: 19.78 (12.0-30.4). It was determined that SR of allergoid was reduced in 87% respect to the native. The products N, P1, P2 and P3 did not produce any response in patients of group 2. To evaluate clinical tolerance, 21 patients of group 1 were treated with the allergoid product with a rush schedule and only two AR were registered (3.2% of doses). These were retarded local reactions with a wheal diameter higher than 5 cm. No systemic reactions were registered and all patients continued the treatment.

**Conclusion:** The allergoid from *A. alternata* produces a significant reduced response to SPT due to its reduced allergenicity. The treatment with an allergoid product in a rush schedule is safety and clinically well tolerated.

## 0872 | A comparative evaluation of clinical and laboratory findings and treatment costs for sublingual and subcutaneous immunotherapy in children with allergic rhinitis and asthma

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**Background:** In our study we aim to determine the more effective, safe and economical method of immunotherapy in children with asthma and allergic rhinitis and to show the benefit of the long term treatment of patients and the financial results of the treatments.

**Method:** 105 (SCIT=54, SLIT=51) patients who had conventional subcutaneous (SCIT) or sublingual (SLIT) treatment with standard preparations for at least 3 years with allergic rhinitis and asthma in our clinic were included in the study. Clinical and immunological efficacy is evaluated. In terms of cost effectiveness, costs such as direct medical expenses and direct non-medical transportation used in the course of asthma and allergic rhinitis treatment and indirect costs such as work and school day losses were evaluated.

**Results:** In terms of demographic characteristics, the two groups have a similar distribution. In clinical terms, when the scores of the pre-treatment and the first, second and third years of treatment were examined for both the SCIT and the SLIT Group, all three of the asthma, rhinitis and drug scores decreased significantly. (for all; *P = 0.000*).

The total cost of 3 years of patients using SCIT was 15665 TL per person whereas the total cost of 3 years of patients using SLIT was 15271 TL per person. When we compare the total cost data of both groups, we found that they are close to each other. While the greatest portion of the cost data of patients with SCIT treatment was direct costs associated with the treatment itself (72%); The remaining part of the total cost was indirect (16%) with non-medical expenses such as transportation (12%). In the SLIT group, direct costs including drug expenditures have a larger percentage (92%) and it was significantly more costly compared to the direct costs of the SCIT group (72%). Transportation costs were found to be more costly in the SCIT group (12%) when compared to the SLIT group (4%). Similarly loss of parent work days in the SCIT group(%16) was found to be significantly more expensive compared with SLIT group (4%).

**Conclusion:** Our study results show that SLIT is a similar treatment for clinically and laboratorially and has a similar efficacy to SCIT to reduce the patients' complaints and to the need for medication. For cost-effectiveness however medicines for treatment of SCIT are less costly; when long term total treatment costs are calculated SLIT and SCIT treatment are economically close treatments.

## 0873 | Development and characterization of a new allergoid from Felis domesticus

Sola JP; Pedreño Y; Cerezo A; Peñalver M
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**Background:** Allergoids from pollen and mites have been used as alternative for allergen immunotherapy with native extracts to obtain a better safety profile and the maintenance of the capacity to induce specific IgG formation. The objective of this study was to develop a new allergoid from cat dander and characterize it by analyzing its protein and allergenic profile.

**Method:** The new allergoid from cat dander (ACD) was developed by modification with glutaraldehyde using a native allergen extract from cat dander (NCD) with a protein concentration of 127.12 μg/mg and a Fel d 1 concentration of 8.3 μg/mg. ACD was characterized in protein content by nitrogen determination in an elemental analyzer and in protein profile by SDS-PAGE and size exclusion chromatography in HPLC (SEC-HPLC). The modification degree of proteins was determined by quantification of the free lysine through reverse phase in HPLC (RP-HPLC). The allergenic profile of ACD was determined by IgE ELISA inhibition e immunoblot using a pool of sera from patients sensitized to cat. The IgG binding capacity of ACD was also evaluated by IgG ELISA inhibition using the same pool of sera. The presence of allergens in ACD was determined by peptide footprint in HPLC-MS/MS after trypsin digestion. The content of major allergen Fel d 1 in ACD was extrapolated based on NCD determination.

**Results:** The protein content of the new ACD was 182.28 μg/mg and the protein profile in SDS-PAGE and SEC-HPLC confirmed the presence of proteins with high molecular weight and the absence of smaller proteins. The content of free lysine in ACD, involved in glutaraldehyde modification, was reduced in 91.96% respect to NCD and it can be considered as the polymerization degree. Regarding to the allergenic profile, through ELISA inhibition was determined a reduction of 18 times in the capacity to bind IgE of the proteins in ACD respect to NCD, whilst the IgG binding capacity was maintained. In immunoblot there was no reaction of ACD proteins to specific IgE from sera. The analysis by peptide footprint determined the presence of Fel d 1 and others allergens in ACD. The content of major allergen Fel d 1 in ACD was determined as 11.9 μg/mg.

**Conclusion:** The new developed and characterized allergoid from cat dander has an excellent safety profile and will allow a safer immunotherapy to treat the allergy to *Felis domesticus*.

## 0874 | Development and characterization of a new allergoid from Alternaria alternata

Sola JP; Pedreño Y; Cerezo A; Peñalver M
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**Background:** Allergoids from pollen and mites have been used as a safer alternative for allergen immunotherapy than native extracts and maintain the capacity to induce specific IgG formation. The objective of this study was to develop a new allergoid from *Alternaria alternata* and characterize it by analyzing its protein and allergenic profile.

**Method:** The new allergoid from *A. alternata* (AAA) was developed by modification with glutaraldehyde using a native allergen extract (NAA) from this mold with a protein content of 44.2 μg/mg extract and a major allergen Alt a 1 concentration of 1.6 μg/mg extract. The protein content of the new AAA was established by nitrogen determination in an elemental analyzer and AAA was characterized in protein profile by SDS-PAGE and size exclusion chromatography in HPLC (SEC-HPLC). The modification degree of proteins was determined by quantification of the free lysine through reverse phase in HPLC (RP-HPLC). The allergenic profile of AAA was determined by immunoblot and IgE ELISA inhibition using a pool of sera from patients sensitized to *A. alternata*. This pool of sera was also used to analyze the IgG binding capacity of AAA by IgG ELISA inhibition. The presence of allergens in AAA was determined by peptide footprint in HPLC-MS/MS after trypsin digestion. The content of major allergen Alt a 1 in AAA was extrapolated based on NAA determination.

**Results:** The protein content of the new AAA was 65.6 μg/mg and the protein profile in SDS-PAGE and SEC-HPLC confirmed the presence of proteins with high molecular weight and the absence of smaller proteins. The content of free lysine in AAA, involved in glutaraldehyde modification, was reduced more than 85% respect to NAA and it can be considered as the polymerization degree. Regarding to the allergenic profile, in immunoblot there was no reaction of AAA proteins to specific IgE from sera and by ELISA inhibition was determined a reduction of 91% in the capacity to bind IgE of the proteins in AAA respect to NAA. The IgG binding capacity in AAA was maintained. The analysis by peptide footprint determined the presence of Alt a 1 and others allergens in AAA. The content of major allergen Alt a 1 in AAA was determined as 2.4 μg/mg.

**Conclusion:** The new developed and characterized allergoid from *A. alternata* shows an excellent safety profile and allows a safer immunotherapy to treat the allergy to this mold.

## 0875 | Stranger things after subcutaneous allergen immunotherapy: Localized hypertrichosis and aspirin-induced recall urticaria in two different patients

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**Background:** Adverse reaction to allergen immunotherapy may be local and systemic and appear within minutes after allergy shot. We present two amazing, rare reactions observed in two different patients which occurred during immunotherapy and four years after allergy vaccine caesation, respectively.

**Method:** Case 1: A 36 years old woman who was being treated with an subcutaneous (sq) glutaraldehyde- modified allergen immunotherapy (AIT) for olive and grass pollinosis, showed within 6-months local growth of hair in the area of injection of allergy vaccine shot in the anterior left arm. She had allergic seasonal rhinitis and molecular allergen profile was consistent with olive and grass sensitization (IgE anti-Ole e 1 24.2 KU/L and anti Phl p 1 + 5b 17.6 KU/L). She was an otherwise healthy woman: she took no drugs and she did not have any remarkable concomitant diseases. The distribution and appearance of the remaining body hair was normal and the hormonal level profiles (LH, FSH, estrogens, progesterone and testosterone) did not show any significant alteration according to her age.

**Case 2:** A 30 year old woman with allergic rhinitis underwent sq glutaraldehyde-modified AIT to house dust mites (D pteronyssinus and G domesticus) without any incidences and complete tolerance to maintenance dose without local reactions during a 5 year period. Two years after AIT discontinuation, patient first experienced a local urticarial reaction with multiple hives at previous sq AIT injection sites 40 minutes after 600 mg of ibuprofen intake. These symptoms recurred at least in seven occasions when patient was exposed to ibuprofen (in five) and metamizol (in two).

**Results:** Case 1: Dermatologist diagnoses localized hypertrichosis.

Case 2: A single blind, placebo controlled oral challenge (SBPCOC) with ibuprofen 600 mg was performed and elicited multiples hives in the circumscribed area in the arm where AIT was conducted. Subsequently, SBPCOC with aspirin was carried out showing the same reaction although a controlled challenge with celecoxib was negative.

**Conclusion:** Local hypertrichosis is a very rare injection-disease associated with injected allergen vaccine treatment. We also firstly described a recall urticaria phenomenon after allergen immunotherapy which has been only elicited after different NSAIDs intake.

## 0877 | Results of a tolerability study of subcutaneous immunotherapy (SKIT) with native depot Olea europaea pollen extract

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**Background:** Grass pollens are the most common allergens responsible for rhinoconjunctivitis in Spain. However, olive pollen is the main cause in certain areas of Andalusia, such as Jaén and Córdoba, where pollen counts in pollination period can reach peaks higher than 15 000 grains/$m^3$.

**Method:** The aim of this phase I, multicenter, open clinical trial was to evaluate the safety and tolerability of subcutaneous immunotherapy (SCIT) in depot presentation. Patients with rhino-conjunctivitis sensitized to *Olea europaea* received an abbreviated schedule consisting of: five weeks of initiation with six injections and a maintenance period of three months with a monthly administration. The primary outcome was the number, percentage, and severity of adverse reactions with this regimen. Secondary endpoint included evaluation of the subrogate efficacy parameters: changes in immunoglobulin titers (specific IgE, IgG and IgG4) and changes in cutaneous reactivity.

**Results:** There were included 47 patients, in five Spanish hospitals. Following ARIA 2010 guidelines, 95.7% of patients were diagnosed of persistent moderate/severe rhinitis. The mean age was 37.7 ± 11.8 years, being 59.6% female. Moreover, 57.4% of the patients had concomitant mild/moderated asthma. The period between the diagnosis of rhino-conjunctivitis and the informed consent signing was 9.8 ± 7.5 years.

According to International 2006 Guidelines, eight systemic reactions were registered, representing 1.9% of the administered doses: five reactions grade 0, (described as nonspecific ocular pruritus, nasal herpes, general discomfort, localized non-specific pruritus plus nausea and non-specific pruritus in throat), a grade I reaction described as rhinoconjunctivitis and two reactions grade II, registered as generalized urticaria and asthma. All reactions were classified of mild or moderate intensity and only two required symptomatic treatment. There were five clinically significant delayed local reactions, which were higher than 10 cm or involved modifications in next dose. Regarding efficacy parameters, Immunoglobulin titers between baseline and final visit according to specific IgG and IgG4 significantly increased. Cutaneous reactivity also decreased significantly in the dose response skin prick test.

**Conclusion:** Results of an abbreviated schedule with *Olea europaea* SCIT in depot vaccine, (Allergovac® ROXALL Medicina España), provides evidence of its adequate safety and tolerability profile and favorable efficacy parameters.

## 0878 | Safety and tolerability of a subcutaneous vaccine (SCIT) with native extract of Parietaria judaica

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**Background:** This was a phase I clinical trial of a SCIT with native extract of *Parietaria judaica* pollen in an aluminum depot preparation, administered following a five increasing doses build-up scheme. Results on safety, cutaneous reactivity, immunoglobulin titers and changes in rhinitis symptoms are shown.

**Method:** This was an open, multicenter clinical trial, in patients aged between 18 to 60 years with rhinoconjunctivitis with or without concomitant mild asthma and sensitized to *Parietaria judaica*. The aim was to evaluate the safety and tolerability of the vaccine. Secondary endpoints were: changes in immunoglobulin levels (specific IgE, IgG and IgG4), changes in cutaneous reactivity and changes in symptoms score. Patients were under study treatment for 17 weeks: five for the induction phase (weekly injections) and 12 for the maintenance phase (monthly injections).

**Results:** 51 patients were included in 4 Spanish sites from May 2015 to March 2016. No patient was withdrawn from the study. 43 patients (84.3%) were diagnosed with persistent moderate/severe rhinitis according to ARIA guidelines and 17.6% had concomitant mild asthma. Previous immunotherapy with *Parietaria judaica* was reported by 9.8% of patients, in all cases ended at least 5 years before starting the present trial. Adverse reactions occurred in 36 patients and were mostly mild reactions in severity. From a total of 470 administered doses, 27.7% elicited adverse reactions: 22.9% local reactions (17.7% late and not clinically relevant) and 4.7% systemic reactions (2.3% nonspecific and 2.3% grade I systemic reactions, being rhinitis and urticaria the most reported symptoms). Concerning the efficacy parameters: cutaneous reactivity at the final visit versus baseline was significantly decreased with all tested vials; specific titers of IgG and IgG4 increased significantly and the percentage of patients with rhinitis symptoms was lower and showed a significant decrease in the rhinitis symptoms score.

**Conclusion:** *Parietaria judaica* SCIT administered in depot vaccine, (Allergovac®ROXALL Medicina España), with an abbreviated updosing scheme showed an adequate safety and tolerability profile and induced *in vivo* and *in vitro* efficacy changes.

## 0879 | Tolerability and safety profile a polymerized depot mixture (100/100) with Olea europaea and phleum pratense pollen extract

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**Background:** Polysensitization in Europe is usually more prevalent than monosensitization, and this prevalence increases with age, being 54% in children under 11 years of age, 61.7% in adolescents and 64.8% in adults.

**Method:** The aim of this phase I, randomized, non-controlled, multicenter, with parallel groups, clinical open trial, was to evaluate the safety and tolerability of subcutaneous immunotherapy (SCIT), in a polymerized mixture (100/100) depot presentation.

Patients with rhino-conjunctivitis polysensitized to *Olea europaea/ Phleum pratense* received an administration schedule consisting of two weeks of initiation with three injections at weekly intervals; or a program comprising two administrations in the same day separated by 30 minutes. Both treatments continued with a maintenance period of three months with a monthly administration. The primary outcomes were the number, percentage, and severity of adverse reactions. Secondary endpoint included subrogate efficacy parameters evaluation: changes in immunoglobulin titers (specific IgE, IgG and IgG4) and changes in cutaneous reactivity at different allergen concentrations.

**Results:** 47 patients were included, 24 to accelerated and 23 to polymerized cluster group schedules. According to ARIA criteria, 89.4% of patients presented persistent moderate/severe rhinitis. The mean age was 31.1 ± 9.9 years, being 40.4% male. Moreover, 61.7% had concomitant mild/moderated asthma. Immunoglobulin titers (specific IgE, IgG and IgG4) at the final visit, increased versus baseline in a statistically significant manner in IgG and IgG4 in both schedules and allergens. There were no changes in IgE. Cutaneous reactivity at the final visit versus baseline decreased significantly in all tested vials and in both schedules.

2 systemic reactions were registered, representing 4.3% of the included patients: one grade 0, described as general discomfort plus dizziness and one grade I, such as rhinoconjunctivitis. There were no local reactions. All were classified as of mild intensity and took place with the polymerized cluster schedule. Symptomatic treatment was not required.

**Conclusion:** Both schedules with polymerized mixture of *Phleum pratense/Olea europaea*, (100/100), presented an excellent safety and tolerability. A good statistically significant response in cutaneous reactivity and immunoglobulin titers to olive and grass allergens was observed after immunotherapy.

## 0880 | Determination and analysis of the protein profile of allergens marketed in Mexico

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**Background:** Allergic diseases affect around 15 to 20% of the world population, in current medical therapy one of the pillars in the comprehensive treatment of allergic diseases and the only one capable of modifying the normal course of the disease is immunotherapy, which consists in the administration of an allergen in demonstrated potencies for each population and induce peripheral tolerance of T cells in addition to influencing the production of regulatory T cells, so it is of utmost importance the administration of allergenic extracts in concentrations which must be provided by the manufacturers of these so that the allergist can establish an individualized and effective treatment to the patient. Goals. To analyze the protein concentrations and its electrophoretic analysis of commercially available extracts in Mexico.

**Method:** The quantification of total proteins in the products was carried out by means of a colorimetric technique using the Bradford reagent (Sigma-Aldrich™, US) in accordance with the manufacturer's instructions. The absorbances of each standard and samples were obtained in a Scinco™ S-3100 spectrophotometer (Seoul, Korea) at 595 nm. All samples were analyzed in duplicate. The electrophoretic profile of the proteins in the tested allergens was obtained according to the procedure described by Laemmli, under denaturing conditions in a polyacrylamide gel at 12.5% concentration and stained in silver. In each lane approximately 30 μg of total proteins were applied. Commercial extracts of the main allergens marketed in Mexico were obtained, Rossel®, ALK®, Alerquin®, Alergomex®, Allerstan®, IPI ASAC®; and they were assigned randomly with the numbers 1, 2, 3, 4, 5 and 6.

**Results:** The following protein concentrations were found in the various extracts analyzed: see table 1

**Conclusion:** Differences were found in the protein profiles analyzed both in concentration and in their electrophoretic profiles of the allergens commercialized in Mexico, this could have consequences in the therapeutic and final concentration in the treatment given to the patient.

Allergen L, Dermatophagoides farinae (A), Phleum spp (B), Dermatophagoides pteronyssinus (C), Fraxinus spp (D), Cynodon dactylon (E).

| Allergen | Concentration (μg/mL) |
|---|---|
| a1 | 39.7 |
| a2 | 70.1 |
| a4 | 46.9 |
| a5 | 29.4 |
| a6 | 54.9 |
| b1 | 33.8 |
| b2 | 81.8 |
| b3 | 61.5 |
| b4 | 38.4 |
| b5 | 63.5 |
| b6 | 49.8 |
| c1 | 36.5 |
| c2 | 63.9 |
| c3 | 31.9 |
| c4 | 51.3 |
| c5 | 29.5 |
| c6 | 58.9 |
| d1 | 36.5 |
| d2 | 82.5 |
| d3 | 55.7 |
| d4 | 44.9 |
| d5 | 40.9 |
| d6 | 56.3 |

## 0881 | Immunogenicity of a new allergoid from Felis domesticus

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**Background:** A new allergoid from cat dander was developed and characterized to determine its reduced allergenicity in a 95% and the maintenance of IgG binding capacity. The objective of this study was to develop an immunogenicity assay in mice with the new allergoid and a native extract from cat dander.

**Method:** The study included 24 female Balb/c mice separated in three groups of 8 mice each: group 1, immunized with a mold allergen extract (control); group 2, immunized with a native extract from cat dander with a Fel d 1 content of 0.525 μg per dose; group 3, immunized with the new allergoid from cat dander with a Fel d 1 content of 2.36 μg per dose. All mice were immunized four times by subcutaneous injections with a volume corresponding to 1/10 of the recommended human maintenance dose with an interval between injections of 2 weeks. One week after the last injection the mice were sacrificed and the serum was obtained. To determine the specific antibody title indirect ELISA were performed using a cat dander extract as antigen, sera from mice as primary antibody and anti-mouse IgG or IgG1 as secondary antibody. ELISA assays were performed using serial dilutions of sera or a simple dilution by duplicate to determine the specific antibody title as arbitrary units/mL (AU/mL).

The data were analyzed by one-way ANOVA and Tukey HSD test to compare the averages of specific antibodies in each group.

**Results:** The immunization with both the native extract and the allergoid from cat dander produces specific IgG and IgG1. Regarding to IgG, a higher title was observed in group 3 respect to group 2 in a curve obtained after ELISA with serial dilutions of sera. The specific IgG title obtained in terms of AU/mL was 18.6 ± 2.6 in group 1, 105.0 ± 15.0 in group 2 and 139.9 ± 16.6 in group 3. Concerning to IgG1 the AU/mL obtained was 5.7 ± 0.4 in group 1, 73.5 ± 16.8 in group 2 and 97.5 ± 18.8 in group 3. The increase of specific IgG or IgG1 in mice from group 3 respect to mice from group 2 and control group was statistically significant ($p < 0.01$).

**Conclusion:** The safety profile of the allergoid from cat dander allows a treatment with higher dose of allergens to produce a greater response to immunotherapy to induce formation of specific IgG and IgG1.

## 0882 | Safety and tolerability of phase I study with a mixture subcutaneous vaccine of native depot Dermatophagoides pteronyssinus and Dermatophagoides farinae (50:50)

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**Background:** This was a Phase I clinical trial of a SCIT with a native mixture extract of *D. pteronyssinus* and *D. farinae* (50:50) in an aluminum depot preparation, administered following a five increasing doses build-up scheme. Results on safety, cutaneous reactivity and immunoglobulin titers changes are shown.

**Method:** This was an open, multicenter clinical trial, in patients aged between 18 to 60 years with rhinoconjunctivitis with or without concomitant mild asthma sensitized to house dust mites (HDM). The aim was to evaluate the safety and tolerability of the vaccine. Secondary endpoints included were: changes in immunoglobulin levels (specific IgE, IgG and IgG4) versus *D. pteronyssinus and D. farinae* and changes in cutaneous reactivity. Patients were under study treatment for 17 weeks: five for the induction phase (weekly injections) and 12 for the maintenance phase (monthly injections).

**Results:** 42 patients were included. There were 6 withdrawals from the trial; no one was related to treatment. The patients mean age was 33.6 years, being 50% female. 71.4% were diagnosed of persistent moderate/severe rhinitis according to ARIA guidelines and 31.0% presented concomitant mild asthma. Regarding to safety results, 22 systemic adverse reactions were registered which corresponded to 7.9% from a total of 277 administered doses. The most of systemic reactions were grade I, (5.4%) described as rhinitis or urticaria, grade 0 or nonspecific (2.2%) and 1 reaction (0.3%), was grade II. All of them were mild or moderate and only 4 needed treatment. Among local reactions, 21 (7.6%) were clinically relevant late local reactions, meaning a wheal at injection site >10 cm and /or requiring a dose readjustment in the next administration; 6 (2.2%) were clinically relevant immediate local reactions meaning a wheal >5 cm. Concerning the efficacy parameters, cutaneous reactivity at the final visit versus baseline was, in average, significantly decreased, and specific titers of IgG and IgG4 against tested HDM increased significantly at final visit.

**Conclusion:** *D. pteronyssinus and D. farinae mixture* (50:50) SCIT in native extract depot vaccine, (Allergovac® ROXALL Medicina España), in an abbreviated updosing scheme, showed an adequate safety and tolerability profile and elicited *in vivo* and *in vitro* efficacy response.

## 0883 | Quality of life improvement in patients with Rhinoconjunctivitis with or without asthma, after one-year immunotherapy treatment. Results of an observational prospective study (ÍCARA)

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**Background:** The purpose of this study was to evaluate the improvement in patients' quality of life after one-year treatment with allergen immunotherapy (AIT), and provide information on the safety and adherence to treatment by patients.

**Method:** This was an observational prospective multicenter study, which included patients sensitized to at least one allergenic source, with or without asthma, receiving SIT in routine practice. Quality of Life questionnaire for Rhinoconjunctivitis (RQLQ) and Visual Analogue Scale (VAS) to assess patients' treatment satisfaction were used. For safety assessment, any adverse reaction was also recorded.

**Results:** 214 patients from 14 centers were recruited, 198 of them were included and analyzed. Mean age was 32.8 years, 49.0% were men, and 66.2% presented associated asthma. A large majority of patients received subcutaneous AIT (98.5%), and 57.1% of them contained a single allergenic source. 56.4% in polymerized formulation, and 40.0% in native depot. Abbreviated conventional schedule was the most prescribed (57.1%), followed by clustered one (34.3%).

162 patients completed the study. Mean values in RQLQ questionnaire (total score) decreased from 2.56 to 1.24 points (51.6% score reduction) in final visit, reflecting a statistically significant improvement ($P < 0.01$). Annual episodes of rhinoconjunctivitis decreased from 13.7 to 9.7 ($P < 0.01$). 43.8% of patients improved from persistent to intermittent rhinoconjunctivitis ($P < 0.01$) and 46.9% from moderate/severe to mild intensity (ARIA) ($P < 0.01$). Moreover, 16.1% of asthmatic patients at baseline, did not have any bronchial symptoms after 1-year treatment ($P < 0.01$). Mean value of treatment satisfaction was 7.2 (SD=1.8) and 7.2 (SD=1.7) for patients and physicians respectively.

For safety assessment, out of 198 analyzed patients, and from 2917 administered doses, 34 systemic reactions were reported in 20 patients (10.1% of patients, 1.2% of total doses). Only 6 were of grade II, and the rest of grade I (EAACI grading system). Less than 1% of the administered doses caused moderate intensity local reactions.

**Conclusion:** The results of this study showed a clear significant improvement in quality of life values as well as high patients' satisfaction values after one year of AIT treatment ($P < 0.01$), together with an adequate safety profile with a low number of systemic adverse reactions, none of them serious.

## 0884 | Evaluation of safety and tolerability of "Allergovac Poliplus" in polysensitized patients with allergic rhinitis-rhinoconjunctivitis with or without asthma: An observational prospective study (APOLO)

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**Background:** The objetive of this study was the safety and tolerance assessment of *"Allergovac Poliplus"* SCIT treatment, with 2 allergen combination-mixtures in polysensitized patients, as well as the evaluation of the clinical improvement and patients' satisfaction after treatment.

**Method:** This is a prospective observational clinical study. *Allergovac Poliplus* treatment is being administered in a "1-day" or in an abbreviated schedule. Polysensitized patients (to pollens or mites), with rhinitis or rhinoconjunctivitis, with or without asthma, and between 5-60 years have been included. All adverse events are being recorded. Visual analog scales (VASs) are being used to evaluate clinical improvement, tolerance and satisfaction after treatment (10 months).

**Results:** A total of 147 patients have been included, with an average age of 31.0 years (16.3% of them under 18 years), 53.7% are women. 68.0% are diagnosed of rhinoconjunctivitis. Most patients present persistent (92.5%), and moderate/severe (91.8%) rhinitis-rhinoconjunctivitis (ARIA). 44.2% have associated asthma, 36.4% of them moderate (GINA). 61.9% of patients are receiving treatment with a 2-pollen mixture (the most frequent one being grass+*Olea europea* (34.7%) combination), while the rest are mixtures with 2-mites: *DPT/DF+Blomia tropicalis* (12.9%) or DPT+*Lepidoglyphus destructor* (25.2%). The "1 day" schedule administration have been the most prescribed (81.7%), compared to abbreviated one.

Currently, 17 patients have already completed the study. These patients have improved in a mean of 24.0% their VAS values in clinical status (mean difference 1.28 points). The mean values obtained in the VAS scale of tolerability are 8.5 (SD=1.8), and 7.3 (SD=2.1) for the patient satisfaction VAS scale. So far, only 23 adverse reactions have been reported. All of them were mild and local (no systemic reactions were reported). 4 are immediate, and the rest are late reactions. Only 2 reactions are clinically relevant. 10 reactions have been presented in the initiation phase of treatments, and most of them with the "1 day" schedule.

**Conclusion:** The safety profile observed so far for the treatment with *Allergovac Poliplus* in polysensitized patients seems to be very acceptable for them. Clinical improvement, tolerability and satisfaction values observed, seem to be also favorable for patients after treatment.

## 0885 | The effectiveness of vaccine prophylaxis of conjugated pneumococcal vaccine in patients with chronic obstructive pulmonary disease for 5 years of observation

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**Background:** GOLD-2017 emphasizes the importance of vaccine prophylaxis against pneumococcal infection. The effectiveness of the PCV13 in patients with COPD has been assessing in the Municipal Pulmonary Center (Chelyabinsk) since 2012.

**Method:** The study included 394 men. The average age of the studied groups were 62.13 years. Patients were divided into 3 groups. The first (n = 150) - patients who were vaccinated with PCV13. The second - not vaccinated (n = 212). The third group consisted of 32 patients vaccinated PPV23. Evaluation of intermediate control points: number of exacerbations, number of hospitalizations, cases of community-acquired pneumonia. The prognostic index BODE is calculated.

**Results:** In all groups prevailed severe forms of the disease and the phenotype of frequent exacerbations. Groups were comparable in age composition and structure of severity. Observations in the group

of vaccinated PCV13 continue the dynamics of decreased dyspnea up to 1.66 (1.11;2.21) points and in the group of PPV23 dyspnea returns to the initial values by the 5th year. Exacerbations COPD was observed in 70% of patients at the time of treatment. In vaccinated patients in both groups after a year of observation, spotted numbers exacerbations in 6.5: from 130 to 25 cases in the group of PCV13 and from 25 to 4 in the group of PPV23. Patients vaccinated with PCV13 after 5 years the number of exacerbations, in comparison with the first year after vaccination, did not change significantly. 95% of the exacerbations were treated as non-communicable, 90% were smokers. Among non-smoking exacerbations patients COPD was not. The number of pneumonias increased in all groups. Microbiological diagnosis of sputum in 62% of cases did not give rise or fixed the flora of the oropharynx in undiagnosed titles. In the group of patients, vaccinated with PCV13, the BODE index had a significant change through year with the effect remaining after 5 years of follow-up.

**Conclusion:** 1. Inclusion vaccine prophylaxis PCV13 in the plan helps to stabilize basic functional parameters of the respiratory system. 2. Using prognostic index assessment indices are a reliable tool for monitoring the effectiveness of the therapy. 3. For nonsmokers the use of PKV13 reliably reduces the number of infectious exacerbations and amount of pneumonia after 5 years. 4. By keeping the effect on all 5 years monitoring vaccination with PCV13 minimizes the number exacerbations of COPD, incidence of pneumonia and the costs of the health system.

## 0886 | Does the number of exacerbation in asthma treated by immunotherapy with dermatophagoides is related to intensity of PRICK reactions?

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**Background:** Immunotherapy of asthma is well established treatment for well documented diagnosis of allergic patterns caused by allergen of dermatophagoides pteronyssinus. Diagnostic procedures should include PRICK test, as the most important and total IgE as well as specific IgE for dermatophagoides pteronyssinus. What is the most important factor in assessing the risk of asthma exacerbations and does the intensity of PRICK reaction is related to asthma exacerbations in patients treated with specific subcutaneous immunotherapy (SCIT), is to be analyzed in this paper.

**Method:** Patients treated with SCIT were analyzed. Diagnostic procedures include PRICK test, measurements of total IgE and specific IgE against dermatophagoides pteronyssinus. Patients were treated at least one year and followed up to evaluated number of exacerbations including assessment of asthma control test. Assessment of PRICK test was conducted by Global Allergy and Asthma European Network (GALEN), and complete PRICK test procedure, so.

**Results:** During three years period we followed up 64 asthmatic patients treated with SCIT, 42 female (66%), and 22 mail (34%), mean age 37 ± 5.6 years. Patients were divided in three steps according to diameter of weal during skin test (I group 3-10 mm, II group 10-20 mm, III group >20 mm). Patients of I group have 0-8 exacerbations yearly, average 4.6 ± 0.4, those of II group 4.9 ± 0.4, and in III group 5.1 ± 0.5 exacerbation per year. There was no significant difference in the severity of exacerbation, nor in the results of the asthma control test. Total IgE was in average 426 ± 54 IU/mL in first group, 466 ± 76 IU/mL in second group, and 482 ± 55 IU/mL in third group. Specific IgE against dermatophagoides was 22.17 ± 3.3 IU/mL, 25.2 ± 4.4 IU/mL and 26.1 ± 5.1 IU/mL respectively.

**Conclusion:** Number of exacerbation and their severity is not related to intensity of PRICK test during diagnostic assessment in asthmatic patients treated by SCIT against dermatophagoides pteronyssinus.

## 0887 | Subcutaneous aeroallergen immunotherapy: To whom? With what?

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**Background:** Allergen immunotherapy is the only treatment capable of altering the natural course of allergic disease. In Portugal there are few studies characterizing the population submitted to this treatment as well as the prescription population profile.

**Objectives:** Evaluate the clinical and sensitization of patients undergoing subcutaneous allergen immunotherapy (SCAIT) and characterize the type and composition of this treatment.

**Method:** Retrospective analysis of SCAIT and patients undergoing this treatment clinical records, between Jan2013-Dec2016 at CHLN. Evaluation of demographic data, clinical parameters and SCAIT.

**Results:** Of a total of 631 pts under SCAIT, 110 were excluded due to data unavailability, and 521 included (♀283 (54%), mean age 32 ± 13 years (minutes: 7 max 73 Md30), age range [18-30] being most prevalent (40%). The most frequent diagnosis was rhinitis/rhinosinusitis (97%), followed by asthma (43%), diagnosis coexisting in

| Comp. | Dermat | Dpt | Dermat+ O.mite | Dermat+ Pollen | Lepido | O.mite | Dermat+ Fungi | Gram | Pariet | Gram+ Olea | Gram+ Pariet | Olea | Gram+ Artem | Phleum | Cat Dander |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N (%) | 140 (26.9) | 123 (23.6) | 85 (16.3) | 20 (3.8) | 6 (1.1) | 2 (0.4) | 1 (0.2) | 87 (16.6) | 23 (4.3) | 12 (2.3) | 11 (2.1) | 4 (0.8) | 3 (0.7) | 3 (0.7) | 1 (0.2) |

Dermat - *Dermatophagoides*; Dpt - *Dermatophagoides pteronyssinus*; Lepido - *Lepidoglyphus destructor*; O. mite - Other mite; Gram - *Gramineae*; Pariet- *Parietaria judaica*; Olea - *Olea europaea*; Artem - *Artemisia vulgaris*; Phleum - *Phleum pratense*.

214 pts (41%). Other diagnosis such as conjunctivitis (24%), atopic eczema (15%) and food allergy (9%) were also found. Mite sensitization occurred in 422 patients (81%) of which 199 (47%) were monosensitized. The pollen sensitization was verified in 288 (55%) with 88 monosensitized pts (31%). The double sensitization mites-pollens was displayed in 189 (36%). Sensitization to epithelia and fungi occurred respectively in 100 (19%) and 42 pts (8%). It was found that 20 pts (4%) presented sensitization to the 4 groups of allergens (mites, pollens, fungi, dander). An average of 58 ± 23 pts started this treatment per year. Prescription included 10 laboratories with the following %: A-39.6; B-29.3; C-13.2; D-5.4; E-4.7; F-4.2; G-2.5; H-0.9; I-0.1; J-0.1. Option for extract of physical modification (5%), physical-chemical (16%) and chemical (79%). Table 1 shows the frequency of distribution of SCAIT composition.

**Conclusion:** In this population sensitization to mites was predominant being the most prescribed SCAIT followed thru sensitization to grasses with the respective SCAIT. The majority of the population was polysensitized. However, in composition preference the choice of 1 group of allergens prevailed and only 5% had more than one sort of pollen and 4% pollen+mites. Polysensitization is a reality, nonetheless the choice of AIT composition should be guided thru scientific criteria and not through the availability of mixtures encouraged by laboratories.

## 0888 | Recombinant allergens in venom immunotherapy treatment

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**Background:** Molecular diagnosis with recombinant allergens allows for the exact pinpointing of the proteins a patient is sensitive to in an allergen source.

The components of recombinant allergens ensure optimum venom immunotherapy treatment. We hereby present two clinical cases in which diagnosis and treatment has been made easier thanks to the aforementioned tool.

**Method:** 40 year old male with high environmental exposure who suffered an anaphylaxis reaction, grade IV according to the Muller classification, having been stung by a non identified vespidae. After a complete patient anamnesis, an analysis was requested with total IgE values, for Apis mellifera, Polistes dominulus, Vespula vulgaris, recombinants Ves v1, Ves v5, Pold d5, triptase and total IgE.

68 year old male with extensive multiple localised reactions having been stung by a wasp, with grade III anaphylaxis. An analysis is requested with total IgE values for Apis mellifera, Polistes dominulus, Vespula vulgaris and triptase.

**Results:** In the first patient, specific IgE (ImmunoCAP®) were detected for Vespula spp 1.21 UI/mL, Polistes dominullus 2.31 UI/mL, Vespula vulgaris 1.28 UI/mL, Rec r Ves v1: 1.28 UI/mL, Rec r

Ves 5: 0 UI/mL, Rec r Pold 5: 0. Pol d1 (ADVIA Centaur): 1.58 kUA/L were detected

IgE values specific to Polistes dominulus were detected, Vespula spp went undetected. There was a second assessment which gave the same result. Recombinants were requested and a new IgE specific to Polistes dominulus 2.16, Véspula vulgaris, Rec r Ves v1, Rec r Ves v5, Rec r Pold5: 0.

**Conclusion:** In the first patient, the IgE levels for phospholipases of both genus (Vespula and Polistes) did not allow for the determination of whether the union to IgE is specific to each phospholipase or it is caused by a crossed reaction. This would be an indication of double immunotherapy.

In the second case, it was not possible to determine Pol d1 and taking into account the IgE values of a complete extract of Polistes dominulus, immunotherapy with 100% Polistes dominulus was prescribed.

In both cases, the dominant allergen (antigen 5) went undetected. The main specific dominant allergens are the Pol d 5 (antigene 5) for polistes; Ves v 1 (phospholipase A1) and Ves v 5 (antigen 5) for vespula.

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## 0889 | Safety of allergen immunotherapy in seniors: Results of a 2 year observational study

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**Background:** Allergen immunotherapy (AIT) has been proven to be an effective treatment of allergic diseases in numerous studies. However, its use in seniors remains limited and questionable, due to common comorbidities and limited evidence of efficacy and safety of AIT in aging population.

The aim of presented study was to assess the safety of AIT in patients over 55 years of age undergoing subcutaneous immunotherapy (SCIT) and analyze the potential risk factors of adverse reactions in this population, compared to younger adults.

**Method:** We followed subcutaneous immunotherapy in a group of 1302 patients treated in the outpatient clinic of Medical University of Lodz, of whom 163 were aged 55 and older (118 between the age of 55-60, 31 aged 61-65 and 14 patients above the age of 65). We recorded detailed information of each administration and corresponding adverse reactions over the period of 2 years. We compiled results of our observations with patients' medical records to compile a database, which we then analyzed using statistical software.

**Results:** 568 patients (43.6%) experienced at least one adverse reaction, local or systemic, after SCIT. We observed no significant difference in AE occurrence between adult (under 55 years of age) and senior group (44.1% and 30.5% respectively). Further analysis showed that while both groups had similar per-patient incidence of local reactions (41.9% vs 40.5%), we observed noticeably fewer systemic events in seniors (10.4% vs 14.7%, $P = 0.047$). Interestingly, while less common, systemic AEs appeared to be more severe in the aged population, with as many as 4.9% of the group having experienced WAO grade 2 reactions, compared to 2.4% in young adult group. No grade 3 or 4 reactions were observed in the course of the study.

While older patients had significantly more comorbidities, multivariate statistical analysis of potential risk factors did not reveal any difference between groups, with both adults and seniors being more likely to experience AEs during immunotherapy with house dust mite compared to other allergens, as well as under treatment with native allergen extracts compared to allergoids.

**Conclusion:** While numerous comorbidities and concomitant medications may promote more intense adverse events in patients of 55 years and above, we observed no severe reactions in this aged population during a 2 year observation period. Our results suggest that allergen immunotherapy in the elderly is safe and well tolerated.

## 0890 | Effectiveness of preseasonal allergoid immunotherapy: Controlled trial in monosensitized and polysensitized patients

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**Background:** The effects of pre-seasonal allergoid immunotherapy on the clinical efficacy and immunologic response in polysensitized patients are not known. The aim of the present study was to compare the clinical efficacy and immunological changes of pre-seasonal allergoid immunotherapy in mono and polysensitized patients.

**Method:** A total of 46 cases with seasonal allergic rhinitis undergoing pre-seasonal immunotherapy and 28 cases followed with conventional drug treatment were included in the study. Immunotherapy and control groups were divided into monosensitized (only pollen) and polysensitized (at least 1 additional allergen except pollens) patient groups according to skin prick test reactivity. All patients were followed between March-September 2013 with symptom and medication scores, and visual analogue scale (VAS). The quality of life was assessed using the Mini-RQLQ questionnaire. Phleum pratense (*Phl p*) specific IgE and specific IgG4 (UNI-CAP 100, Phadia) measurements were performed before and after 7 weeks of immunotherapy in all patients. Gramineae pollens were counted during the grass pollen seasons.

**Results:** Mean age was 34.9 ± 10.6 and 34.2 ± 12 years, female/male ratio was 29/17 and 17/11, the number of monosensitized/polysensitized patients were 37/9 and 20/8 in immunotherapy and control groups, respectively. In the immunotherapy group, June-July symptom scores, May-June-July-August VAS scores and June combined symptom-medication scores were lower than the control group ($P = 0.005$). Furthermore, improvements in activities-practical problems and other quality of life scores were significantly different between two groups ($P < 0.05$). In immunotherapy group, *Phl p* specific IgE and *Phl p* specific IgG4 levels measured after immunotherapy were significantly higher compared to those before immunotherapy ($P < 0.001$, $P < 0.001$, respectively). *Phl p* specific IgG4 levels measured after immunotherapy were also significantly higher in the immunotherapy group than in the control group ($P < 0.001$). There was no difference in terms of clinical and immunologic parameters in monosensitized and polysensitized patients ($P > 0.05$).

**Conclusion:** Clinical improvement with pre-seasonal allergoid immunotherapy is accompanied by an important increase in specific IgG4 blocking antibodies despite short-term injections. Our findings show that pre-seasonal allergoid immunotherapy has similar clinical

efficacy and B cell response in polysensitized subjects compared to monosensitized patients.

## 0891 | The safety trial of sequential sublingual immunotherapy with Japanese cedar droplet and house dust mite tablet

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**Background:** Sublingual immunotherapy (SLIT) is recognized as the only treatment option with the potential to provide long-term post-treatment benefits. In Japan, the prevalence of Japanese cedar (JC) pollinosis is very high, about 30% of the population, of which the majority are co-sensitized to HDM. SLIT is now well established, safe and convenient treatment form for allergic disease, and recently, JC SLIT-droplet and HDM SLIT-tablet products were approved in Japan for treatment of JC and HDM induced allergic rhinitis, respectively. However, the safety of sequential JC SLIT-droplet and HDM SLIT-tablet has not yet been investigated. Therefore, we investigated the safety trial on SLIT combined with JC droplet and HDM tablet in allergic patients.

**Method:** Eleven subjects with JC pollinosis and HDM rhinitis were enrolled. Patients were treated once-daily with JC SLIT-drops for 4 weeks, followed by 24 weeks of sequential SLIT treatment where the JC SLIT-drops and the HDM SLIT-tablets were administered daily with a 5 minute interval (1st: JC-SLIT drops, 2nd: HDM SLIT-tablet). The primary endpoint was the frequency and severity of adverse events (AEs) during sequential SLIT by Common Terminology Criteria for Adverse Events (CTCAE) v4.0 and SLIT grading system. Serum antibodies were measured as the secondary endpoint.

**Results:** Eleven patients were recruited. AEs after JC SLIT-drops administration were found in 9 patients out of 11 cases (82%). AEs after sequential SLIT were found in 8 patients out of 10 cases (80%). All AEs were graded 1 or 2. No severe AEs were observed during the study period. The levels of JC- and HDM-specific IgE and IgG4 in serum were increased during treatment.

**Conclusion:** Sequential-administration of JC SLIT-drops and HDM SLIT-tablets was well tolerated by patients suffering from both JC pollinosis and HDM rhinitis.

## 0892 | Sublingual Immunotherapy with a liquid Phleum pratense extract is effective in grass pollen allergic patients—Results of a phase II allergen exposure chamber (AEC) trial

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**Background:** According to the EMA guideline on the clinical development of products for specific immunotherapy products should be tested in phase II at different doses in several study-arms to establish a dose-response relationship for clinical efficacy before confirmatory trials can be initiated. Allergen exposure in an AEC may be used as primary endpoint.

**Method:** The study was a single-center, randomized, double blind, placebo-controlled, phase II trial, treatment duration 10 months. 168 grass pollen allergic patients (18-65 years of age) with seasonal rhinitis/rhinoconjunctivitis (ARC) with (mild, GINA I) or without concomitant asthma were randomized to three different dosages of a liquid *Phleum pratense* extract (10 000 AUN/mL; 40 000 AUN/mL; 80 000 AUN/mL) or placebo for sublingual administration (maximum dose 5 drops, up-dosing in 4 days). The primary efficacy endpoint was the mean Total Symptom Score (TSS: sum of individual scores for eight nasal and non-nasal symptoms, rated on a scale of 0-3) at the end of the trial. For TSS assessment a validated AEC was used with a standardized controlled grass pollen exposure at an average concentration of 3500 ± 500 $ppm^3$ for 6 hours ensuring aeroallergen exposure under controlled and reproducible conditions.

**Results:** According to the pre-specified Emax model a borderline significant dose-response relationship for TSS was observed ($P$ = 0.050 per protocol population, 0.057 ITT). At the end of the trial all patients (ITT) treated with the different doses of the liquid *Phleum Pratense* extract showed an improvement in the TSS compared to placebo (LS Means (SE): placebo 10.01 points (0.80), 10.000 AUN/mL 8.06 (0.85), 40.000 AUN/mL 8.19 (0.82) and 80 000 AUN/mL 7.69 (0.83), respectively). The TSS reduction compared to placebo ranged from 18.2% to 23.2%. The treatment emergent adverse events (TEAE) were primarily local reactions, of mild intensity with a dose-response relationship. The incidence of patients developing at least one systemic reaction (all Grade I), were similar between the active treatment groups and the placebo group.

**Conclusion:** A consistent improvement of ARC symptoms was observed with all doses of the liquid *Phleum pratense* extract, including the current marketed dose of 10 000 AUN/mL, compared to placebo in this AEC model. The safety profile was comparable to other sublingual immunotherapy (SLIT) products.

## 0893 | Relation between grass pollen count and Combined Symptom and Medication Score in grass allergic patients

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**Background:** The Combined Symptom and Medication Score (CSMS) has been recommended by EAACI as primary endpoint for pivotal Phase III studies in allergic rhinoconjunctivitis (ARC) (Pfaar, Allergy 2014). Currently, a Phase II study with a modified grass allergen subcutaneous immunotherapy (SCIT) product (1.0 mL) with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants will read out in 2018 and a subsequent pivotal Phase III study is in preparation. As part of an effort to prepare the analysis plan using the CSMS as primary endpoint, the grass pollen data of the European Aeroallergen Network (EAN) was used to identify the window within the grass pollen season (GPS) with optimal correlation between the grass pollen counts and the CSMS.

**Method:** EAN currently includes information from more than 400 active and 300 historical pollen-monitoring stations in Europe including 39 countries. The EAN database used for analysis included grass pollen data collected during 2009-2016. The daily allergy symptoms and medication were recorded spontaneously using an APP questionnaire on the subject's smart phone. The CSMS was re-calculated using the EAN database, using the recorded symptom scores with estimation of the medication score using similar methods as recently published. The correlation between the daily grass pollen count and the daily CSMS was analyzed with a mixed effects model accounting for patient-specific correlations and symptom levels.

**Results:** Days of the GPS with higher grass pollen counts had significantly higher CSMS values. Irrespective of the pollen counts, for earlier days during the grass pollen season statistically significant higher CSMS values were observed. Furthermore, during the overlap of the GPS and the birch pollen season (BPS) lower CSMS values were reported.

**Conclusion:** These results confirm a statistically significant correlation between grass pollen counts and the CSMS. Importantly, these findings suggest that the optimal window to observe treatment effects after immunotherapy may be a short interval after start of the GPS and during the peak GPS, due to generally higher CSMS values. This provides sufficient basis to consider additional sensitivity analyses to evaluate the treatment effect of grass MATA MPL SCIT on the primary CSMS endpoint during a shortened window after the start of the GPS and to consider excluding the overlapping period between the BPS and GPS from the primary analysis.

## 0894 | Combo-VAS as a tool to assess efficacy of allergen immunotherapy

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**Background:** Allergen Immunotherapy (AIT) is at present the unique cure for respiratory and venom allergy. Usually, AIT lasts for some years, but its efficacy is longstanding. Criteria for assessing AIT efficacy are mainly based on symptom severity improvement and saving of symptomatic medications. In this regard, there are different score grading for both measuring symptom severity and drug use. Visual analogue scale (VAS) is a well-defined and validated method widely used in many diseases, including allergic disorders. VAS is a psychometric tool measuring the patient's perception of symptoms, emotions, pain, drug use, etc.

**Method:** Recently, it has been published an EAACI position paper concerning the recommendations for the standardization of clinical outcomes used in AIT trials for allergic rhinoconjunctivitis, but it is complex. So we would propose a simpler way to measure AIT efficacy by VAS, in particular a combo-VAS based on one VAS for symptom and one for medications.

**Results:** Globally 150 patients were retrospectively evaluated. All of them were treated with a 3-year AIT course: 120 were defined as responders and 30 as non-responders. In Responders group the Combo-VAS mean value was 14 (IQR 12-15) at baseline and 4 (IQR 3-6) after AIT treatment. In Non-Responders group Combo-VAS mean value was 13 (IQR 10.5-14) at baseline and 11 (IQR 9-12.5) at the end of AIT. The difference was significant ($P = 0.012$). The D Combo-VAS was −66.67% in Responder Group and −10% in Non-Responders group ($P < 0.0001$).

**Conclusion:** Combo-VAS, i.e. the sum of VAS for symptoms and medications, could be an easy and quick tool for assessing AIT efficacy and reflects the patient's perception. Therefore, it could be very fruitful in clinical practice.

## 0895 | Rapid up-dosing in sublingual specific immunotherapy is safe, well-tolerated and effective in patients suffering from tree pollen allergic rhinitis

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**Background:** An optimised up-dosing period of specific immunotherapy (SIT) is desirable for better patient compliance

because a long or complicated up-dosing scheme is sensitive to disruption. The aim of this study was to compare the safety, tolerability and effectiveness of an optimised up-dosing scheme with two pre-existing schemes of sublingual SIT (SLIT) in patients under standard medical care.

**Method:** This was a prospective, open, active controlled, multi-center non-interventional study in Germany and Austria to document the treatment of children and adults with allergic rhinoconjunctivitis and/or allergic asthma treated with a SLIT containing purified, aqueous extracts of birch, alder and hazel pollen. The investigators were free to select an up-dosing scheme for included patients: scheme A consisted of an up-dosing period of up to 12 days at the patient's home using three different solution strengths to reach the maximum dose; ultra-rush scheme B performed only with the highest solution strength at the physician's office within 2 hours, and the optimised scheme C which was initiated at the physician's office and continued at home using exclusively the highest solution strength within 2 (long-term) or 4 (pre-seasonal) days. Data on up-dosing and maintenance treatments were documented by physicians during 5 patient visits and by patient diaries. The study was approved by ethic committees, and all patients or parents gave their informed consent.

**Results:** In total, 164 patients aged 3-76 years were included into this study. Scheme A was applied by 90 patients, 29 patients decided on regimen B, and 45 patients on the optimised scheme C. 106 valid patient diaries documented comparable proportions of patients without any local reaction nor any systemic reactions during the up-dosing phase (A: 50.8% and 84.7%, B: 45.5% and 72.7%, and C: 51.9% and 77.9%, respectively). For all groups, more than 90% of the patients and investigators evaluated the overall tolerability of treatment as "very good" or "good". Compared to the previous year, a clear decrease in the severity of rhinitis symptoms (A: 66.2%, B: 44.4%, C: 63.2% of patients) and in the use of symptomatic treatment (A: 36.6%, B: 15.5%, C: 25.0% of patients) was shown.

**Conclusion:** The evaluated SLIT was well tolerated and shown to be beneficial. No relevant difference in tolerability and safety was found between the gentle up-dosing scheme A and the schemes B or C, which used only the highest strength solution.

## 0896 | Compatibility of an accelerated dose escalation with a high-dose, hypoallergenic birch pollen allergoid

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**Background:** Subcutaneous specific immunotherapy (SCIT) with a high-dose birch pollen allergoid is an effective and tolerable treatment method. This study examines the safety and tolerability of a dose escalation scheme reduced to 4 injections with a hypoallergenic birch pollen preparation.

**Method:** 130 adult patients were included in an open controlled multicentre phase II trial. The compatibility of an accelerated dose regimen (4 injections, n = 63) was compared to the standard dose regimen (7 injections, n = 67). Both groups additionally received 2 maintenance doses. All adverse events were recorded. Patients and investigators assessed the tolerability of the treatment using a 5-point Likert scale.

**Results:** Frequency and severity of adverse events were comparable in both treatment arms. Local reactions occurred in 54.0% of patients in the accelerated and 56.7% of patients in the standard dose regimen. Systemic reactions occurred in 6.3% of patients in the accelerated and in 3.0% of patients in the standard dose regimen. More than 85% of the patients as well as the investigators rated the accelerated dose regimen as good to very good tolerated.

**Conclusion:** The accelerated dose regimen with a high dose, hypoallergenic birch pollen allergoid provides an additional safe dosing regimen for patients suffering from an allergic rhinoconjunctivitis with or without bronchial asthma. Treatment of adult patients with the hypoallergenic birch pollen preparation can be initiated about 4 weeks before the pollen season.

## 0897 | Updated safety analysis of a high-dose hypoallergenic birch pollen allergoid from clinical trial data

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**Background:** Subcutaneous high-dose hypoallergenic allergen immunotherapy (AIT) using a birch pollen allergoid has been well-established for decades in birch-pollen specific immunotherapy of allergic rhinitis and asthma. Recently performed new clinical trials prompted a reappraisal of the overall safety data pool from clinical trials.

**Method:** 800 patients diagnosed for grass pollen allergic rhinoconjunctivitis (+/-) asthma were included in 3 randomized, controlled trials. The pooled active safety set (PASS) comprised all patients receiving active AIT via the standard dose escalation scheme (7 injections) either as preseasonal or perennial treatment for a maximum of 3 years. Adverse events (AE), adverse drug reactions (ADRs) as well as routine biochemical and hematological laboratory safety parameters were analysed. The Medical Dictionary for Regulatory Activities (MedDRA 19.0) terminology was used throughout for coding with recoding of AE terms from lower MedDRA versions where appropriate. All codes were assessed to their primary system organ class (SOC).

**Results:** 304 (159 female, 145 male) patients with a mean age of 36.8 years and a mean duration of allergic rhinoconjunctivitis of 13.3 years were included in the safety analysis. 83 (27.3%) Patients were diagnosed for having bronchial asthma at study entry. More

than 40% of treatment emergent AEs were observed in the following SOCs: General disorders and administration site conditions (n = 137) as well as infections and infestations (n = 152). 8.9% of patients (n = 27) had systemic reactions. No treatment related serious adverse events were observed. The most frequent drug related adverse events (ADRs) were injection site reactions like pruritus (28.3%, n = 86), reaction (24.3%, n = 74), and swelling (reported for 22.7% of patients, n = 69). No notable differences in changes of laboratory measurements following AIT compared to placebo were observed.

**Conclusion:** The updated overall analysis of safety data from randomized, controlled clinical trials confirmed previous analyses of clinical trial data and was found in accordance with the long-term experience from the use of the high dose hypoallergenic birch pollen allergoid in the market.

## 0898 | Safety of ultra-rush schedule of subcutaneous allergen immunotherapy with house dust mite extract in patients with atopic dermatitis conducted in an outpatient clinic

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**Background:** Ultra-rush schedule of subcutaneous allergen immunotherapy (UR-SCIT) administering maximum maintenance dose of allergen extract within one-day can save time and effort in patients with allergic diseases. However, UR-SCIT is associated with an increased risk of systemic reaction compared to conventional subcutaneous allergen immunotherapy and is usually conducted in a hospital admission setting. To overcome these limitations of UR-SCIT, we evaluated the safety of one-day UR-SCIT in patients with atopic dermatitis (AD) conducted in an outpatient clinic.

**Method:** UR-SCIT was performed in 421 patients with moderate-to-severe AD sensitized to house dust mites (HDM). A maximum maintenance dose of tyrosine adsorbed HDM extract (1 mL of maintenance concentration) was divided into 4 increasing doses (0.1, 0.2, 0.3, and 0.4 mL) and administered to the patients by subcutaneous injections at 2-hour interval for 8 hours in an outpatient clinic. Systemic reactions associated with UR-SCIT were classified according to the World Allergy Organization grading system.

**Results:** Systemic reaction was observed in 8 of 421 patients (1.9%) during UR-SCIT. Severity of systemic reaction was grade 1 in 5 patients (1.2%) and grade 2 in 3 patients (0.7%). Severe systemic reaction (grade 3 to 5) was not observed. Prescheduled 4 increasing doses of HDM extract could be administered in 420 of 421 patients except one patient who experienced a systemic reaction at 1.5 hours after the first dose injection. Systemic reactions were observed within 2 hours in 7 patients and at 5.5 hours in one patient who experienced a grade 2 systemic reaction after administration of the last dose of HDM extract.

**Conclusion:** One-day UR-SCIT conducted in an outpatient clinic was safe and well-tolerated in patients with AD sensitized to HDM. UR-SCIT can be a safe and useful option to start a subcutaneous allergen immunotherapy for AD.

## 0899 | Factors affecting on adherence to allergen specific immunotherapy

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**Background:** Allergen specific immunotherapy (AIT) is known to be the only therapeutic modality to alter the natural course of allergic diseases. However, at least 3 years treatment duration is required to achieve the long-term disease-modifying effect through AIT. This study aimed to investigate clinical factors associated with its non-adherence in real world practice.

**Method:** We retrospectively reviewed medical records of patients who were diagnosed as allergic rhinitis, asthma, conjunctivitis or atopic dermatitis and sensitized to common allergen such as house dust mite and/or pollens. Total 1162 patients had taken AIT from January 2007 to August 2014. Clinical factors including demographics, their diagnosis of allergic diseases, schedule of build-up phase, associated diseases other than allergic disease, follow up schedule to other departments in the same hospital, the kinds of allergens contained in AIT, and patients' address were analyzed to affect the adherence to AIT.

**Results:** Among 1162 enrolled patients, 228 (19.6%) patients failed to complete at least 3 years of AIT, which were regarded to be non-adherent in this study. Univariate analysis revealed that male, younger age group less than 40 years, cluster and ultra-rush schedules, atopic dermatitis, the absence of associated diseases, and follow up of other department were found to be associated with non-adherence to AIT. In multivariate analysis, younger age group less than 40 years (OR 2.31, 95% CI 1.55-3.45), cluster (2.37, 1.56-3.60) and ultra-rush schedules (6.03, 3.18-11.42), and absence of follow up of other department (2.11, 1.31-3.40) were independently associated with non-adherence to AIT. No association was found in gender, diagnosis of allergic diseases, kind of allergen extracts, and patients' distance from hospital.

**Conclusion:** Various factors are related with AIT non-adherence to interfere the effectiveness of immunotherapy. Clinicians need to be aware of the factors associated with non-adherence to AIT and consider them when choose to maximize AIT adherence.

## 0900 | Cost-effectiveness of allergen immunotherapy to grass in patients with allergic rhino-conjunctivitis and asthma

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**Background:** Allergen Immunotherapy (AIT) has been shown to reduce symptoms and medication use in subjects with rhino-conjunctivitis and asthma. However, long-term cost effectiveness of this therapy needs to be evaluated. Our aim was to assess cost effective of AIT, both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), *vs.* pharmacotherapy alone in subjects with rhino-conjunctivitis, with or without allergic asthma, to grass pollens.

**Method:** A Markov cohort state-transition model with a time horizon of 9 years was used to assess the costs and effects of 3-year AIT in adults. Relative efficacy of the treatments expressed as standardized mean difference was estimated using an indirect comparison on symptom and medication score extracted from available meta-analyses. The Rhinitis Symptom Utility Index was used as a proxy to estimate utility values for symptom score. The societal perspective, through the Human Capital technique, was used to estimate indirect costs, to represent the scenario of a country with nationalized medicine. Data on drug and other medical costs were derived from published sources as well as AIT duration and asthma occurrence. Additional sensitivity analyses were performed to test the robustness of our results.

**Results:** In the base case analysis, using Italy clinical practice patients with moderate-to severe allergic rhino-conjunctivitis (SS ranging from 6 to 15 points) and a mean age at entry of 21 years, both SCIT and SLIT were associated with increased cost but superior efficacy compared to pharmacotherapy alone. The results were most sensitive to variation in efficacy estimates and AIT persistence rates.

**Conclusion:** This analysis suggests that AIT is cost effective relative to pharmacotherapy alone. SCIT, despite significantly higher indirect cost burden, seems to be the most cost effective option. The results should be interpreted in the context of the data input and modelling assumption used.

## 0901 | iELISA as a tool to measure IgE binding towards single modified peanut allergens

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**Background:** Immunotherapy has shown to be a potential treatment for food allergies but needs further research to improve safety. Modification of peanut allergens to reduce their allergenicity is a promising approach to develop a safe and effective immunotherapy as shown by the successful completion of a first-in—human safety and tolerability study using HAL-MPE1 in adult patients with peanut allergy (EudraCT 2013-004238-13). In order to assess the impact of modification on individual peanut allergens and to assess its impact on IgE binding by individual patient sera, we have developed peanut allergen-specific inhibition ELISAs. With this methodology we are able to identify patients with residual IgE binding to modified peanut allergens.

**Method:** IgE inhibition ELISAs (iELISAs) were developed and performed to test IgE binding towards purified Ara h2 and Ara h6 and their reduced and alkylated (modified) versions, using the individual responses of single patient sera.

**Results:** Ara h6-specific iELISAs showed that modification of Ara h6 results in >95% reduction in IgE-binding for all individual sera tested. Ara h2-specific iELISAs showed that modification of Ara h2 also results in >95% reduced IgE-binding for most of the sera, but some sera were identified which showed residual, 10%-20% IgE binding to mAra h 2. In some of the latter sera, the presence of IgE binding to a linear hydroxyproline-containing peptide could be confirmed as a possible source for the residual IgE binding to mAra h2.

**Conclusion:** We have developed a methodology to assess residual IgE binding to modified peanut allergens. The sensitivity of the allergen-specific iELISAs allowed us to discriminate between patient sera in which IgE binding to mAra h2 and to mAra h6 was virtually completely absent and sera in which 10-20% residual IgE binding to Ara h2 was observed. The clinical importance of these observations is yet unknown. Future clinical studies will need to reveal whether the patient-specific IgE binding profiles to individual modified peanut allergens do correlate with the adverse events profile of immunotherapy with modified peanut extract.

## 0902 | Design of a phase II allergen immunotherapy study to determine the optimally effective and safe dose of subcutaneously administered tyrosine adsorbed modified grass allergen+MPL

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**Background:** A Phase II study is being conducted [EudraCT 2017-000333-31] as part of a clinical development program to support the marketing authorization application of a modified grass allergen subcutaneous immunotherapy (SCIT) product (1.0 mL) with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A

(MPL) adjuvants for the treatment of allergic rhinoconjunctivitis (ARC) due to grass pollen.

There is increasing evidence that the effectiveness of allergy immunotherapy to control ARC symptoms is related to the cumulative allergen (or allergoid) dose administered. Previously, two clinical studies have been conducted using a conjunctival provocation test (CPT) as primary efficacy measure for a similar SCIT MATA MPL product for birch allergy [EudraCT 2012-004336-28 and 2015-000984-15]. These studies showed a 5.5 fold increase in cumulative dose to achieve ~ 50% increase in efficacy, with a relative reduction in total symptom score (TSS) of 32.3% compared to placebo and no safety signals of concern. The shape of the dose response curve was curvilinear, where this high dose almost reached plateau.

**Method:** This is a multi-center (~ 47 clinical study centers across Europe), randomized, double-blind, placebo-controlled, parallel-group study in ~ 440 adult patients with moderate to severe seasonal ARC with or without mild asthma. A positive CPT is to be achieved at screening and verified prior to randomization. The primary outcome is the post-treatment TSS following CPT. A wide range of cumulative dose regimens is used (5100, 14400, 27600 and 35600 SU) applied over 6 weekly injections to establish the shape of the dose response to support dose selection for Phase III.

**Results:** The design of the current Phase II grass allergoid SCIT study will be discussed, including the rational of using 4 cumulative dose regimens and placebo and the pre-selected shapes of the dose response curves. In addition, the number of patients screened and randomized will be presented by country, gender and/or age category and screen failures will be categorized.

**Conclusion:** This Phase II study was initiated to establish the dose response of a grass MATA MPL SCIT product, using CPT to measure the effect of a wide range of cumulative dose regimens. The achievement of its aim will be an important milestone in the development of an efficacious and safe state-of-the-art grass SCIT.

## 0903 | Cationic peptides are the inductors of selective apoptosis in tumor cells

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**Background:** Development of targeted drugs with selective antitumor activity is a global challenge. Earlier, cationic peptides (CPs) with high apoptosis effectivity for cutaneous melanoma cells were specially designed. Probable cellular targets for CPs are chaperone proteins nucleolin/C23 and nucleophosmin/B23 involved in the regulation of the cell cycle, molecular transport, signaling, transcription, ribosome biogenesis, etc. C23/D23 are overexpressed in most of tumors, C23 molecules are receptors for many ligands including endostatin, a potent inhibitor of angiogenesis. Receptor C23 activation is likely effected by the interaction of the cationic cluster of endostatin and anionic cluster of C23. Proposed mechanism of C23/B23 interaction with CP is similar. Objective is to analyze the cytotoxicity mechanisms of CPs with different molecular structure.

**Method:** 8 CPs with different charge and molecular mass were synthesized by solid phase method using the Fmoc-protective strategy, their structures were confirmed by HPLC and MALDI-MS. Human tumor cell lines of cutaneous melanoma—melIS, melH; glioblastoma—Glb-Sh and Glb-17; ovarian cancer—CrovCel; multidrug-resistant breast cancer HBL-100/Dox; hepatocarcinoma - Huh7; 4 pancreatic cancer cell lines- Panc1, MiaPaCan2, AsPc1, CaPa2; renal cancer - Rpoch1-KK and control fibroblast line H1036 were studied. CP $R_8K_4K_2$KAC-$NH_2$ was labelled fluorescently by Cy5 for visualization in cells. For western blotting and immunohistochemical assay (IHA) proteins p53, C23/B23 were labelled by commercial mAbs.

**Results:** High cytotoxicity of 5 CPs in relation to all tumor cell lines was found. Cell viability was varied as 8-25%, while cytotoxicity was not detected in control. Analysis by RT PCR, blotting and IHA has revealed the high expression of C23/B23 and encoded genes *NCL/NPM* in all tumor cell lines under study. The level of *NCL* gene expression before the incubation with CPs was 8.5 times higher than in normal cells, for *TP53* gene it was 2.8 times lower. After 3-day incubation, the level of *NCL* gene expression drops sharply, and p53 gene increases 2.5-fold. Tumor cell apoptosis induction was proved by cytofluorometry with labeled caspases 3, 8, 9, DAPI and Höchst staining.

**Conclusion:** Possible mechanism of selective cytotoxicity of CPs is a competitive interaction with C23/B23 after intracellular transport, subsequent accumulation of p53 via MDM2 negative regulation capacity and apoptosis.

## 0904 | Inflammatory mediators in the nasal lavage of patients with allergic rhinitis before and after specific immunotherapy with Dermatophagoides pteronyssinus extract after specific nasal challenge

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**Background:** The Allergic Rhinitis is the clinical expression of the link between the IgE-antibodies and antigens in the nasal mucosa resulting in inflammation. In daily practice, There are patients with a clinical picture suggestive of allergic rhinitis, but who do not present specific systemic IgE. Some of these patients have local specific IgE and are diagnosed with local allergic rhinitis. There are authors who advocate the use of immunotherapy in these cases. However, little is

known about the changes produced by immunotherapy in the nasal mucosa of patients with RA who present systemic specific IgE. Our objetive was to determine the local inflammatory response by examining the nasal lavage fluid after nasal challenge tests of patients with allergic rhinitis before and after treatment with specific allergen immunotherapy to house dust mite for a period of 6 months using the standard inflammatory Th1/Th2 and Th17 responses.

**Method:** We selected patients sensitized to *Dermatophagoides pteronyssinus* diagnosed with persistent allergic rhinitis and performed the collection of pre and post nasal lavage fluid after nasal challenge with *Dermatophagoides pteronyssinus*. After 6 months of treatment and placebo the patients were reevaluated. We performed the analysis of the Th1/Th2 and Th17 cytokines responses.

**Results:** We analyzed 19 patients in the immunotherapy group and 17 in the placebo group. The dosage of the free cytokines in nasal lavage were not significantly changed by 6 months of immunotherapy, but it was observed an increase in the levels of IL-13, IL-10 after nasal challenge in both groups; there was also a significant increase in GM-CSF levels in both groups.

**Conclusion:** We observed that the specific nasal challenge with house dust mite generates an inflammatory response within the first hours, but we did not demonstrate any correlation with the response to immunotherapy after six months.

## 0905 | Tolerability of a two week rush up-dosing with modified allergens in pollen allergic subjects in the day-to-day practice

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**Background:** In two Phase IV studies the tolerability of a subcutaneous Rush up-dosing, using three injections in two weeks, has been tested and proven to be save in adults. In the course of a non-interventional study (NIS) now the tolerability of this treatment scheme was tested in the day-to-day practice.

**Method:** The prospective NIS was performed in 116 doctor's offices in Germany. The Rush up-dosing with 3 injections (0.1, 0.3 and 0.5 mL) was documented in patients getting a subcutaneous immunotherapy with modified Tree or modified Grass pollen or a mixture of those. After each injection the patients recorded any side effects within 24 hours after the injection in a diary. By using an electronic case report form (eCRF) every participating doctor's office documented four injections per patient.

**Results:** Data from 1069 patients, of which 529 were male (49.5%), and with a mean age of 38 years, were collected. Of the patients with a fully documented Rush up-dosing (n = 993) 97.9% (n = 972) could reach the highest dose of 0.5 mL.

Early local reactions were reported in 15% (n = 157), early systemic reactions in 1.1% (n = 12) of patients with available data (n = 1048) and late local reactions in 31.6% (n = 327), late systemic reactions in 7.8% (n = 81) of the patients (n = 1035). No severe systemic reactions were observed.

Mono-sensitized patients (n = 364; 34.7%) showed a difference in comparison to poly-sensitized patients (n = 684; 65.3%) only with regard to the early local reactions (12.4% vs 16.4%). In patients with rhino-conjunctivitis (n = 813) versus patients with rhino-conjunctivitis and allergic asthma (n = 235) a difference could be observed in early local reactions (13.2% vs 21.3%), late local reaction (30.4% vs 35.6%) and late systemic reactions (6.4% vs 12.9%).

A subgroup of 29 patients (2.7%) was treated with two therapies (e.g. Trees 100% and Grasses 100%) in parallel. Early local reactions were observed in 13.8% (n = 4), late local reactions in 10.3% (n = 3) and late systemic reactions in 3.4% (n = 1). No early systemic reactions occurred. All patients reached the maintenance dose.

**Conclusion:** Over 97% of the patients could reach the highest dose of 0.5 mL. The overall tolerability is very good. The data from daily practice confirm the data that were previously obtained in two Phase IV studies.

## 0906 | Molecular allergens contribution in the selection of grass and/or olive immunotherapy

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**Background:** Quantification of specific IgE against molecular allergen components (sIgE-CRD) may be relevant for a precise choice of candidates to immunotherapy (IT) and its respective composition, in patients that are allergic to both grass and olive pollens.

**Objectives:** Evaluation of the usefulness of sIgE-CRD determination compared to sIgE for total extract (sIgE-tot), in the choice of the correct IT's candidates/composition.

**Method:** Anonymous survey applied to allergists, including clinical information and results of aeroallergens skin prick tests (SPT) and

sIgEs from 40 patients, evaluated during the 1st semester of 2017 at an outpatient clinic. All patients presented persistent moderate-severe allergic rhinitis, in pollen season and had not been submitted to IT. All patients had positive SPT for grasses (grass) and olive (olea). sIgE-tot for *Phleum pratense* and *Olea europaea* and some sIgE-CRD (rPhl p 1, rPhl p 5, rPhl p 7, rPhl p 12, rOle1 and nOle7) were determined. Physicians were divided into 2 groups (group 1 if <10 years of practice and group 2 if≥10 years of practice) and were asked to choose which IT to prescribe for each patient (none, only grass, only olive or both grass and olive), according to SPT and *sIgE* results.

**Results:** Fifteen physicians (60% with ≥10 years of practice) participated in the survey. Considering only the sIgE-tot results, the IT choice (group 1/2) was: no vaccine in 10%/3%; grass vaccine 50%/58%; olive vaccine 5%/10% and both grass and olive vaccines in 35%/30% of the patients ($P = 0.42$), the intergroup agreement was 70% (kappa 0.612). According to the sIgE-CRD results the physicians chose (group1/2): no vaccine at 10%/13%; grass vaccine in 63%/60%; olive vaccine in 10%/5% and both vaccines in 18%/23% of patients ($P = 0.79$), with intergroup agreement of 78% (kappa 0.591). Based on the *mode* ($M_o$) of response for each of the patients, after the evaluation of sIgE-CRD the IT choice was changed in 25% (10) of the patients.

**Conclusion:** The determination of sIgE-CRD had important impact in IT prescription in 25% of the patients. The prescription of vaccines to both grass and olive decreased and the number of patients with no indication to vaccine increased. This difference, although lower than reported in similar studies, emphasizes the importance of sIgE-CRD determination for a precise IT choice in patients sensitized to both grass and olive pollens.

## 0907 | Long-term effect of Grass-pollen SLIT on symptom control of patients with allergic rhinitis

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**Background:** Allergen immunotherapy in patients with allergic rhinitis has been shown to have disease—modifying properties with clinical benefits that can persist for several years. Long-term efficacy of grass pollen sublingual immunotherapy (SLIT) on symptom and medication scores as well as quality of life has been established. However, data on control of allergic rhinitis (AR) after discontinuation of therapy are insufficient. The aim of our study was to assess sustained control of AR in three consecutive years after Grass-pollen SLIT discontinuation.

**Method:** A total number of 35 patients [24 (68.57%) males; mean age 32 years, age range 15-56] well-controlled after a three-year course of SLIT with grass pollen extract were prospectively evaluated in three consecutive years after discontinuation of therapy. Control of disease was assessed by Rhinitis Control Assessment Test (RCAT). Each patient was evaluated by the same physician in May and June—months with the highest grass pollen concentration. Pollen count was measured.

**Results:** When assessed one year after SLIT discontinuation 33 (94.26%) patients were well controlled. On the second year 32 (91.41%) patients were classified as well-controlled according to RCAT questionnaire. The proportion of well-controlled patients was the same on the third year. No significant difference in the number of patients, well controlled on the third year of SLIT with Grass pollen extract and three year after discontinuation of therapy was established ($P > 0.10$).

**Conclusion:** A three- year course of Grass-pollen SLIT seemed to have a long-term effect on control of symptoms in patients with AR. The authors declare no conflict of interest.

SUNDAY, 27 MAY 2018
TPS 17
DIAGNOSIS OF FOOD ALLERGY 1

## 0909 | Birch/Alnus sensitization profile in patients with oral allergy syndrome in Mexico city

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**Background:** Oral allergy syndrome (OAS) is an allergic reaction to fresh fruits, vegetables or seeds, which is caused by cross-reactivity between food and pollens. Apart from Birch, Alnus sensitization has shown to very common among people living Mexico City. As it already known birch and alnus pollen cross-react. This study aimed to investigate the birch/alnus sensitization profile in a case series of patients with OAS.

**Method:** This study was based on a data analysis of 24 patients ages 15-62, (of which 66% were female and 33% male). They were diagnosed with OAS in a Private Allergy Clinic in Mexico City. This study was conducted to investigate OAS sensitization profile to clinically relevant pollen allergens.

**Results:** All patients showed a positive sensitization profile by skin prick test to either Betula and/or Alnus. In 40% of patients this profile was furtherly confirmed with serum specific IgE levels to Betv1, (mean 13.56 kU/L). Allergic symptoms in patients with birch/alnus pollen allergy after ingestion of certain food can result from cross-reactivity of Bet- v1-specific IgE to homologous pathogenesis-related proteins, particularly the PR-10 protein.

**Conclusion:** Within the allergy history we emphasize on focusing on SAO symptoms as many patients under-recognize them. Among the sensitization profile of these patients it is quite important to highlight cross reactivity between Bet v1 and Alnus.

## 0910 | Anaphylaxis to lettuce in two patients as part of LTP- syndrome

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**Background:** Lettuce (*Lactuca sativa*) is a vegetable of *Asteraceae* family, widely consumed raw as salad, but also in cooked forms. As an elicitor of allergic reactions lettuce is often associated with LTP syndrome. However, in the Allergology Department of Laiko General Hospital of Athens in Greece, only recently were identified two patients with LTP syndrome who demonstrated allergic symptoms after consuming lettuce.

**Method:** The patients referred to the Allergology Department in 2017 with allergic reactions of varying severity to several LTP containing foods including lettuce in raw form. Both patients were females in their early 20's. Lettuce induced severe anaphylactic reaction (GRADE III) in the first patient after consuming a full serve of lettuce salad, while mild exercise (walking) enhanced the reaction. The other patient suffered from anaphylaxis(GRADE II) induced by minimum amount of lettuce consumption without co-factors. Both patients suffered from oral allergy syndrome to peach and allergic rhinitis.

SPTs to foods and pollens were performed with commercial extracts, prick-through-prick with fresh plant foods, while specific IgE was determined accordingly. LTP syndrome was defined as a sensitization to Pru p 3 and symptoms elicited by at least 2 unrelated plant foods. Co-factors were also investigated.

**Results:** The first patient was sensitized to lettuce, peanut, hazelnut, sunflower's seed, peach and banana, and plane tree, olive tree, grasses, parietaria and mugwort. sIgE to lettuce was 2.04KUA/L, to Pru p 3 was 20.8KUA/L and total IgE was 703.4U/mL. Co-factors, such as exercise, were involved. The second patient was sensitized to peanut, walnut, hazelnut, almond, sunflower's seed, cashew, lettuce and peach, and, plane tree, olive tree, grasses, parietaria, mugwort and willow. sIgE to lettuce was 27.6kUA/L, to Pru p 3 was 37 and total IgE was 1705.9kU/L. No co-factors were identified.

**Conclusion:** Although several patients with LTP syndrome have been investigated in our Department, in only two lettuce was involved in allergic reactions. They were both sensitized to plane tree and mugwort, in concordance with LTP and food pollen syndrome described in Mediterranean area. Lettuce is part of LTP syndrome with the potential of life-threatening reactions and should not be ignored in the evaluation and guidance of the patients.

## 0911 | Allergy to garlic in a 9-month infant

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**Background:** Garlic (*Allium sativum*) is a vegetable that belongs to *Amaryllidaceae*'s family. Hypersensitivity to garlic is not very common. It has been mainly reported in occupational allergy but it also may cause contact dermatitis, rhinoconjunctivitis, asthma, urticaria, gastrointestinal symptoms and anaphylaxis after its ingestion. Some studies have identified Alliin lyase, a 56 kDa protein, as a major garlic allergen and it seems to be a heat-sensitive allergen.

**Method:** We report on a 9-month-old infant who presented, 15 minutes after an accidental ingestion of garlic sauce, generalized erythema and cough. She was still breastfeeding and she had never

eaten garlic before (although the mother usually consumed garlic). The patient had never tasted other vegetables belonging to *Amaryllidaceae*'s family either but zucchini, with good tolerance. We performed skin tests and specific IgE (sIgE) to different vegetables. A raw garlic extract was also carried out and analysed in the patient by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE).

**Results:** Prick by prick with garlic was positive (10 mm) and negative to onion, leek, asparagus, zucchini and saffron. Skin prick tests to commercial extracts of mugwort, grass pollen, peach LTP and profilin were negative as well. Specific IgE to garlic was 3.15 KU/L (out from a total IgE 32 kU/L) and 0 kU/L to onion and asparagus. SDS—PAGE immunoblotting assay with patient's serum revealed IgE reactivity with proteins of 6 kDa and 8 kDa.

**Conclusion:** We report a garlic IgE-mediated anaphylaxis case in an infant with proteins of 6 and 8 kDa as the relevant allergens. The mechanism of sensitization in the present case remains unclear. The authors hypothesized that breastfeeding, cutaneous contact or inhalation might be possible mechanisms involved.

## 0912 | Predictive value of peanut skin prick test and specific IgE in peanut-sensitized children in Singapore

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**Background:** The predictive decision points for both peanut skin prick test (SPT) wheal size and serum IgE concentrations, in peanut-sensitized children, have not been evaluated in Singapore. We aim to assess these for purposes of risk stratification and prediction of oral food challenge (OFC)s' outcomes by means of a retrospective chart review.

**Method:** Patients with a positive SPT to peanut, performed during a 4-year period between 2012 and 2016, were included. The patients were assessed for their peanut allergy status based on a convincing clinical history. Their first SPT and serum IgE results done at presentation to our centre were used.

**Results:** The number of patients evaluated was 328, of which 269 had clinical diagnosis of peanut allergy based on recent immediate reaction to peanut (PA group) and 59 were tolerating peanuts regularly (PT group). The mean age of both groups were similar, 3.9 ± 3.2 and 3.7 ± 3.3 years in PA and PT groups respectively. There was a high prevalence of atopic diseases in both groups, with atopic dermatitis (75.8% in PA, 79.7% in PT), and other food allergies (55.4% in PA, 44.1% in PT). Presence of rhinitis was statistically higher in the PA group compared to the PT group, with odds ratio of 2.52 (95% CI: 1.42-4.47). A wheal size of ≥8 mm and a peanut-specific IgE of ≥6 kU/L provided for a 95% positive predictive value. The larger the wheal size on SPT, the higher the probability of a clinical reaction to peanuts.

**Conclusion:** The results will help us in deriving preliminary cut-off values when conducting future prospective studies with OFCs in our peanut-sensitized cohort (whom had no prior peanut exposure), and to eventually reduce the need for expensive and potentially risky food challenges.

## 0913 | Ginger: flavory, spicy …allergenic? A report of four patients with allergy to ginger

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**Background:** Ginger (Zingiber officinale) belongs to the family Zingiberoidae, along with cardamom and turmeric. The edible portion is the horizontal rhizome, and it is very appreciated for its aroma and spicy flavor. It also presents great interest for its therapeutic and culinary use. Hypersensitivity to ginger is rare and has been scarcely reported. We report 4 cases (P1, P2, P3, P4) of adverse reactions to ginger after its ingestion and with good tolerance to cardamom and turmeric.

**Method:** Skin prick tests (SPT) to environmental allergens and prick-by-prick with ginger were carried out. Total IgE, and specific IgE to ginger were also determined. A raw ginger extract was prepared. This extract was analyzed in all the patients by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE).

**Results:** SPT to environmental allergens were positive to pollens in the four patients. Prick-by-prick and specific IgE were positive in all the patients. SDS-PAGE IgE immunoblotting assays with the patients' sera revealed IgE-reactivity with proteins of 30 kDa and 32 kDa in the four patients, and proteins of 8 kDa and 10 kDa for P3 and P4.

**Conclusion:** We present 4 cases of allergy to ginger, demonstrated with positive skin tests, specific IgE, and SDS-PAGE IgE immunoblotting assays. Proteins bands of 8, 10, 30 and 32 kDa seem to be the relevant allergens involved in the reaction. To our knowledge we describe the largest series cases of allergy to ginger… a plant which is not only flavory and spicy.

## 0914 | Classical food allergy categorization: Is it applicable in daily practice?

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**Background:** Food allergy is divided into 3 groups according to pathophysiology: IgE-mediated, IgE- and non-IgE (mixed type), and non-IgE (cellular type). However, in clinical practice, patients who fall under more than one group may be observed.

**Method:** Patients who were diagnosed with food allergy at our clinic from January 2012 to December 2016 were included in the study. The medical files of patients were retrospectively evaluated, their symptoms and findings after consumption of foods were recorded, and they were categorized into 3 groups (IgE-mediated type, non-IgE type, and mixed type) according to their symptoms and findings.

**Results:** A total of 587 patients (63.5% male) with food allergies were included in the study. According to categorization via symptoms and findings, the distribution of patients was as follows: 140 (23.8%) IgE-mediated type, 44 (7.5%) non-IgE type, 195 (33.2%) mixed type. The remaining 208 (35%) patients were found to show various combinations of symptoms and findings that fit more than one group.

**Conclusion:** In this study, we observed that food allergy symptoms and findings were distributed in a broad range which caused difficulties in the categorization of more than one-third of our patients.

## 0915 | Crocodile parvalbumin is a new allergen: The fish-crocodile syndrome

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**Background:** Fish allergic patients suffer a lifetime of strict dietary restrictions. Crocodile meat is a nutritious alternative choice in many countries around the world; however, it has recently been reported to also trigger severe allergic reactions. In these two case reports from 2017 pediatric patients were sensitised to the major fish allergen parvalbumin (PV), a potential cross-allergen. Bony fish contain predominantly PVs of the β-lineage, which are the most common trigger of allergic reactions in fish allergic patients. In most other vertebrates, PVs of the α-lineage are most abundant, which have been reported as a causal allergen in frog, cartilaginous fish, and chicken allergies. We aimed to evaluate the allergenicity of crocodile meat in fish allergic children, with focus on PV.

**Method:** Over 70 children with clinical history of IgE-mediated fish allergy were identified, skin tested to commonly consumed fish species using commercial and in-house preparations, and serum samples were collected. A sub-cohort was skin tested to crocodile using heat-treated tail muscle tissue from Saltwater crocodile (*Crocodylus porosus*). Extracted proteins and purified PVs were analysed by SDS-PAGE, immunoblotting, and mass spectrometry. Serum from all fish allergic children was analysed for IgE reactivity to the crocodile PV. This reactivity was compared to those of raw and heated crocodile protein extracts as well as protein extracts and purified PVs from frequently consumed fish species.

**Results:** More than 5 fish allergic children were positive on skin testing to crocodile (wheal size>3 mm), demonstrating its clinical reactivity. *In vitro* analyses revealed IgE reactivity to crocodile PV in serum from more than half of all patients. Two β- and one α-crocodile-PV isoforms were identified. PVs constituted approximately 90% of total proteins in heated crocodile extracts, with β-PV (11 kDa) being 10 times less abundant, but up to 500 times more IgE-reactive than α-PV (13 kDa). α- and β-PVs from crocodilians, including alligators and crocodiles, share more than 96% and 74% of their amino acid sequence, respectively.

**Conclusion:** Crocodile PV is a new allergen as per the IUIS guidelines. Fish allergic patients may be at risk of severe allergic reactions upon ingestion of crocodile meat due to strong IgE cross-reactivity of β-PVs. This study suggests that fish allergic individuals and health professionals need to be aware of potential allergic reactions to meat from crocodilians, termed 'fish-crocodile syndrome'.

## 0916 | Allergy to green pepper

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**Background:** We present a 39-year-old nonatopic woman that in December 2016 after eating a seafood paella with green pepper presented asthenia, nasal obstruction, incoercible vomiting and diarrhea. Later she ate a grilled loin sandwich in a bar and she had the same symptoms (she asked the waiter at the bar and the chef had cooked her sandwich in the same pan where he had cooked green pepper just before). After that, she suffered from abdominal pain, nausea, abdominal distension without diarrhea two hours after she ate an omelet sandwich with certain flavor of green pepper. At present even the casual smell of pepper causes her nausea. The woman eats everything including spices and just avoids pepper.

**Method:** Skin prick tests were performed using extracts from food (nuts, fish, mollusk, fruits, vegetables, legumes), aeroallergens (mites,

pollens and epithelia) and purified proteins (Pru p 3, profilin, polcalcin, alfalactoalbumin, betalactoglobuline, casein). We also performed prick by prick to raw and cooked green pepper.

SDS-PAGE immunoblotting according to Laemli under reducing conditions (with 2-mercaptoethanol) was performed to study the molecular mass of the IgE- reactive proteins. Extracts from green pepper and green pepper seed were used.

**Results:** The prick tests were all negative and the prick by prick test to raw and cooked green pepper was positive in both cases. Total IgE was 66.4 U/mL and specific IgE to rPru p 3 (recombinant Lipid Transfer Protein from peach)<0.10 $k_A$U/L.

The immunoblotting showed IgE binding bands of 80 kDa, 67 KDa and 55 kDa with the green pepper extract, and 68 kDa and 29 kDa bands with the green pepper seed extract.

**Conclusion:** We present a case of anaphylaxis by green pepper ingestion. IgE-reactive proteins from green pepper and green pepper seed were detected.

The patient signed a written informed consent for presentation and publication of the case report.

## 0917 | Lipid transfer protein allergy in poland: a dominant role for mugwort pollen as a primary sensitizer

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**Background:** Lipid transfer proteins LTP are the most common cause of food-induced allergies in adults living in the Mediterranean area. Peach fruit, which is an important component of the diet in the Mediterranean countries, is the most common cause and precursor of allergies associated with LTP.

**Method:** The study group included 50 adult patients, 30 women and 20 men, aged 18-74 with confirmed allergy and who suffered from adverse symptoms after consuming food. The study included patients under the care of the Department and Clinic of Allergology, Clinical Immunology and Internal Disease of Collegium Medicum in Bydgoszcz. Criteria for exclusion from the study group were severe chronic diseases, auto-immunological diseases and cancer. The study also excludes minors and women during pregnancy and breast-feeding. The control group included 20 healthy persons, 12 women and 8 men, aged 18-62 years with a negative personal and family interview towards atopy, no infectious signs and no drugs use.

Blond was taken from all patients to specify the levels of allergen-specific IgE against 112 allergen components of ImmunoCAP ISAC test, the result≥0.30 ISU-E was assumed as positive.

**Results:** In the study group, in 12 patients (24%) specific antibodies against LTP were detected, the ISU-E level range 0.3-34 average 5.26 ISU-E

On average, in patients with detected LTP IgE was detected for 3.5 components belonging to the LTP, however the highest number 41% patients were detected IgE only for 1 LTP. In 9 subjects (75% of respondents with detected LTP), IgE was detected against Art v 3 and this is the only LTP component whose occurrence was statistically significant ($P$ = 0.044). In 6 patients IgE was detected against Pru p 3, Jug r 3, Pla a 3,; 5 patients IgE to Ara h 9; 4 patients Cor a 8; 3 patients Ole e 7, 2 patients Tri a 14, and in 1 person Para j 2. The highest mean levels of IgE were obtained for: Art v 3 8.36 ISU-E; Ara h 9 6.16; Pru p 3 5.45; Cor. 8 5.28; Jug r 3 4.8; Pla 3.36; Tri a 14 3.15; Par. J 2 1.5; Ole e 7 0.93.

**Conclusion:** Mugword protein Art v 3 is a primary sensitizer and plays a dominant role in LTP allergy in Poland.

## 0918 | Skin prick test responses with commercial sesame extract and raw tahini as predictors of sesame allergy in children

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**Background:** Sesame allergy is an increasingly recognized health burden, especially in developed countries including European countries, United States, and Japan. In Israel it is a major cause of severe IgE-mediated food allergic reactions. Studies suggest that sesame specific IgE concentration and skin prick test (SPT) with commercial sesame extract has a poor diagnostic performance. Our aim was to assess the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) using commercial SPT and raw Tahini in a big cohort of Israeli children who perform oral food challenge.

**Method:** The study included 98 participants (54 Males,44 Females) with suspected sesame allergy. Sixty children were skin pricked with commercial sesame extract and tahini and 38 children were skin pricked only with commercial Sesame extract. All participant underwent oral food challenge.

**Results:** Thirty-eight children out of 98 (38.7%) had a positive sesame food challenge. Age at oral food challenge was 38.69 ± 37 (3.5-183.6) months. Thirty-one (31.6%) children had atopic dermatitis, 24 (24.4%) had asthma and 47 (47.9%) had history of allergy to other food allergens. SPT with commercial sesame had sensitivity of 41.7% (25.5-57.8) and specificity of 93.3% (86.9-99.6), PPV of 78.9% (60.5-97.2) and NPV of 72.7% (62.7-82.6). SPT with raw tahini had a sensitivity of 73.95% (55.9-91.8), specificity of 70.3% (55.6-85.0), PPV of 60.7% (42.6-78.8) and NPV of 81.3% (67.8-94.8) (diameter >3 mm as cutoff). Using commercial extract and raw tahini together had sensitivity of 76.9% (53.9-99.8), specificity of 95.7%(87.4-100), PPV of 90.9% (73.9-100) and NPV of 88.0% (75.2-100). Positive

food challenge in children less than 3 years was associated with atopic dermatitis [odds ratio (OR)=6.8, 95% confidence interval (CI): 2.2-21.3], and in children above 3 years with asthma [odds ratio (OR) =6.7 95%CI (1.1-40.5). Children with positive food challenge had a higher percent of allergy to other food allergens, 26/38 (68.4%) vs. 20/60 (33.3%), $P$ = 0.0009.

**Conclusion:** Using both commercial and raw tahini improve sesame diagnosis process. Atopic dermatitis under the age of 3 years and asthma above 3 years are risk factor for positive sesame food challenge.

## 0919 | Food-SPT is not a useful marker in the diagnosis of a birch pollen-associated oral allergy syndrome

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**Background:** The birch pollen-associated oral allergy syndrome (OAS), an IgE-mediated local allergic reaction, is the most common manifestation of pollen-associated food allergies. Its origin is explained by cross-reactions between birch pollen- and food-allergens belonging to the pathogenesis-related protein subfamily 10 (PR-10). [1]

So far, there is no marker available for its detection and no standardized test established to evaluate objectively the subjective feelings experienced by OAS. The diagnosis is based on a characteristic history and on detecting the sensitization to triggering allergens in skin prick test (SPT) and laboratory examination.

**Method:** The aim of this study was to evaluate whether the food skin prick test could be a helpful marker in the diagnosis of a birch pollen-associated OAS.

For this exploratory study, data from 2016-2017 was collected retrospectively at the dermatological outpatient department of the Ordensklinikum Linz Elisabethinen.

Patients with positive SPT results for birch pollen were included. The variables age, gender, tree pollen- (birch, alder, hazel) and food-SPT, laboratory tests (IgE, Bet v 1, Bet v 2, Gly m 4) and symptoms (OAS, rhinoconjunctivitis allergica, atopic dermatitis, anaphylaxis) for statistical analysis.

**Results:** There was an association between food-SPT and OAS but also between the negative OAS patients and food-SPT ($P$ = 0.9-0.1). All of the Bet v 1 sensitized patients with positive Gly m 4 results had also a positive food-SPT result.

**Conclusion:** There was no evidence for a possible role of food-SPT as helpful markers in the diagnosis of birch pollen associated OAS. Maybe Gly m 4 could be a helpful marker, but more data are needed. Bet v 1 seems to be the cause of birch-pollen associated OAS, due to the dominant sensitization pattern to major allergens in Austria.

**Literature::** [1] Worm M. et al., 2014, 23:1. Nahrungsmittelallergie infolge immunologischer Kreuzreaktivitäten mit Inhalationsallergenen. Allergo J Int.

## 0920 | Anaphylaxis to duck egg

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**Background:** Eggs are among the foods most frequently causing allergy. The most common one is hen egg, although we may consume other bird's eggs such as duck's, those of goose, quails and seagulls. Clinical and serological crossreactivity between hen egg proteins and those of other birds eggs have been described. Allergy to other species eggs are less frequent and are usually described in patients allergic to hen eggs. We report a case of food allergy after ingestion of duck egg in an adult patient without hen egg allergy.

**Method:** The patient was a 50 year-old man who had symptoms of generalized itching, swelling uvula, erythema neck and deglutition difficulty immediately after he ate eggs from duck and hen. He claimed to have eaten hen eggs almost daily without clinical symptoms and he had not previously ingested duck egg. He denied allergic reactions to any other food but did complain of seasonal allergic rhinoconjunctivitis in the spring. We performed skin prick test with extracts of egg and feathers, prick by prick test with cooked and fresh yolk and white from duck and hen egg and oral challenge with hen eggs. Specific serum IgE was measured to hen proteins and we carried out a western blot with the proteins of allergenic extracts from different eggs (white and yolk of quail, chicken, goose and duck) and an inhibition of western blot with ovalbumin as inhibitor allergen.

**Results:** Skin test with extracts of eggs and feathers, cooked and fresh hen and duck eggs were positive. Total serum IgE was 29.2 KU/L. Specific IgE to hen's egg was class two for hen egg white, ovoalbumin and class one for yolk and ovomucoid. Oral challenge with heated egg yolk negative and with egg white was positive. The patient's serum recognized mainly and intensely several proteins of white and egg yolk of quail and duck with a molecular mass around 45 to 50 kDa respectively. On the other hand a protein around 45 and 50-52 kDa was unique recognized in white eggs of hen and goose. The Western blot inhibition revealed ovalbumin inhibited the protein recognized in the egg white but not egg yolk involved in.

**Conclusion:** We report a case of anaphylaxis IgE mediated to egg white from duck. OVA seems to be the responsible protein. A person who is allergic to other bird's eggs could tolerate hen egg, but we may not know if eventually he may present a cross-reaction in

the future. While most allergic reactions have been reported to hen egg, patients have been known to develop hypersensitivities to other avian eggs due to cross reactivity of antigens.

## 0921 | Food allergy to tree nuts, peanut and sesame seeds: sensitization and clinical reactivity patterns

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**Background:** Management of tree nut allergy is usually based on the avoidance of the suspected tree nut (TN), as well as peanuts and seeds, either because of the risk of cross-reactivity and/or contamination, or due to the clinical severity.

**Objective:** To assess the sensitization pattern and clinical reactivity patterns to different TN, peanut and sesame seeds (SS) in patients with a history of reaction to at least one of these foods.

**Method:** Clinical records of all patients evaluated between January 2011 and June 2017 in the food allergy unit of a University hospital center for suspected allergy to TN, peanut and/or SS (n = 116) were reviewed. Demographic data and the results of skin prick (SPT), prick-to-prick (SPTT) tests, specific IgE (sIgE) and/or oral food challenges (OFC) were analysed. A definite diagnosis of nut allergy was considered if the patient had a positive OFC or a reproducible clinical history with concordant skin tests/specific IgE.

**Results:** A total of 47 patients with confirmed nut allergy were included; 70% female, median age [interquartile range] of 28 [18-46] years; 72% were atopic. The most frequently involved foods were walnuts (53%), hazelnuts (40%), almonds (32%) and peanuts (38%). Anaphylaxis was the clinical presentation in 51% of the patients.

In those with a history of reaction to only one nut (24), the most prevalent was peanut (42%). In the 23 patients that reacted to more than one nut, the most frequent combinations were walnut/hazelnut (15), walnut/almond (12) and almond/ hazelnut (10). Of these patients, 5 tolerated other nuts. Two had sesame seed allergy, one reacted only to SS. Nine patients (19%) were sensitized to foods that they tolerated. Fourteen (30%) patients were sensitized to LTP and 8 of them reacted to more than one nut.

**Conclusion:** These data concur with the existence of different sensitization profiles (primary, concomitant or cross-reactive), which may predict different clinical reactivity patterns and therefore, influence dietary recommendations.

## 0923 | Anaphylaxis caused by buckwheat, an unusual food allergen

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**Background:** Buckwheat (*Fagopyrum esculentum*) is a Polygonaceae weed, not a cereal, which is increasingly been consumed and used as an alternative food in the diet of celiac patients. Despite its wide use, allergy to buckwheat has unfrequently been reported in our setting.

**Method:** Two female patients, aged 37 and 58, suffered an immediate severe allergic reaction after eating a bread and a pancake containing buckwheat among its ingredients. The first patient presented generalized urticaria, palpebral angioedema and pharyngeal occupation. The second one showed those same symptoms, as well as abdominal pain, nausea, dyspnea, dizziness, hypotension and loss of consciousness.

Skin tests and specific IgE determination to aeroallergens and food allergens were carried out, including prick-prick test with buckwheat and all other components contained in the food involved. Buckwheat allergens were studied by SDS-PAGE and IgE-Immunoblotting of one of the patients.

**Results:** Prick-prick tests yielded strongly positive results to the food itself and buckwheat, and negative to the remaining food components in both cases. CAP was positive to buckwheat (11.30 kU/L and >100 kU/L, respectively). Basal serum tryptase levels were normal. Both patients were not sensitized to cereals, LTPs, profilins or PR-10 proteins. For the first patient, the skin tests were negative for other foods, seeds and nuts. The CAP was negative for LTPs, profilins and storage proteins of peanut and other nuts. The second patient who had the most severe reaction, was also sensitized to hazelnut(CAP 13.7 kU/L), pistachio (1.44kU/L), almond(0.66kU/L), walnut(29.7kU/L) and sesame(4.47kU/L), which were not included in the pancake. The buckwheat Immunoblot of the first case, under non-denaturing conditions, revealed a IgE-binding protein of 60-kDa. IgE-immunoblotting under reducing condition showed protein bands of 30, 20, 17 and 14 kDa in the buckwheat extract.

**Conclusion:** Two cases of anaphylaxis by buckwheat flour contained in two frequently consumed foods are presented. The absence of sensitization to LTPs, together with the pattern of specific IgE binding in the immunoblot in one of the cases suggests that the responsible allergen could correspond to a storage protein of buckwheat, without cross-reactivity with other seed and nut allergens. Buckwheat must be taken into account as an unsuspected food allergen capable of causing severe allergic reactions.

## 0924 | Linseed allergy: A case series

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**Background:** Allergy to linseed (Linum usitatissimum) has infrequently been reported despite of its wide use in bread and in a range of "health food" products. Linseed contains potent allergens which have not yet been characterized.

**Method:** We studied three patients who presented allergic reaction after eating different foods which contain linseed. Two of them (Patient P1 and patient P2) had anaphylaxis and the third one (patient P3) had oral syndrome, abdominal pain and diarrhoea. P2 was also allergic to mustard and P3 to sesame seed. All of them tolerated the remaining seeds, nuts and food. Baseline tryptase levels were in normal range in all patients.

Skin tests and specific IgE determination to inhalants and food allergens were carried out. Linseed allergens were studied by SDS-PAGE and IgE-immunoblotting.

**Results:**

**Skin tests:** Patient 1: Prick tests were positive to pollens and Linseed, and negative to LTP, profilin, nuts, seed and the remaining food; Patient 2: Prick tests were positive to linseed and mustard and negative to other food and inhalants; Patient 3: Prick tests were positive to linseed, pollens, sesame and nuts (peanut, hazelnut, almond, pistachio).

**Specific IgE:** P1: CAP was positive to linseed (4.59 kU/L); P2: CAP was positive to linseed (0.86 kU/L) and mustard (15.0 kU/L). P3: CAP was positive to linseed (10.5 kU/L), rPru p 3 (1.33), peanut (1.90), Hazelnut (0.73). CAP to Ara h 1, Ara h 2, Ara h 3, Ara h 9, Cor a 8, Bet v 1, Bet v 2, other nut and food extracts was negative in all patients.

IgE-immunoblotting assays under non-denaturing conditions revealed an intense IgE-binding protein band of 14 kDa with sera from the patient 1, a band of 50 kDa from the patient 2, and bands of 50 kDa and 14 kDa from the patient 3. Under reducing condition, the IgE-binding bands detected were 8 kDa (patient 1), 30 kDa and 20 kDa (patient 2) and 30 kDa (patient 3).

**Conclusion:** We present three cases of severe allergic reactions to linseed. The pattern of specific IgE binding in the immunoblot seems to lead to storage proteins as the responsible allergens.

## 0925 | PR-10 sensitization—looking it up in food allergy

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**Background:** PR-10 protein group sensitization is found in patients with respiratory allergy, mainly in areas inhabited by trees of the *Betulacea* or *Fagacea* families. Its role in food allergy is, however, more frequently described in the context of cross reactivity.

Our aim was to characterize the pattern of molecular sensitization of food allergic patients sensitized to PR-10 protein group with ImmunoCap ISAC® (ISAC).

**Method:** A group of patients in whom ISAC study was performed between January 2009 and June 2017 were analyzed. Subjects with PR-10 sensitizations and a concomitant history of plant food allergy (PFA) were selected and their clinical records reviewed.

**Results:** Out of 234 ISAC studies performed, only 16 were positive for PR-10. Of the latter, 9 (56%) corresponded to patients with a positive history of PFA. Most common triggering food groups were fresh fruit (n = 7 patients), tree nuts and peanuts (n = 5), legumes and cereals (n = 2 each). Clinically, 3 patients had oral contact urticaria (OCU), 4 had systemic non-anaphylactic reactions (SNA), and 2 had a history of anaphylaxis. Two of the patients with OCU were sensitized only to PR-10 and 1 was co-sensitized to Profilin and LTP. The remaining patients, with more severe reactions, were all co-sensitized to either LTP and/or Storage Proteins (SP). Only 2 of the 7 patients without PFA were co-sensitized to LTP or SP versus 7 of 9 with PFA ($P < 0.05$).

**Conclusion:** PR-10 sensitization is rare in our population. Approximately half of the patients had allergy to plant foods, but the majority were co-sensitized to LTP and/or SP. The few patients only sensitized to PR-10 had minor reactions. Among the patients without plant food allergy, co-sensitization to LTP and SP was significantly less common. According to these results, in our population, PR-10 seems to be less relevant to food allergy, when compared to reported results from other European countries.

## 0926 | Characterization of the children with pistachio allergy

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**Background:** Pistachio is a tree nut belonging to "*Anacardiacea*" family, and constitutes 7% of tree nut allergies. This nut most often

cross-reacts up to 95% with cashew which is located in the same family. Pistachio allergy is mostly seen in Iran, Turkey, the United States, and China where this tree nut is frequently consumed. In this study, we analyzed age and cut-off values for development of tolerance to pistachio.

**Method:** Children who had reported allergic reactions with pistachio, and who have not consumed pistachio, but had positive SPT and/or specific IgE levels were enrolled into the study. SPT and specific IgE levels were measured in all patients.

**Results:** A total of 112 patients (M/F: 74/38) with a median age of 58.45 months (IQR: 40.38-88.32) was enrolled into the study. Fifty-six patients had reported allergic reactions with pistachio, and the remaining 56 patients who have not consumed pistachio, had positive SPT and/or specific IgE levels. The median age of the first consumption of pistachio nut was 47.0 months (IQR: 31.0-62.0 months). Oral provocation(OP) tests with pistachio were performed by 82 patients, and 21 of them had positive test result. The median age of tolerance development was 60 months (IQR: 48.0-89.0 months). The most commonly involved systems during OP tests were skin (90%, n = 19), gastrointestinal system (33%, n = 7), and lower respiratory tract (24%, n = 5). Concomitant allergic diseases were atopic dermatitis (70%), asthma (40%) and allergic rhinitis (17%). There was a positive correlation between skin prick test diameter (SPT) and specific IgE levels (spIgE) ($r = 0.331$, $P = 0.001$). SPT of$\geq$8.25 mm to pistachio nut was found as highly predictive of clinical allergy (AUC: 0.83, 95%CI: 0.73-0.94, $P < 0.001$). Any relation was not determined between eosinophil, basophil counts, triptase levels, and OP test positivity.

**Conclusion:** Pistachio allergy is one of the frequently seen nut allergies in Turkey which may cause serious allergic reactions including anaphylaxis. OP test showed that tolerance was achieved by the median age of 60 months, and a cut-off level of 8.25 mm was best predictor for positive reaction.

SUNDAY, 27 MAY 2018
TPS 18
MANAGEMENT OF FOOD ALLERGY 1

## 0927 | Omalizumab facilitates rapid oral desensitization for peanut allergy

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**Background:** Food allergy is a major cause of anaphylaxis among children and young adults, with increasing prevalence. About 0.6% of the Danish population has peanut allergy.

The standard treatment for food allergy is allergen avoidance. Oral desensitisation schemes for food allergens are being developed, and Omalizumab (anti-IgE) has been used to prevent reactions during oral desensitization.

**Aim:** We report a successful oral desensitisation of a young adult with severe, provocation-verified peanut allergy under the cover of anti-IgE.

**Method:** A 19-year-old man presented, with a convincing history of allergic reactions after ingestion of peanut, with Grade 1 and 2 symptoms on the Brown scale in 2014, and in 2016 with Grade 2 symptoms. s-IgE for peanut extract was over 100, titers for Ara h1 60.4, Ara h2 71 and Ara h3 5.8 $kU_A$ / L.

In an oral challenge test, the patient responded with generalized urticaria, swelling of the lips and difficulty breathing at a cumulative dose of 0.1 g peanut protein, however, without blood pressure drop. (Grade 2, Moderate Symptoms). The patient was treated with anti-IgE for 3 months (with 450 mg every 4 weeks sc). Oral desensitization began with ingestion of 500 μg peanut, escalating to 500 mg, on the first day and escalating weekly doses of peanut from 500 mg to 4000 mg (8 peanuts). Then anti-IgE was discontinued while the patient ingested 8 peanuts every day. We have followed the patient's sensitivity to peanuts from before anti-IgE treatment to after anti-IgE washout with basophil testing.

**Results:** The patient completed desensitization without side effects, and continues to ingest 8 peanuts a day. Basophil sensitivity was reduced 13-fold by anti-IgE treatment, but returned to baseline levels after anti-IgE washout.

**Conclusion:** Anti-IgE allows rapid desensitisation of peanut allergic subjects with peanut oral immunotherapy. In the majority of subjects, this desensitization is sustained after anti-IgE is discontinued. Additional studies will help clarify which patients would benefit most from this approach. The return of basophil response to pre-treatment levels suggests that the patient is desensitised, and depends on the daily ingestion of allergen.

## 0929 | Biologic prosthesis allergic sensitization: What do we (not) know?

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**Background:** The use of biologic prosthesis is a well-established surgical procedure. Acute and delayed complications may occur, but accurate epidemiologic data about allergic reaction to graft tissue is lacking.

**Methods:** A 9 years old boy referred to our Unit for urticaria and gastrointestinal symptoms which developed a few years before. He received a biologic porcine vascular duct during a cardiovascular surgery at 20 days of life. At the age of 5 urticarial episodes occurred, and a diagnosis of beef allergy was made. After the exclusion of beef meat from the diet, most symptoms resolved, but the child began to complain about occasional episodes of vomit and diarrhoea.

**Results:** Skin prick tests confirmed the beef meat sensitization and prick-prick test resulted positive against raw pork meat but not against cooked pork meat. In vitro tests demonstrated the presence of pork meat specific IgEs (14.1 kUA/L). Component-resolved diagnostic tests revealed allergy sensitization toward Bos d 6 (bovine serum albumin, BSA; porcine serum albumin was not tested due to lack of a specific test). After accurate exclusion of pork meat from diet, a complete remission was achieved, and the diagnosis of pork meat allergy was confirmed.

**Conclusion:** BSA is a major beef allergen, responsible for the raw beef-cow milk cross-reactivity but with a scarce importance in milk allergy. It is highly homologous with human serum albumin and other mammalian serum albumins, including porcine albumin. Porcine albumin is also highly homologous with cat serum albumin and therefore responsible for cross-reactivity in patients affected by cat-pork syndrome. We hypothesize that the implanted porcine tissue was the trigger for pork meat allergy in our patient, as this condition is exceptional in childhood and that our patient never owned a cat.

Few cases of pork allergy due to porcine tissue implantation have been reported so far. Of interest, pig sensitization was recognized as a rare but possible cause of blood-culture negative endocarditis in patients with porcine bioprosthesis according with anamnesis, increased IgE level against pork, tissue eosinophilia during autopsy.

At least two final questions arise: 1) what is the risk of allergic sensitization in patients with biologic prosthesis? 2) Our patient will need the substitution of the prosthetic duct very soon, and the biologic material would be the cardio-thoracic surgeons preferred option: what kind of reaction could we expect?

## 0931 | Allergy to quail's egg in patient desensitized to chicken's egg

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**Background:** Desensitization to foods is assuming a new paradigm in food allergy. This technique is becoming widespread especially for patients with egg and milk allergy, but the effect of desensitization on the consumption of similar but not identical foods is still uncertain.

**Material and Methods:** We describe the case of a 16-year-old patient, with a history of chicken egg allergy, who had been successfully desensitized tolerating cooked and raw chicken eggs for a year. The patient came to the office after presenting an episode of anaphylaxis immediately after eating fried quail eggs. An immunological study was carried out. We performed skin prick test with chicken egg′s proteins (white, yolk, ovoalbumin and ovomucoid). An Immunoblotting to detect specific IgE to egg proteins was also performed. For this purpose, the following extracts were used: chicken egg white and yolk (Commercial extract form ALK) and quail egg white and yolk prepared following a similar procedure (extracted in 10% phosphate buffer (w/v)).

**Results:** Skin prick test with chicken′s egg proteins (white, yolk, ovoalbumin and ovomucoid) were all negatives. A double band of high intensity of a molecular weight between 50-70 kDa was detected in the immunodetection with yolk and quail clear. It could be Ovotransferin (66-78 kDa). This band is obtained after a development of only 30s, which indicates a very significant positivity. No band was detected in the immunoblotting in the case of chicken eggs. Following immunoblot the patient tolerated again chicken′s egg without problems.

**Conclusion:** We present the case of a patient with specific allergy to quail egg white and yolk, probably through ovotransferin, but not to chicken egg. The desensitization against chicken eggs does not allow the consumption of eggs of other species of birds, such as quail eggs, and this indication must be made specifically to patients after a protocol of desensitization against chicken′s eggs.

## 0932 | First case of spontaneous tolerance in lettuce allergy

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**Background:** Lettuce (*Lactuca sativa*) is a vegetable belonging to the *Compositae* family. Lac s 1 LTP, Thaumatin and Aspartil protease have been identified as three major lettuce allergens.

**Case Report:** Seven years ago we presented the case of a 32-year-old male, who suffered two acute episodes of oral pruritus, lip angioedema, epigastric pain, generalized urticaria and dizziness after ingesting lettuce. He previously tolerated salads (including lettuce). He was later diagnosed with non-LTP-dependent lettuce anaphylaxis and an Aspartyl protease was identified as a new lettuce allergen with cross-reactivity with other members of the *Compositae* family. Since the diagnosis he has avoided lettuce and all the other *Compositae*. We present the patient's curious outcome after 7 years of follow up.

**Methods:** Total IgE, basal tryptase, specific IgE to lettuce by ImmunoCAP, prick-prick and oral challenge tests with lettuce and other *Compositae*. SDS-page, Immunoblotting and molecular characterization of IgE binding bands by mass spectrometry. Skin prick tests and specific IgE to lettuce were repeated on several occasions in the following years. After 7 years an oral challenge test with lettuce was carried out.

**Results:** Prick-prick test was positive to fresh lettuce (11 × 15 mm) and to other *Compositae* (raw endive, chicory, thistle, artichoke and chamomile). Prick-prick test was negative with these boiled *Compositae*. Basal tryptase was 7.07 μg/L. Total IgE in serum was 189 Ul/mL. Specific IgE by ImmunoCAP was positive to lettuce (7.35 kU/L) and negative to profilin, LTPs and thaumatin. Oral challenge test with endive was positive and negative with cooked *Compositae* (artichokes and thistle). SDS-page and Immunoblotting detected an intensely binding IgE band about 46 kDa, common for endive and chicory, which was identified by mass spectrometry as an Aspartyl protease. No bands were detected at LTP (9 kDa) and profilin (16 kDa). In the first two years after the diagnosis, prick-prick test and specific IgE to lettuce remained positive (CAP 1.91 kU/L and 0.44 kU/L, respectively). After 7 years, prick- prick test and specific IgE to lettuce became negative (CAP 0.08 kU/L). With this findings a new oral challenge test with lettuce was carried out which result turned out negative.

**Conclusion:** We report the first case of spontaneous tolerance to lettuce in a patient who previously presented lettuce anaphylaxis and identify an Aspartyl protease as the causative allergen.

## 0933 | Eosinophilic esophagitis after introduction of baked milk, report of case

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**Introduction:** Eosinophilic esophagitis (EoE) is an emergent allergic inflammatory disease that is triggered by food allergens and characterized by progressive esophageal dysfunction. Recently, it has been seen that EoE develops in up to 2.7% of patients with IgE- mediated food allergy undergoing oral Immunotherapy (OIT). Ingestion of baked milk and egg was associated with increased development of tolerance to regular milk and Immunologic changes have been

reported in subjects ingesting baked milk and egg, similar to those seen in food Oral Immunotherapy studies.

**Case description:** We present the case of a 13-year-old girl, with history of IgE mediated Cow′s milk allergy and rhino conjunctival and bronchial asthma symptoms. Prick test against milk proteins showed: milk 6 mm, alpha- lactalbumin 6 mm, casein 3 mm and to beta-lactoglobulin: negative. Total IgE: 469 KU/L. Specific IgE to milk: 3, 15 alpha- lactalbumin: 3, 16 KU/L; casein: 2 KU/L and beta- lactoglobulin: 0.10 KU/L. We performed an oral food challenge with baked milk which was well tolerated. Then, we performed an oral food challenge with fresh milk and she presented facial urticaria and pharyngeal pruritus. After 3 months eating baked milk every day, she had symptoms of dysphagia and esophageal food impaction. For this reason, we performed an Esophagogastroduodenoscopy (EGD) and biopsies which showed white exudates and vertical furrows. The histological study showed eosinophil count>20 per high- power field. Eosinophilic esophagitis was diagnosed and she started treatment with Esomeprazole 20 mg. The EGD was repeated 8 weeks later with similar results in the biopsy. She was treated with a comprehensive diet free of cow′s milk proteins. After 8 weeks she was asymptomatic and endoscopy and biopsy findings were normal.

**Conclusion:** We report the case of a Cow′s milk allergic patient who developed EoE after introduction baked Cow′s milk which apparently was tolerated in her diet. The avoidance proved efficacy in inducing the remission of EoE.

## 0934 | Vitamins sufficiency in bottle-feeding children with food allergy

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**Background:** Food allergy management in bottle-feed children depends on balanced nutrition intake including vitamins supplement.

**Aim:** Asses vitamins sufficiency in bottle-feeding children with food allergy.

**Method:** We examined 87 bottle-feeding infants with food allergy aged from 1 to 12 months. Serum vitamin levels were measured by immunoassay methods (retinol binding protein (RBP), vitamin B6, 25-hydroxy vitamin D), biochemistry methods (vitamin C, vitamin E) and microbiology methods (vitamin B1, vitamin B2). As criteria for complete sufficiency standards adopted in the Russian Federation were used (the lower limit of normal levels: RBP — 0.52 μmol/L; B6—8 ng/mL; 25-hydroxy vitamin D—15 ng/mL; vitamin C — 0.4 mg/dL, vitamin E — 0.8 mg/dL; vitamin B1 — 28 μg/mL; vitamin B2 — 6 ng/mL).

**Results:** Complete sufficiency were observed in 21 infants (25.9% cases), one vitamin deficiency in 33 infants (40.7%), two vitamins deficiency in 23 infants (28.4%), three and more vitamins deficiency in 6 infants (7.4%).

**Conclusion:** Vitamin supplementation in infants with food-allergy should be used after vitamin status asses, mainly using monovitamin medication.

## 0935 | Omalizumab for patients refractory to milk oral immunotherapy

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**Background:** Oral immunotherapy (OIT) is a new treatment option for children with cow milk allergy (CMA) who had not achieved tolerance by the age of four. Serious and frequent adverse reactions (AR) may cause 20% of patients to quit the treatment. Having previous anaphylactic reactions, concomitant asthma and evidence of very high sensitization to milk in diagnostic tests may predict OIT failure. Adjuvant therapy with anti-IgE antibodies during OIT may be a hope for these patients.

**Method:** Milk OIT had been performed in Ege University Pediatric Allergy Department since 2008. Seven patients who would have to leave OIT due to serious AR could continue with the addition of Omalizumab (OMZ).

**Results:** Patients were followed with the diagnoses of CMA and asthma. Age at the beginning of symptoms and start of OIT were in the range of 3-6 months and 4-19 years, respectively. They had high total IgE (139-843 IU/mL), milk spIgE (2.9-418 kUA/L), casein spIgE (3.8-112 kUA/L) and beta-lactoglobulin spIgE (0.42-42.8 kUA/L) levels. The induration diameters in prick-to-prick skin test with CM were 6-30 mm. Symptoms-triggering doses in oral challenge test were 1.5-7.5 mg of milk protein in six children. One patient showed no symptoms until he had a severe anaphylaxis reaction at 800 mg of milk protein. All patients experienced frequent or severe AR in acceleration phase of OIT. After addition of OMZ at this stage, safe milk dose increments could be achieved. Five patients are in the maintenance phase receiving more than 6.5 gr milk protein/day, whereas two of them are in acceleration phase yet.

**Conclusion:** We recommend addition of OMZ for patients having severe and/or frequent AR during OIT treatment to decrease the AR and increase the chance of OIT success.

## 0936 | Policy on food allergy management in preschools and primary schools

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**Background:** Food allergies may affect up to 6% of school-aged children. It has been shown that approximately 20% of all anaphylactic reactions caused by food allergy are firstly presented at (pre) school. Therefore, it is of high importance that (pre)schools have a policy on food allergy management and the use of an epinephrine auto-injector (EAI). To our knowledge, limited is known on the policies of food allergy management at (pre)schools. The aim of this study was to investigate the policy on food allergy management in preschools and primary schools in the Northern part of the Netherlands.

**Method:** A cross-sectional survey containing 29 questions was send by email to the board of preschools and primary schools in 3 provinces in the Northern Part of the Netherlands. The survey contained questions on participant characteristics, experience with children with food allergies and the policy on food allergy management and use of the EAI.

**Results:** We included 87 preschools and 110 primary schools in this study. We showed that 80.5% of the preschools and 73.6% of the primary schools had a child(ren) with food allergy. Only 13.8% of the participating preschools and 27.2% of the primary schools had a policy on allergen avoidance and only 35.6% of the preschools and 35.8% of the primary schools had a policy for the use of an EAI.

**Conclusion:** The majority of the pre- and primary schools in the Northern part of the Netherlands have children with food allergy. However, only a limited number of (pre)schools do have written guidelines for food allergy management in (pre)schools. Additionally, there is limited experience how to use an EAI at (pre)schools. Therefore, an evidence-based policy on food allergy management in (pre) schools is needed.

## 0939 | SOTI to cow's milk in 3 cases with anaphylaxis after cow's milk consumption

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**Background:** Food allergies are the most common cause of anaphylaxis in childhood. Here we present 3 cases had anaphylaxis due to cow ‘s milk allergy, and treated with specific oral tolerance induction (SOTİ) to cow’ s milk.

**Method:** SOTI protocol was administered according to previously published by Longo et al. Skin prick test were performed according to standard methods with allergens. Cow's milk specific IgE was investigated with immunoCAP system. In all cases, the wheal size of the cow's milk in skin prick tests or the specific IgE levels was higher than level of positive predictive value of 95%.

**Results:** Case 1: A 7 years old male patient who had 3 anaphylaxis after milk consumption. SOTI treatment was started one year ago. There was no complications during the dose increasing phase. However, he had two episodes of anaphylaxis during the maintenance phase. In the final visit, we observed that he could drink 200 mL milk and could consume dairy products.

Case 2: Eight-year-old male patient has an intensive care-of-hospitalization story due to anaphylaxis three times after milk consumption. His accordance to strict diet was bad, and had frequent asthma attack. Anaphylaxis developed 2 times during the dose increasing phase in SOTI protocol. After SOTI treatment, he could consume 200 mL cow's milk and dairy products without problems.

Case 3: A 7-year-old male patient followed-up for asthma and cow's milk allergy. It was learned that anaphylaxis developed 2 times after milk consumption. He was fed in accordance with the milk-free diet. He has used fluticasone nebules, montelukast, mometasone nasal spray, and cetirizine. Anaphylaxis developed 4 times during the dose increase phase of SOTI administration. There were many mild to moderate anaphylactic episodes during the maintaining phase. After the SOTI treatment, he could consume 150 mL milk and dairy products.

| Before the SOTI to cow's milk | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| Skin Prick Test (cow's milk induced wheal size) | 9 × 8 mm | 8 × 8 mm | 10 × 8 mm |
| Eosinophil % | 8.07 | 7.88 | 9.10 |
| Total IgE | 199 kU/L | 305 kU/L | 1188 kU/L |
| Cow's milk specific IgE<br>Casein | 20.8 kUA/L (class 4)<br>5.55 kUA/L | 140 kUA/L (class 6)<br>65.6 kUA/L | 453 kUA/L (class 6)<br>112 kUA/L |
| After the SOTI to cow's milk | | | |
| Skin Prick Test (cow's milk induced wheal size) | 7 × 5 mm | 8 × 8 mm | 8 × 5 mm |
| Eosinophil % | 4.3 | 4 | 2.28 |
| Cow's milk specific IgE<br>Casein | 9.8 kUA/L<br>2.06 kUA/L | 71.7 kUA/L<br>21.6 kUA/L | 192 kUA/L<br>39.3 kUA/L |

**Conclusion:** The use of SOTI to cow's milk has been an increasing in recent years. Anaphylactic reactions may occur during the treatment, but most of them are mild or moderate. SOTI should only be applied in experienced allergy clinics.

**Reference:** 1. Longo G, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. J Allergy Clin Immunol. 2008;121:343-7.

## 0940 | Sustained patient satisfaction and effectiveness of dietetic group sessions in management of cow's milk protein allergy

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**Background:** Cow's milk protein allergy (CMPA) is one of the most common food allergies in early childhood. Small dietetic group sessions for parents of infant with non-IgE mediated CMPA were held to meet increasing demands and reduce waiting times. Parents were given information on CMPA, advice on weaning and milk reintroduction using a locally designed milk ladder. Parents were also advised to contact the dietitians via telephone if they had further questions. We aim to evaluate the sustained effectiveness and patient satisfaction of the group sessions.

**Method:** Parents and carers who attended the group dietetic sessions held between November 2015 and July 2016 were included in the survey. Feedback were obtained via a self-designed questionnaire using a Likert-type scale, rating several questions from 1 (least satisfied) to 5 (most satisfied). Initial feedback was obtained directly after the session. We followed these patients up a year after the initial session via telephone and postal questionnaire.

**Results:** Overall attendance rate of the 9 group sessions held was 58% (n = 40). During the initial survey, participants found the group session useful (mean score 4.7 out of 5) and felt more confident in managing CMPA (mean score 4.8).

We successfully obtained follow up feedback from 13 participants. Majority agreed that the group sessions have been informative (mean score 4.8). They also said they felt confident weaning their child on milk-free diet (mean score 4.8), and in reintroduction of cow's milk in diet (mean score 4.3).

30% (n = 4) said that they would have preferred an individual session. 38% (n = 5) have contacted the dieticians via telephone after the initial session, and 15% (n = 2) had requested individual consultations. 69% (n = 9) have attempted reintroduction of cow's milk in their child's diet using our local milk reintroduction guide. The mean age at first challenge was 14 months (age range 6 to 26 months), with average of two attempts. 31% (n = 4) have been successfully challenged and are managing well on a normal diet.

**Conclusion:** We recognised the limitation in obtaining feedback via telephone and postal questionnaire, which resulted in the poor follow-up response rate.

Overall, parents felt more confident in managing CMPA and the positive responses were sustained a year on, highlighting the success of these group sessions. Follow up opt-in sessions could be offered to provide additional support and allay parental anxiety in challenging their child with cow's milk at an appropriate age.

SUNDAY, 27 MAY 2018
TPS 19
IMMUNOTHERAPY: FROM ALLERGEN CHARACTERISTICS TO THERAPEUTIC

## 0941 | Characterization of primary and secondary aluminum adsorbate particles in products for subcutaneous allergen immunotherapy

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**Background:** Aluminum compounds are extensively used as adjuvants in prophylactic vaccines and products for subcutaneous allergen immunotherapy (SCIT). The most frequently used salts are aluminum potassium sulfate (potassium alum), aluminum hydroxide and aluminum phosphate. During the manufacturing of SCIT products, the allergens or allergoids are adsorbed to the insoluble aluminum salts. The drug product is a parenteral suspension that contains visible adsorbate particles. The objective of this work was to assess the morphology and size distribution of adsorbate particles of a SCIT product. Chemically modified grass pollen proteins (allergoids) adsorbed to aluminum hydroxide were analyzed by scanning electron microscopy (SEM) and laser diffraction analysis.

**Method:** Twenty batches of the drug product were obtained from Allergopharma's routine manufacturing. The particle size distribution of the visible particles was assessed with a Mastersizer 2000 laser diffraction device equipped with a Hydro 2000 μP dispersion unit (Malvern Instruments Ltd). Results were provided by a volume distribution profile. The dv(0.5), the median of the distribution, as well as the dv(0.1) and dv(0.9) values for determining the width of the distribution, were calculated by the system software. For SEM a Supra 35/ LEO 1530 microscope (Zeiss) was used.

**Results:** The particle size distribution profiles of the twenty batches were comparable shown by the obtained dv values: dv(0.5): 20-28 μm (mean: 23 μm), dv(0.1): 10-13 μm (mean: 11 μm) and dv(0.9): 36-56 μm (mean: 44 μm). The SEM images revealed that the visible particles consist of tightly agglomerated small primary particles with a subvisible size of 16-20 nm. Hence, the visible particles in the suspension are agglomerated primary particles.

**Conclusion:** The results offered a detailed insight into the formation, structure and size distribution of the visible particles in an aluminum hydroxide based SCIT product. High-resolution SEM uncovered the nanostructure of the visible particles which are based on primary particles. The close insight into the particle morphology offers the possibility to elucidate variations during drug product development and routine manufacturing. The low batch-to-batch variation regarding the morphology and size distribution of the adsorbate particles demonstrated the high reproducibility of the production process. A drug product of high quality is crucial for a consistent and successful therapy.

## 0942 | Development of an inhibition-assay for the determination of specific IgG reactivity of allergoid-based allergen preparations

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**Background:** Chemically modified allergens, so called allergoids, are reduced in their IgE-binding reactivity but still contain structural features mandatorily needed for T cell recognition and the formation of the allergen-specific IgG antibodies. The Guideline on Allergen Products demands the use of animal sera based potency assays to verify the IgG reactivity of allergoids. Therefore, in the present study a microtiter plate based inhibition-assay was to be developed, to determine the relative specific IgG activity of allergoids and aluminum-adsorbed-allergoid-based allergen preparations (manufactured from pollen of grasses, birch, mugwort and olive).

**Method:** The established immunological method consists of allergoid-reactive polyclonal antibodies, a secondary antibody and HRP/TMB as detection system. The allergoid-preparation in the soluble phase of the assay competes with the allergoids coated on the surface of the microtiter plate for the binding of the anti allergoid-antibodies. The relative potency of the allergoid-preparation is inversely proportional to the optical density determined in the assay and is calculated as the relation of the dilution factor at 50% inhibition of sample to reference (Prel_DF). For further evaluation of the method for routine the parameters linearity, accuracy, precision, reproducibility and robustness have been assessed.

**Results:** Goats and rabbits were immunized with specific allergoids, the allergoid-specific IgG titer determined and sera pools produced. The allergoid reference material was comprehensively characterized. While IgE reactivity of the allergoids was not detectable anymore, IgG reactivity was maintained. Allergoid-specific assay parameters as serum dilution, reference dilution and sample dilution factor to obtain at least six data points within the pseudo-linear range of the inhibition curve were determined. With these set parameters the evaluation of the analytical method was performed. The assay showed very good results in terms of linearity, accuracy, precision, reproducibility and robustness for all investigated allergoids as well as aluminum-adsorbed allergoid-preparations.

**Conclusion:** With the developed immunological inhibition assay, it is possible to determine the specific IgG reactivity of allergoids in different preparations. The performance of the analytical method

met all pre-defined acceptance criteria, which will be confirmed in the next step by a validation procedure according to ICH-guidelines.

## 0943 | Late reaction to specific immunotherapy? Not all is allergy

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**Case report:** We present the case of a 32-year-old patient, diagnosed with rhinitis and asthma due to sensitization to pollens, as well as dyshidrosis and allergic contact dermatitis to Cobalt.

The patient presented a cutaneous pattern consisting of erythematous papules, some scaly, very pruritic, of initial appearance in the upper limbs 2-3 days after initiation of administration of specific immunotherapy extract (DEPIGOID forte grasses, Leti®). Subsequently generalize lower limbs and neck. She presented them repeatedly and late after 2-3 days of the first 3 doses administered. She referred partial control of pruritus with oral antihistamines, without total resolution of lesions for weeks. Immunotherapy was suspended persisting the skin lesions for 3 more weeks.

According to the personal history of sensitization to metals, and the clinic presented in a temporal relationship with the use of an extract of immunotherapy with aluminum hydroxide, a study was requested with epicutaneous tests with aluminum hydroxide as well as with epicutaneous tests with immunotherapy extract.

Aluminium hydroxide and Depìgoid Forte grasses extract epicutaneous test were negative. In subsequent visits the patient reported that coinciding with the start of immunotherapy, presented at home and mainly in her bedroom a plague of Cimex lectularius, popularly known as bedbugs, proving that they had been the cause of bites on their skin, and later skin reaction. Patient reported that with the elimination of said pest the skin lesions disappeared. The administration of its immunotherapy extract was tolerated.

Cimex lectularius, commonly known as bed bugs, is a hemiptera insect of the family Cimicidae. The clinical picture usually corresponds to multiple pruriginous lesions from the prurigo type, to multiple erythematous plaques, some infiltrated and others with a urticarial appearance, or even bullous. The lesions last for 3 to 6 weeks without treatment, and while the older ones heal, new ones may appear. In our patient it was not considered as an initial diagnosis, having considered immunotherapy as an etiological factor, but we must not forget that although in our country it is not a reason for frequent consultation, either due to underdiagnosis, because of the transitory nature of the pathology or because of scarce number of causative agents, it is important to consider insect bites in the differential diagnosis of dermatosis.

## 0944 | Heterogeneity of commercial house dust mites extracts

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**Background:** House dust mites (HDM) are one of the most important allergens involved in childhood respiratory diseases, and the most frequently prescribed extract for sublingual immunotherapy in children (SLIT).

Despite the improvement of standardization methods for the production of SLIT, the differences in cultivation and purification processes used to produce raw materials for specific immunotherapy extracts may still impact on the final composition of mite allergen extracts.

Our study investigated the total protein and main allergen content of five commercial HDM sublingual immunotherapy extracts using SDS-PAGE and immunoblotting. Recombinant allergens of group 1 and group 2 major allergens were used to test the immunogenicity of such extracts.

**Method:** HDM SLIT extracts were purchased from five Italian suppliers (ALK-Abellò, Allergy Therapeutics, Anallergo, Lofarma, Stallergenes).

The protein composition of extracts was evaluated analysing equal volumes (15 mL/lane) by SDS–PAGE (12% separating gel) and subsequent immunoblotting. For identification of allergens in the extracts, western blot analyses were performed with rabbit monoclonal antibodies (RayBiotech) against Der p 1 and Der p2.

**Results:** The total protein content in the five tested commercial extracts showed a relevant variability. The protein contents ranged from 32.9 to 44.2 μg/mg for what concerns Der p1, while Der p2 showed a greater variability, ranging from 4.2 to 14.6 μg/mg.

SDS-PAGE showed a similar pattern of distribution in 3 of the tested extracts, which showed protein bands of comparable intensity, while 2 extracts showed a lower total protein count. Extract 2 showed a higher intensity band corresponding to the molecular weight of tropomyosin.

Western-blotting showed a similar concentration of Der p 1 in most extracts, while Der p2 was more variable.

**Conclusion:** Our analysis of five commercial extracts commonly used for sublingual specific immunotherapy against HDM showed important variations in term of total protein content. A less evident but still relevant difference was also evidenced when testing the major allergen content, with up to 25% variation in Der p1 and up to a 3-fold variation in Der p2 concentration. This differences, likely related to the different production and extraction methods, could still be responsible of a different immunological response in children who underwent SLIT.

## 0945 | Treatment effect of grass-pollen immunotherapy for children with allergic rhinoconjunctivitis in a district general hospital

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**Background:** Allergic Rhinoconjunctivitis affects 10-20% of adults and up to 40% of children in the UK. Symptoms can be disruptive with uncontrolled symptoms causing disturbed sleep and poor school performance. Immunotherapy is the only treatment that can alter the course of this disease and results are widely reported in specialist centres. A rural district general hospital in the UK, Worcestershire Acute NHS Trust has been using immunotherapy for patients with uncontrolled symptoms of rhinoconjunctivitis. We evaluated the efficacy of the treatment in our local population since 2010 using a validated questionnaire on quality of life with regards to symptoms of rhinoconjunctivitis, the Mini Rhinoconjunctivitis Quality of Life Questionnaire (mRQLQ) taken before and after the treatment course of 3 years.

**Method:** We evaluated 29 children who had completed their immunotherapy treatment. Along with demographic data we were able to record skin prick test (SPT) results and mRQLQ at start and end of treatment. We only included patients who had completed pre and post treatment questionnaires in the study to allow a comparison. The scores were evaluated using a student T test.

**Results:** Patients' starting age ranged from 6 to 17 years (mean 11 years). 29 of the 48 children had completed pre and post treatment questionnaires. All 29 had grass pollen allergy confirmed on SPT at the start of treatment. 10 patients (34%) had isolated grass pollen allergy on SPT and 19 (66%) had multiple allergies. Mean start treatment score for all patients was 37 on mRQLQ. Mean score at end of treatment was 24, indicating a 35% reduction in total mRQLQ score (*P* value <0.05). For those with multiple allergies the mean total mRQLQ scores were 33 at start of treatment and 25 at end of treatment, indicating a 27% reduction (*P* value 0.16). For those with isolated grass pollen allergy scores were 44 at start of treatment and 23 at end of treatment indicating a 50% reduction (*P* value <0.05).

**Conclusion:** For children with uncontrolled symptoms of allergic rhinoconjunctivitis, grass pollen immunotherapy is associated with statistically significant improvement in quality of life. This improvement is most beneficial for patients with isolated grass-pollen sensitivity on SPT. Those with multiple aeroallergen sensitivities on SPT did show an improvement (not statistically significant) post-treatment. Grass-pollen immunotherapy is an effective treatment for rhinoconjunctivitis to offer patients in a rural DGH setting.

## 0946 | Clinical analysis of specific immunotherapy for allergic asthma

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**Background:** Allergic asthma is a common clinical refractory disease, most patients with asthma are accompanied by varying degrees of allergy. In clinical practice, treatment of this disease using specific immunotherapy has proven effective. In the current study, we examined the effectiveness of specific immunotherapy in a total of 99 patients admitted to our hospital from 2015 to 2016.

**Method:** To investigate the clinical efficacy of allergic asthma-specific immunotherapy. 99 patients were selected, of which 49 were males, aged 22 to 61 years, 50 females, aged between 23 to 64 years old, all patients were clinically diagnosed only as allergic asthma. The 99 patients were randomly divided into two groups, including the observation group containing 50 cases, the control group of 49 cases. All patients were first treated with conventional basic treatment. The observation group was subsequently treated with specific immunotherapy. Both groups were followed-up and the treatment efficiency were analyzed.

**Results:** After treatment, both two groups of patients showed improvement, in the observation group, the effective rate was 93%, while for the control group, the effective rate was 75%. Observation group showed significantly better outcomes than the control group.

**Conclusion:** In allergic asthma treatment, adding specific immunotherapy on the basis of routine treatment is beneficial and could be widely used in clinic.

## 0947 | Application of component resolved diagnostics in treatment of severe atopic dermatitis

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**Case report:** Atopic dermatitis(AD)is the most common itchy dermatosis that affects millions of children and adults. During recent years, diagnosis and treatment based on component resolved diagnostics (CRD)is recommended. We report a 9-year-old boy with severe Atopic dermatitis. He had positive family history of atopy. The atopic dermatitis was developed since infancy. He was referred to our clinic when he was 5 years old. He had generalized xerosis with ulcerative eczematous lesions on his neck, popliteal and antecubital

areas. He had mild eosinophilia and his serum total IgE level was 590 IU/mL. Daily bleach bath, moisturizing agents, topical steroids and systemic antibiotics in addition to antihistamine were prescribed. He had multiple food and aeroallergen sensitization in skin prick test (SPT). He started to eliminate some foods according to the SPT results. He was suffering from recurrent relapse even after strict food avoidance; so treatment with cyclosporine was initiated for him, with partial response. CRD showed sensitization to Alternaria alternata (Alt a1 specific IgE:10.97 kU/L). Allergen immunotherapy by Alternaria alternata was started. After accomplishment of buildup phase, he had significant improvement and we were successful to taper and finally discontinue cyclosporine. Now he is on maintenance phase of immunotherapy, his skin is in optimal condition only by hydration and moisturization.

**Conclusion:** Alternaria alternata immunotherapy is an effective treatment in Alternaria alternate sensitized patients with severe atopic dermatitis unresponsive to other treatments. Trials have suggested that desensitization to specific allergens may improve atopic dermatitis.CRD can help in accurate allergen diagnosis and patient treatment in selected patients with severe Atopic Dermatitis.

## 0949 | Efficacy of cat sublingual immunotherapy in a Thai girl with severe asthma

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**Background:** Subcutaneous immunotherapy (SCIT) in severe asthmatic patients can increase the risk of systemic reactions. Sublingual immunotherapy (SLIT) is thus considered as an alternative treatment for these patients. Many studies showed good efficacy of SLIT in grass and mite allergic patients, but there is limited data for the efficacy of SLIT in cat allergic patients.

**Method:** We reported the efficacy of SLIT in a Thai cat allergic girl with severe asthma.

**Result:** A 15-year-old Thai girl is a known case of severe asthma since one year old. Her asthma was uncontrolled asthma even treatment with high dose combination of inhaled corticosteroid and long acting beta agonist (ICS/LABA), montelukast and Omalizumab. Spirometry revealed the force expiratory volume in one second (FEV1): 34% predicted, FEV1/forced vital capacity (FVC): 48% predicted and 14% improvement of FEV1 after salbutamol 400 ug inhalation. Allergic sensitization showed specific IgE to cat: 2.04 KUA/L. SLIT with cat allergen started at the dose of 450 AU per month and increased to 1500 AU per month (SCIT dose is 1000 AU per month) for three-year-and-six-month course. After SLIT, her asthma symptom improved significantly. She can exercise without exacerbation and plays sport at school. Her last episode of asthma exacerbation was 1.5 year ago. Her FEV1 (% predicted) was improved from 34% predicted to 48% and the FEV1 bronchodilator response decreased from 14% to 6%.

**Conclusion:** An improvement of pulmonary function and asthmatic symptoms of the presenting case would support the efficacy of SLIT of cat allergen in a patient with severe asthma.

## 0951 | Rheumatoid arthritis developed during subcutaneous pollen allergen immunotherapy: A case report

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**Case report:** Allergen specific immunotherapy is used widely, yet there is less evidence of its long-term-safety. Here a patient who developed rheumatoid arthritis (RA) during subcutaneous allergen-immunotherapy (SCIT) was described. A 39-year-old-physician presented with allergic rhinitis (AR), due to pollen sensitization in skin-prick-tests/sIgE. As she was exposed to indoor passive smoking since her birth and respiratory bronchiolitis with mosaic pattern in computed tomography, fixed airway obstruction (best FEV1 70%). was diagnosed. However, she had mild dyspnoea but was concerned of progression of airway obstruction. She underwent SCIT with grass mix in December, since she was unresponsive to medical treatment for severe AR during pollen season. She had no dyspnoea or adverse events during increasing phase of SCIT, and maintenance dose was reached successfully. However, she had developed finger and wrist pain in both hand joints after 11 months of SCIT, and used non-steroid anti-inflammatory drugs regularly for almost 1-week. Although pain was relieved, her symptoms recurred the next month, with morning stiffness lasting longer than 30 minutes and fatigue, as well as symmetrical multiple joints swelling, redness, tenderness and was consulted to rheumatology department. Hand MRI was normal, serologic tests for collagen disease including RF or anti-CPP were found to be negative. She was diagnosed sero-negative RA, but positive inflammatory blood test results (sed:48/hr), and symmetrical polyarthritic symptoms. Treatment with low-dose-corticosteroid and hidroxyclorocin-sulphate was started, and continued with hidroxyclorocin-sulphate regularly. The relation with RA and SCIT was unclear, and the patient wanted to continue SCIT since her rhinitis was improved, and had no arthritis till August. After 20 months of SCIT, she had an arthritis attack right after SCIT injection, and was treated with low-dose corticosteroid. After SCIT was discontinued, no arthritis attack was observed within 6 months. The patient is still using hidroxyclorocin-sulphate regularly, and although she is asymptomatic, her systemic inflammation persists (sed:56/hr). In conclusion, SCIT was found to be effective and safe for most of the patients with rhinitis/asthma,

RA developed during pollen SCIT in this case might be related with immunomodulation effect of immunotherapy.

## 0952 | The importance of molecular diagnosis in allergen-specific immunotherapy

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**Background:** We report a case of 20-year-old woman with allergic rhinoconjunctivitis and mild persistent asthma due to sensitisation to seasonal pollens and molds with bad clinical evolution and not response to conventional drug therapy.

We decided to start subcutaneous allergen specific immunotherapy with *Alternaria* extract in our Immunotherapy Unit in accordance with the guidelines of the European Academy of Allergology and Clinical Immunology (EAACI) and we used a cluster regimen.

The immunotherapy was not well tolerated: the patient had two grade 2 systemic reactions with the first dose in two attempts.

**Method:** Sensitisation was diagnosed through skin prick test with aeroallergens standard panel and serum specific IgE by ELISA.

Due to the bad tolerance to immunotherapy, molds molecular diagnosis by ImmunoCAP, study of the molecular weight to specific IgE binding proteins by SDS-PAGE IgE immunoblotting, and cross-reactivity study by means of Immunoblotting-inhibition assay were performed.

**Results:** Serum specific IgE level was positive to *Alternaria alternata* (1.48 $kU_A/L$), *Aspergillus fumigatus* (3.31 $kU_A/L$) and negative to *Cladosporium herbarum* (< 0.1 $kU_A/L$)

Molds molecular diagnosis was negative to Alt a1 (< 0.1 U/L) (major allergen from *Alternaria*).

SDS-PAGE immunoblotting analysis of *A. alternata* extract showed an intense 38 kDa IgE binding band, and some other faint bands.

*A. fumigatus* extract was able to produce a total IgE binding inhibition on the 38 kDa band of *A. alternata* extract when IgE Immunoblotting assay was performed.

**Conclusion:** Respiratory allergic disease due to *Alternaria* is difficult to control, the use of subcutaneous specific immunotherapy could be of significant benefit.

Most of the allergic patients to *A. alternata* are sensitized to Alt a1, major allergen from *A. alternata*. However, our patient is sensitized to a 38 kDa *Alternaria* protein due to cross-reactivity with *A. fumigatus* allergens, this sensitization could explain the bad tolerance to the *Alternaria* immunotherapy.

## 0953 | Adaptive immune responses in allergic subjects in response to natural allergen exposure

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**Background:** The association between natural pollen exposure, clinical symptoms as well as allergen-specific immune responses has not been investigated at a molecular level. Our aim was to monitor the effect of seasonal birch and grass pollen exposure on clinical symptoms as well as specific B cell and T cell responses to defined allergen molecules in sensitized subjects during two consecutive years.

**Method:** Grass pollen sensitized (n = 10) and birch pollen sensitized (n = 13) subjects were included in this study and were followed for two consecutive years (2013-2014). Subjects were taking part in a clinical trial for the recombinant grass pollen vaccine (BM32) but did not receive immunotherapy for the allergen they were sensitized to. Before, during and after the respective seasons IgE and IgG levels as well as T cell responses to the major birch pollen allergen Bet v 1 and the major grass pollen allergens Phl p 1, 2, 5 and 6 were measured. Pollen counts were recorded throughout the year and patients kept a daily diary including symptom medication score (SMS) and visual analogue scale (VAS).

**Results:** We noted that IgE levels specific for Bet v 1 and the grass pollen allergens increased most in the seasons in which patients experienced the highest peak symptoms according to VAS and SMS but not depending on cumulative pollen counts. Increases in allergen-specific T cell responses were observed in the pollen seasons as compared to shortly before the pollen seasons in the grass pollen-allergic patients also in association with VAS and SMS but not in the birch pollen allergic subjects. No relevant changes of allergen-specific IgG levels were observed during the two years observation in grass and birch pollen allergic patients.

**Conclusion:** We found an association of increases of allergen-specific IgE increases shortly after the pollen season with clinical symptoms in the pollen season as reflected by VAS and SMS which was not necessarily reflected by cumulative pollen counts in the season. These results may be important for the analysis of allergen-specific immunotherapy trials.

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MONDAY, 28 MAY 2018
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CLINICAL FEATURES AND COMORBIDITIES OF ASTHMA

## 0954 | Characteristics of adult severe refractory asthma in Korea analyzed from severe asthma registry supported by severe asthma work group of the Korean academy of asthma, allergy and clinical immunology

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**Background:** The morbidity and mortality of severe asthma is much higher than that of mild to moderate asthma. This study was performed to understand the clinical characteristics of severe asthma in Korea.

**Method:** We registered the patients with severe refractory asthma into Severe Asthma Registry supported by Severe Asthma Work Group of the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI). The patients were enrolled from the 15 university hospitals nationwide in Korea since 2010. Severe asthma was defined as modified European Respiratory Society/American Thoracic Society criteria. Information for demographics, medical history, pulmonary function tests, and skin prick tests were collected and clinical characteristics of severe asthmatics were analyzed from the collected data.

**Results:** A total of 494 patients were enrolled with a mean age of 62.0 and 45% of them were male. The most common comorbidities were allergic rhinitis (52.0%) and hypertension (30.0%). Aspirin hypersensitivity was observed in 11.3% and non-smokers were 53.4%. Positive bronchodilator response was proven in 34.1% and allergen skin prick test showed positive in 50.2% of patients. In terms of asthma medications, ICS and long-acting β-agonists fixed dose combination inhalers were dominantly prescribed (95.3%) followed by leukotriene antagonists (70.0%), methylxanthines (56.3%), and short-acting β-agonist (37.2%). Systemic corticosteroids and anti-IgE monoclonal antibody (omalizumab) have been used in 58.5% and 1.8% of the patients, respectively. The mean FVC, FEV1, and FEV1/FVC were 78.8%, 67.6%, and 68.1% of predicted values, respectively. The mean score of asthma control test (ACT) and quality of life questionnaire in adult Korean asthmatics (QLQAKA) were 16.5 out of 25 and 59.5 out of 85, respectively.

**Conclusion:** Herein, the baseline characteristics of severe asthma patients of the Severe Asthma Registry in Korea were firstly analyzed and reported. With this cohort, further prospective studies should be performed to search ways for improving management of severe refractory asthma.

## 0955 | Refractory asthma: Clinical characteristics in patients in Reunion Island

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**Background:** Refractory asthma (RA) is a condition where large amount of medication is required to maintain disease control. Although RA is uncommon (likely-10% of patients with asthma), clinical characteristics and risk factors for the development of the condition has to be details to improve management of affected individuals.

The aim of the present study is to characterize RA by comparing with non-RA.

**Method:** 131 patients with "problematic asthma" (female: 67, mean age: 49 years) were recruited in our Allergy Outpatient Clinic over a 2-year period, between July 2015—June 2017, presenting the diagnostic criteria for RA included continuous requirements for systemic corticosteroid or high dose inhaled corticosteroid to maintain control (Innovative Medicines Initiative -2011). For each patient, we recorded anamnestic data, respiratory function, body Mass Index (BMI), presence and type of comorbidities. Serum IgE and complete blood count (CBC) were obtained while disease control was stable.

**Results:** 14 patients fulfilled the diagnostic criteria of RA. Patients with RA displayed significantly lower $FEV_1$/FVC compared with patients with non-RA ($P$ = 0.012). Reversibility to $B_2$ agonist tended to be lower in patients with RA. The CBC showed higher percentage of neutrophils ($P$ = 0.0081) for RA patients. Regression analysis identified significant association between RA and chronic sinusitis ($P$ = 0.01) and of drug allergy ($P$ = 0.0001). The presence of gastro-esophageal reflux disease (GER) were significantly higher ($P$ = 0.001) among RA patients, 65% RA reported symptoms of asthma associated with GER. Severe obstructive sleep apnoea was observed in RA (mean Apnea Hypopnea Index of 37.5 ± 25.5/h vs 18.2 ± 5.3/h) with mean BMI ($Kg/m^2$) 35.6 vs 26.7.

**Conclusion:** A systematic evaluation of patients with RA should include the confirmation of the diagnosis of asthma, assessment of disease severity, evaluation of risk factors, comorbid conditions and other factors that prohibit asthma control.

## 0958 | The prevalence of bronchial asthma and allergic rhinitis among pregnant women in St.-Petersburg

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**Background:** Data on the prevalence of allergic diseases among pregnant women is contradictory. At present, no studies on the prevalence of bronchial asthma (BA) and allergic rhinitis (AR) in pregnant women have been performed in Russia. Aim of study was investigate the prevalence of allergic diseases (BA and AR) in pregnant women of St. Petersburg.

**Method:** We evaluated 4 000 pregnant women in St. Petersburg to clarify the prevalence of asthma and AR. European Community Health Survey (ERCHS) for evaluation of BA and special questionnaire developed by the Pulmonology Research Institute for evaluation of AR were used.

**Results:** Data from the questionnaire showed that bronchial asthma was diagnosed before pregnancy only in 193 women (4.83%). 43 patients (1.1%) were diagnosed with chronic bronchitis at the pregestation stage. Asthma attacks were experienced repeatedly during a lifetime in 4.2% of patients, 12.7% of patients noted long periods of dry cough at night, among them 8.1% had wheezing. The cold did not precede the wheezing breathing in 5.1% of patients. Difficulty in breathing on waking was noted in 2.6% of patients, at night—4.3%. After examination, the diagnosis of asthma was confirmed in 14.65% of the respondents (586 people). Symptoms of rhinitis are noted in 58% of women surveyed, 18% of rhinitis was allergic. Before examination, the diagnosis of AR was only in 3.5% of patients.

**Conclusion:** The incidence of symptoms of asthma and AR in pregnant women is significantly higher than the reported cases of these diseases, which leads to untimely initiation of treatment.

## 0960 | Identification of asthma phenotypes in Turkey

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**Background:** Asthma is a heterogenous disease that can be seen in different clinical features. Recognition of phenotypes may further our understanding about the pathophysiology, treatment response and genetic basis of the disease. Our aim is to define the asthma phenotypes in adult Turkish patients.

**Method:** A total of 117 nonsmoker asthmatic patients without concomitant pulmonary pathology are recruited to our study. All patients underwent spirometry tests, measurement of fraction of exhaled nitric oxide and sputum induction to asses sputum cell counts, demographic features and current medications were recorded. Using the variables of age at onset, BMI, allergy status, FEV1%, FEV1/FVC, asthma severity and induced sputum cytology cluster analysis is performed.

**Results:** 4 clusters are identified. Cluster1: (n = 43) Early onset atopic asthma, consists of mild asthmatics with a good asthma control and lower BMI. Cluster 2: (n = 14) Severe atopic asthma, consists of lowest spirometry measurements with a least ACT scores. Induced sputum cytology shows a neutrophilic character, while having also the highest percentage of eosinophils. Cluster 3 (n = 27) Late onset obese asthma, nonatopic asthmatics having high spirometry measurements, with a lower ACT scores. Cluster4 (n = 33) Nonatopic mild asthma, consists of patients with the best respiratory functions and least inflammation in means of lowest total IgE, FeNO, sputum cell counts.

**Conclusion:** Identification of asthma phenotypes in different countries will improve our understanding on the heterogeneity of the disease among the different geographies.

## 0961 | Clinical features of obesity in children with bronchial asthma

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**Background:** Scientific researches made in recent years have shown that obesity is accompanied by an increased risk of developing bronchial asthma.

The purpose of the research: to identify the clinical features of obesity in children with bronchial asthma.

**Method:** Characteristics of children and methods of research: 125 children aged 7-14 years, 101 boys and 24 girls were examined. 84 patients had found mild asthma and 31 had a moderate severity. The control group consisted of 100 children aged 7-14 years who did not have bronchial asthma. All children underwent analysis of the history of development, examination, measurement of length and body mass index, inspection of the endocrinologist to exclude secondary forms of obesity. For the diagnosis of obesity, the SDS indices of body mass index (BMI) were determined. Obesity—more than +2.0 (I degree: SDS BMI 2.0-2.5, II degree: SDS BMI 2.6-3.0, III degree: SDS BMI 3.1-3.9, IV degree: SDS BMI ≥4.0).

**Results:** *Results and discussion*. In the course of analysis, obesity was more common in children with bronchial asthma −25% than in the comparison group-in 9.3%. Obesity of the 1st degree was diagnosed in 10 patients of the main group, II degree—in 8, and III degree- 5 and IV degree—in 2 patients e diagnosis of obesity, the SDS indices of body mass index (BMI) were determined. Obesity—more than +2.0 (I degree: SDS BMI 2.0-2.5, II degree: SDS BMI 2.6-3.0, III degree: SDS BMI 3.1-3.9, IV degree: SDS BMI ≥4.0).

**Conclusion:** Thus, the results obtained indicate a high prevalence of constitutional-exogenous obesity in children with bronchial asthma and precedes the formation of the underlying disease *e diagnosis of obesity, the SDS indices of body mass index (BMI)* were determined. Obesity—more than +2.0 (I degree: SDS BMI 2.0-2.5, II degree: SDS BMI 2.6-3.0, III degree: SDS BMI 3.1-3.9, IV degree: SDS BMI ≥ 4.0).

| Group | 1 degree | 2 degree | 3 degree | 4 degree |
|---|---|---|---|---|
| Main | 10% | 8% | 5% | 2% |
| Control | 5% | 3% | 2% | — |

## 0963 | Relation of systemic comorbidities in asthma with disease control, severity and phenotype

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**Background:** Asthma is a heterogeneous and chronic inflammatory disease that can accompany many comorbidities during the course. It is thought that different comorbidities are seen in different phenotypes of asthma. Our aim is to establish the relationship between systemic comorbidities seen in asthmatic patients and asthma control, severity and phenotypes.

**Method:** Patients who were followed up with asthma diagnosis in Polyclinics of Ankara University Faculty of Medicine Department of Immunology and Allergy Diseases were questioned about demographic characteristics. Their control status and disease severity were determined. They were classified whether r atopic, eosinophilic or obese. Systemic comorbidities were questioned and Charlson comorbidity indices (CCI) were calculated. The difference between the groups in the terms of CCI was evaluated.

**Results:** 229 patients (29E/200K, 12.7%/87.3%) with a mean age of 51.25 ± 12.02 were included in the study. CCI was significantly higher in patients without asthma control than in those with partial control and well control. (CCI: 2.22, 1.69, 1.50, respectively) ($P$ = 0.03). There was also a linear correlation between asthma severity and CCI (CC: 0.22, $P$ = 0.001). Allergic comorbidities were more frequent in the eosinophilic phenotype ($P$ = 0.01) (OR:2.20, 95%CI: 1.2-3.8) but did not increase the likelihood of accompanying systemic comorbidity. (OR: 1.05, 95%CI: 0.8-1.2) ($P > 0.05$) The likelihood of systemic comorbidity, especially HT, coroner artery diseases, depression, was higher in nonatopics than in atopic patients. (OR: 2.03, 95%CI: 1.04.11) ($P$ = 0.03) Obesity was found to be a risk factor for systemic comorbidities. (OR: 1.36, 95%CI: 1.09-1.84) ($P$ = 0.04).

**Conclusion:** Severe, uncontrolled, obese or nonatopic asthma patients should be examined for systemic comorbidities. There is a need for further study to assess the relationship between treatment of established comorbidities and asthma course.

ORAL PRESENTATION

ASTHMA/ASTHMA: MECHANISMS

## 0964 | Differences in viral etiologies in asthma and wheezing illness in young children

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**Background:** The pattern of viral infections associated with the diagnosis of "asthma" or "wheezing illnesses" are largely the same. In particular, HRV is the most common virus being detected. Longitudinal studies and carefully designed intervention studies are needed to determine if earlier use of asthma treatment may result in "better control" of children who have received a diagnosis of 'wheezing illness'.

**Acknowledgement:** Suppoted by the TS Lo Foundation.

**Method:** A total of 642 patients with 728 admissions during the study period (male 63.5%, mean age at first admission 3.2 ± 0.1 years) were enrolled. There were 201 cases of asthma and 257 of wheezing illness while 81% of the admitted children were under 5 years of age. Compared with patients diagnosed with 'asthma', the prevalence rate of human rhinovirus (HRV) being detected in the NPA was similar in those diagnosed with 'wheezing illness' (54.1% vs. 63.2%, p = 0.254), whereas the detection of HRV was significantly lower in patients diagnosed with 'bronchiolitis' (39.1%, p = 0.03) where more respiratory syncytial viruses were detected (2.4% vs. 24.6%, p < 0.001). Other types of viruses, such as influenza and parainfluenza were mainly detectable in patients with URI, croup and pneumonia. Many children with 'wheezing' illnesses had recurrent symptoms highly suggestive of asthma.

**Results:** This was a prospective study of pediatric patients admitted to the Prince of Wales Hospital, September 2016 to November 2017 due to respiratory complaints including asthma exacerbations, wheezing illness, bronchiolitis, and shortness of breath. Nasopharyngeal aspirates (NPA) were obtained by standardized techniques. The detection of viruses was determined by immunofluorescence and multiplex PCR testing. The other investigations were up to the discretion of the attending doctors. The attending physicians were not aware of the NPA-PCR results. The demographic data, treatment details and discharge diagnoses were recorded prospectively for subsequent analyses.

**Conclusion:** Proper diagnosis is the first important step for optimal management of asthma. A variety of diagnoses such as wheezy bronchitis, viral wheeze and recurrent bronchiolitis are being used instead of asthma in young children due to lack of objective measure for the diagnosis of asthma. As a result, proper asthma treatment may not be prescribed. The aim of the current study is to determine the viral etiologies associated asthma and related wheezing disorders in young children.

## 0965 | Self-reported nasal hyperreactivity in patients with asthma

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**Background:** Nasal hyperreactivity (NHR) is a novel phenotype found in two-thirds of rhinitis patients, irrespective of the atopy status. In line with the concept of united airway diseases, 90% of asthma patients have rhinitis and 30% of patients with allergic rhinitis suffer from asthma. Data on the prevalence of NHR in patients with asthma are lacking, as well as data on the nature and number of triggers, and correlation between NHR and phenotypes of asthma.

**Method:** Postal questionnaires were distributed to an unselected group of asthma patients (n = 190). Healthy non-asthmatic volunteers were recruited amongst university and hospital co-workers (n = 53). The presence of self-reported NHR, the type of triggers evoking nasal symptoms, asthma phenotype, medication use and environmental factors were evaluated.

**Results:** 114 patients and 53 controls completed the questionnaire (responder rate of 60% and 100% respectively). NHR was reported in 71% of asthma patients and 22% in non-asthmatic controls ($P < 0.0001$), with changes in temperature being the most important inducer of nasal symptoms (74% of asthmatics), followed by strong odours (62%) and cigarette smoke (61%). Interestingly, NHR was more prevalent in patients with severe (79%) compared to mild (50%) asthma symptoms ($P = 0.015$), and more prevalent in atopic (77%) compared to non-atopic (55%) asthmatics ($P = 0.028$). Most asthma patients reported more than one trigger evoking nasal symptoms, with 44% of patients reporting 3 or more triggers evoking nasal symptoms.

**Conclusion:** We here demonstrate for the first time the high prevalence of self-reported NHR in asthma. Novel therapeutic strategies targeting NHR in asthma might reduce the burden of disease.

## 0966 | Behavioral disorders in children with and without asthma that referred to children medical center in Qom, Iran

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**Background:** Asthma is a chronic medical condition that is common in childhood. This disorder can lead to complications, extra costs, hospitalization and poor quality of life in patients and their families. Asthma-like other chronic diseases can be associated with mood disorders, anxiety, and behavioral change. In some cases, this combination can negatively affect the clinical course of the underlying disease. The purpose of this study was to compare the behavioral disorders in children with and without asthma referred to a children's hospital.

**Method:** This case-control study was performed on 134 children aged 7-15 years old referred to children medical center in Qom. Sixty-seven children with asthma, as the case group and 67 healthy children as a control group, were included. Questionnaire on demographic and clinical information, and the Child Behavior Checklist (CBCL) and Global Assessment of Functioning (GAF) (for parents) were completed. Data were analyzed by t-test and Chi2 test in SPSS18.

**Results:** The mean score of CBCL questionnaire in case group with 28.12 ± 2.06 was significantly higher than in comparison with a control group with 17.33 ± 9.7 ($P$ = 0.01). The mean scores of the subscales of social isolation (the case group: 5.83 vs control: 1.18, $P$ = 0.006), anxiety-depression (4.99 vs 2, $P$ = 0.22), intellectual problems (4.8 vs 2.3, $P$ = 0.000), and aggressive behaviors (5.1 vs 2.3, $P$ = 0.003) were significantly higher in children with asthma than in healthy children. The study showed a significant correlation between the mean duration of asthma and a general score of CBCL ($P$ = 0.012, CC=0.8). Moreover, there was also a significant correlation between asthma severity and CBCL scoring ($P$ = 0/001, CC=0.03).

**Conclusion:** Behavioral disorders in children with asthma are significantly more than healthy children. The duration of asthma and the severity of asthma, are related to and can predict behavioral disorders in children with asthma.

## 0967 | Uncontrolled asthma symptoms amongst severe asthma patients: Impact of comorbidities and prediction of exacerbation risk. Findings from the Singapore general hospital severe asthma phenotype study

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**Background:** Assessment of asthma control is an integral part of the management of asthma. Whilst Asthma Control Test (ACT) is a commonly used questionnaire to assess symptom control, its utility in predicting long term risk of exacerbation has not been well studied.

Aim: To analyze the factors associated with uncontrolled asthma symptoms using ACT and its impact on predicting future exacerbation.

**Method:** Severe asthma patients on at least Step 4 of GINA and being followed up at our severe asthma clinic from 2011 to 2016 as part of the Singapore General Hospital Severe Asthma Phenotype study were included. Clinical, laboratory, health care utilisation information and asthma control test (ACT) scores were derived from the hospital electronic medical records. Patients were divided into two groups according to their baseline average ACT scores over 2011: Average ACT<20 (uncontrolled) vs. ACT≥ 20 (well-controlled). Data was analysed using SPSS.

**Results:** N = 204 patients were included with a mean age of 53.48 ± 18.3 years, 52.5% were female. 106 patients (52%) had uncontrolled asthma symptoms and they had higher prevalence of Gastro-oesophageal reflux disease (GERD) ($P$ = 0.004), eczema ($P$ = 0.04), significantly higher incidence of emergency department visits for asthma ($P$ = 0.003), and mean number of admissions from 2012-2016 ($P$ = 0.02) than patients with well-controlled asthma symptoms. In the multivariate analysis, factors predictive of exacerbations requiring admissions were increasing body mass index (BMI) (OR 1.065, 95 CI 1.0-1.13, $P$ = 0.036), ACT <20 (OR 2.866, 95%CI 1.35-5.50, $P$ = 0.005) and factors predictive of exacerbations requiring emergency visits were increasing BMI (OR 1.081 (95%CI 1.020-1.147, $P$ = 0.009) and ACT <20 (OR 3.914, 95%CI 1.98-7.75, p=<0.001).There was no significant difference in age, gender, allergen sensitisation pattern, lung function, eosinophil count, prevalence of smoking, anxiety, depression or obesity between the two groups.

**Conclusion:** Uncontrolled asthma symptoms were associated with GERD and eczema and predicted future risk of exacerbation. Comorbidities impact severe asthma outcomes and systematic evaluation of these comorbidities are integral to the overall management of severe asthma.

## 0968 | Non-Pharmacological factors and asthma control in children: A factor analysis

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**Background:** Most of the asthma-scoring tools detect the asthma severity from patients' symptoms but there is no scoring tool using parameters to define risk of asthma exacerbation. Thus, this study use factor analysis to evaluate the relationship of parameters in childhood asthma.

**Method:** The descriptive study using factor analysis in asthmatic children aged less than 15 years old, who attended Thammasat University, the center of excellence for allergy, asthma and pulmonary diseases, Thailand. The participants or caregivers were interviewed by using the 52 items questionnaire divided in seven parts, including cooking smoke exposure, egg consumption, vegetable and fruit consumption loaded on factor 1. Having indoor furry pets on factor 2. Lighting incense stick in the house and having dolls on factor 3. Changing bed sheets and vacuuming the bedroom less than once per month on factor 4. Using dust mite-proof bed sheets and using trash can with lid in the house on factor 5. Having cockroach in the house and having depressed mood on factor 6. Using mosquito coils and having carpets on factor 7.

**Results:** The subject consists of 158 asthmatic children, 105 male and 53 female. The parameters are separated in 7 different factors. The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.548. There were 14 items related with asthma control in descending order as follows: changing bed sheets less than once per month (KMO=0.825), using dust mite-proof bed sheets (KMO=.80), using mosquito coils (KMO=0.78), furry pets (KMO=0.775). Indoor pets and lighting incense(KMO=0.738), having dolls (KMO=0.714), having cockroach in the house (KMO=0.712), vacuum the bedroom less than once per month (KMO=0.707), having depressed mood (KMO=0.705), cooking smoke (KMO=0.67), using trash can with lid in house (KMO=0.66), egg consumption (KMO=0.633), vegetable and fruit consumption (KMO=0.58).

**Conclusion:** The factors which have the major impact on asthma control are changing bed sheets less than once per month and using dust mite-proof bed sheets. This study is supporting non-pharmacological strategies but further studies are needed to create a more efficient asthmatic symptom checker.

## 0969 | Environmental factors associated with uncontrolled asthma

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**Background:** Asthma can be triggered by many factors such as infections, exercise, emotions, and environment. However, there has been no study that shows the difference of each environmental factor that affects asthma control. Thus, the study determine the environmental factors that effects asthma control among asthmatic patients in the Center of Excellence for Allergy, Asthma and Pulmonary Diseases (TU-CAAP), Thammasat University, Thailand.

**Method:** Patients aged Ages between 1 to 80 years old with confirmed asthma diagnosis were recruited from the TU-CAAP during May 2016 to November 2017. The patients were divided into 2 groups classified by controlled and uncontrolled conditions using the Global Initiative for Asthma (GINA).The participants were interviewed using an online questionnaire that composed of 3 domains and 28 items about environmental factors: smoke (active smoking, secondhand smoking, stove smoke during cooking, incense smoke, and mosquito repellent coil smoke), allergen (allergens from furred pets, dust exposure related to having carpets and dolls, use of dust mite covers, and frequency of bed sheets changing), and hygienic condition (trash and cockroaches control).

**Results:** The subjects consist of 231 patients, 129 males and 102 females. The mean age was 19.55 years old. There were 75 patients (32.47% %) in uncontrolled asthma group. The mean age and sex were not different between the controlled and uncontrolled group. The ACT score in the controlled group was significantly higher than the uncontrolled group ($P < 0.001$). The study showed that cigarette smoke is one of the significant factors that can trigger asthma exacerbation ($P < 0.001$) and mosquito repellent coil smoke is also significantly associated with asthma exacerbation ($P < 0.03$). However, the effects of exposure to other types of smoke including other domains are non-significant.

**Conclusion:** The result shows that cigarette smoke and mosquito repellent coil smoke are significantly associated with uncontrolled asthma. According to the results of this study, the health care provider should educate the patients and caregivers of asthmatic about the effects of stove smoke during cooking and mosquito repellent coil.

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## 0972 | Serum concentration of TNFSF14/LIGHT in asthma patients

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**Background:** Experimental studies have demonstrated that tumor necrosis factor family member 14 (TNFSF14/LIGHT) plays an important role in airway remodeling. There is little data available concerning in vivo regulation of TNFSF14/LIGHT expression in humans. The aim of this study was to evaluate serum concentration of TNFSF14/LIGHT in different subsets of asthmatic patients.

**Method:** The study was performed on 36 nonsmoking asthmatic patients (A), including 24 mild-moderate-severe asthmatics controlled on inhaled corticosteroids (AICS) and 12 asthmatics evaluated twice during asthma exacerbation (AEX) and during subsequent remission (AREM). In addition age and sex matched 24 nonsmoking healthy controls were included (HC). Serum TNFSF14/LIGHT concentration was evaluated using ELISA method. In asthmatic patients lung function tests, exhaled nitric oxide concentration (FeNO), serum total IgE concentration (t-IgE), allergen-specific IgE concentration (s-IgE) and peripheral blood eosinophilia were evaluated.

**Results:** The mean TNFSF14/LIGHT serum concentration in A (250 + /-134 pg/mL) was significantly greater than that in HC (72 + /-32 pg/mL; $P < 0.001$). Among all asthmatic patients studied the greatest TNFSF14/LIGHT serum concentration was demonstrated in AEX (357 + /-79 pg/mL), which was significantly greater than that in AICS (194 + /-123 pg/mL $P < 0.001$). During resolution of asthma exacerbation a significant decrease in serum TNFSF14/LIGHT concentration (118 + /-70 pg/mL; $P < 0.001$) was demonstrated. In AREM the mean serum TNFSF14/LIGHT concentration was comparable to that seen in AICS ($P = 0.06$) but was still significantly greater than in HC ($P < 0.01$). No significant correlation could be demonstrated between serum TNFSF14/LIGHT concentration and baseline lung function parameters, exhaled nitric oxide concentration, serum t-IgE or s-IgE concentration or peripheral blood eosinophilia.

**Conclusion:** Enhanced production of TNFSF14/LIGHT seen in asthmatic patients, which is further upregulated during asthma exacerbations may play an important role in asthma pathogenesis.

## 0973 | Implication of neutrophils in allergic airway inflammation

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**Background:** Neutrophils are known to be regulatory infiltrate airways and release inflammatory mediators triggering asthma development, however in allergic airway inflammation they are replaced by eosinophils. Here we investigate the mechanisms underlying the switching from neutrophil- to eosinophil-mediated response.

**Method:** Two models of Aspergillus fumigatus-induced allergic airway inflammation were used in the study: long terms (4 weeks) and short terms (2 weeks). Acute neutrophil-mediated inflammation that was induced by one high dose oropharyngeal *A. fumigatus* extract application inflammation served as a control. The numbers of bronchoalveolar lavage neutrophils and the levels of cytokines were measured by flow cytometry. The levels of lavage fluid and peripheral blood immunoglobulins were measured by ELISA.

**Results:** Comparison of both types of allergic and acute airway inflammations to intact mice revealed significant increase in total bronchoalveolar lavage cell numbers. In both types of allergic inflammations these cells were mainly represented by eosinophils, while acute inflammation was mediated primarily by neutrophils. The level of neutrophils was the highest in acute inflammation but in long term allergic airway inflammation it was higher than in short term model. The elevated levels of pro-allergic IL-4 as well as allergen-specific blood IgG and lavage fluid IgA were detected only in long term allergic airway inflammation. Mice with acute inflammation showed significantly elevated levels of TNF-alpha and IFN-gamma. In spite of bronchoalveolar lavage eosinophilia mice with short term allergic inflammation revealed no elevated level of IL-4 in lavage fluid and no peripheral blood IgG. The only detected feature of pro-allergic humoral response in mice with short term allergic airway inflammation was the increased level of local allergen-specific IgA.

**Conclusion:** Thus we have shown that allergic airway inflammation can be induced in the absence of adaptive immune response activation. Moreover our findings supported the evidence that upregulation of eosinophil-mediated response and downregulation of neutrophil-mediated inflammation in allergic inflammation development could be independent processes.

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## 0974 | CXCL12 neutraligand chalcone 4 inhibits migration of intraganglionic DC in an OVA-sensitized mouse model for allergic airway inflammation

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**Background:** Chalcone 4 is identified as an inhibitor of the interaction between CXCR4 or CXCR7 and their ligand CXCL12. Therefore it is called a neutraligand. The chemokine CXCL12, interacting with the CXC-receptor4 (CXCR4) can play a role in the progression and development of bronchial asthma. Asthma is defined as a chronic disease characterized by episodes of obstructive events which affects about 300 million people over the world. The aim of this study is to approach the mechanism of the anti-inflammatory effect of the CXCL12 neutraligand chalcone 4 and also to assess its impact on the migration of dendritic cells in a murine model of allergic airway inflammation.

**Method:** Chalcone 4 is administered intranasally to BALB/c ovalbumin (OVA) asthma mice and control groups as well.

**Results:** Our results indicate that the CXCL12 neutraligand chalcone 4 can modify the inflammatory reaction in an airway allergic hypereosinophilia model. Furthermore, found out that CXCL12 neutraligand chalcone 4 prevents DC migration to the airways and airway JNC ganglia during allergic airway inflammation.

**Conclusion:** The detection of the CXCR4-CXCL12 pathway and its role in the pathophysiological actions of asthma offers a promising target for allergic diseases treatments.

## 0976 | In vitro and in vivo analyses of the PTGDR involvement in allergic asthma and response to the treatment with corticosteroids

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**Background:** The prostaglandin D2 receptor (PTGDR) has been related to allergic asthma. We aim to verify the implication of PTGDR in allergic asthma using a cell and a murine model, and to analyze the effect of a corticosteroid treatment.

**Method:** Four groups of Balb/c mice were defined: control and asthmatic, with and without treatment. Asthmatic groups were sensitized with intraperitoneal ovalbumin (OVA) and provoked with intranasal OVA (0.1% OVA three times a week for 12 weeks). Treated groups received 0.2 mg/kg dexamethasone before each challenge. RNA was extracted from lung tissue and *PTGDR* expression was analyzed by qRT-PCR. Kruskal-Wallis test was performed through the SPSS 19.0 program. To deeper analyze the involved mechanism, A549 cells were transfected with *PTGDR* expression vectors for 12 hours. Cell culture cytokines levels were analysed using Bio-Plex System.

**Results:** In the murine model, OVA stimulation caused an increase in the expression of *PTGDR*, while corticosteroid treatment reduced it. Control groups, without and with dexamethasone, presented a median of 2.17 (RI=3.25) and 1.02 (RI=0.89), respectively. Asthmatic groups, without and with dexamethasone, presented a median of 84.45 (RI=77.96) and 36.08 (RI=26.32), respectively ($P$ = 0.013). Overexpression of *PTGDR* in pulmonary cells associated to a generalized increase of cytokine expression.

**Conclusion:** In a mouse model we confirmed the involvement of *PTGDR* in allergic asthma by the increase of its expression levels after ovalbumin sensitization. We also identified a reduction of *PTGDR* levels in response to dexamethasone treatment. The *in vitro* model suggests that *PTGDR* induces an inflammatory response, increasing the cytokines levels.

| pg/mL | Control | PTGDR expression |
|---|---|---|
| IP-10 | 2020.58 | 3035.51 |
| MIP-1b | 51.83 | 84.97 |
| IL12 | 46.1 | 65.26 |
| IL6 | 24.07 | 39.08 |
| IFN-γ | 11.68 | 34.6 |

## 0977 | The miR-23b-3p plays a negative regulatory role in inhibition of influenza A virus replication

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**Background:** Exacerbations of asthma are most frequently associated with infections of respiratory viruses or bacteria with concomitant deterioration of lung functions. The most common causative respiratory tract viruses are influenza virus and rhinovirus, and interestingly, asthmatic subjects are susceptible to these viral infections compared to healthy control subjects.

MicroRNA (miRNA) is a small non-coding RNA molecule, and their functions are known to modulate the activity of specific mRNA target by post-transcriptional regulation of target gene expression, and they act as key effector molecules between virus and host in the complicated interaction network. Therefore, studies on miRNA level could contribute to further understanding of the mechanisms of the interaction between virus and the host cells. The miR-23b can down regulate rhinovirus 1B infection via the low density lipoprotein receptor family for viral entry. Its effect on Influenza viruses has not unproven up to date. Aim of the present study was to check the inhibitory possibility of miR-23b on influenza virus replication using.

**Method:** Viral DNA and RNA including miRNA were extracted from 30 induced sputum of 16 asthma patients with acute exacerbation. National Center for Biotechnology Information were used to extract the influenza A virus (A/Korea/426/1968(H2N2)) sequences. Mature human miRNA sequences were obtained from the miRBase website. The analysis of miRNA predicted targets was determined using miRanda using default parameter. The miR-23b-3p expression level measured using real-time PCR on the sputum

**Results:** Respiratory viruses were identified in 14 samples. Parainfluenza virus 1/2/3 was detected frequently in 5 (16.67%), rhinovirus in 5 (16.67%), influenza A virus in 4 (13.33%). Sixteen patients (53.33%) were not infected with a respiratory virus. Quantitative PCR detection showed a significant decrease in miR-23b-3p expression in patient infected with Influenza A virus and rhinovirus than control subjects and parainfluenza-infected patients.

The miR-23b-3p may have target sites in the conservative sequence of influenza A virus genome, which was incompletely matched with influenza A virus genome and was predicted having the four target sites: one location in PB2 and three locations in HA.

**Conclusion:** The miR-23b-3p expression changes in patient infected with Influenza A virus and plays a negative regulatory role in inhibition of influenza A virus replication.

## 0979 | Immune imbalance between transcription factor t-bet/gata3 and allergic asthma

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**Background:** Exposure to allergens in asthmatic patients leads to over-activation of CD4 + T cells, excessive production of Th2 cytokines, and a significant decrease in Th1 cytokines, whereas antagonism of Th1 cytokines and Th2 cytokines eventually leads to an unbalanced Th1/Th2 ratio, leading to the selective expression of transcription factors that are predominantly Th2. Accordingly, responsive to allergic inflammation is a regulatory element that plays a key role in the directed differentiation of Th cells.

**Method:** To investigate the role of transcription factor T-bet/GATA3 in immune imbalance in patients with allergic asthma. T-bet/GATA3 mRNA expression in peripheral blood mononuclear cells (PBMCs) from 57 patients with allergic asthma and 30 healthy controls was detected by real-time fluorescence quantitative PCR. Th1 and Th2 cells were detected by flow cytometry.

**Results:** T-bet mRNA expression of peripheral blood lymphocytes in patients with allergic asthma was lower than that of the normal control group, and the expression level of GATA-3 mRNA was higher than that of the normal control group ($P < 0.05$). The Th1 percentage of peripheral blood lymphocyte subsets was lower than that of the normal control group ($P < 0.05$), the percentage of Th2 cells was significantly higher than that of the normal control group ($P < 0.05$), and the changes in T-bet/GATA3 expression and Th1/Th2 ratio was highly correlated.

**Conclusion:** Changes in the level of T-bet/GATA3 mRNA expression and the Th1/Th2 ratio were highly correlated in allergic asthma patients.

## 0980 | A new approach to understanding the effect of bmps protein in asthma in response to a specific and non-specific trigger

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**Background:** Asthma is a heterogenic disease of the respiratory tract, in which various cytokines, including TGF-ß, are responsible for inflammation and remodelling. Bone morphogenetic protein(BMP) is a member of the Transforming Growth Factor beta(TGF-β) superfamily. Both BMPs and TGFs have similar signal transduction mechanisms and common co-mediating protein. The role played by BMP is regulation of degradation and remodelling of the extracellular matrix, which is one of the elements involved in the reconstruction of the structure of the bronchi in severe asthma.

Our objectives were to assess the changes of BMP4 and BMP7 serum levels in the response to allergen and methacholine challenge tests and the correlation between BMP4 and BMP7 serum levels and FEV1 before and after allergen and methacholine challenge tests.

**Method:** Study group consisted of 59 patients with asthma and 48 healthy volunteers. Spirometry, skin prick tests, allergen and methacholine challenge tests were performed in compliance with EAACI, ERS and ATS guidelines. Personalized clinic surveys including ACT™ were performed. Venous blood was collected before and after 1 hour, and 24 hours afterwards the provocation to EDTA-KE-filled test tubes. Evaluation of BMP4 and BMP7 serum protein levels was performed using specific ELISA immunoassay kits according to the manufacturer's protocol.

**Results:** The increase in BMP4 and BMP7 serum level 24 hours after provocation test correlates significantly with the concentration methacholine during provocation time ($P < 0.05$).

BMP7 serum level before the provocation, 1 hour and 24 hours after provocation, correlates negatively with FEV1 change ($P < 0.05$). The median BMP7 level 24 hours after provocation was significantly lower in patients with negative methacholine challenge test compared to the control group ($P = 0.03$).

The median BMP4 level 24 hours after provocation was higher in patients with positive allergen provocation test than in patients with negative test results ($P = 0.03$).

**Conclusion:** The BMP7 serum level 24 hours after positive methacholine test is lower and correlates inversely with FEV1 change in every time point, which could indicate that serum level of BMP7 is a predictive factor of FEV1 change. The higher BMP7 serum level, the lower FEV1 change was observed. This could suggest the protective influence of BMP7 in patients with obstructive pulmonary disease, i.e. asthma. The higher BMP4 serum level 24 hours after positive allergen provocation test result shows that the BMP4 could be an indicator of the response to a specific trigger.

## 0981 | Thrombin lag time is increased in children with mild asthma

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**Background:** Inflammation and coagulation are closely linked events. Thrombin is the key enzyme in coagulation system. Besides its well-known functions in hemostasis, thrombin plays a role in inflammation. The aim of our study was to evaluate thrombin generation in children with mild asthma and demonstrate associations between thrombin levels and control of asthma.

**Method:** Forty-two children with mild asthma and forty-nine healthy children included in the study. Asthmatic children had no asthma exacerbation during the last 6 months. Patients (n = 27) who had mild persistent asthma, were using either inhaled steroid or montelukast. All patients performed spirometry. Thrombin levels were measured by thrombin generation test. Thrombin peak levels, endogenous thrombin potential, thrombin lag time, time to thrombin peak and thrombin tail time were recorded.

**Results:** Thrombin lag time was significantly longer in children with asthma (3.98 ± 1.2) compared to those in control group (3.29 ± 0.6) ($P < 0.01$). Children with asthma also had longer thrombin tail time compared to control group (19.5 ± 8.9 vs 16.7 ± 2.9, $P = 0.02$). Thrombin peak was inversely correlated with FEF 25-75 (-0.41, $P < 0.01$). Thrombin lag time was inversely correlated with FEF 25-75 (-0.39, $P < 0.01$). Thrombin generation parameters did not show difference according to asthma control treatment, asthma control scores and having atopy.

**Conclusion:** Coagulation/anticoagulation balance is disturbed in mild asthma but this disturbance may not be as strong as to increase thrombin levels. Factors increasing inflammation may cause an increase in lag time, and increase in inflammation and excessive fibrin deposition may contribute to airway narrowing.

## 0983 | IL-31 in patients with asthma and COPD

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**Background:** Cytokines represent key mediators in the onset and persistence of inflammatory process, in both asthma and COPD. IL-

31, which belongs to IL-6 family, it might act in a similar way with IL-6 at the beginning of the inflammatory process. Its role in atopic skin diseases has already been demonstrated, but there are conflicting results related to its role in respiratory allergic diseases.

The aim of the study was the evaluation of IL-31 plasmatic level in patients with asthma and COPD and the its correlation with clinical and lung function parameters.

**Method:** Fifty consecutive patients with bronchoobstructive diseases were included in the study. Thirty-two patients presented asthma and 18 patients had COPD. The evaluation included: number of exacerbation in the last year, disease's severity, spirometry. Plasmatic levels of IL-31 and IL-10 were determined in all patients.

**Results:** The mean age was higher in patients with COPD (43.4 ± 13.3 vs 64.94 ± 6.95 years, $P = 0.02$). COPD was most frequently observed in males (73.7% vs 26.3%, $P = 0.01$), while asthma was diagnosed frequently in females (81% vs 19%, $P = 0.01$). IL-31 was significantly higher in patients with asthma [median 1269 (338.36-2785.99)] pg/mL versus COPD [median 481.79 (178.74-1402.72)] pg/mL ($P = 0.015$). IL-31 was positively correlated with the number of exacerbation in the last year ($R = 0.456$, $P = 0.033$) and asthma severity ($R = 0.541$, $P = 0.009$) and negatively correlated with FEV1 ($R = -0.413$, $P = 0.05$) in patients with asthma. In patients with asthma, IL-31 negatively correlated with IL-10 plasmatic level ($R = -0.459$, $P = 0.032$). In patients with COPD the number of exacerbation was negatively correlated with vital capacity ($R = -0.523$, $P = 0.026$), but there were no correlations between IL-31 level and clinical, functional parameters or with plasmatic level of IL-10.

**Conclusion:** IL-31 had increased plasmatic levels in patients with asthma. IL-31 may play a role in the severity and regression of lung function in asthmatic patients, but not in COPD patients.

## 0987 | Aerobic exercise reduces asthma phenotype involving SOCS-JAK-STAT signaling in airway epithelium and peribronchial leukocytes

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**Background:** Asthma is a chronic airway inflammatory disease, which impairs physical capacity and quality of life. Aerobic training (AT) decreases airway inflammation and dyspnea in asthmatic patients, resulting in improved physical capacity and quality of life. However, the cellular and molecular mechanisms involved in the beneficial effects of AT for asthma are still not completely understood. Thus, we aimed to evaluate the participation of SOCS-JAK-STAT signaling in the effects of AT on airway inflammation, remodeling and hyperresponsiveness in a model of allergic airway inflammation.

**Method:** C57Bl/6 mice were divided into 4 groups: Control (Co), Exercise (Ex), HDM (HDM), and HDM+Exercise (HDM+ Ex). *Dermatophagoides pteronyssinus* [house duste mite (HDM), 100ug/mouse] were administered oro-tracheally on days 0, 7, 14, 21, 28, 35, 42 and 49. AT was performed in a treadmill during 4 weeks in moderate intensity, from day 24 until day 52.

**Results:** AT inhibited HDM-induced total cells ($P < 0.001$), eosinophils ($P < 0.01$), neutrophils ($P < 0.01$) and lymphocytes ($P < 0.01$) in bronchoalveolar lavage (BAL), and eosinophils ($P < 0.01$), neutrophils ($P < 0.01$) and lymphocytes ($P < 0.01$) in peribronchial space. AT also reduced BAL levels of IL-4 ($P < 0.001$), IL-5 ($P < 0.001$), IL-13 ($P < 0.001$), CXCL1 ($P < 0.01$), IL-17 ($P < 0.01$), IL-23 ($P < 0.05$), IL-33 ($P < 0.05$), while increased IL-10 ($P < 0.05$). Airway collagen fibers ($P < 0.01$), elastic fibers $P < 0.01$) and mucin ($P < 0.01$) were also reduced by AT. AT also inhibited HDM-induced airway hyperresponsiveness (AHR) to methacholine 6.25 mg/mL ($P < 0.01$), 12.5 mg/mL ($P < 0.01$), 25 mg/mL ($P < 0.01$) and 50 mg/mL ($P < 0.01$). Mechanistically, AT reduced the expression of STAT6 ($P < 0.05$), STAT3 ($P < 0.001$), STAT5 ($P < 0.01$) and JAK2 ($P < 0.001$), similarly by peribronchial leukocytes and by airway epithelial cells. SOCS1 expression ($P < 0.001$) was upregulated in leukocytes and in airway epithelial cells, SOCS2 ($P < 0.01$) was upregulated in leukocytes and SOCS3 down-regulated in leukocytes ($P < 0.05$) and in airway epithelial cells ($P < 0.001$).

**Conclusion:** AT reduces asthma phenotype which is followed by positive modulation of SOCS-JAK-STAT signaling in peribronchial leukocytes and in airway epithelial cells.

## 0988 | Effects of a training session on the skin barrier function in swimming vs football elite athletes

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**Background:** The benefits of swimming on asthma have been extensively accessed. Swimming pools contain chlorine and other

potentially irritating chemicals that may have a cutaneous drying side effect. This study aimed to evaluate if skin barrier function, as measured by transepidermal water loss (TEWL), is affected by a training session in swimmers compared with football players.

**Method:** Elite swimmers enrolled in the SWAN trial—Swimming Pool Environment Impact on the Human Respiratory Health (ClinicalTrials.gov Identifier: NCT03017976) and football players were invited to participate. Due to the lack of prior information no sample size calculation was possible and all athletes that provided informed consent were included in the analysis (n = 58, 29 females, aged 12 to 21 years). TEWL was measured using the Tewameter® TM 300 before, immediately after, and 30 minutes after a 2 hours training session. The probe was held on the dorsum of hand, the volar forearm and the antecubital flexure for 60 s. The average of two consecutive measurements was recorded. Non-parametric statistic was used were appropriate. Ethical approval was obtained from the University Clinical Research Ethics Committee and informed consent provided.

**Results:** Mann–Whitney U Test showed significantly higher baseline median TEWL level on football players hand's dorsum compared with swimmers, median (P25-P75) respectively 17.1 (14.7 to 21.7) and 13.7 (11.9 to 16.2); $P = .001$. Friedman test revealed a significant effect of swimming on TEWL on the hand's dorsum, volar forearm and antecubital flexure ($P < .001$) while football training affected only the hand's dorsum ($P = .008$). Differences in changes after swimming and football training were significant only for TEWL in volar forearm ($P = .028$).

**Conclusion:** In conclusion, our exploratory findings do not provide support for a specific deleterious effect of swimming, compared with football training, on the training induced changes in TEWL.

## 0989 | Increased sputum uric acid levels and serum CC16 levels reveal early epithelial damage in young high-school elite athletes

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**Background:** Exercise-induced bronchoconstriction (EIB) is defined as transient, reversible airway narrowing occurring during or after exercise, is common among elite athletes and associated with epithelial damage. However, little is known about the existence of EIB in young athletes. The goal of this study is to investigate the presence and to evaluate potential (bio)markers of EIB in young high-school elite athletes in different sport disciplines versus age-matched control subjects.

**Method:** High-school selected elite athletes (12-13 years) from different sport disciplines: basketball (n = 26), football (n = 44) and swimming (n = 47) performing at least 12 hours of sport per week (median=13 h) and 17 control subjects (performing less than 6 hours of sport per week) were recruited. The eucapnic voluntary hyperventilation (EVH) test was performed according to ATS guidelines and adapted for this age group. Lung function was measured before, immediately after and 5, 10, 15 minutes after the EVH test. The test was considered positive if a maximal fall in FEV1 of 10% was measured on at least one time point and exhaustion was excluded. A blood sample was obtained at baseline. Sputum induction and skin prick test for the most common allergens were performed after the EVH test.

**Results:** Fifteen swimmers had a positive EVH test (33.3%), which is higher than in basketball players (18.2%), football players (17.95%) and controls (17.65%). 40.4% of the swimmers were atopic which is also higher than in basketball players (23.1%), football players (31.8%) and controls (23.5%). Serum Clara cell secretory protein (CC16) levels are significantly higher in swimmers (7.6 ± 2.5 ng/mL) compared to indoor athletes (5.1 ± 2.2 ng/mL) and controls (5.2 ± 1.2 ng/mL). A significant positive correlation was found between the magnitude of maximal fall in FEV1 and CC16 levels ($r = –0.194$; $P = 0.026$). A significant increase in sputum uric acid levels is seen in swimmers (89.1-95.3-106.2) compared to controls (61.4-76.3-94.7).

**Conclusion:** Young elite swimmers have a higher prevalence of EIB compared to basketball and football players. Atopy and/or chlorine is a risk factor for the development of EIB in young elite athletes. CC16 levels and sputum uric acid levels are increased in athletes compared to control subjects suggesting the presence of epithelial damage already at young age. This is especially observed in young elite swimmers, pointing to a probable role of exposure to chlorine-by-products in combination with intensive exercise.

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## 0990 | Relevance of free-run screening test (FRAST) for diagnosis of exercise-induced bronchospasm with and without asthma

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**Background:** Free-run screening test (FRAST) consists in a sequential evaluation of FEV1 after an outdoor run for 6 minutes. During the exercise challenge, the individual should reach at least 90% of his maximal heart rate. The test is positive if FEV1 is reduced (ΔFEV1%) by more than 10% after the challenge. This study aims to disclosure the relevance of FRAST in diagnosis of exercise-induced bronchoconstriction in patients with and without previous diagnosis of asthma.

**Method:** Data from subjects referred for FRAST by Immunoallergology Department, from January 2014 to December 2017, were retrospectively collected. Demographic characteristics, previous diagnosis of asthma, presence of respiratory symptoms exclusively with exercise (RSEE), BMI, sport practice and smoke cigarette exposition were evaluated.

**Results:** Data from 237 subjects (134 females, 56.5%) were analyzed. FRAST was positive in 97 (40.9%) patients (55 females, median age of 14 years (IQR 11-18)). In this group, 55 (56.7%) had a previous diagnosis of asthma, 27 (27.8%) practiced federated sports, 18 (18.6%) had smoke cigarette exposition and 3 (3.1%) had a BMI >30 kg/m$^2$. 82.5% of patients showed a ΔFEV1% >10% in the first 5 minutes after finishing the challenge. Median FEV1 reduction was 13.4% (IQR 11.5-16.85) and 390 mL (IQR 307.5-495).

FRAST was more frequently positive in patients with previous diagnosis of asthma ($P < 0.01$). There were no differences related to FRAST positivity and smoke cigarette exposition.

In patients with a previous diagnosis of asthma (n = 93), 55 (59.1%) had a positive FRAST and 52 (56%) performed spirometry with bronchodilator test (SBT). In the 32 patients with negative SBT, 17 (53%) had positive FRAST.

In patients with RSEE (n = 144), 42 (29.2%) had a positive FRAST, and 65 (45%) performed SBT. SBT was negative in 61 patients, and in this group 17 (28%) patients had a positive FRAST.

**Conclusion:** FRAST is an important tool to diagnose exercise-induced bronchospasm without asthma ($EIB_{wa}$), as well as to diagnose asthma. In our study, FRAST was fundamental to access $EIB_{wa}$ in 28% of patients with RSEE, and confirmed asthma diagnosis in 53% of cases with previous asthma diagnosis and negative SBT.

## 0991 | Free-run asthma screening test (FRAST), feno and atopy in patients with exercise-induced respiratory symptoms

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**Background:** The association of exercise-induced respiratory symptoms (EIRS) with atopy and fractional exhaled nitric oxide (FENO) is under investigation. The free-run asthma screening test (FRAST) is a diagnostic tool to access patients with EIRS and consists in a sequential evaluation of FEV1 after an outdoor run for 6 minutes. The test is positive if FEV1 is reduced (ΔFEV1%) by more than 10% after the challenge. This study aims to evaluate the association between FRAST, atopy and FENO in patients with EIRS.

**Method:** Data from subjects referred for FRAST by Immunoallergology Department, from January 2014 to December 2017, were retrospectively collected. Demographic characteristics, previous diagnosis of asthma, presence of respiratory symptoms exclusively with exercise (RSEE), atopy and FENO were evaluated.

**Results:** Data from 237 subjects (134 females, 56.5%) were analyzed. FRAST was positive in 97 (40.9%) patients (55 females, median age of 14 years (IQR 11-18)); in this group, 55 (56.7%) had a previous diagnosis of asthma, 74 (76.3%) were atopic and the median FENO value was 34 ppb (IQR 16.5-49.25).

Patients with positive FRAST had higher FENO ($P = 0.001$). Atopic patients in the entire sample and in the FRAST positive group had significantly higher FENO values ($P < 0.001$, $P < 0.001$).

There was no difference in the prevalence of atopy between patients with positive and negative FRAST.

Patients older than 9 years-old presented higher ΔFEV1% compared to younger patients ($P = 0.04$).

Higher levels of FENO were observed in patients with positive FRAST ($P = 0.032$, $P = 0.045$), both in patients with and without previous diagnosis of asthma.

A positive correlation was observed between FENO levels and ΔFEV1% in the whole sample ($r = 027$, $P = 0.009$); when these data were analyzed considering a previous diagnosis of asthma, only patients with this condition showed a positive correlation of FENO and ΔFEV1% ($r = 0.29$, $P = 0.031$).

**Conclusion:** Our results evidenced that higher FENO was associated with atopy and a positive FRAST, both in patients with and without previous diagnosis of asthma. Higher FENO seems to correlate with ΔFEV1% in patients with previous diagnosis of asthma.

## 0992 | Managements of specific immunotherapy in professional footballer: Case report

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**Background:** Specific immunotherapy is the casual treatment for allergic rhinitis.

A 28 year old professional footballer suffer from severe allergic rhinitis since two years. During May, June and July his level of playing, concentration and durability decreased about 20%. Patient was complaining of runny nose, nasal blockage, each eyes, sneezing, tearing.

**Method:** We did skin prick tests -which showed greatest allergy to grass pollen. We confirmed the allergy by specific IgE and nasal provocation tests. Spirometry was done-FEV1 116%. The patient was qualified to undergo specific immunotherapy. However, because of his profession, it was hard to find a day without trainings to get the vaccine. After long discussion, patient decided to start specific immunotherapy- SCIT.

**Results:** The patient start the immunotherapy. He was attuning very irregularly, because of matches, injuries, trips, trainings, and lack of time. Several times we had to call the patient to remind him about the immunotherapy. After one year of SCIT the patient felt big improvement. During grass pollen season he suffered from mild allergic symptoms, and just for few days. After next year of immunotherapy, the patient had no symptoms of allergic rhinitis during the grass pollen season. However, it was the reason for him, to stop SIT, before 3rd year of immunotherapy.

**Conclusion:** Such a treatment—specific immunotherapy-is a burdensome method for both, for professional athletes and doctors. Such a patients need to be on special observation, and cooperation with trainers must be obtained, if we want to see results. To improve compliance we have to keep in touch with patients, to remind them about next visit.

## 0993 | Comparison of bronchial response to mite and cat allergen in asthmatics in ALYATEC Environmental Exposure Chamber (EEC)

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**Background:** Late allergic response (LAR) is a good asthma model. It has been shown, in individual challenge tests that mite allergen induces more frequently late allergic responses (LAR) than cat allergen. The aim of this study is to compare the frequency of LAR in asthmatic subjects allergic to mite with asthmatic subjects allergic to cat.

**Method:** 24 asthmatic subjects allergic to mite were compared to 21 subjects allergic to cat (GINA 1 or 2). The subjects had prick tests≥5 mm compared to the negative controls and specific IgE ≥ 0.70 KU/L. The dose selected for the mite and cat allergen was the airborne allergen concentration inducing the most frequently early asthmatic response (EAR) (a 20% drop in FEV1) and LAR (a 15% drop in FEV1).

**Results:** The frequency of LAR with mite allergens was 66.6% and 20% with cat allergens ($P$ = 0.007). The frequency of EAR for mites was 78.2%; of 91.3% for EAR or LAR, and 50% for EAR and LAR. In contrast, with cat allergens, 55% of patients had an EAR, 60% had EAR or LAR and 25% had an EAR and LAR. No significant differences was observed between cat and mite allergen regarding the severity and the time necessary to obtain an EAR and LAR. No significant differences was observed between cat and mite allergen regarding the severity and the time necessary to obtain an EAR and LAR.

**Conclusion:** The frequency of LAR in asthmatic subjects allergic to dust mite exposed in ALYATEC® EEC was higher than in asthmatics sensitized to cats. Our results confirmed previous results with individual bronchial challenge. Therefore, it appears that the mite model is more interesting in the study of asthma.

## 0994 | Clinical validation of Environmental Exposure Chamber in Strasbourg (ALYATEC®) in asthmatic patients allergic to cat allergens

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**Background:** As recommended by the Task Force on Environmental Exposure Chamber (EEC), allergenic and non-allergenic exposure must be better controlled in EEC. It is the aim of ALYATEC's EEC.

The aim of the study is to validate ALYATEC's EEC by determining the concentration of Fel d1 inducing 50% of early asthmatic response (EAR) and/or late phase asthmatic response (LAR) in subjects sensitized to cat.

**Method:** It was a randomized, double blind, cross-over study including group A:20 asthmatic subjects allergic to cat and group B:10 asthmatic subjects allergic to another allergen. All subjects were first exposed to placebo. Group A was exposed to 2 Fel d1 concentrations. The number and size of particles were recorded online during the exposure. Group B was exposed to the concentration of Fel d1 which fulfills the objective of the study.

**Results:** The mean age of subjects was 29 years (±8). For the 2 concentrations of Fel d1, we obtained more than 50% EAR and/or LAR. The mean time necessary to obtain an EAR was: 59.7 ± 8 minutes and 138.6 ± 90 minutes for the LAR. The mean fall in FEV1 during EAR and LAR was −29.22% and −17.64% respectively. We

didn't observe any severe reaction. No subjects in group B experienced any symptoms during exposure.

**Conclusion:** We have validated ALYATEC's EEC in asthmatic subjects allergic to cat allergens. We also demonstrated its specificity. That is of interest for future clinical studies.

## 0995 | What is the best way to diagnose asthma in patients without reversibility?

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**Background:** The best test and strategy for diagnosing asthma especially in those patients with negative bronchodilator reversibility tests still remains unclear. In this study we aimed to investigate the diagnostic yield of peak expiratory flow (PEF) variability for the patients with symptoms suggesting asthma but negative bronchodilator reversibility tests.

**Method:** Subjects referred to our outpatient clinic with suspicion of asthma were enrolled in this study. Demographics and referral symptoms were recorded, asthma control test (ACT) scores and health related quality-of-life scores (AQLQ, SF36) were calculated. Monitoring of PEF variability during 2-weeks and bronchial challenge test with methacholine (BPT) were analyzed. Asthma was diagnosed by having PEF variability ≥20% and/or positive BPT.

**Results:** Thirty out of 50 enrolled patients were diagnosed as having asthma. When we compare asthmatic patients with nonspecific respiratory symptomatic subjects there were statistically-significant differences regarding to wheezing ($P$ = 0.020), activity limitation ($P$ = 0.058), total symptom score ($P$ = 0.028) and basal $FEF_{25-75}$ ($P$ = 0.050) in the favor of asthma cases. Multiple logistic regression analysis revealed that lower basal $FEF_{25-75}$ was an independent predictive factor of asthma diagnosis ($P$ = 0.05). When the BPT positivity was assessed as gold standard for the diagnosis of asthma, the sensitivity and specificity of PEF variability for different cut-off-values (≥20%, >15% and >%10) were 61.5-83.3%, 88.5-62.5% ve 100-16.7%, respectively.

**Conclusion:** $FEF_{25-75}$ is an important diagnostic parameter for asthma. Although current guidelines recommend PEF variability of 10% for the diagnosis of asthma in general, this cut off level may not be appropriate for this defined group of subjects. Our results suggest to use a cutoff level of >15% while excluding asthma and ≥20% while confirming the diagnosis of asthma for patients with asthma suspicion but without shown reversibility.

## 0996 | Assessment of pulmonary function and use of medications in obese asthmatic patients before and after bariatric surgery

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**Background:** In recent years obesity has been considered as a factor that contributes to the development of asthma, increases exacerbations and leads to poor control of it due to resistance to drugs to control this pathology. It is known that obesity produces chronic systemic inflammation; one of the markers that are affected is the levels of C-reactive protein (CRP), which are increased.

**Objective:** Evaluate, lung function, the use of medications to control asthma and systemic inflammation, after bariatric surgery.

**Method:** A prospective longitudinal correlation study in 46 obese asthmatic and non-asthmatic patients aged 23 to 71 years attending the Bariatric Surgery Center and the Department of Allergy and Immunology. Classification of the severity of asthma according to the GINA criteria, body mass index (BMI), C-reactive protein (CRP). They were performed before surgery, 6 months later and at 12 months.

Statistical analysis through Infostat, ANOVA, Kruskal Wallis, Chi square, Student Test.

**Results:** 15 obese asthmatic patients with surgery, 15 non-asthmatic obese patients with surgery, 16 obese asthmatic patients without surgery.

A significant difference was found between the severity of obesity and forced expiratory volume in patients with asthma and without asthma of 1 second (FEV1) before surgery with an average of 87.9% at the beginning of the study and 105.5% at 12 months ($P$:0.0004). In the non-operated group, FEV 1 at the beginning was 69% and 83.04% at 12 months ($P$: 0.0018).

The CRP, before surgery in all operated patients had CRP: 9, at 12 months after surgery they became negative, CRP: 0 ($P$: 0.004).

In obese asthmatics with surgery at the beginning, 100% used medication, and at 12 months only 20% In obese asthmatic patients without surgery, 93.75% used the medication at the beginning, at 12 months 62.5% ($P$:0.0006).

**Conclusion:** Bariatric surgery achieved a great improvement in asthma control in asthmatic patients with surgery; decreased use of medications and even without using them in most cases, also achieved improvement of systemic inflammation with negative CRP in all patients post surgery.

## 0997 | Impact of cough provocation test on clinical variables in patients with asthmatics

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**Background:** Cough is a common and important respiratory symptom. Inhaled capsaicin (8-methyl-N-vanillyl-6-nonenamide) has long been used to induce cough in a safe and dose-dependent manner, and the degree of induced cough reflects the reactivity of sensory C-fibres in the respiratory mucosa.

**Method:** 385 patients with chronic cough [capsaicin provocation test (+, n = 152)] vs. [capsaicin provocation test (–, n = 233)] who has done with capsaicin provocation test recruited and evaluated by asthma diagnosis and clinical variables.

**Results:** Capsaicin positivity was more prevalent in patient with asthma diagnosis than in patients without asthma diagnosis (128/304 vs. 24/81, $P = 0.042$). Capsaicin positivity was more prevalent in female patients than in male patients (122/271 = 45% vs. 30/114 = 26.3%, $P = 0.001$). Capsaicin amount for provocation correlated with smoke amount. Capsaicin positivity was more prevalent in non-smoker patients than in smoker patients. Capsaicin amount for provocation negatively correlated with methacholine PC20. Capsaicin amount for provocation correlated with BMI. Capsaicin amount for provocation negatively correlated with FEV/FVC.

**Conclusion:** Capsaicin test for asthma diagnosis should be considered for variable clinical factors.

## 0998 | A novel asthma monitoring device methacholine challenge study

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**Background:** Biomarkers of lung function in asthma rely heavily on peak flow and spirometry measurements which are forced manoeuvres and relatively difficult to perform. A Bluetooth and Cloud enabled asthma home monitoring device is being developed which uses a deep, steady breathing technique to produce an Exhaled Breath Condensate ($ECB_1$) breath profile. The breath profile is based on changes in the humidity of expired air as a result of airflow obstruction. The primary study objective was to determine if the device could effectively measure airflow obstruction induced during a methacholine challenge. The secondary objectives were to determine the ease of use, sensitivity and specificity and safety of the device.

**Method:** 20 patients with asthma aged 18 to 80 and a predetermined positive methacholine Pc20 were recruited and underwent a single challenge to cause bronchoconstriction of ~20% comparing the outcome of the device with spirometry. The subjects were monitored at baseline, after a ~20% fall in $FEV_1$ and after bronchodilation back to baseline.

The study protocol allowed for an interim analysis of the initial 8 subjects at which point the sensor was calibrated to optimise sensitivity. A further 12 subjects were studied using the optimised sensor.

**Results:** All 20 subjects successfully completed the study. The device was found to be straightforward to use by both operator and subject with no concerns regarding safety. The initial sensitivity of the device was found to be suboptimal in the first eight patients to reliably detect changes in lung function.

After adjustment to the device the tests results of the remaining 12 subjects were analysed. 66.6% of subjects were female. The mean age of all subjects was 45.8 years. An average baseline $FEV_1$ value of 2.575 (S.D. 0.881) was observed.

Changes in lung function were detected in 100% of subjects. A baseline value, drop in lung function and reversal were measured in 66% of subjects. The mean percentage drop observed in 66% of subjects using the investigational device was 13.04 %. The mean percentage increase observed using the investigational from drop to reversal was 25.36 %.

**Conclusion:** The device (using $EBC_1$) was able to detect changes in lung function tracked using $FEV_1$. This provided proof of concept that the device could potentially be used to monitor lung function more effectively in the home than peak flow and supports further development to optimise the device and demonstrate functionality in clinical asthma.

## 0999 | Non-specific bronchial hyperreactivity measured by methacholine in the diagnosis of asthma in children

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**Background:** Methacholine challenge test (MCT) is the most widely used method of quantification of bronchial hyperreactivity (BHR), one of the main features of asthma. It is performed in patients with asthma symptoms, normal spirometry and negative bronchodilator response (*criteria Guide GEMA 4.2*), and it is considered positive if there is a decrease of 20% in $FEV_1$ at a concentration of methacholine ($PC_{20}$) <8 mg/mL (*criteria ATS*). We present a descriptive study of MCT performed in children under 18 during 2016 and 2017 at the University Hospital Fundación Jiménez Díaz

(*Madrid, Spain*), aiming to calculate the incidence of positive results and their relation with the symptoms and risk factors for asthma.

**Method:** Ninety four patients under 18 years of age seen in the Allergy Department due to common asthma symptoms (wheezing, dyspnea, cough, chest tightness) with normal spirometry and negative bronchodilator response, underwent MCT during 2016 and 2017. The variables studied were: sex, age, body mass index (BMI), asthma symptoms, exercise symptoms, rhinoconjunctivitis, family history of atopy, sensitization to respiratory allergens, spirometric data and fractional exhaled nitric oxide (FeNO).

**Results:** Of the total sample, half were women (51.06%) and the other half were males (48.94%). Mean age was 11.8 years. BMI was normal in most of them (with an average of 19.55 Kg/m$^2$). The most common symptom among the patients with positive MCT was cough (79.8%), followed by dyspnea (62.76%), wheezing (34%) and chest tightness (11.7%). 43.6% had symptoms of asthma with exercise and 70.2% had rhinoconjunctivitis. 37.23% had a family history of atopy. 74.4% were sensitized to aeroallergens, mainly to pollens (grass and olive tree). 75.5% of the MCT′s were positives, with a mean $PC_{20}$ of 1.89 mg/mL. 62.7% had a moderate-severe result ($PC_{20}$ ≤4 mg/mL), 7.4% mild ($PC_{20}$ 4-6 mg/mL) and 5.3% bordering ($PC_{20}$ 6-8 mg/mL). The mean FeNO was 19.62 ppb.

**Conclusion:** In our series, the completion of a test of HRB was decisive to confirm the diagnosis of asthma in most patients of a pediatric population with symptoms of suspicion (cough, mainly), normal spirometry and negative bronchodilator response (with normal FeNO in most of them). Therefore, we consider it important to include in the routine clinical practice HRB tests in the pediatric population with suggestive symptoms of asthma, despite normal functional and/or inflammation tests.

## 1000 | Cut-points of the ′Control of allergic rhinitis and asthma test′ (CARAT) asthma subscale based on an international survey

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**Background:** Control of Allergic Rhinitis and Asthma Test (CARAT) was designed and validated to measure control of both asthma and Allergic Rhinitis (AR). CARAT is the only control of asthma tool that reflects control of AR. However, cut-points of the asthma and AR subscale of CARAT are unknown. From a clinicians point of view the purpose of the upper cut-point (between controlled vs partly/uncontrolled) is to exclude uncontrolled disease and the purpose of the lower cut-point (between controlled/partly controlled vs uncontrolled) is to confirm uncontrolled disease. This is similar in structure to the Asthma Control Questionnaire (ACQ). The aim of the current study is identifying the cut-points of the CARAT asthma subscale to differentiate between controlled, partly controlled and uncontrolled asthma using the ACQ.

**Method:** Asthma patients from the Netherlands, Greece and Portugal completed CARAT together with the ACQ. Decisions were based on NPV≥.850 for the upper cut-point and on PPV≥.850 for the lower cut-point, supported by: Area Under the Curve (AUC), sensitivity (SS), specificity (SP), percentage correctly classified patients (PCCP).

**Results:** Data from 653 asthma patients (49.3% with rhinitis; ACQ: 46.7% well controlled, 17.3% partly controlled, 17.5% uncontrolled; 35.4% men, mean age 51.6 yrs), suggested an upper cut-point of 14.5 (SS 83%, SP 79%, AUC 0.891, PCCP 80.8%, PPV 76%, NPV 86%) and a lower cut-point of 8.5 (SS 46%, SP 99%, AUC 0.93, PCCP 87%, PPV 88%, NPV 87%). The characteristics of the AR group did not meet statistical demands to result in a AR cut-point.

**Conclusion:** We defined cut-points of 14.5 (to exclude uncontrolled disease) and 8.5 (to confirm uncontrolled disease) for the CARAT asthma scale. Further analysis should reveal cut-points for the AR subscale.

## 1001 | The use and willingness of asthma patients toward mobile phone functionalities in support of self-management

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**Background:** Information technology-based interventions such as mobile health have potential to enhance self-management in Patients with chronic illness through the provision of supports (e.g., information, education, and reminders). An important factor in successful implementation of mobile health interventions is the positive attitude of users, especially patients, towards these interventions. The aim of this study was to assess the current use of mobile functionalities (Phone call, SMS, Application, Internet, Email and Social networking) in asthma patients and their willingness to use these functionalities to receive self-management services.

**Method:** This descriptive-cross sectional study was conducted in 2017. The study population included 145 patients with asthma in Asthma and Allergy Clinic (The only center providing services to

patients with asthma) in Kashan, Iran. The data collection tool was a questionnaire with 38 questions, designed to gather information on demographic asthma patients, the current use of mobile functionalities, and the willingness to use these functionalities to receive self-management services, which was distributed among patients with informed consent. The collected data were analyzed by descriptive statistics method using SPSS software.

**Results:** The most use of patients from mobile phone functionalities was to receive information about asthma symptoms and allergens and irritants via mobile internet (42.1%). Patients were most likely to use social networking (31.7%) in comparison with other mobile phone functionalities, to receive reminders about appointments and medication. The respondents were most likely to use social networks through mobile phone functionalities, to receive asthma self-management information (53.1%), to communicate with other patients (55.9%), to receive reminders about medication use, and to perform a peak flow meter test (52.4%) and to get an alert when the asthma is not controlled (53.1%).

**Conclusion:** The findings show that asthma patients are currently using the internet search for educational information and they have a tendency to use social networks to receive asthma-related services. Patients believe that mobile health is an appropriate intervention for providing educational information, reminders, and alerts and communication with other patients.

## 1002 | Concordance between the determination of asthma control through the GINA 2015 guidelines and the ACT questionnaire—Results of the EFIMERA study

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**Background:** The exacerbation of asthma, progressive worsening of acute episodes, is one of the most frequent attending reasons at hospital emergency unit [1]. Several factors causing poor control of asthma, such as inadequate therapy, have been described. In the present study, estimations of asthma severity by researchers were assessed by comparing the concordance between the assessment of asthma control through the GINA 2015 guidelines and the ACT questionnaire

**Method:** Cross-sectional observational study on the evaluation of factors related to treatment that influence the poor control of asthma was assessed through the GINA guidelines and the ACT questionnaire. Patients referred to a pneumologist or allergist by a primary care for the first time were evaluated. Two variables were collected for the assessment of asthma control: one derived from the GINA 2015 guidelines and another derived from the ACT questionnaire. Regarding the GINA assessment, researchers' evaluations guidelines were compared with the scoring calculated from the variables registered in the CRD. Both measures were compared in terms of sensitivity-specificity to determine their ability to classify patients.

**Results:** The patients included in this study (n = 1682) had a mean age of 45 ± 17 years, with a 64% of women and an average disease evolution of 14.9 ± 14.1. The control of asthma according to "GINA researcher" and "GINA calculated score had a concordance Kappa index of 0.87 and a rho correlation coefficient of 0.92 and $r^2$ = 0.846. The control of asthma according to GINA researcher compared to the of the ACT questionnaire score (grouped into 3 categories:<= 15; 16-19; 20 = <) showed a Kappa=0.458 and rho=0.688; $r^2$ = 0.478. The control of asthma according to GINA score compared to the ACT questionnaire score presented a Kappa=0.458 Rho=0.709; $r^2$ = 0.503.

**Conclusion:** A number of specialists did not correctly apply the scoring algorithm of the 2015 GINA Guidelines, tending to underestimate the severity of their patients' asthma. In comparison with the assessment using GINA guidelines (both, GINA researcher and GINA calculated score), the ACT questionnaire, measuring the severity of the asthma, underestimated the poor control of asthma.

## 1003 | Follow-up interviews to assess patient-centred outcomes in the Salford Lung Study in Asthma (SLS Asthma)

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**Background:** SLS Asthma, a 12-month, open-label, clinical trial (UK primary care), assessed effectiveness/safety of initiating fluticasone furoate/vilanterol (FF/VI) vs continuing usual care (UC) for asthma. In this analysis, we aimed to provide additional descriptive data on treatment outcomes not measured in SLS Asthma, as perceived by participants (pts).

**Method:** 400 pts were sampled from SLS Asthma and interviewed post-SLS exit. Pts answered study-specific, closed-ended questions on symptoms, impact on daily life, triggers, self-management/disease awareness, asthma attacks, treatment, quality of life (QoL) and background/lifestyle. A subset (n = 40) completed 17 additional open-ended questions. Interview data were analysed descriptively.

**Results:** Pts were reasonably representative of those in SLS Asthma (at SLS baseline: 43.8% male; mean age 48.4 yrs; mean Asthma Control Test [ACT] score 16.5). The most frequently reported symptoms during SLS Asthma for these pts were cough/breathlessness, followed by wheeze, phlegm and chest tightness; breathlessness and wheeze were perceived as the biggest impactors

| Pts, n (%) | Cough | Breathlessness | Wheeze | Phlegm/ mucus | Chest tightness | Tiredness/ fatigue | Sleep Problems | Chest pain |
|---|---|---|---|---|---|---|---|---|
| Experienced symptom | 304 | 295 | 268 | 250 | 220 | 174 | 159 | 92 |
| Improved | 122 (40.1) | 141 (47.8) | 122 (45.5) | 89 (35.6) | 96 (43.6) | 46 (26.4) | 40 (25.2) | 36 (39.1) |
| No change | 152 (50.0) | 125 (42.4) | 125 (46.6) | 121 (48.4) | 100 (45.5) | 100 (57.5) | 94 (59.1) | 44 (47.8) |
| Worsened | 30 (9.9) | 29 (9.8) | 21 (7.8) | 40 (16.0) | 24 (10.9) | 28 (16.1) | 25 (15.7) | 12 (13.0) |

on pts' lives. The aspects of daily life most impacted by asthma were reported as walking at a hurried pace, strenuous physical activity, and asthma-related frustration. Since SLS began, 50% of pts in this subset reported improvements in overall asthma (44% no change; 6% worsening). Perceived changes in symptoms are shown (Table). Most pts (66.0%) reported avoiding places with dust, smoke or fumes. Most pts (57.5%) perceived no change in overall QoL; 36.3% reported improvement.

Being an ACT responder during SLS (total ACT score ≥20 or ≥3 change at end of SLS) was associated with reported improvements in overall asthma symptoms, lower impact of asthma on QoL, and higher perceived confidence/control in managing asthma. More pts (65.8%) in the FF/VI arm reported an overall improvement in asthma vs UC (34.3%); the most evident differences between treatment groups were for breathlessness, wheezing and chest tightness. Improvements in confidence/control in managing asthma were reported by 53.8%/49.3% of pts (FF/VI) vs 31.3%/25.3% (UC).

**Conclusion:** Breathlessness and wheezing were key symptoms in SLS Asthma and had the biggest impact on pts' daily lives. This patient-centred study enriches the findings of SLS Asthma.

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## 1004 | Asthma and COPD treatment adherence and breach using TAI questionnaire

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**Background:** Adherence is defined as medication (inhalator) intake following the dosage and schedule prescribed. Adherence mistakes are a public healthy problem according to the big morbi-mortality presented in patients with an incorrect intake. Our aim is to evaluate the adherence level and fulfillment in patients with asthma or COPD using TAI (Inhalators Adherence Test) questionnaire.

**Method:** Patients with a diagnosis of persistent asthma or COPD were selected. We used to size adherence and breach type the TAI questionnaire. Adherence is defined as good when patient's test reaches 50 points, medium (46-49 points) and bad (less than 45 points). Breach type is defined as erratic when points between questions 1 to 5 are less than 25, deliberate when questions 6 to 10 are less than 25, and unconscious when questions 11 and 12 are less than 4 points.

A correct fulfillment is defined when questionnaire reaches 50 points plus 4 points of conscious fulfillment.

**Results:** Fifty-five patients more than 14 years old (mean age 50.61 years and 50.9% males) were selected. A 67.27% of them were asthmatics, 30.9% COPD and 1.81% a mix phenotype. A 21.81% presented a correct fulfillment with conscious fulfillment, and the other 78.18% presented good, medium or bad adherence with a breach type.

According to adherence level, a medium adherence was defined in 16 patients (29.09%), with an erratic mistake in 8 patients (50%). Bad adherence was seen in 21 patients (38.14%), with the three breach types in 9 patients (40%). Good adherence with unconscious breach type was defined in 6 patients (10.9%).

**Conclusion:** TAI questionnaire confirms a good adherence and fulfillment in less than 30% patients.

An erratic mistake is the most frequent breach type defined in our patients.

Educational protocols should be applied to improve adherence and fulfillment.

## 1005 | What is adhesion to treatment of asthmatic patients like in Argentina according to the TAI questionnaire?

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**Background:** Asthma is a chronic inflammatory disease of the airways, which requires an adequate treatment and control.

The adhesion of a patient to an asthma treatment is a critical factor in order to achieve and maintain control. This adherence arises from a consensual agreement of the doctor-patient relationship; it is a complex multifactorial variable in which the variability in human behaviour in relation to its environment influences.[1]

The Test of Adherence to Inhalers (TAI) identifies the patient with low adherence to the treatment, determines their degree of adherence (good, intermediate or poor) and the patient's type or pattern of non-compliance: (sporadic, deliberate or unconscious) based on its technique and knowledge of the inhaler.[2 3.]

Poor adherence to inhalers is associated with increased morbidity and mortality. Knowing the type of non-compliance and degree of adherence in our population, allows us to incorporate specific corrective measures to achieve disease control.

**Method:** It is an observational, prospective, transversal, multicentric study in Argentina (Cordoba, Marcos Juarez, La Plata, Rosario, Parana). The TAI was performed on patients between 18 and 80 years old, diagnosed with asthma according to Gina 2016 in inhaler treatment from February to July 2017 at the Allergy Services of these cities. Variables were analysed: age, sex, type of inhaler treatment: single-dose/combined, public and/or private area, and health insurance.

**Results:** A total of 124 patients participated. Average age were 45 years old, 59% female. 56% belong to the private sector. 88% were on combination therapy and 22% on mono drugs.

The non-compliant patients were 101 (81.5%), 64 of them had poor adhesion (54.1%), 34 intermediate adhesion (27.4%) and 23 patients had good adhesion (18.5%). The types of defaults found were: Sporadic 89.11%, Deliberate 87% and Unconscious 18.5%. The private sector showed better compliance (83% p.0.05).

**Conclusion:** It is prevalent a high rate of non-compliance (81.5%) with inhaled treatments in patients with asthma. Sporadic and Deliberate types of non-compliance were the most frequent. The private sector presented better compliance (p0.05). This study makes us rethink new strategies to improve therapeutic efficacy, better adherence, education and disease control in our population.

## 1006 | Pharmacoeconomic evaluation of oral corticosteroid adverse events in patients with severe asthma

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**Background:** Five to ten percent of patients with asthma can be classified, according to the latest ERS/ATS definition, as affected by severe asthma, a condition in which patients are not well controlled and/or with frequent exacerbations despite high dose of standard therapy and/or chronic use of oral corticosteroids (OCS). The regular use of OCS in severe asthmatics is a frequent finding (about 61.5% in the Severe Asthma Network Italy—SANI—registry) and it is well known to be the cause of several unwanted adverse events.

**Method:** We aimed to perform a pharmacoeconomic evaluation of OCS-related adverse events in severe asthmatics. The study consisted in: 1) evaluation of the existing published literature on the type and frequency of OCS-related adverse events and their direct and undirect costs; 2) attribution of an annual economic value to each individual OCS-related adverse event, according to Italian standards of care for each single diagnosis-related group (DRG).

**Results:** The articles selected for extrapolating type and frequency of OCS-related averse events are reported in Table 1.

4860.04 Euros was thee total annual cost of OCS-related adverse events in the asthmatics, corresponding to 193% (2344.32 Euros) more than subjects without asthma.

**Conclusion:** The use of OCS in severe asthmatics has a high impact, both in terms of frequency than under a pharmacoeconomic point of view of its adverse effects. Therefore one of the most relevant unmet need in severe asthma is the reduction (possibly with novel biologic agents) of regular use of oral corticosteroids.

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## 1007 | Short-acting b2-agonists (saba) bronchodilator sales and pollen concentrations in central France over a 5 year period

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**Background:** The association between ambient pollen and asthma has been studied intensively with inconsistent results, attributed to differences in study population, geographic factors (geoclimatic features), data sources, measurement of pollen (different types of traps), and different outcome occurrence (hospitalizations or emergency department visits). We investigated the associations between daily sales of short-acting β2-agonists (SABA) and outdoor pollen concentrations in the central France area.

**Method:** The relationship between daily changes in pollen concentrations and daily SABA sales obtained from the social security database was analysed with generalized additive models, taking into account confounding factors such as air pollution, weather conditions, and day of the week.

**Results:** The daily SABA sales (mean, SD) rose from 46.5 (23.6) in 2010 to 59.0 (30) in 2015. The relative risk (RR [95% CI Confidence Interval]) of SABA sales associated with an interquartile increase in pollen concentration was significant for *Fraxinus* 1.079 [1.037-1.222], *Betula* 1.130 [1.063-1.202], *Carpinus* 1.032 [1.019-1.046], *Platanus* 1.079 [1.037-.1.122] *and Quercus* 1.014 [1.003-1.025] across the whole population.

**Conclusion:** This study indicates that outdoor pollens contribute to asthma morbidity in the general population. It confirms the highly allergenic role of *Fraxinus*, *Betula* and *Quercus* pollens, but also shows a relatively unknown association between treated asthma and *Carpinus* and *Platanus* pollens, despite their counts being less than 1% of overall pollen concentration.

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## 1008 | Total cost of health care resource utilization for asthma patients in Sweden with different exposures to oral corticosteroids

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**Background:** Asthma is one of the most common chronic diseases in the world, and published studies report greater use of continual oral corticosteroid (OCS) therapy by patients with severe, uncontrolled, or eosinophilic asthma. Regular use of OCS puts patients at risk for systemic corticosteroid-related complications (e.g., osteoporosis and diabetes). The aim of this study was to investigate the total cost of health care resource utilization for asthma patients in Sweden with different dosages of OCS.

**Method:** Patients in primary care, ≥18 years of age with a record of a drug claim for obstructive pulmonary diseases (ATC R03) during 2007-2009, and a physician-diagnosed asthma (ICD-10 J45-J46) established prior to drug collection were identified (index). Patients with a concomitant diagnosis of polymyalgia rheumatica (ICD-10 code M35.3) or rheumatoid arthritis (ICD-10 code M05) were excluded. Primary care medical records data were linked to national Swedish health registries. Patients were classified by their OCS claims from pharmacy during 1-year post index (baseline): regular OCS (≥5 mg per day); periodic OCS (<5 mg per day); and no OCS (no OCS claim). Numbers of any cause inpatient, outpatient, primary care contacts, and medication were extracted and direct health care costs were estimated from 1-year post index until death or end of study (December 31, 2013).

**Results:** Of 15 437 asthma patients (mean age 47.8 years, female 62.6%), regular OCS use was identified for 223 patients (1.4%), periodic OCS use for 3054 patients (19.7%), and no OCS use for 12 160 patients (78.7%) 1-year post-index. Regular OCS users had a greater mean age, were more often male, and had greater eosinophil counts, lower lung function, and greater prevalence of comorbidities than did the periodic and no OCS users ($P < 0.001$). Total yearly cost was greatest for the regular OCS users (€ 5509), followed by periodic OCS users (€ 2892) and no OCS users (€ 2042) ($P < 0.001$). Among regular OCS users, hospital admissions were the main cost driver (41.5% of total cost), while GP consultations were driving the total cost in periodic and no OCS users (48.0% and 52.9% of total cost, respectively).

**Conclusion:** In this sample of patients with asthma in Sweden, the total yearly cost of health care resource utilization for a regular OCS user is twice as high as for a patient with no OCS use, demonstrating substantial economic and clinical burden in asthma patients on regular oral steroid treatment.

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## 1009 | Serum periostin levels are associated with asthma severity in children

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**Background:** Serum periostin might be a biomarker in the pathogenesis of T helper 2-type allergic diseases and its significance has been emphasized in several adult studies. The aim of this study was to investigate the association of serum periostin levels with disease features in children with asthma.

**Method:** Children with physician-diagnosed asthma who attended to an outpatient pediatric allergy and asthma center were enrolled in the study along with control subjects. Asthma severity and control status of the patients were evaluated according to recent GINA guidelines. Laboratory investigations including skin prick tests, complete blood counts with differential, total IgE levels, serum periostin levels and pulmonary function tests were performed.

**Results:** A total of 158 children (125 with asthma and 33 age and sex-matched control subjects) with a median age of 10.2 years (range 5.9-17.0) were enrolled. Asthma severity was mild in 41 (32.8%), moderate in 63 (50.4%) and severe in 21 (16.8%) children. Children with asthma had significantly higher periostin levels than controls (53.1 ± 13.1 vs 43.0 ± 11.2 ng/mL; $P < 0.001$). The mean serum periostin levels of children with severe asthma (63.8 ± 10.8) were significantly higher than in children with moderate asthma (53.3 ± 12.7) and mild asthma (47.4 ± 11.1) ($P < 0.001$). Serum periostin levels were found to be significantly correlated with asthma severity (Spearman's rho [r]=.41, $P < 0.001$). Analysis using ROC curves identified the role of
periostin levels in determining children with severe asthma (AUC: 0.77, 95% CI: 0.67-0.87, $P < 0.001$].

**Conclusion:** Serum levels of periostin, a novel asthma biomarker, were higher in asthmatic children, and were associated with asthma severity.

## 1010 | The evolution of bronchial asthma in children with bronchiectasis

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**Background:** Appreciation of evolutionary particularities of bronchial asthma in children with bronchiectasis.

**Method:** In this study, 103 children with asthma aged 7-18 years were enrolled in the pneumology clinic. The imaging evaluation of the bronchopulmonary lesions in children was performed by thoracic computed thoracic HRCT (Aquilion 32, Toshiba, Japan).

**Results:** The pulmonary imaging assessment of children with asthma detected 1.94% of cases of bronchiectasis. These children were diagnosed with severely uncontrolled asthma. In the first case, the child was diagnosed at age 9 with mixed bronchiectasis in the lower left pulmonum (segments 8, 9, 10). At the age of 14 he is undergoing surgery: lower lobectomy on the left. Subsequently, the condition of the child with improvement and the evolution of bronchial asthma became controlled, spirometric indices and quality of life improved. Another child diagnosed with uncontrolled severe BRCA at 7 years of age has been confirmed to have bilateral mixed bronchiectasis in the lower lobes. After the combination of antiasthmatic treatment with gastroesophageal reflux disease therapy and treatment for bronchiectasis, partial bronchial asthma control was achieved, and then the evolution to controlled bronchial asthma.

**Conclusion:** The presence of bronchiectasis in children with bronchial asthma causes a severe evolution and absence of control of the disease. Control of asthma can be obtained after the treatment of bronchiectasis and comorbidities.

## 1011 | Alternaria alternata sensitization and clinical manifestation at the children of preschool age

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**Background:** Nowadays, data from several epidemiological studies confirm the important role of fungi in respiratory disease in the indoor as well as in the outdoor environment. In general, exposure to fungi occurs via inhalation, skin contact, or ingestion. Alternaria alternata is one of the most common fungi associated with presence asthma and persistence and severity of asthma. Although exposure to *A. alternata* is also may represent a risk factor for development of asthma. In Ukraine has been an increase in the number of the mold

sensitized children for the last few years. At the same time we can see increasing frequency BA at the children of pre-school age.

**Method:** Thirty five children aged 3-7 years with allergic rhinitis and high level of asthma predictive index (API) sensitized to *A. alternata* were included in a 2-year cohort study of the efficacy and safety of SLIT (Diater Laboratories, Spain) using standardized sublingual extracts containing molds (Alternaria alternata). Treatment efficacy was analyzed using the score of symptoms such as difficulty in nasal breathing, rhinorrhea, sneezing, itching of the nasal mucosa (upper palate) and discharge from the nose and recurring wheezing. We also have analyzed the level API during the period investigation. Symptoms were measured before starting treatment, and at 4, 12 and 24 months after starting immunotherapy.

**Results:** SLIT significantly reduced both symptoms and medication score: nasal symptoms (38% vs. control group) and the use of rescue medications (38% vs. control group), and improved FEV1 (in children aged≥5 years). In the SLIT group, API decreased by 15% for the first year, by 31% for the second year. No patient had a systemic reaction during therapy.

**Conclusion:** Our results have shown that SLIT is an effective treatment in pediatric patients suffering from allergic rhinitis and high API with significantly improved clinical outcomes (less symptoms and less medication intake) in comparison with children treated with symptomatic drugs only. In this study, large and statistically significant differences in symptom and medication scores were demonstrated in patients receiving SLIT compared to control group. Sublingual immunotherapy is effective for allergic rhinitis in children especially early age and is generally advantageous because of the convenient administration and safety profile and ensure prevention of developed BA.

## 1012 | Clinical form of asthma and vaccine immunity in preschool children

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**Background:** The classification of asthma based on the severity of its clinical course has been recommended by GINA since 2008. This division is useful for the patient's initial assessment when asthma is being diagnosed and essential decisions concerning an appropriate therapy are made. The objective of the work is to evaluate the influence of a clinical form of asthma on vaccine immunity in preschoolers following three years after the programme of mandatory vaccination has been realised.

**Method:** The study encompassed 172 preschool children (mean age of 5.22 ± 0.34 years old) with asthma being newly diagnosed, including 140 patients with mild asthma and 32 ones with moderate asthma, whose vaccine immunity (IgG specific antibody titer) was assessed after the mandatory early childhood vaccines had been administered. Monovalent vaccines (HBV+IPV+Hib) along with a three-component combined vaccine (DTwP) were given to 86 children while a six-component vaccine (DTaP+IPV+Hib+HBV) was given to the remaining 86 children. The vaccine doses were consistent with the Polish Immunisation Programme and manufacturers' recommendations. The ELISA immunoenzymatic method was applied to assess titer of specific antibodies to diphtheria, tetanus, pertussis, poliomyelitis and *H. influenza* type B. The level of HBV antibodies was measured chemiluminescently. The immunity class for particular vaccinations was assessed according to the test manufacturers' instructions.

**Results:** Children suffering from mild asthma had considerably more frequently vaccinations on time ($P < 0.001$) and the type of vaccines (monovalent, highly-combined) administered to them did not have a significant influence on a clinical form of asthma in the children examined ($P > 0.6951$). Apart from the vaccines against hepatitis B and rubella where considerably more frequently a high antibody titer occurred in children with mild asthma, the titers of antibodies to other vaccines, namely diphtheria, tetanus, pertussis, Hib and mumps, were not associated with a clinical form of asthma. The protective antibody titers in the children with asthma were found in 100% after vaccinating them against poliomyelitis (≥12U/mL) and measles (≥300 mL U/mL). Significantly higher current weight was solely found in the children with mild asthma (M = 20.80, SD=3.77; $P < 0.05$).

**Conclusion:** The results achieved indicate a possible influence of asthma severity on post-vaccine response in the case of hepatitis B and rubella.

## 1013 | Chronic atypical respiratory infections (Mycoplasma pneumoniae, Chlamydophila pneumoniae) and asthma control in children

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**Background:** An association between intracellular bacterial respiratory pathogens and the pathogenesis of asthma is still under debates. Some authors advocate the possible role of *M. Pneumoniae/Chl. Pneumoniae* in new- or late-onset asthma, and acute asthma exacerbations. The data about the influence of *M. pneumoniae* and *Chl. pneumoniae* infections on asthma control in children are limited.

**Method:** 159 children aged 6-12 years were examined: non-asthmatics (22), asthmatics (controlled—63, uncontrolled—74, in

| Antibodies subclasses | Non-asthmatics (n = 22) 0 | Controlled asthmatics (n = 63) 1 | Uncontrolled asthmatics (n = 63) 2 | P |
|---|---|---|---|---|
| M. pneumoniae | | | | |
| A | 0 | 4.8 (3) | 16.2 (12) | $P_{0\text{-}2} = 0.046 P_{1\text{-}2} = 0.035$ |
| M | 0 | 27.0 (17) | 39.2 (29) | $P_{0\text{-}1} = 0.008 P_{0\text{-}2} < 0.001$ |
| G | 22.7 (5) | 19.0 (12) | 21.6 (16) | |
| Chl. pneumoniae | | | | |
| A | 4.5 (1) | 4.8 (3) | 14.9 (11) | $P_{1\text{-}2} = 0.054$ |
| M | 13.6 (3) | 11.1 (7) | 24.3 (18) | $P_{1\text{-}2} = 0.048$ |
| G | 22.7 (5) | 31.7 (20) | 35.1 (26) | |

accordance with GINA-2016 recommendations). All children had no any signs of acute respiratory infection and did not receive antibiotic therapy prior to the examination. Asthmatics were on inhaled corticosteroids therapy with no differences in total equivalent dose. For the diagnosis of *M. pneumoniae/Chl. pneumoniae* infections we determined specific antibodies classes A, M, and G using ELISA test systems SeroMP/SeroCP (Savyon®). Chi-square with Yates correction and two-sided Fisher's exact tests were used.

**Results:** The presence of IgA and IgM against both *M. pneumoniae* and *Chl. pneumoniae* were associated with poor asthma control (Table 1). The uncontrolled asthma group exhibited threefold increase in proportion of children with IgA presence against intracellular respiratory pathogens, a good serological marker of chronic course of *M. pneumoniae/Chl. pneumoniae* infection.

**Conclusion:** Chronic *M. Pneumoniae/Chl. Pneumoniae* infection is associated with poor asthma control in children. We suppose that intracellular respiratory pathogens may be involved in the asthma pathogenesis through the induction of inflammation. On the other hand, asthma itself and/or inhaled corticosteroids therapy may predispose to activation of chronic intracellular infection.

## 1014 | Determinants for asthma control, quality of life and use of complementary and alternative medicine in asthmatic pediatric patients in four cities

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**Background:** Asthma is a significant chronic health problem worldwide. Management aims at disease control by reducing functional impairment and exacerbations and improving quality of life (QoL). We report a multi-center study to survey asthma control and QoL in four cities in the Pearl River Delta Region of Southern China.

**Method:** The conjoint survey involved 10 Hong Kong pediatric hospitals/units, 2 Shenzhen hospitals, 2 Macau hospitals and 2 Guangzhou hospitals on asthma control (using Asthma Control Test, ACT) and QoL (Pediatric Allergic Disease Quality of Life Questionnaire, PADQLQ). Acceptability of a treatment is graded as very good/good/fair/poor.

**Results:** Good asthma control was only reported in 80% subjects in Hong Kong but higher in sister cities (85-94%, $P < 0.001$). Allergic rhinitis, "incense burning" and "smoker in family" were prevalent among the four cities. Logistic regression showed better control of asthma was associated with better PADQLQ (B = −0.029, $P < 0.001$), better acceptability of bronchodilator (B = −1.488, $P = 0.025$), negatively with "smoker in family" (B = −0.83, $P = 0.015$) and various PADQLQ domains. Conversely, worse PADQLQ was associated with allergic rhinitis severity (B = 4.77; $P < 0.001$), poor control of asthma (B = 7.56; $P < 0.001$), increase frequency of traditional Chinese medicine use (B = 1.7; $P < 0.05$), increase frequency of bronchodilator usage (B = 1.05; $P < 0.05$), "smoker in family" (B = 4.05; $P < 0.05$), and incense burning at home (B = 3.9; $P < 0.05$).

**Conclusion:** There are some clinical and cultural differences among the four southern Chinese cities within the Canton province. This study identifies potentially modifiable environmental and treatment factors associated with poor asthma control and QoL for healthcare interventions. Having a smoker in the family is independently associated with poor asthma control and QoL.

## 1015 | Assessment of thrombocyte parameters in children with asthma

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**Background:** It is known that thrombocytes have been implicated in many inflammatory and immunologic conditions, including allergic

inflammation. In this study, it was aimed to evaluate thrombocyte parameters in children with asthma.

**Method:** It was recorded age, gender, asthma severity, asthma control status, atopy and parameters of thrombocyte (mean thrombocyte volume-MPV, thrombocyte distribution weight-PDW, thrombocyte counts) of the patients with asthma in the allergy outpatient clinic in our hospital.

**Results:** In this study, we evaluated 933 patients. The mean age of the patients was 10.44 ± 4.25 years, and 61% (n = 568) were male. 56.3% (n = 526) of the patients had atopic asthma, 55.1% (n = 514) were mild persistent asthma, 74.3% (n = 693) were well controlled. 173 (18.5%) of the patients had allergic disease in their families. When the platelet parameters are evaluated, MPV(fL)= 8.03 ± 0.87 fL, PDW (%)=16.25 ± 0.55, thrombocyte counts (103/mm3)=318.463.02 ± 83.137.48. Asthma control status, asthma status, gender and atopy status did not show any correlation between the parameters of thrombosis ($P > 0.05$).

**Conclusion:** In the patients with asthma, parameters of thrombocytes are not associated with asthma control status, asthma severity and atopy.

## 1016 | Assessment of leukotriene E4 as a marker of inflammation in allergic rhinitis children with antihistamine and leukotriene receptor antagonist

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**Background:** Recent studies have shown that the cysteinyl leukotriene (cysLT) of exhaled breath condensate (EBC) could be predictive of inflammatory status and effectiveness of treatment in allergic disease. The aim of this study was to evaluate the inflammation and therapeutic effectiveness with cysLT in EBC of pediatric allergic rhinitis (AR).

**Method:** We enrolled 54 healthy children (median age, 4 years 7 months) and 87 AR children (median age, 4 years 11 month). All of AR patients received intranasal steroid (fluticasone furoate) once per day for 2 weeks. After 2 week fluticasone furoate treatment, they were classified into two groups (levocetirizine group (L) and montelukast group (M)) and we treated each group for another 10 week. To evaluate the therapeutic effectiveness, we used symptom score (SS) and EBC leukotriene E4 (LTE4). EBC samples were collected with RTube. Each parameter was checked at 0, 2, 12 week therapeutic period.

**Results:** Most AR patient showed clinically improvement with 2 and 12 week fluticasone therapy (0 wk SS=6.6, 2 wk SS=3.2, 12 wk SS=1.9 $P < 0.01$ in L group; 0 wk SS=6.8, 2 wk SS=3.6, 12 wk SS=2.0 $P < 0.01$ in M group). LTE4 levels of AR were higher than control (0 wk 77 vs. 12 pg/mL), and were reduced after 2 week fluticasone treatment (86.2 → 41.6 pg/mL, $P < 0.01$ in L group; 83.5 → 43.1 pg/mL, $P < 0.01$ in M group). After 12 wk treatment, there were no different level of LTE4 in L and M group.

**Conclusion:** LTE4 in EBC assessment may be useful in the evaluation of inflammation of allergic rhinitis.

## 1017 | Asthma predictive index external validation in Russian population

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**Background:** About a third of children under the age of 3 report episodes of wheezing, however, most of them do not develop asthma later in life. Detection of those at a highest risk of asthma development is an important goal.

Asthma Predictive Index (API) originally developed by Castro-Rodriguez et al. is the most widely used tool for asthma prediction. This pilot study aims to externally validate API performance in Russian high-risk population.

**Method:** Clinical notes of all patients 0-4 years of age admitted in 2013 to the respiratory infections department of Speransky Hospital №9, Moscow, Russia were screened. Those diagnosed with wheezing were included into the study. Comprehensive patient data related to the time of admission were collected.

A telephone survey of parents was conducted when children were 6-7 years of age. Questionnaire included detailed information on family/child allergy history, environment and data on asthma symptoms (ISAAC questionnaire).

Loose API was considered positive if child was an early wheezer—at least one episode of wheezing in the first 3 years of life plus at least one of two major criteria (MC) or 2 of 3 minor criteria (MiC). Stringent API: early frequent wheezer—frequency of episodes ≥3 on a scale from 1 (very rarely) to 5 (most of the time) plus at least 1 of 2 MC or 2 of 3 MiC.

MC were: parental medically diagnosed (MD) asthma or MD eczema in the child.

MiC were: MD allergic rhinitis, wheezing apart from colds, eosinophilia ≥4%.

Outcome was defined as MD asthma and at least 1 episode of asthma during the previous year or more than 3 episodes of wheezing during the 12 months regardless of asthma diagnosis.

**Results:** From a total of 144 of parents approached, 86 (58%) agreed to participate in a phone interview. 18 (21%) children were diagnosed with asthma. The age at the time of admission (mean,

(SD)) was 27.0 (9.9), at the time of phone survey 77.6 (10.9) months, respectively.

Positive loose API at 2-3 years of age had sensitivity of 77.8%, specificity 75%, positive predictive value (PPV) 45.2%, negative predictive value (NPV) 92.7%.

Positive stringent API at 2-3 years of age had sensitivity of 50%, specificity 91%, PPV 64.3%, NPV 85%.

**Conclusion:** API performance in Russian population is comparable to the original study. High NPV shows decent ability of API, particularly loose, to rule out asthma. However, asthma development predictivity is very weak. Future research should focus on predictive performance improvement, using index modifications.

## 1018 | Comparable lung function improvements with tiotropium in adult and pediatric patients with asthma confirm the validity of the extrapolation concept

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**Background:** Asthma is the most common chronic airway disease in childhood, with a high unmet need for new treatments due to insufficient symptom control in a relevant percentage of patients. Ethics and resource factors limit the feasibility of large, long pediatric trials required to assess outcomes such as exacerbations and symptoms. For diseases like asthma, where the disease process is largely similar in children and adults, with the same expected therapy outcome, the International Council for Harmonisation advise extrapolating adult data to those of a younger age, reducing unnecessary pediatric trials. Here we assess the partial extrapolation used in the clinical development of tiotropium.

**Method:** We compare lung function and other endpoints from Phase 3 trials in adults (aged 18-75), adolescents (aged 12-17) and children (aged 6-11) with symptomatic severe (PrimoTinA-/PensieTinA-/VivaTinA-asthma) or moderate asthma (MezzoTinA-/RubaTinA-/CanoTinA-asthma), respectively. Trials lasted 12-48 weeks, all with tiotropium Respimat 5 μg add-on vs placebo as two puffs once daily.

**Results:** In adult trials, lung function, symptoms and exacerbation endpoints were evaluated in a confirmatory manner: tiotropium significantly improves lung function and asthma control, and reduces risk of exacerbation, vs placebo (Table 1). In pediatric trials, where only lung function endpoints were confirmatory, the peak and trough $FEV_1$ improvements with tiotropium vs placebo are generally

| Trial | Asthma severity | Age, years | Trial duration / time of endpoint reporting, weeks | Patients, n, tiotropium 5 μg / placebo | Baseline $FEV_1$ in all patients, % predicted normal, mean (SD) | Peak $FEV_1$ response vs placebo, L, mean (95% CI) | Peak $FEV_1$ vs placebo, % predicted (95% CI) | Trough $FEV_1$ response vs placebo, L, mean (95% CI) | Trough $FEV_1$ vs placebo, % predicted (95% CI) | ACQ responder rate vs placebo, OR (95% CI) | Time to any asthma exacerbation vs placebo, HR (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PrimoTinA-asthma replicate pooled trials | Severe | 18-75 | 48/24 | 422/429 | 55.96 (13.14) | 0.110 (0.063, 0.158) | 3.63 (2.12, 5.15) | 0.093 (0.050, 0.137) | 3.01 (1.55, 4.48) | 1.32 (1.01, 1.73) | 0.69 (0.58, 0.82) |
| PensieTinA-asthma | Severe | 12-17 | 12/12 | 130/132 | 79.52 (11.49) | 0.090 (−0.019, 0.198) | 1.64 (−1.25, 4.54) | 0.054 (−0.061, 0.168) | 0.83 (−2.35, 4.01) | 0.99 (0.55, 1.76) | 0.60 (0.32, 1.14) |
| VivaTinA-asthma | Severe | 6-11 | 12/12 | 128/130 | 81.64 (11.45) | 0.139 (0.075, 0.203) | 6.33 (3.26, 9.39) | 0.087 (0.019, 0.154) | 3.85 (0.58, 7.12) | 1.26 (0.67, 2.40) | 0.69 (0.44, 1.06) |
| MezzoTinA-asthma replicate pooled trials | Moderate | 18-75 | 24/24 | 481/492 | 75.06 (11.51) | 0.185 (0.146, 0.223) | 5.80 (4.61, 6.98) | 0.146 (0.105, 0.188) | 4.63 (3.33, 5.92) | 1.32 (1.02, 1.71) | 0.87 (0.69, 1.09) |
| RubaTinA-asthma | Moderate | 12-17 | 48/24 | 131/137 | 82.79 (10.56) | 0.174 (0.076, 0.272) | 4.49 (1.70, 7.29) | 0.117 (0.010, 0.223) | 3.21 (0.21, 6.20) | 1.47 (0.84, 2.58) | 0.82 (0.51, 1.33) |
| CanoTinA-asthma | Moderate | 6-11 | 48/24 | 134/126 | 84.06 (10.79) | 0.164 (0.103, 0.225) | 6.52 (3.72, 9.32) | 0.118 (0.048, 0.188) | 4.44 (1.21, 7.67) | 2.43 (1.23, 4.93) | 0.77 (0.54, 1.10) |

comparable to adult responses within same severity groups. Symptoms and exacerbations in pediatrics (exploratory analysis) showed trends for improvement in a comparable range to adult data. Safety data were similar with tiotropium vs placebo, with low numbers of exacerbations in pediatrics.

**Conclusion:** Based on similarities in disease profile and magnitude of treatment responses between age groups, it is reasonable to expect tiotropium add-on to produce clinically meaningful improvements in exacerbation and symptom endpoints in children and adolescents, as in adults. The robust tiotropium clinical program supports using a partial extrapolation to avoid overly long and large trials in pediatrics.

## 1019 | Clinical state of treatment and examination during last 3 years before remission about asthmatic children in long-term remission cases

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**Background:** I have been presented the characteristics and clinical usefulness of airway hyperresponsiveness about asthmatic children at the congress of EAACI 2014, EAACI 2015, EAACI 2016 and EAACI 2017. Last year I reported clinical characteristics of asthmatic children during last one year before remission. This time I studied clinical state (background, treatment, examination) during last 3 years before remission. Then I tried to discuss about the clinical indicator when we will quit the treatment for leading long-term remission.1.

**Method:** Remission cases (no symptom and no therapy) for 3 years of asthmatic children were studied. Clinical background and treatment (drugs) was studied during last 3 years before remission annually.

Acetylcholine inhalation test by standard method was performed, and respiratory threshold of acetylcholine (RT-Ach) was obtained. FEV1%, and serum IgE also examined. These data were compared before remission with 3 years after remission.

**Results:** Mean age of 25 cases at 3 year before remission was 9.2 years old. Male to female ratio was 1.3.

Severity of asthma was all mild type, and number of attack was 2 to 8 times in a year. There was no admitted case during this study.

The long-term therapeutic drugs were leukotriene receptor antagonist (Anti LT) in 20 cases, and/or inhaled corticosteroids (ICS) in 12 cases, but 5 cases had no treatment for the control.

Geometric mean of RT-Ach (after then: 3 years before and after remission) was 2900 μg/mL and 5800 μg/mL. The mean FEV1% was 83% and 90%. Geometric mean of serum IgE level was 360 IU/L and 410 IU/L. Complicated cases of atopic dermatitis decreased after remission, but the incidence of allergic rhinitis increased slightly.

**Conclusion:** Characteristics of asthmatic children during last 3 years before remission were mild type, had several times of attack in a year, and the treatment was mainly Anti LT and/or ICS. FEV1% was within normal range, and serum IgE level was not changed after remission. RT-Ach had the tendency to improve during 3 years before and after remission. These data is supposed that airway hyperresponsiveness is one of the indicators for quitting treatment.

## 1020 | Clinical aspects of polyvalent mechanic bacterial lysate (PMBL) treatment in children with uncontrolled asthma

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**Background:** Uncontrolled or inadequately treated asthma can reduce the functioning of children with asthma and their families in all areas of daily activity. The factors that worsen the course of the disease include, among others, acute and chronic infections of the respiratory tract. Therefore, the search for methods of prevention of respiratory tract infections in children who have not been successfully treated for asthma is of particular importance. The aim of the study was to determine the clinical significance of polyvalent mechanic bacterial lysate (PMBL) treatment in children with uncontrolled asthma.

**Method:** The study data were obtained from the patient's medical records and the physical examination of the children. The assessment of the quality of life of a child with asthma was made using the Paediatric Asthma Quality of Life Questionnaire—PAQLQ and Asthma Control Questionnaire (ACQ or ACQ-IA) was used to estimate asthma control. Children were evaluated at the time of inclusion in the study, after 3 months of additional therapy and after 6 months from its completion.

**Results:** In the years 2014-2015 a randomized, double-blind, placebo-controlled study included 78 children aged 6-16 years who were treated with SABA on demand and ICS (inhaled corticosteroids) or iCS+LABA for chronic IgE-dependent asthma. The population consisted of 26 girls (33%) and 52 boys (67%) with an average age of 9.73 ± 2.6 years. Statistically, PMBL group and the placebo group did not significantly differ (). At the time of inclusion, all children had confirmed uncontrolled asthma based on the results of the ACQ I questionnaire (PMBL-1.9 ± 1.0 points vs. placebo—2.1 ± 1.1 points, $P = 0.6$). Both after 3 months of treatment and during the 6-month follow-up, the influence of the type of additional therapy on the degree of asthma control in children was not observed (ACQ II: PMBL- 1.1 ± 0.86 points vs. placebo- 0.95 ± 0, 78 points, $P = 0.6$, ACQ III: PMBL-0.84 ± 0.65 pts vs. placebo—1.0 ± 0.77 pts, $P = 0.4$). In the 6-month follow-up period, in the PMBL group, there was a

significantly better improvement in the quality of life of the child with asthma in the domain „symptoms" compared to placebo (PAQLQ III-II: PMBL- +0.59 points vs. placebo- + 0.005 points; $P = 0.005$).

**Conclusion:** Adding PMBL treatment to standard anti-asthmatic therapy in children with chronic uncontrolled asthma may reduce the limitation of their daily functioning associated with the symptoms of the disease.

## 1021 | 4-6 years experience of targeted therapy with omalizumab in children with uncontrolled severe persistent asthma

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**Background:** Omalizumab is the only biological medication, which was authorized in Russia as an add-on therapy in children aged>6 years with uncontrolled severe persistent asthma during treatment with high doses of inhaled corticosteroids plus long-acting beta2-agonist. Analysis of available literature showed that the data on real-life outcomes for more than 2 year of omalizumab treatment were limited in children.

Objective: To analyze the efficacy of the long-term therapy with Omalizumab (more than 4 years) to maintain disease control in children with uncontrolled severe persistent asthma in real life practice.

**Method:** Data of the long-term follow-up monitoring in children with uncontrolled severe persistent asthma were analyzed. A patient registry included data of 104 children (31.73% girls) from 6 y to 17 y 11 mo (average age 13.4 y), receiving Omalizumab in addition to basic therapy. 26 children (27% girls) received targeted therapy for more than 4 years (Me 62.5 mo [47;91 mo]).

**Results:** 26 children have received therapy of Omalizumab for 4 years, the average point of ACT before the therapy of Omalizumab was 14.42 ± 3.36, in 4 years—21.86 ± 2.56 ($P = 0.001$). 15 patients (57.7%) achieved partial control, 5 (19.23%) became well controlled. The average dose of the amount of basic therapy before Omalizumab was 575 ± 279 μg, Me 500 (250;1250), after 4 years the basic therapy volume was reduced by 14.5%—524 ± 342 μg; $P = 0.065$), Me 500 (100;1000)

17 children received Omalizumab for 5 years, the average point of ACT in 5 years of therapy—22.059 ± 3.45. 12 patients (70.58%) achieved partial control, 2 (11.76%) became well controlled. The average dose of basic therapy of Omalizumab after 5 years was 444.85 ± 277.2 μg, Me 500 (100;1000),

After 6 years of Omalizumab treatment (n = 7) the average point of ACT was 21.57 ± 3.40. 3 patients (42.8%) achieved partial control, 2 became well controlled. The average dose of basic therapy of Omalizumab after 6 years was 339.29 ± 212.54 μg, Me 250 (100;750),

After 2 years of Omalizumab treatment, the number of exacerbations and requirement of quick-relief medications have been reduced. There was no severe exacerbation requiring emergency admissions.

**Conclusion:** Our results indicate that long-term treatment with Omalizumab in children can help to achieve better asthma control and reduce the amount doses of basic therapy.

## 1022 | Comparison of diagnosed patients with allergic rhinitis and rhinoconjunctivitis

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**Background:** Conjunctivitis accompanies some patients diagnosed with allergic rhinitis. The purpose of this study was the evaluation of patients with the diagnosis of allergic rhinitis and allergic rhinoconjunctivitis.

**Method:** Allergic rhinitis (AR) and allergic rhinoconjunctivitis (ARC) diagnosed-patients' demographic information, accompanying-asthma, the allergic history of the family, the onset of symptoms, types of aeroallergens sensitivity were noted from patients' files in our hospital's pediatric allergy clinic.

**Results:** In this study, 675 patients were evaluated. The mean age of the patients were 11.65 ± 3.85 years and 61% (n = 412) were male. 452 (67%) patients had AR and 223 (33%) patients had ARC. Asthma were accompanying to 395 patients (87.4%) who are diagnosed with AR, and 166 (77.4%) patients who are diagnosed with ARC ($P < 0.001$). 20.8% (n = 94) of AR-diagnosed patients and 28.7% (n = 64) of ARC-diagnosed patients had allergy in their family history ($P = 0.02$). 175 (38.7%) patients with AR and 38 (33.2%) patients with ARC had other aeroallergen allergies ($P = 0.16$). There was no statistical difference between the two groups in terms of other aeroallergen allergies. The distribution of non-pollen aeroallergens was different between the two groups. However, considering the distribution of non-pollen aeroallergen allergy, in patients with AR, the majority of other aeroallergen allergies were house dust mites (53.8%; n = 94); while in patients with ARC, the majority of other aeroallergen allergies were cat and dog dander (63.5%; n = 47), ($P = 0.01$). There was no statistical difference between AR and ARC diagnosed patients in terms of eosinophil count, percentage of eosinophil and levels of IgE ($P = 0.35, 0.77, 0.43$, respectively).

**Conclusion:** Patients diagnosed with AR and ARC should also be evaluated for non-pollen aeroallergen allergies.

## 1023 | Assessment of pollen season and out of season pulmonary function test of patients with allergic rhinitis

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**Background:** Allergic rhinitis (AR) is a disease characterized by symptoms of nasal discharge/congestion, sneezing, and pruritus, and is caused by an IgE-mediated immunological response to inhaled allergens. We aimed to evaluate pollen season and out of pollen season pulmonary function tests (SFT) of patients with AR in our study.

**Method:** In our study, the demographic characteristics and aeroallergens were recorded from patients' files with AR diagnosed. In addition, pollen season and out of pollen season SFTs were evaluated and compared.

**Results:** 114 patients were evaluated in the study. The mean ages of the patients were 11.37 ± 3.74 years and %64 (n = 73) were male. %16.7 (n = 19) of the patients had atopic dermatitis. When the distribution of aeroallergens is evaluated, in 60.5% of patients (n = 69) only pollen, 39.5% (n = 45) had pollen and non-pollen aeroallergen allergy. When the SFTs of the patients are compared; seasonal FVC=90.97 ± 9.74 FEV1 = 87.18 ± 9.62; out of season FVC=91.40 ± 9.19 FEV1 = 95.44 ± 8.78; both parameters were lower during the season ($P < 0.001$). When SFTs of patients with only pollen allergy and patients with pollen+non-pollen aeroallergen allergy were compared, FVC and FEV1 values were found to be lower during the season ($P < 0.001$). There was no statistical difference between FEV1 / FVC and FEF25-75 values.

**Conclusion:** In patients with AR, FEV1 and FVC values are seen to be lower during the season even though there is no lower respiratory symptom. Therefore, SFTs of patients with AR should be evaluated during pollen season.

## 1024 | Peculiarities of clinical manifestations of pollinosis in children and adults

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**Background:** The purpose of the study: to study the specific features of clinical manifestations of pollinosis in adults and children of different age groups in the comparative aspect.

**Method:** There were examined 1154 patients with hay fever at the age of 3-70 who were divided into several age groups: children: 3-7 years old (118 children); 8-12 years old (143 children); 13-18 years old (70 children) and adults: 19-29 years old (252 people); 30-49 years old (422 people); over 50 years old (79 people). The examination included: (allergological—ImmunoCAP (Phadia), skin prick-tests (pollen allergens DIATER (Spain), nasocytogram, spirography (including provocation tests), etc. as well as specialist consultations (ENT and ophthalmologist).

**Results:** Among the clinical manifestations, the most common combination of allergic rhinitis (AR) and conjunctivitis (AC) is noted in 83.80% of adults and 55.11% of children, but in children aged 3-7, the combination of AR and AC is observed only in 48.40%, among 8-12 years old—51.25%, while in the remaining age groups it is encountered in more than 80%. Higher percentage of isolated AR is also observed among young children—17.55%, and those of the average age—13.99%, whereas in the group of 13-18 years old—it is in 4.29%, and in adults—in 5.05%. Isolated AC was detected in 9.09% of children aged 8-12, in 3.19% of children of 3-7 years old and only in 1.43% of older children and 1.33% in adults. The high frequency of isolated forms of AR and AC is observed at the age of 7 years old—20.74% and 8-12 years old—23.08%, while at the age of 13-18 it makes 5.71%, at 19-29 years old—4.76%, at 30-50 years old—6.87%, over 50 years old—8.86%. The presence of bronchial obstruction is most common in young children—30.85%, decreasing with age (among patients of 8-12 years old—25.87%, 13-18 years old—12.86%, 19-29 years old—8.33%, 30-50 years old—10.19%, over 50 years old—12.66%).

**Conclusion:** Thus, the age-related peculiarities of the body affect the presence of clinical manifestations of pollinosis: the frequency of combination of AR and AC is noted in more than 80% of adults and only in half of children under 12 years old; isolated forms of AR and AC occur in children under 12 years old several times more frequently than in adults; the presence of bronchial obstruction is detected in more than 30% of children under 7 years old, which is almost 3 times more than in adults, significantly decreasing with age.

## 1025 | Pollen-related food allergy in children with seasonal allergic rhinitis

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**Background:** Pollen-food syndrome (PFS) is common in adults sensitized to pollen and homologous food allergens. Seasonal allergic rhinitis (SAR) and bronchial asthma still remain a typical manifestation in this group of age. There is limited information regarding the sensitization patterns of pollen-related food allergy in children with SAR and its impact on the course of disease.

The aim of study was to evaluate the prevalence of SAR in children with pollen-related food allergy and assess the role of food allergens in exacerbations of nasal symptoms.

**Method:** A group of 43 children with pollen-food sensitization aged from 2 to 14 years were evaluated for evidence of SAR. The inclusion criteria was IgE-mediated sensitization to pollen and homologous food allergens evaluated by skin prick tests (SPT) and/or measurement of specific IgE antibodies. The diagnosis of SAR was based on clinical symptoms appearing seasonally according to the profile of sensitization. The control group consisted of 31 children with SAR caused by pollen.

**Results:** Allergic rhinitis was a main symptom in 69.8% of children with pollen-food sensitization. In all of them concomitant allergic disorders were noticed: bronchial asthma (77.7%), atopic dermatitis (77.8%). Only in 26.7% temporal association between ingestion of pollen-related foods and nasal symptoms was observed (mainly apple and peanuts); occurring also outside the pollen period. The simultaneously sensitization to animal origin food allergens was stated in 63.3% of children with SAR, but only in two of them milk and white egg proteins were an additional exacerbation factor of nasal symptoms. In 18.5% anaphylactic reactions to food allergens were registered. 36.7% of children were asymptomatic despite pollen-food sensitization. The statistically significant differences were noticed in comparison to the control group.

**Conclusion:** 1. Allergic rhinitis in children, similar to adults, is a common manifestation of pollen-food syndrome and this type of sensitization should be taken into account regardless to age.

2. Children with pollen-related food allergy have the predisposition to multiorgan clinical manifestation.

3. The lack of association of symptoms with plant-origin foods in the majority of cases and the asymptomatic course of food sensitization in more than one third of patients indicate the need for follow-up.

## 1026 | Clinical benefit of the screening of suspected food allergen using multiple allergen simultaneous test in the patient with pollen-food allergy syndrome (PFAS)

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**Background:** The quantitative Fluoresce Enzyme Immunoassay ImmunoCAP (IC) system has been widely used for detection of allergen-specific IgE for the diagnosis of allergy. However, the system can only detect IgE against a single allergen, the multiple antigen simultaneous tests has been developed such as the Fluorescence Enzyme Immunoassay View Allergy 39 (VA) or Chemiluminescent Enzyme Assay MAST IV (MA) and both assay detect more than 39 allergen-specific IgE. In this study we examined the diagnostic capability of these two systems for screening test in the patient with PFAS.

**Method:** Total number of participants are 37 (Male/Female: 20/17), aged 12.0 ± 3.9 (range 3~20) years old. All the patients showed oral allergy syndrome (OAS) to Rosaceae family plants (apple, peach) and/or kiwi and/or banana, also showed tree pollen allergy. Specific IgE assay were performed using IC, MA or VA. Results of greater than Class 1 were to be regarded as positive, and the concordance rates between the assays were assessed.

**Results:** The correlation of sensitivity between PR-10 (rBet v1, rMal d1, rPru p1, measured by IC) and specific IgE to apple (measured by VA), specific IgE to peach (measured by MA) in 27 OAS patients to Rosaceae family plants were assessed. rBet v1, rMal d1, rPru p1 were found to be 96.0%, 96.3%, 92.6% positive measured by IC while the specific IgE to apple (supposed to be including PR-10) were found to be 100% positive measured by VA. On the other hand, the specific IgE to peach (supposed to be including PR-10) were found to be only 33.3% positive measured by MA, this detection rate was lower than that of VA ($P < 0.0001$). Also, the correlation of sensitivity between PR-10 (rAct d8, measured by IC) and specific IgE to kiwi in 17 patients with OAS to Kiwi were assessed. rAct d8 were found to be 76.5% positive measured by IC while the specific IgE to kiwi (supposed to be including PR-10) were found to be 64.7% and 17.6% measured by VA and MA, respectively ($P < 0.005$). Additionally, all the 3 OAS patients to banana found to be positive for the specific IgE to banana measured by VA, but only 1 patient was detected as positive measured by MA.

**Conclusion:** In this study, we found that VA showed better agreement of sensitivity and specificity with IC compared to MA in the OAS patients to Rosaceae family plants, kiwi, or banana.

Therefore, it may be clinically useful for screening of allergen specific IgE in patient with PFAS by VA and follow the observation the subsequent transition quantitatively by IC.

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## 1027 | The frequency of occurrence of sensitization to the alternaria alternata in patients with seasonal allergic rhinitis and sensibilization to ragweed

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**Background:** Seasonal allergic rhinitis (SAR) is one of the most common chronic diseases. Often concomitant sensibilizations may worsen the outcomes of patients with SAR. At present, ragweed allergy is the second most common cause of pollinosis in Ukraine, after grass allergy. Alternaria alternate is another allergen that may cause symptoms of the allergic diseases of the respiratory tract. In Ukraine, elevated concentration of Alternaria spores in the air is present between July and September, with the peak air concentration at the end of the summer-beginning of the fall. This coincides with the peak of ragweed bloom. In patients sensitized to ragweed, exposure to Alternaria spores may add to the morbidity, aggravating respiratory symptoms and extending duration of the allergic season.
The aim of this study was to determine the prevalence and clinical significance of sensitization to Alternaria alternate in patients with SAR who are already sensitized to ragweed. To our knowledge, no other group has attempted to perform such an investigation in Ukraine.

**Method:** Patients with SAR (N = 91) underwent clinical examination, skin prick tests, and analysis of levels of specific IgE to pollen allergens. Patients were from the Kyiv region (north-central region of Ukraine). Of all patients, 56% were men. The mean age was 22.6 ± 13.2 years (3-50 years). All patients underwent a skin test for the ragweed. Then, all patients were analyzed for specific IgE to the ragweed and Alternaria alternate through ImmunoCap.

**Results:** All patients had sensibilization to ragweed. 36% of the patients had sensibilization to Aletrnaria alternata. Sensibilization to Alternaria alternate in children was higher than in adults: 61% in patients ages 5-10; 44% in patients ages 11-20. There was a trend for decreased sensibilization with age: 43% in patients ages 2130; 9% in patients ages 31-40; no sensibilization in patients ages 41-50.

**Conclusion:** In this study, we demonstrated that a third of patients in Kyiv region with SAR and sensibilization to ragweed had sensitization to Alternaria alternate. Given the overlapping pollination seasons of Alternaria and ragweed, physicians should consider testing for sensibilization to Alternaria in patients with SAR and sensibilization to ragweed. According to our findings, this is especially relevant in younger patients (20 years and under), who showed higher levels of sensibilization to Alternaria.

## 1028 | Role of humic substances in the hygiene hypothesis for autoimmune and allergic diseases

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**Background:** The hygiene hypothesis for autoimmune and allergic diseases, which exists nowadays, shows that human immune system is dependent on various environment factors. We consider the effects of humic substances (HS) to be important in understanding the hygiene hypothesis. Due to urbanization, the amount of human interaction with HS found in soil has significantly dropped. The goal of our work was to study allergenic potential and antimicrobial activity of HS.

**Method:** Various fractions of HS were researched: humic (HA), hymatomelanic (HMA), fulvic (FA), and humic-fulvic acids (HFA). The research of allergenic potential of HS was conducted in vivo with methods for estimation of levels of IgE-antibodies after HS injetion, and for propagation of anaphylactic reaction and development of sensibilization in mice after HS injection. The study of HS antibacterial activity and chelate complexes of HS was conducted on: *E. coli* (ATCC 25922), Ps. aeruginosa (ATCC 27853), St. aureus (ATCC 25293), *B. subtilis* (ATCC 6633). The results were estimated in reference to the growth suspension zone of test culture on Mueller-Hinton agar.

**Results:** Injection of HS showed decrease of levels of allergen-specific IgE-antibodies almost twice in comparison with mice in reference group against the background of developing allergic IgE-response to ovalbumin. Study of anaphylactic effect showed an absence of specific homocytotrophic IgE-antibodies, specific towards HA components and able to cause anaphylaxis, in test animals. Study of antibacterial properties showed, that HS exhibit bacteriostatic activity towards the growth of studied gram-negative bacteria, and stimulate growth of gram-positive bacteria. Study of chelate complexes of HS revealed cytolytic activity towards test cultures of microorganisms. The least antimicrobial activity was observed in chelate complexes of FA containing zinc and iron (II), and the most—in chelate complexes of HA containing silver and mercury (II).

**Conclusion:** HS appear to be exogenous immunocorrectors, and also to have an ability of suppressing propagation of allergic reactions and sensibilization, which leads to conclusion that they seem to play a major role in hygiene hypothesis. Moreover, HS selectively interact with bacterial cell wall, and this effect could be used in order to create antimicrobial drugs based on HS.

## 1029 | Peach tree pollen and molecular components: Sensitization and clinical relevance in Madrid

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**Background:** Peach tree pollen has been identified as having relevant allergens (the third most prevalent after olive tree and grass pollen) in areas of high cultivars (Murcia, East-Spain). When analyzing molecular components in sensitized patients, along with Pru p 3, we have identified other relevant inhalant allergens one of which was named Pru p X.

Because pollen of different species share allergens and with plant-derived food, we have also studied Peach tree pollen sensitization in a non-exposed population (Madrid, Central-Spain).

The aim was to study the association between Peach Tree Pollen and several panallergens, as well as the relevance of Pru p X in our area (Madrid).

**Method:** A total of 328 patients who came to our Allergy Unit (November 2016-December 2017) reporting seasonal respiratory symptoms (RC/Asthma) were evaluated. The study included clinical history and skin prick tests (SPT) to a panel of relevant inhalant pollen as well as peach LTP, Polcalcin and Profilin from other sources in order to assess potential cross-reactivity.

In those patients with positive SPT to at least one pollen we also performed Peach tree pollen SPT. If positive, we tested Pru p 3, Pho d 2, Pho d 3 and Pru p X.

To study the clinical relevance of these findings, we also performed Nasal Provocation test (NPT) with Peach tree pollen and Pru p X.

**Results:** A total of 57 patients were sensitized to Peach tree pollen. From these, 33% had also positive SPT to Pru p 3 and none of them to Pru p X. Positive SPT to Polcalcin were found in the 33% of the cases and to Profilin in the 13%.

In 7 patients sensitized to Peach tree pollen NPT was performed being 4 cases positive to Peach tree pollen and none to Pru p X.

**Conclusion:** Peach tree pollen sensitization in non-exposed patients with allergy to other pollens is high although primary sensitization is unlikely. These patients present clinical response when exposed to that pollen that needs further evaluation. In our study, one third of the patients were also sensitized to Polcalcin and Pru p 3 and none to Pru p X. We have not found clinical response to this new inhalant allergen identified in highly exposed Peach tree pollen population.

## 1030 | Cross validation of the candidate European Pharmacopoeia standard method for quantification of the major birch pollen allergen, Bet v 1

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**Background:** The goal of the BSP090 program initiated by the European Directorate for the Quality of Medicines & Healthcare (EDQM) is to establish reference standards for the quantification of major allergens in allergen products. A candidate standard method for measuring Bet v 1 was developed using monoclonal antibodies (Stallergenes Greer) in an ELISA. Our aim was to cross-validate improvements in the ELISA which would make the assay more suitable for routine use.

**Method:** Hybridoma cell lines producing anti-Bet v 1 monoclonal antibodies validated in the BSP090 multi-center ring trial were acquired. Antibodies were purified and used to develop a two-site ELISA (ELISA 2.0-EP) using recombinant Bet v 1 (rBet v 1) as the assay standard, which was sub-standardized against the EDQM rBet v 1 Chemical Reference Substance (CRS). The Bet v 1 ELISA 2.0-EP was validated under the auspices of the Paul-Ehrlich Institute and the EDQM.

**Results:** The Bet v 1 ELISA 2.0-EP complete kit format (including pre-coated plates and all buffers and reagents) allowed for the consistent measurement of Bet v 1 in birch pollen extracts within the same lab (IntraLab CV=5.5%) and between different labs (InterLab CV=13.5%). The average recovery from matrix spiked samples (CRS in birch pollen extracts) ranged from 75-112%, with an average recovery of 91% (n = 10). Assay time was reduced from several days to two hours compared to the original method.

**Conclusion:** The performance of the Bet v 1 ELISA 2.0-EP kit was comparable to that of the Stallergenes Greer candidate standard method and has been successfully cross-validated. This will enable allergen manufacturers and regulatory authorities to adopt a standard method for Bet v 1 determination, which, ultimately, may be included in the European Pharmacopoeia. The development of a certified ELISA represents a major step forward in the standardization and quality control of allergen products.

## 1031 | An isoform of the Ole e 7 allergen assembled by proteomics could explain the cross-reactivity with pollen and food nsLTPs

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**Background:** Olive tree pollen is an important cause of allergy worldwide. Ole e 7, a non-specific lipid transfer protein (nsLTP) from olive pollen, is a major allergen responsible for severe symptoms such as anaphylaxis in extensive regions with high olive pollen counts. Despite the clinical relevance of this allergen, its cloning has been impossible since the late 90's mainly due to its high polymorphism, what prevented the analysis of the implication of Ole e 7 in cross-reactivity.

The aim of this work consists of determining the whole Ole e 7 amino acid sequence by proteomics for its subsequent cloning, expression and analysis of its structural and immunological features.

**Method:** Ole e 7 purified from olive pollen was separated by 2DE-gel electrophoresis, in-gel digested with trypsin and analyzed by nLC-MS/MS in an LTQ-Orbitrap Velos for *de novo* peptide sequencing. The obtained peptides were used to complete the full-length amino acid sequence of Ole e 7. After optimizing the codon usage for the production in *Pichia pastoris* yeast, the DNA codifying for Ole e 7 was synthesized and used to produce the recombinant protein. Once purified to homogeneity, a comprehensive immunological analysis by ELISA and immunoblotting, and an analysis of the release of allergic mediators in cell-based assays (RBL-2H3 mast cell model and Basophil Activation Tests) using sera and blood of allergic patients' sera.

**Results:** A total of 457 peptides were obtained by *de novo* sequencing. Ten of them allowed the completion of the full-length amino acid sequence of the allergen. After purification, rOle e 7 was obtained with a yield of 1.5 mg/L of cell culture. Immunological assays confirmed that the recombinant isoform of Ole e 7 shared most of the allergenic and antigenic properties of the natural allergen. Moreover, we observed its implication in cross-reactivity with pollen extracts, and plant-derived food extracts.

**Conclusion:** These results suggest that the presence of this isoform in the olive pollen could explain the co-sensitization observed in some allergic patients between Ole e 7 and nsLTPs from food-derived extracts and might be used for a more effective clinical diagnosis of olive pollen sensitized patients.

## 1032 | Identification and immunochemical characterization of aeroallergens from penicillium oxalicum

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**Background:** *Penicillium oxalicum*, one of the prevalent airborne fungi in India, was selected to detect its spores as potential source of allergens and also to identify and characterise its major IgE-reactive component.

**Method:** The airborne spores of *Penicillium oxalicum* was detected by Andersen 2-stage air sampler at different parts of West Bengal. The allergenic potency of *P.oxalicum* was tested by SPT, ELISA and immunoblotting. Total protein was resolved in 1-D and 2-D gel electrophoresis and allergens were identified by 1-D and 2-D immunoblots. Identification of major IgE-reactive protein spots was made by mass spectrometry based MALDI-TOF-TOF. Major allergen was partially purified by ion exchange chromatography.

**Results:** Aerobiological investigation clearly indicated the predominance of *P. oxalicum* spores (56 CFU $m^{-3}$) in the air of West Bengal, India. Sensitivity of patients to spore antigens was highly correlated with rhinitis. In SDS–PAGE, 80 bands were detected with molecular weight range of 16-180 kDa. The allergenic potency of spores was confirmed by skin-prick test, ELISA and dot-blotting. Eleven IgE-reactive proteins were detected as allergens by 1-D and 2-D immunoblots, of which 43% patients were sensitized to 22 kDa allergen. This 22 kDa protein was found to be the major allergen which was further characterized by mass spectrometry based MALDI-TOF-TOF. This major allergen (pI 6.08) was partially purified by ion exchange chromatography.

**Conclusion:** The eleven allergens were identified from spore of *Penicillium oxalicum* fungi for the first time from India. Immuno-proteomic identification of major IgE-reactive protein (22 kDa) may be used for proper diagnosis and immunotherapy of atopic diseases and vaccine designing.

## 1033 | Skin test reactivity to indoor inhalant allergens among children with respiratory allergic diseases

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**Background:** There have been studies demonstrating cross reactivity among protein families with indoor allergens in children with

respiratory allergic diseases. However, there are only few studies evaluating the correlation of skin test responses among indoor allergens in these children.

**Objective:** To evaluate the concordance of skin test response between the pairs of indoor allergens among children with respiratory allergic diseases.

**Method:** This study was a retrospective medical chart review of children aged 2 to 18 years old who presented with symptoms of allergic rhinitis and/or asthma at the Pediatric Allergy Clinic of Thammasat Hospital, Pathumthani, Thailand. The skin prick test results of mites *(Dermatophagoides farinae*, *Dermatophagoides pteronyssinus)*, cockroaches (*Periplaneta Americana*, *Blatella germanica*), cat and dog were collected. The sensitization was defined as≥3 millimeters in wheal diameter. The kappa coefficient (k) was used to analyze the concordance of sensitization for each pair of allergens.

**Results:** A total chart of 300 children were reviewed, of which 187 (62.3%) were male. The mean age was 7.4 ± 3.3 years. 216 (72%) children were diagnosed as allergic rhinitis alone, 13 (4.3%) children as asthma alone, and 71 (23.7%) as both allergic rhinitis and asthma. There were 183 (61%), 140 (46.7%), 45 (15%), 30 (10%) of 300 children who were sensitized to mites, cockroaches, cat and dog, respectively. 126 children had co-sensitization to mites and cockroaches. The concordance of sensitization between mites and cockroaches was moderate agreement, k = 0.53. There were 18/45 (40%) children with cat sensitization had co-sensitization to dog while 18/30 (60%) children with dog sensitization had co-sensitization to cat, k = 0.41. Mite-sensitized children had poor concordance of sensitization to cat and dog, k = 0.1, 0.06, respectively. Also, there were poor concordance between cockroach-sensitized children to both cat and dog sensitization, k = 0.19 and 0.08, respectively.

**Conclusion:** This study showed moderate agreement of skin test response between dust mite and cockroach, dog and cat. This could be due to cross-reactivity or parallel sensitization. Component resolving diagnosis should be considered in children with co-sensitization of these pairs of allergen.

## 1034 | Metabolomics: A new tool to characterize epithelial barrier damage

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**Background:** Airway epithelium (AE) is one of the largest cellular surfaces exposed to the environment. AE constitutes a physical barrier due to the presence of intercellular apical junctional complexes between neighboring cells. In the past years evidence indicates an association between epithelial airway dysfunctionality and allergic asthma. It is still unclear if an impaired epithelial barrier could be the cause of allergy development as opposed to the consequence. One of the most common comorbidities of asthma is house dust mite (HDM) allergy. It has been shown that HDM allergen Der p 1 can disrupt the epithelial airway due to its protease action against cellular apical junction complexes damaging the epithelial monolayer. In the last decade, metabolomics has been successfully employed as a new approach to describe metabolic changes in biological systems. Metabolomics focuses on describing and identifying small molecules to explain complex biological processes. We theorized that metabolomics could be used as a new tool to detect damage of epithelial barrier *in vitro* after Der p 1 exposure.

**Method:** Human cell line Calu-3 cultured at air-liquid interphase (ALI) was used as an *in vitro* model of bronchial epithelium. ALI culture system allows establishing 2 different compartments, mimicking the conditions found in the human airways: a basolateral compartment in which basolateral surface of the cells is in contact with the culture medium, and an apical compartment where the apical cell-surface is exposed to air. After 7 days in ALI, the cells were exposed to either Der p 1 or PBS as a control in the apical side for 24 hours. Then, apical and basolateral media were collected and processed for metabolomics analyses.

**Results:** Metabolic profiles from samples were obtained, these were composed by 248 and 397 features for apical and basolateral media, respectively. Of these, using Mann-Whitney unpaired test as statistical analysis, 108 and 15 features were found changed within the apical and basolateral compartments, respectively. Specifically, in the apical compartment there were 104 signals significantly increased and 4 decreased after Der p 1 exposure; whereas for the basolateral compartment, 11 signals were found to be significantly decreased and 4 increased after exposure.

**Conclusion:** The difference in the amount of metabolite signals suggest that metabolomics can detect difference in the epithelial damage suggesting the application of this technology for other complex cell culture systems.

## 1035 | The microbiome of Dermatophagoides farinae, Dermatophagoides pteronyssinus and Tyrophagus putrescentiae grown in autoclaved medium

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**Background:** Mites are one of the major causes of allergies. It is known that allergen concentration varies depending on the species of mites and the degree of allergy induction is different, but the difference in microbiota according to mite species is not known. In addition to allergen, endotoxin or bacterial DNA, adjuvants of

allergen derived from the microbiota in the mites, are also present in the feces. Bacterial endotoxin is found in gram-negative bacteria, acting on TLR4 and acting as an adjuvant to allergies.

**Method:** Three species of mites (*D. farinae*, *D. pteronyssinus*, and *T. putrescentiae*), known to cause allergies, are cultured in same condition(autoclaved media, 80%RH, 25°C)and analyzed for microbiota of each species. Using the next generation sequencing that complements the existing Sanger sequencing, we analyze the difference of microbiome according to the dust mite species and measure the level of endotoxin.

**Results:** Three species of mites, *D. farinae*, *D. pteronyssinus*, and *T. putrescentiae*, grew under the same conditions had different patterns of microbiota depending on species. The *D. pteronyssinus* grown in the aseptic medium were unusually bacterium-free in contrast to the other two species. The concentration of endotoxin derived from the extract of mites was confirmed and the results corresponded to the distribution of the microbiota.

**Conclusion:** The microbiota of three species of mites grown under the same conditions is different. Endotoxin, derived from microbiota, is an adjuvant of allergens and affects allergic reaction. Endotoxin concentrations were high in *D. farinae* and *T. putrescentiae*, which corresponded to the distribution of microbiota, but endotoxin concentrations were very low in *D. pteronyssinus* with few bacteria.

## 1037 | Validation of air sampling technique for control of Fel d1 levels in cat allergen exposure chamber

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**Background:** Cat allergen can cause a significant allergic response in affected patients. Monitored exposure to cat allergen, Fel d1, can provide a better understanding of patients' allergic responses in a controlled environment. However, controlling the allergen level in the chamber remains challenging. Previous work evaluated the use of fans and blanket shaking as a means to aerosolize the cat dander. It was found that blanket shaking provided more consistent levels of airborne Fel d1 over a period of time. The purpose of this study is to standardize and validate the blanket shaking technique to provide controlled levels of Fel d1 in the chamber for future cat allergen exposure studies.

**Method:** The Natural Exposure Chamber, with a volume of 520 $ft^2$ (14.7 $m^3$), was designed and built to accommodate two neutered cats and 1 to 2 subjects at a time. To quantitate Fel d1 levels, three surface swabs, using glass fiber filters (Milipore), were collected from the chamber walls and floor. Air samples at 4 L/min were collected at four different locations in the chamber using portable air sampling pumps (Gilian 5000) with glass fiber filters. Fel d1 collected on the filters was quantified using ELISA (Indoor Biotechnologies).

**Results:** Two variations of blanket shaking were performed. The first procedure collected dander for cumulative sampling times of 15, 30, 45 and 60 minutes while the second procedure collected four 15-minute samples at 15, 30, 45 and 60 minute time points. In both cases the cats' blanket was shaken for 1 minute every 15 minutes just before sampling start. The average of all the tests performed show stabilized air concentrations of Fel d1 in the cat chamber with 44.12 ± 39.34 ng/$m^3$ in the first procedure and 39.17 ± 24.36 ng/$m^3$ in the second procedure.

**Conclusion:** The obtained results demonstrate controlled levels of Fel d1 in the Exposure Chamber validating the air sampling techniques which will be used for future clinical studies.

## 1038 | Prevalence of skin sensitisation to pollen of salsola oppositifolia in the east coast of Spain

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**Background:** The first aim of this study was to know de prevalence of skin sensitisation to pollen of *Salsola oppositifolia* in patients with pollinosis residing in the area of Cartagena, in the East Coast of Spain. A secondary objective was to describe the different patterns of skin sensitisation to pollen of *Salsola oppositifolia*.

**Method:** Six hundred and thirty five patients (51.8% males and 48.2% females, mean age 30.2 years old, range 3 to 82 years old) were included.

All of them referred respiratory symptoms (Rhinitis, conjunctivitis or bronchial asthma) and had skin prick tests positive with any pollen.

Patients were skin prick tested with a battery of common pollens in our area, including three species of Chenopodiaceae: *Chenopodium album*, *Salsola kali* and *Salsola oppositifolia*.

**Results:** Three hundred and forty tree (54%) patients were sensitised to pollen of any Chenopidaceae species: 255 (40.2%) to *Chenopodium album*, 245 (38.6%) to *Salsola kali* and 220 (34.6%) to *Salsola oppositifolia*.

The prevalence of skin sensitisation to pollen of *Salsola oppositifolia* was 34.6% in the population studied and 64.1% in patients sensitised to Chenopodiaceae pollen.

Patients sensitised to pollen of *Salsola oppositifolia* showed different patterns of skin sensitisation: 139 (63.2%) were sensitized to the three Chenopadiaceae species studied; 41 (18.6%) to two species: 21 (9.5%) to *Salsola kali* and *oppositifolia* and 20 (9.1%) to *Chenopodium album* and *Salsola oppositifolia*; 40 (18.2%) were sensitised only to *Salsola oppositifolia*. 36 (16.4%) out of the last group were also sensitised to olive pollen.

**Conclusion:** 1.- More than half of patients with pollinosis residing in our area were sensitised to pollen of Chenopodiaceae, and more than third to pollen of *Salsola oppositifolia*.

2.- Skin sensitisation to pollen of *Salsola oppositifolia* showed different patterns.

3.- The results suggest cross-reactivity between pollen of *Salsola oppositifolia* and the other species of Chenopodiaceae and olive pollen.

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MOLECULAR PROFILES OF SENSITISATION

## 1040 | Allergic sensitization profile of polysensitized asthmatic patients in Southern China using molecule-based IgE technique

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**Background:** Data of allergic sensitization profile for polysensitized asthmatic patients in China are lacking. This cross-sectional study aimed to analyze the sensitization profiles of polysensitized asthmatic patients in Southern China utilizing molecule-based IgE diagnostic technique.

**Method:** Serum samples from 63 polysensitized asthmatic patients in a tertiary referral centre of Southern China were tested with Immuno ISAC for specific immunoglobulin E (sIgE) against 112 single allergen components.

**Results:** In this group of polysensitized asthmatic patientsin, 79.36% showed sIgE positive to more than three allergen components. Dust mite allergen components rDer f 2 (68.25%), nDer f 1 (66.67%) and nDer p 1 (65.08%) showed the highest positive rates, followed by a *Felis domesticus* allergen component rFel d 1 (26.98%) and a *Canis familiaris* allergen component rCan f 1 (12.70%). Polysensitized asthma patients complicated with rhinitis showed higher positive rates of the allergen components Phl p 4 and nCyn d 1 than patients without rhinitis ($P < 0.05$). Among food allergen components, the walnut allergen component nJug r 2 showed the highest positive rate (9.52%). An optimal scaling analysis indicated that a positive test of rDer p 10 was associated with food allergy.

**Conclusion:** Asthma patients with polysensitization in southern China were mainly sensitized to the dust mite allergen components. Polysensitized asthma patients complicated with rhinitis showed higher positive rates for nPhl p 4 and nCyn d 1 than without. Polysensitized asthma patients with positive test results for rDer p 10 was associated with food allergy.

## 1041 | Determination of the profile of sensitization in patients living in Ukraine using the ImmunoCAP ISAC®

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**Background:** The purpose of this study is to analyze the profile of the sensitization of the Ukrainian population using the ImmunoCAP ISAC® panel.

**Method:** Serum samples of 256 patients (adults and children) living in different regions of Ukraine who during the last two years applied to the Forpost Clinic of Immunology and Allergology with dermatitis, rhinitis or asthma and were tested using the ImmunoCAP ISAC panel®.

**Results:** In patients aged 1- 60 years of age in 80.5% of the cases IgE reactivity was at least to one allergen tested. The majority of patients (more than 2/3) had a complex sensitization profile and reacted on average to more than 5 allergens. The highest frequency of sensitization in Ukraine among patients who turned to the clinic among adults was found Phl p1 (34.1%), Amb a1(33.3%), Fel d1 (33.3%), Bet v1 (30.2%) and children (29.2%, 34.6%, 38.5%, 36.9%), respectively. When analyzing the results of tests for the source of the allergen, most often among house dust mites (HDM) allergens in adults and children is sensitization to Fel d1 (35.9%), as well as to HDM: in adults (Der f2- 15.1% Der p2 –15.1%, Der f1- 12.7%, Der p1-11.9%) and in children (12.3%, 13.1%, 9.2%, 10.8%), respectively. Among fungal allergens the most common is sensitization to Alt a1 and varies from 2.4% in adults to 26.9% in children. Among pollen allergens in adults is sensitization to Phl p1 (34.1%), Amb a1 (33.3%), Bet v1 (30.2%), Cynd1 (23.8%), Art v1 (22.2%), Bet v2 (11.1%) and in children (29.2%, 34.6%, 36.9%, 19.2%, 16.9%, 21.5%), respectively. Tests for food allergens in adults and children are more common on PR-10 proteins. In children, sensitization to milk and egg proteins is more common than in adults.

**Conclusion:** Most patients who came to the clinic have a complex IgE reactivity profile in which pollen sensitization predominates. Among HDM allergens, more than 1/3 of the examined have sensitization to the cat's proteins. Sensitization to mold Alternaria alternata in children occurs 10 times more often than in adults.

## 1042 | Characteristics of sensitization profiles in children with atopy living in Ukraine

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**Background:** This study aimed to identify the most frequently recognized allergen components in children living in Ukraine and were directed to the examination to the clinic "Forpost".

**Method:** Identifying the specific IgE with method ImmunoCAP ISAC were conducted according to the instruction of the manufacture.

**Results:** Total 130 children were examined, aged 1-16 years (median 5 years). 72% children were sensible to two and more components 57.7% - to 5 and more components. The frequency of sensitization to inhalation components was 65.4%, to food

components—33.1%. Among the most frequent inhalation components were Feld 1-39%, Betv1-37%, Amba1-35%, Phlp1-29%, Alta1-27%, the sensitization to house dust mites (HDM) was most often observed to Der p2-13%. However, the analysis of these protein by the level of ISU showed that the highest levels were for Der f1 - median 19 (IQR 9.4-47.0), whereas for Fel d1-6.9 (IQR 2.6-15.0). Among food allergens, sensitization was most commonly observed to PR-10 proteins - 42%. Children sensitized to PR-10 proteins were in most cases sensitized to - Mal d1(28%), Cor a1.0401(27%), Pru p1 (22%).This co-sensitization was accompanied by a high correlation of ISU levels among these components. Sensitization to celery and kiwi was less common, the level of these proteins was also low. The frequency of sensitization to storage proteins was 38%, among which the highest level of ISU was in Ara h6 median 13(IQR 5.9-16.5). Sensitization to LTP proteins was detected in 22% of children, among which the most commonly detected Pru p3 protein was 9.2%. The sensitization to profilins, which was evaluated at the level of Bet v2, was found in 21% of children, but the levels of these proteins were not high. Among the food products of animal origin, the most frequent was sensitization to egg component Gal d2 −13.1%, however, ISU levels were the highest to milk component Bos d4 −9.8 (IQR 1.2-21.0).

**Conclusion:** The most frequent causative inhalation allergens were epidermal allergens and weed pollen, however, the highest level of ISU was to HDM and mould. Among food allergens, the most commonly observed sensitization was to PR-10 proteins.

## 1043 | Allergy from the position of molecular diagnostics in children with allergic diseases

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**Background:** The increase in the prevalence of allergic diseases (AD) is a serious medical and social problem in all countries of the world.

The aim of the research was to evaluate the results of molecular allergodiagnosis in children and to optimize the methods of treatment.

**Method:** Immunological examination was carried out on an automatic analyzer ImmunoCAP 100 (Phadia AB).220 children aged 1 to 17 years were examined, among them boys −130, girls 90. The first group consisted of 151 patients with allergic rhinitis and atopic dermatitis. The second group consisted of 69 patients with bronchial asthma, allergic rhinitis and atopic dermatitis.

**Results:** In our study, an elevated level of total IgE was detected in all patients, an average level of 32, 6±2.3 PAU / I ($P < 0.005$). The average level of total IgE in the 1st group of the examined children was 29.2 ± 2.8 PAU / I, in the second group - 40.1 ± 4.1 PAU / I, the average level of JgE of the blood was significantly higher in the 2nd group of children, in comparison with the 1st group. Hypereosinophilia of peripheral blood was observed in 87 children under study, which was 50% (4.7%). As a result of testing patients with a wide panel of allergens, 98% of the patients had diagnostic levels of antibodies to allergens sIgEd1, 91.2% - to allergens sIgEd2. In 50% of cases, a significant level of antibodies to plantain allergens sIgE w8 was detected, 30.8% to dandelion allergens sIgE w9, 35.7% to evergreen trees sIgE t23, to maple sIgE t11 to 33.3%, to allergens of olive tree sIgE t9 — 40%, to the banana allergens sIgE f92 — 63.6%, to the egg protein sIgE f1 in 24.5%, in 34% to the milk allergens sIgE f2, to the food mixture sIgE f x5 — 37.7%, to allergens of mold fungi mx2 −17.8%. Among the leading household allergens were registered in the 1st group and in the 2nd group of the investigated children - D pteronyssinus (80.3%, 97.8%), and *D. farinae* (86.6%, 97.8%).

**Conclusion:** The average level of specific IgE in the patients of the second group was significantly higher for domestic allergens ($P < 0.05$) and D farinae (86.6%, 97.8%)The average level of specific IgE in patients of the 1st group was significantly higher for fungal, pollen and food allergens ($P < 0.05$). As a result of the analysis of the obtained material, the high significance of diagnosing patients with molecular diagnostics is shown and an algorithm for choosing the tactics of treatment of patients with AD has been developed.

## 1044 | Sensitization to lipid transfer protein and PR-10 in Georgian allergic patients

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**Background:** Panallergen sensitizations are clinical 'warning signs' for elevated risk of multiple allergies as well as severe symptoms. Panallergens comprise a variety of protein families of plant and animal origin and are responsible for wide IgE cross-reactivity between different allergenic sources. The most important panallergens are lipid transfer proteins (LTP), profilins and PR-10 (pathogenesis-related proteins). The aim of this study was to describe the LTP and PR-10 allergen sensitization in Georgian allergic patients.

**Method:** 221 allergy patients were studied by ImmunoCAP-ISAC-112 microarray analysis (Thermo Scientific, Sweden), among them 47 patients with atopic dermatitis, 80 with allergic rhinitis and 51 with asthma. Prevalence of sensitization to LTP and PR-10 was calculated with 95% confidence interval. Associations were assessed by the Fisher's exact test. Values of $P < 0.05$ were considered statistically significant.

**Results:** The prevalence results are expressed in the Table 1.

We have not observed any significant association in allergic rhinitis patients group with any LTP or PR-10 molecules. For atopic dermatitis only rAra h 9 (OR with 95% CI - 10.2 (1.9-54.6) and nJug r 3 (OR with 95% CI - 6.7 (1.6-29.5)) were associated significantly. For asthma, the most important molecules were rBet v 1, rAln g 1, rCor

a 1.0101, rCor a 1.0401, rMal d 1, rPru p 1 and rApi g 1 (*P*-values for OR less than 0.05).

**Conclusion:** Future studies focusing on the evaluation the association of cross-reactive molecules with allergy phenotype should be done.

| LTP | Atopic dermatitis (%) | Allergic Rhinitis (%) | Asthma (%) |
|---|---|---|---|
| rAra h 9 | 10.6(4.6-22.6) | 1.2(0.2-6.7) | 2.0(0.3-10.3) |
| rCor a 8 | 4.3(1.2-14.2) | 1.2(0.2-6.7) | 2.0(0.3-10.3) |
| nJug r 3 | 10.6(4.6-22.6) | 1.2(0.2-6.7) | 2.0(0.3-10.3) |
| rPru p 3 | 10.6(4.6-22.6) | 2.5(0.7-8.6) | 3.9(1.1-13.2) |
| rTri a 14 | 2.1(0.3-11.1) | 0.0 | 2.0(0.3-10.3) |
| nArt v 3 | 4.3(1.2-14.3) | 1.2(0.2-6.7) | 5.9(2.0-15.9) |
| nOle e 7 | 0.0 | 5.0(0.2-12.2) | 3.9(1.0-13.2) |
| rPla a 3 | 6.4(2.2-17.2) | 2.5(0.7-8.6) | 3.9(1.0-13.2) |
| **PR-10** | | | |
| rBetv1 | 14.9(0.7-27.7) | 17.5(10.7-27.3) | 27.5(17.1-40.9) |
| rAlng1 | 4.3(1.2-14.3) | 2.5(6.9-21.5) | 19.6(11.0-32.5) |
| Cora1.01 | 6.4(2.2-17.1) | 15.0(8.8-24.4) | 21.6(12.5-34.6) |
| Cora1.04 | 10.6(4.6-22.6) | 13.8(7.8-23.0) | 21.6(12.5-34.6) |
| rMal d1 | 6.4(2.2-17.1) | 13.8(7.8-23.0) | 23.5(14.0-36.7) |
| rPru p1 | 8.5(3.3-19.9) | 12.5(6.9-21.5) | 21.6(12.5-34.6) |
| rGly m 4 | 4.3 (1.1-14.2) | 3.8 (1.3-10.5) | 3.9 (1.0-13.2) |
| rAra h 8 | 4.3 (1.1-14.2) | 3.8 (1.3-10.5) | 7.8 (3.1-18.5) |
| rAct d 8 | 0.0 | 2.5 (0.7-8.6) | 5.9 (2.0-15.9) |
| rApi g 1 | 2.1 (0.4-11.1) | 1.2 (0.2-6.7) | 7.8 (3.1-18.5) |

## 1045 | Molecular allergy explorer test based on new state-of-the-art multiplex nano-bead technology in Asteraceae-hazelnut association

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**Background:** Pollen-food syndromes and associations are multiple and diverse, with different molecular allergic sensitization profiles.

**Methods:** We report the case of a 28-year-old female patient from Southern Romania with fall seasonal allergic rhinoconjunctivitis, history of two episodes of anaphylaxis to ingestion of hazelnuts and sunflower seeds, and contact angioedema to pot marigold. Molecular allergy diagnosis was performed using a new *in vitro* multiplex allergy explorer test (MacroArray Diagnostics, Vienna, Austria) allowing simultaneous measurement of serum specific IgE against a plethora of allergen extracts and molecular allergens, based on nano-bead technology, with immunoassay protocol integrating powerful cross-reactive carbohydrate determinants inhibitor during serum incubation and results quantification based on colorimetric image acquisition.

**Results:** Molecular serum biomarkers for genuine sensitization to *Asteraceae* weed pollen were detected as specific IgE to ragweed pectate lyase Amb a 1 (46.37 $kU_A/L$) and mugwort defensin Art v 1 (28.34 $kU_A/L$). No sensitizations were found to other region relevant pollen-specific molecular allergens from weeds (Pla l 1), grasses (Phl p 1, Phl p 5.0101), trees (Bet v 1, Cor a 1.0103, Fra e 1, Pla a 1) or to cross-reactive polcalcins and profilins (Phl p 7, Phl p 12, Bet v 2). High serum specific IgE levels to non-specific lipid transfer protein (nsLTP) molecules were measured: hazelnut Cor a 8 (1.1 $kU_A/L$) and mugwort pollen Art v 3 (27.07 $kU_A/L$), a similar LTP being also present in sunflower seeds (Hel a 3). Specific IgE to ragweed pollen Amb a 4 was detected (1.75 $kU_A/L$), this Art v 1-like defensin being homologous with sunflower Hel a 4 defensin. Amb a 1-like Hel a 6 present in sunflower pollen must be mentioned, because pollen contamination of sunflower seeds was not excluded. No sensitization was found to hazelnut storage proteins: 11S globulin Cor a 9, 7/8S globulin Cor a 11 and 2S albumin Cor a 14. In addition, positive skin prick tests to commercial extracts of hazelnuts (3 mm diameter wheal), *Helianthus annuus* pollen (8 mm diameter wheal), and *Calendula officinalis* flores pulvis suspension (4 mm wheal) are relevant.

**Conclusion:** We propose the use of a new allergy term, *Asteraceae*-hazelnut association, to describe the cross-reactive nsLTP IgE-mediated *Asteraceae* weed pollinosis-associated hazelnut food allergy, and we suggest that multiplex allergy explorer test assesses its molecular diagnosis.

## 1046 | Study profiles of sensitization to panallergens of food allergy in extremadura

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**Background:** We conducted a multicentre, follow-up study at a specialized Allergy section including patients with suspected food allergy from Coria Hospital (CoH), Plasencia Hospital (PH) and Caceres Hospital (CH) into Caceres province.

**Objectives:** Our study aimed to classify different profiles of sensitization of food allergy (FA) based on IgE sensitization to panallergens.

**Method:** We examined Spanish patients adults and children with food allergy symptoms and/or seasonal allergic rhinoconjunctivitis and/or asthma. Foods triggering allergic symptoms were acquired by questionnaire. Patients included were classified into three groups: mild, severe and no reactors based on clinical history. IgE to

panallergens Phpl p12 or Bet v2 (profilin), Bet v1 (PR-10) and Pru p3 (nsLTP) were tested by immuno CAP.

**Results:** We identified different profiles linked to panallergens IgE sensitization: 1- mono-panallergens FA: sensitization to either profilin or nsLTP, or PR-10. 2- cosensitization to two panallergens: profilin and nsLTP, or profilin and PR-10. 3- cosensitization to three panallergens (multipanallergens FA): profilin, nsLTP and PR-10.

The most frequent was profilin monopanallergen profile: PH >80%, CoH >70%, CH >60%. The group of patients with severe reactions to foods (oral allergy syndrome plus systemic symptoms, or uvula edema, or life threatening reactions) were most frequent in CoH (40%). Relevant differences were observed in this group, the most important profile was monopanallergens: profilin (>50% CoH, >70% PH and >30% CH), nsLTP was less important, and PR-10 was infrequent. The second profile, cosensitization to two panallergens: profilin+nsLTP was observed in CoH and CH (<20%) while the third one, multipanallergen FA only was found in PH.

**Conclusion:** Patients in Caceres province present a phenotype of food allergy profilin mediated.. Monopanallergen FA profile reported severe reactions more frequently, but differences were observed, while profilin was more important in PH and CoH, both located in north of the province, in CH (located in the south) profilin and also LTP were observed. Multipanallergen FA only was found in PH. This classification may be useful for diagnostic and therapeutic purposes in the clinical practice.

## 1047 | Evaluation of LTP's sensitization patterns according to component resolved diagnosis and protein alignment tools

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**Background:** LTP's are the main elicitors of food allergy in Spanish Mediterranean shore and there is a high cross-reactivity among them. However, there is not a systematic approach to provide dietary recommendations to patients.

**Objective:** To evaluate the LTP's sensitization patterns by the application of component resolved diagnosis (CRD) tests and protein alignment tools (BLAST).

**Method:** 210 patients (both gender, older than 14 y.) attended at Allergy Department were included. CRD was performed by ImmunoCAP© ISAC 112 (Phadia AB, Uppsala, Suecia). Results>0.35 ISU to LTP's were considered positive. The protein sequence alignment were performed by BLAST system. Cross-reactivity was considered when the homology rate≥75%. The Pearson rank order correlation and determination coefficient ($R^2$) were used to measure the strength of the relationship between component-specific IgE ISU levels.

**Results:** Four LTP's profiles were identified according the higher level of sensitization to a specific LTP component (CRD): peach profile (PP): (Pru p 3 > Jug r 3 > Ara h 9 > Cor a 8) in 46% of patients, walnut profile (WP): (Jug r 3 > Pru p 3 > Ara h 9 > Cor a 8) in 37.22%, peanut profile (PeP): (Ara h 9 > Pru p3 > Jug r 3 > Cor a 8) in 5.11% and hazelnut profile (HP): (Cor a 8 > Pru p 3 > Jug r 3 > Ara h 9) in 2.91%. The results obtained by BLAST analysis showed a high correlation with CRD, with little differences for PP (Ara h 9 > Jug r3), WP (Ara h 9 > Pru p 3), PeP (Jug r 3 > Pru p 3) and HP (Jug r 3 > Ara h 9 > Pru p 3). Cor a 8 was the component showing lower cross-reactivity in PP, WP and PeP. In HP patients, Ara h 9 was the component eliciting lower cross-reactivity by CRD and BLAST and Pru p 3 showed the lowest correlation coefficient.

**Conclusion:** The four LTP sensitization patterns showed a high degree of concordance when analyzing the cross-reactivity by the two methods: CRD and BLAST. In patients with PP, WP and PeP patterns should be subsidiary to challenge with hazelnut, while those with HP pattern should be challenged with peanut and/or peach. This new approach aims to avoid unnecessary dietary restrictions. The safety of this procedure should be evaluated by a DBPC clinical trial.

## 1048 | Molecular allergy diagnosis approach in a patient with kiwifruit anaphylaxis

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**Background:** The fuzzy/green kiwifruit (*Actinidia deliciosa*), widely grown commercially, contains various pulp allergenic molecules, including the major allergen cysteine protease actinidin.

*Methods*. This case report is about a 40-year-old male patient with house dust mite allergic persistent rhinitis and intermittent asthma, presenting a convincing history of anaphylaxis immediately after eating a kiwifruit on empty stomach, followed, a few months later, by a severe oral allergy syndrome after licking a slice of raw kiwi. Previously, the patient ate kiwi without any problems and had no manifestations of pollen or latex allergy. Skin prick testing was done with commercial allergen extracts, while prick-prick testing was performed with raw kiwifruit, avocado and banana. Molecular approach consisted in assessment of serum specific IgE to native extracts and molecular allergen components using patient-friendly allergen nanobead array multiplex test and singleplex capsule-enclosed activated cellulose solid phase fluorescence enzyme immunoassay.

*Results*. Regarding kiwifruit allergy, the patient presented positive prick-prick tests with raw edible kiwifruit components: outer pericarp and inner pericarp (each 15 mm wheal) and columella/core (19 mm wheal) and negative with kiwifruit whole seeds, avocado and banana, and pollen extracts. Serum specific IgE to kiwifruit were detected

(0.5 kU/L), but specific IgE values were negative (≤0.01 FIU/mL) for actinidin Act d 1, thaumatin Act d 2, kiwellin Act d 5, nsLTP type 1 Act d 10, Bet v 1-like major latex/ripening-related protein Act c 11, Act c chitinase_IV, Act d 9 cross-reactive profilins Bet v 2 (birch pollen profilin) and Hev b 8 (latex profilin), and also negative (<0.1 kU/L) for PR- 10 rAct d 8. Moreover, specific IgE to avocado were nor found (≤0,01 FIU/mL). Although IgE against seed proteins cupin/11S globulin Act d 12 and 2S albumin Act d 13 were not determined, this was not considered of great importance since allergic symptoms were also induced by licking kiwi pulp, in which abundantly expressed actinidin enzymatically degrades seed storage proteins, and prick-prick test was negative to kiwifruit seeds.

*Conclusion*: In a patient with anaphylaxis to kiwifruit, positive skin tests to its pulp and detectable serum specific IgE to *Actinidia deliciosa*, a detailed molecular allergy diagnosis is necessary, including assessment for Act d 3 glycoallergen or other molecules, not performed in this patient.

## 1049 | Is PR-10 sensitization a Portuguese phenomenon as well?

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**Background:** Bet v 1, a major allergen found in birch pollen, belongs to the PR-10 protein group. In our practice, some Bet v 1 sensitized patients have been identified, residing in areas without this tree genus in its flora.

Our aim was to characterize a Portuguese patient population with PR10 sensitization.

**Method:** A group of patients in whom ImmunoCap ISAC® (ISAC) study was performed, between January 2009 and June 2017, were analyzed. All subjects with one or more PR-10 sensitizations were selected, and their clinical records reviewed. A sequential sample of the last subjects (n = 80) who underwent ISAC study, was then used for comparison.

**Results:** Out of 234 ISAC studies performed, only 16 were positive for PR-10 protein group. Median age was 18.3 years, 68% (n = 11) were male. PR-10 sensitized individuals were more likely to live in Portalegre district compared to the control group (7/16 vs 1/80; $P < 0.001$). 15 patients were positive for PR-10 family pollens (93.7%), frequently Bet v 1 (n = 13), followed by Aln g 1 (n = 10) and Cor a 1 (n = 8). 14 out of the 16 patients were sensitized to PR-10 foods, mostly Cor a 1.0401 (n = 13) and Mal d 1 (n = 12). Skin prick tests revealed birch as the main sensitizing pollen as well (14/16). Moreover, only four patients were skin prick tested for *Fagaceae* trees which were positive for oak (4), chestnut tree (3) and cork tree (1). All patients were co-sensitized to other pollens, namely grass and all had respiratory allergy. Nine patients were food allergic, although seven of them were co-sensitized to other cross reactive (LTP/profilin) or species specific proteins.

**Conclusion:** Although PR-10 sensitization is known to be rare in our population, mostly Alto Alentejo inhabitants showed sensitization to this protein family in our sample, either by in vitro and/or in vivo methods. This phenomenon is consistent with the native plant species of this region, which should be taken into account when studying the allergic profile of these patients. In our sample, all PR-10 sensitized patients had respiratory allergy while this protein didn't seem to be relevant when it comes to food allergy. Further studies are needed to characterize which plant species belonging to this protein family are more significant for our country's aerobiology context and to determine its clinical relevance.

## 1050 | Artemisia pollen allergy in China: Component resolved diagnosis reveals asthma patients have significant multiple allergen sensitization

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**Background:** *Artemisia* pollen allergy is a major cause of asthma in Northern China. Possible associations between sIgE responses to *Artemisia* allergen components and clinical phenotypes have not yet been evaluated.

**Method:** Two hundred and forty *Artemisia* pollen allergic patients, 178 from Shanxi and 30 from Shandong Provinces in Northern China, and 32 from Yunnan Province in Southwestern China, were included. Allergic asthma, rhinitis, conjunctivitis and eczema allergic symptoms were diagnosed. All patients were tested by ImmunoCAP with mugwort pollen extract and the natural components nArt v 1, nArt ar 2, nArt v 3, and nArt an 7.

**Results:** The positive frequency and sIgE levels of the four components in the *Artemisia* allergic patients from Southwestern China were significantly lower than that from the north. Art v 1 and Art an 7 were the highest recognized allergens, followed by Art v 3 and Art ar 2. Patients from Northern China were more likely to have

asthma (50%) than patients from Southwestern China (3%), and being sensitized to more than two allergens increased the risk of asthma. Sensitization to Art v 1, Art v 3 and Art an 7 played a significant role in the development of asthma.

**Conclusion:** Component-resolved diagnosis of Chinese *Artemisia* pollen allergic patients is helpful to assess the potential risk of asthma.

## 1051 | Clinical and molecular correlations in ragweed pollen allergy

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**Background:** Ragweed is an invasive species in Europe and worldwide. Ragweed pollen has a high potential for eliciting allergic reactions, in late summer and fall. Sensitization rates in atopic patients range from 47% in France to 70% in Northern Italy. In Western Romania, ragweed allergy accounts for 40% of the monosensitized and 60% of the polysensitized patients (2008-2014 data, PREVALERG project).

**Method:** A number of 97 participants matching inclusion criteria were prospectively enlisted in an observational cross-sectional study. They were clinically evaluated and skin prick test (SPT) to a standard panel of 18 inhaled allergens was performed. A current symptoms score (CSS) was calculated and the subjects were asked to grade the allergy impact on quality of life from 1 (lowest) to 10 (highest). Serum specific IgE (sIgE) to 176 allergens was determined by ImmunoCAP ISAC microarray.

**Results:** Among the 97 subjects, positive SPT to ragweed pollen extract (RPE) was recorded in 84 cases, the other 13 registered as controls. Increased ragweed sIgE were determined in 73 cases. One individual displayed no SPT reactivity to RPE, with low Amb a 1 sIgE (class 1) and no allergy symptoms, while 10 subjects were positive for RPE sensitization, with negative sIgE. Clinical manifestations of allergy included asthma (23 cases) and rhinoconjunctivitis (total of 87, including 84 ragweed allergy cases and 3 house dust mite allergy cases).

**A comprehensive correlation analysis revealed::** - weak correlation between the overall self-assessed impact of disease and CSS (Spearman's rho=0.25, $P = 0.0317$) and moderate correlation between the current self-assessed impact of disease and CSS (rho=0.584, $P < 0.0001$)

- weak correlation: severity, duration of allergy vs total SPT score (rho =0.25, $P = 0.0224$)

**- weak correlation: RPE SPT score vs total SPT score (rho=0.325, $P = 0.0025$):** - moderate correlation: Amb a 1 sIgE level (ISAC class) vs total ISAC class sum (rho=0.510, $P < 0.0001$).

**Conclusion:** A small but significant part of the population react to ragweed pollen extract and are not identified as disease-positive by standard sIgE tests. There is a need for targeted tests towards a larger spectrum of allergen molecules.

In ragweed allergic individuals, this allergy can be the main cause of overall sIgE levels and also of in vivo reactions (tested by SPT).

## 1052 | Molecular profile of pollen sensitization of Tashkent residents with respiratory allergy

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**Background:** Advances in molecular allergology have allowed to determine the specific IgE to trigger molecules of allergy development and to characterize the sensitization profile of a particular patient.

Purpose: conduct a study on the molecular profile of sensitization of Tashkent residents.

**Method:** We present the pilot examination of 42 patients with respiratory allergy (25 men and 17 women, average age of 30 ± 1.3). The examination results were analyzed in the general group, as well as separately for diseases: allergic rhinitis (20 people) and / or bronchial asthma (22 people). Sera were tested for specific IgE to 112 molecules of allergens by using microchip (ISAC, Thermo Fisher Scientific).

**Results:** ISAC results showed that patients with respiratory allergy have a wide profile of allergen-specific IgE sensitization, as their reaction to 51 out of 112 components was positive. Clinically significant sensitization to one pollen component was detected in 4.7% of the patients; to two allergens—in 16.6%, to three—in 14.3%. Positive values of polysensitization to 5-10 components were detected in 33% of the patients. More than 28% of the patients had a positive response to 11-17 components. The maximum number of detected allergenic molecules amounted to 17.

**Conclusion:** Molecular diagnostics of allergy is viable both for identifying the genuine sensitization and for the correct selection of SIT (specific immunotherapy) and efficiency forecast thereof. Identifying the cross-reactions to allergens of the same protein family predetermines the launch of development of sensitization to an additional source. Studying the molecular profile of sensitization at the preclinical stage enables to develop personalized programs to prevent the progression of the allergic process.

## 1053 | Comparison of sIgE levels to mite extracts and allergen components between asthmatic and non-asthmatic house dust mite allergic patients

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**Background:** In paediatric cohorts, a correlation between specific IgE (sIgE) levels to house dust mite extract or allergen components and the occurrence of asthma has been shown. Higher levels of sIgE to mite extract were associated with a higher risk of wheezing. Moreover, asthmatic children recognized more allergens and had higher sIgE levels to nDer p 1 as well as rDer p 2, 5 and 23. We sought to investigate potential differences in sIgE levels or sensitization patterns between asthmatic and non-asthmatic patients in a mixed paediatric and adult house dust mite allergic cohort.

**Method:** Total IgE and specific IgE against house dust mite extracts (Dermatophagoides pteronyssinus and farinae) and allergen components (rDer p 1, 2, 10, and 23) were determined in 190 house dust mite allergic patients. 35 patients had diagnosed asthma ("asthmatic", 54% females, mean age 27 ± 15 years, 31% younger than 18 years), whereas 155 had rhinitis (and conjunctivitis) without respiratory symptoms ("non-asthmatic", 54% females, mean age 28 ± 15 years, 29% younger than 18 years).

**Results:** Total IgE levels were markedly higher in asthmatic compared to non-asthmatic patients (315 vs. 144 kU/L, $P = 0.022$). Positivity to rDer p 1 (71 vs. 52%, $P = 0.039$) as well as rDer p 10 (9 vs. 1%, $P = 0.044$) differed between both groups. Specific IgE levels to house dust mite extracts and allergen components (rDer p 1, 2, 10, and 23) and positivity to rDer p 2 and 23 did not differ between both groups.

**Conclusion:** In contrast to previously published data, sIgE levels to house dust mite extracts or allergen components were not statistically different between asthmatic and non-asthmatic patients in our mixed paediatric and adult house dust mite allergic cohort. Only higher total IgE levels and a higher reactivity to rDer p 1 and 10 were found in asthmatic patients. However, larger studies are needed to confirm clinical relevance of these findings.

## 1054 | Analysis of sensitization to cat and dog allergen components

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**Background:** Component resolved allergen diagnosis allows for a precise evaluation of the sensitization profiles of patients sensitized to felines and canines. An accurate interpretation of these results allows better insight into the evolution of a given patients sensitizations, and allows for a more precise evaluation of their prognoses.

**Method:** 70 patients (42 female and 28 male), 18-65, 35.5) with a positive feline or canine allergy diagnosis were included in the research group. 30 patients with a negative allergy diagnosis were included in the control group. The allergen-specific IgE to feline and canine allergen extracts and to canine (Can f 1, Can f 2, Can f 3, Can f 5) and feline (Fel d 1, Fel d 2, Fel d 4) allergen components were measured with ImmunoCap method.

**Results:** 30% of patients were monosensitized to only one canine or feline allergen component. The main feline allergen was Fel d 1, which sensitized as many as 93.9% of patients sensitized to felines. Among 65 patients sensitized to at least one feline component, for 30 patients (46.2%) the only sensitizing feline component was Fel d 1. Only 19 patients in that group (63.3%) were not simultaneously sensitized to dogs. In 11 (36.7%) cases the isolated sensitization to feline Fel d 1 did not exclude concurrent sensitizations to one of the canine allergen components. Fel d 4 sensitized 49.2% of the research group. 64.3% of patients sensitized to canine components had heightened levels of specific IgE to Can f 1. Monosensitization in that group occurred for 32.1% of the patients. Sensitization to Can f 5 was observed among 52.4% of the patients.

**Conclusion:** Concurrent sensitizations to a few allergic components, not only cross-reactive but also originating in different protein families, are a significant problem for patients sensitized to animals.

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ASPECTS OF URTICARIA

## 1055 | Adherence to treatment guidelines for chronic spontaneous urticaria is poor: 1-year findings of the multicentre observational aware study

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**Background:** Chronic urticaria (CU) is defined by recurring hives and/or angioedema for ≥6 weeks; either linked to specific triggers, in inducible urticaria, or not, in spontaneous urticaria (CSU). AWARE is a global study of CU in the real-world setting. Here, we report on physician treatment patterns for pts with CSU in Germany and compare them with current international guidelines.

**Method:** Adults with $H_1$-antihistamine (AH)-refractory CU for ≥2 mths were included. Physician treatment patterns were assessed in relation to pts' disease control (Urticaria Control Test [UCT]), symptoms, and QoL (dermatology life quality index [DLQI]; CU-related QoL questionnaire [CU-$Q_2$oL]; angioedema-related QoL questionnaire [AE-QoL]).

**Results:** Prior treatments reported at Baseline (BSL) included: 17.3% of pts were receiving 1 or more second-generation $H_1$-AH at approved dose (recommended first-line), 23.9% were receiving them at increased dose (second-line); 8.5% were receiving omalizumab (third-line); 29.9% had no treatment. The majority of pts (78.2%) had uncontrolled CSU (UCT<12) at BSL (Table). Treatment changes were most evident at the BSL visit, with an increase in pts receiving omalizumab (21.4%) and a decrease in those receiving no treatment (12.8%) vs. prior therapy. These changes were associated with improvements in rates of hives and/or angioedema, UCT and QoL scores at Month 3, but only modest improvements thereafter (Table). A sub-analysis of 528 pts with UCT<12 and who were receiving the approved (36.9%) or increased dose $H_1$-AH (63.1%), revealed that few pts had recommended escalation from the approved to increased dose $H_1$-AH (0.0-6.7%) or from increased dose $H_1$-AH to omalizumab (0.0-11.1%) (Table).

**Conclusion:** Poor physician adherence to guidelines was evident throughout AWARE. Initial improvements in disease activity and QoL plateaued after Month 3, possibly owing to fewer changes to recommended therapies. Greater physician adherence to guidelines is needed for better symptom control in pts with uncontrolled CSU.

| Category | Baseline | Month 3 | Month 6 | Month 9 | Month 12 |
|---|---|---|---|---|---|
| Patients with uncontrolled urticaria (UCT <12), % (n/N)[a] | 78.2 (1188/1520) | 60.0 (921/1534) | 52.2 (802/1537) | 51.7 (796/1539) | 48.9 (753/1541) |
| Hives, % (n/N)[a,b] | 91.1 (1407/1545) | 71.4 (855/1197) | 66.2 (859/1298) | 65.0 (853/1313) | 60.3 (800/1326) |
| Angioedema, % (n/N)[a,b] | 43.9 (678/1544) | 23.3 (277/1191) | 20.0 (260/1298) | 18.9 (248/1313) | 16.6 (220/1325) |
| DLQI, mean±SD[a] | 8.3 ± 6.9 | 5.9 ± 6.1 | 5.3 ± 5.9 | 5.1 ± 5.9 | 4.9 ± 5.8 |
| CU-$Q_2$oL, mean±SD[a] | 36.5 ± 20.0 | 28.6 ± 19.3 | 26.6 ± 19.3 | 25.8 ± 19.5 | 24.9 ± 19.6 |
| AE-QoL, mean±SD[a] | 42.8 ± 22.9 | 38.3 ± 22.8 | 36.8 ± 22.5 | 35.7 ± 22.7 | 33.3 ± 22.5 |
| Treatment escalation from the approved dose to increased dose $H_1$-AH in patients with UCT<12,% (n/M)[c] | 5.6 (11/195) | 1.6 (2/124) | 0.0 (0/90) | 6.7 (5/75) | 0.0 (0/109) |
| Treatment escalation from increased dose $H_1$-AH to omalizumab in patients with UCT<12,% (n/M)[c] | 11.1 (37/333) | 1.1 (2/187) | 1.5 (2/132) | 1.9 (2/106) | 0.0 (0/66) |

[a]Data were analyzed in the full analysis set using last observation carried forward. [b]The time period for which symptoms were reported at Baseline differed from that of subsequent visits (6 months vs. 12 weeks); [c]Data are reported as observed

AE-QoL, angioedema-related QoL questionnaire; CU-$Q_2$oL, chronic urticaria-related QoL questionnaire; DLQI, dermatology life quality index; $H_1$-AH, $H_1$-antihistamine; M, number of patients with UCT<12 at each visit; N, number of evaluable patients; SD, standard deviation; UCT, urticaria control test

## 1056 | Clinical features and autoimmunity in patients with dermographic urticaria

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**Background:** Dermographic urticaria (DU) or symptomatic dermographism is the most common form of chronic induced urticaria (CIndU), with a prevalence of up to 5% of the general population. DU is characterized by pruritic hives that occurs in response to friction, about 10 minutes after that, it disappears within 1 to 2 hours of the stimulus. The underlying cause is not known. Antihistamines are the most effective symptomatic treatment option to control the disease. Symptomatic dermographism may be related to autoimmunity in many cases. Our aims were to assess the clinical characteristics and the presence of autoimmunity in patients with dermographic urticaria.

**Method:** This was a retrospective study of electronic medical records of patients with DU, attended at a tertiary hospital. Time of disease, association with chronic spontaneous urticaria (CSU), type of treatment, and frequency of autoimmune disease and/or autoantibodies were assessed.

**Results:** We assessed 97 patients with DU in a follow-up period of more than 6 months. Eighty-one patients (83.5%) were female, with a mean age of 46.8 years and a time of disease of 8.5 years. The association with CSU was observed in 22.7% of the patients, autoantibodies was observed in 36.5% of them, and the autoimmune disease was present in 12 patients (12.4%) of the patients. In regard to the association DU and CSU (22 patients), autoimmunity was observed in 3 patients (13.6%), and autoantibodies, in 8 (36.4%) of them. The majority of the patients had good response to antihistamine (AH): 74.2% of them responded to second generation AH alone, and 51% of the patients needed first generation AH added or not to the second generation AH. Some patients (6%) had used prolonged oral corticosteroids therapy to control their symptoms, previously.

**Conclusion:** DU was associated with CSU in almost a quarter of the patients. The prevalence of autoimmunity and/or autoantibodies was high, regardless of the association between DU and CSU. This study observed that the majority of the patients with demographic urticaria had good response to AH for symptom control.

## 1057 | Molecular genetic mechanisms of urticaria

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**Background:** Urticaria is a common skin condition with pruritic raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. It affects about 20% of people at some time during their lives. Urticaria is a complex disease with pathogenesis involving allergic inflammation, skin lesions and hyperreactivity to environmental triggers. Cytokines play crucial role in all stages of allergy and inflammation development and maintaining; loss-of-function mutations in filaggrin (FLG) gene coding for the major component of the stratum corneum lead to epidermal barrier abnormality; Toll-like receptors (TLR) play a crucial role in innate immunity. Therefore we analyzed common changes in genes of filaggrin (c.2282del4, p.R501X), cytokines (rs2243250 of IL4, rs20541 of IL13, rs1800872 of IL10, rs1800629 of TNFA) and toll-like receptors (rs5743571 of TLR1, rs5743794 of TLR6, rs11466617 of TLR10) in urticaria patients and healthy individuals from Volga-Ural region of Russia.

**Method:** The patients group includes 103 individuals of different ethnic origin (Russians, Tatars, Bashkirs and individuals of mixed origin). The control group consists of 106 healthy donors without atopic diseases of respective ethnic background. Genotyping was performed by PCR-RFLP.

**Results:** We revealed that in Russians urticaria is associated with rs20541*Arg/Gln genotype of the IL13 gene ($P = 0.02$) and rs5743794*CC genotype of TLR6 ($P = 0.0011$) gene polymorphism. In Tatars the association with disease development was shown for rs5743571*TT genotype of TLR1 gene SNP ($P = 0.0054$). The rs5743794*C allele of TLR6 gene polymorphism is associated with acute and chronic forms of urticaria ($P = 0.0209$ and $P = 0.0063$, respectively) and rs2243250*C allele of IL4 gene polymorphism - with acute urticaria ($P = 0.0247$). The study of FLG gene mutations revealed two individuals (1.9%) with urticaria (one with acute and one with chronic from) in patients group who have c.2282del4 deletion. The allelic frequency of this mutation is 0.96% in patients and 2.12% in healthy donors. Three patients (2.9%) with urticaria (two with acute form and one—with chronic) are heterozygous for the p.R501X mutation. The allelic frequency of the mutation in patients is 1.4% while in controls it is 0.53%. However all shown differences are not of statistical significance.

**Conclusion:** Thus, we found an association of urticaria with rs2243250 of the IL4, rs20541 of the IL13, rs5743571 of the TLR1 and rs5743794 of the TLR6 gene polymorphisms.

## 1058 | Chronic spontaneous urticaria and thyroid autoimmune disease: A follow up study of patients with chronic urticaria for 17 years

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**Background:** Approximately 40% of patients with chronic spontaneous urticaria (CSU) have a concomitant autoimmune disease, and thyroid autoimmune disease was the most frequent of those diseases. In addition, CSU is associated with the presence of IgG anti-IgE or IgG anti-high affinity receptor for IgE in about 50% of patients. The aim of this study was to evaluate the frequency of autoimmune thyroid disease (ATD) and/or anti-thyroid autoantibodies patients with chronic spontaneous urticaria during a period of 17 years.

**Method:** Retrospective study of the electronic medical record of adults patients with CSU followed up in an Urticaria Outpatient Clinic at a tertiary center in the Clinical Immunology and Allergy Division, University of Sao Paulo, Brazil, between 2000 and 2017. Patients were assessed for the presence of ATD or autoantibodies concomitant to CSU and if CSU diagnosis preceded or followed the ATD diagnosis.

**Results:** This study assessed 988 patients with CSU. ATD and/or anti-thyroid autoantibodies were present in 101 patients (10.2%). Of these, 89.1% were female, the mean age was 53 years and the mean time of CSU was 13 years. Of the 101 patients, 48 (47.5%) had ATDs, the most prevalent being hypothyroidism. Anti-thyroid autoantibodies without ATD were present in 53 patients (52.4%). CSU preceded (mean time of 7.3 years) the diagnosis of ATD in 19 patients (39.5%) and CSU developed after

ATD diagnosis (mean time of 3.7 years) in 18 patients (37.5%). CSU concomitant to ATD was diagnosed in 11 patients (22.9%).

**Conclusion:** The link between CSU and ATD isn't yet fully understood, however, several studies showed a high prevalence of this association. In this study, the association between CSU and ATD and/or autoantibodies was observed in 10.2% of the patients over a 17-year period.

Correction added on 31 October 2018, after first online publication: the author sequence has been changed. The correct order is as follows: Mouco C. C., Zanadrea A., Brugnolli R.M., Kalil J., Motta A. A., Agondi R. C.

## 1059 | Identification of anti-TPO IgE and other causes of skin exacerbation in patients with CSU

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**Background:** Patients with chronic spontaneous urticaria (CSU) have periods of clinical control and skin exacerbation. Although patients frequently recognize different events or substances as triggers of their skin symptoms, there are few studies evaluating in a controlled way the clinical impact of these triggers. IgE autoantibodies against thyroid-peroxidase (TPO) have been demonstrated in a group of CSU patients in higher frequency than healthy subjects. However, if these IgE autoantibodies can trigger urticaria it's still a matter of study. The aim of this study was to evaluate the role of anti-TPO IgE and triggers most frequently reported by patients as causes of skin exacerbations in CSU.

**Method:** 100 CSU patients from the URTICA cohort (ClinicalTtrials.gov number: NCT01940393) participated in the study. A questionnaire was carried out evaluating the triggers identified by the patients, the comorbidities and the treatments received. Patients with a self-report of skin exacerbation by foods, nonsteroidal anti-inflammatory drug (NSAID) or physical triggers were subjected to a controlled provocation test with the suspect food, medication or physical stimuli report by the patient. the levels of anti-TPO IgE were measured during a period of clinical control and during two exacerbations in all patients.

**Results:** 30% of the patients had at less one inducible urticaria demonstrated by provocation tests (24% dermographism, 10% cold, 8% pressure). Self-reported exacerbation for a food (60%) or medication (30%) were high, but positive provocation tests were low (1% and 14% respectively). 30 patients had (+) anti-TPO IgE during the baseline period. Among them, 60% presented a significant elevation of anti-TPO IgE during at less one of the two exacerbations. 18.5% of patients (n = 13) with (–) anti-TPO IgE, presented elevation of anti-TPO IgE one of the two exacerbations.

**Conclusion:** Foods, drugs and physical triggers must be verified by challenge tests to avoid unnecessary lifestyle restrictions in patients with CSU, nevertheless self-report is usually greater than positive provocation tests. Increase concentrations of Anti-TPO IgE seems to be implicated in urticaria exacerbations in some patients with CSU.

## 1060 | Does leptin play a role in the pathogenesis of chronic spontaneous urticaria?

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**Background:** Chronic spontaneous urticaria is an interdisciplinary problem with unknown pathogenesis. Overweight and metabolic disturbances are supposed to be more frequent in chronic spontaneous urticaria patients. It is well proved that fatty tissue is the source of

adipokines. The aim of the study was to evaluate the possible contribution of leptin to chronic spontaneous urticaria pathophysiology.

**Method:** The study included 48 chronic spontaneous urticaria patients and 41 healthy subjects. The leptin level in both examined groups was measured.

**Results:** No statistically significant difference in leptin level was determined between the studied subgroups.

**Conclusion:** We are among the first to present the effects of exploration aimed at assessment of the possible role of adipokines in chronic spontaneous urticaria pathogenesis. In this study we did not prove any difference in leptin level. In our opinion it is valuable to perform further studies in this area.

## 1061 | The role of lesional skin biopsy in the diagnosis of chronic urticaria

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**Background:** Skin biopsy plays an important role in the diagnosis of many skin diseases, mainly neoplastic lesions, bullous and inflammatory diseases. But it is not a routine diagnostic test recommended for the investigation of urticaria etiology.

**Method:** The records of the patients who applied to the Immunology and Allergy Polyclinic and underwent skin biopsy because of chronic urticaria between January 2013 and September 2015 were reviewed retrospectively.

**Results:** The forty patients (16 men and 24 women, aged 19 to 74 years) with chronic urticaria were applied skin punch biopsy. These patients did not benefit from high-dose antihistamine and steroid therapy. The lesions of the patients generally lasted longer than 24 hours, and sometimes pain, burning, and hyperpigmentation accompanied to the itching. Laboratory tests revealed 3 patients with ANA, 2 patients with ANA and AntidsDNA, and 1 patient with ANA and MPO ANCA positivity. Histopathological and immunofluorescence (IF) examination of the punch biopsies revealed findings of urticarial vasculitis in 6 patients (IF examination revealed C3 and fibrinogen accumulation in the walls of vessels in the upper dermis and / or in the basal layer of the epidermis). Only one of these patients had ANA and AntidsDNA positivity. Unidentified non-specific findings were detected in 14 of the biopsied patients. In the remaining 20 patients, pathologic findings that were not specific but consistent with chronic urticaria (minimal superficial perivascular dermatitis (lymphocyte predominant), increased fibroblastic activity in the upper and middle dermis).

**Conclusion:** According to the skin biopsy results, pathologic urticarial vasculitis was detected in only 6 patients. Therefore, skin biopsy should be performed when clinical history, physical examination and laboratory results of the patients were suspicious in terms of urticarial vasculitis.

**Key words:** Urticaria, skin, biopsy, vasculitis.

## 1062 | Pilot study, to evaluate the presence of specific IgE antibodies anti microorganisms, in patients with chronic idiopathic urticaria

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**Background:** The pathogenesis of chronic idiopathic urticaria (CIU) is unclear. Since the early 1900s, an association between CIU and infections has been reported. Recently, anti-IgE therapy (Omalizumab) has shown efficacy, even in patients without evidence of IgE sensitivity.

The purpose of this pilot study is to investigate if microbial antigens are capable of triggering an IgE response.

**Method:** Four patients with CIU were selected. Microbial antigens were obtained from cultures of *Alcaligenes faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomona aeruginosa*, *Streptococcus faecalis*, *Neisseria catarrhalis*, *Propionibacterium acne*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus viridans* and *Candida albicans*. To retain their antigenic "natural" structure, lysing or wall destruction techniques were not used.

The microorganisms were inactivated with phenol, and the concentration was adjusted to 1 000 000 microbial cells/mL (labeled as a 1/1). Dilutions 1/2 and 1/4 were made from the product labeled 1/1.

The Dot blot technique was used to detect the presence of specific IgE to the different microbial antigens and controls (anti IgE 1/1 and 2 fold dilution ½ and ¼).

| Germ Name | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| Alcaligenes faecalis | | X | X | |
| Escherichia coli | | | X | |
| Haemophilus influenzae | | X | X | |
| Klebsiella pneumoniae | | | X | |
| Proteus mirabilis | | | | X |
| Pseudomona aeruginosa | | X | X | X |
| Streptococcus faecalis | | X | | X |
| Neisseria catarrhalis | | X | X | X |
| Propionibacterium acne | | X | X | X |
| Staphylococcus aureus | | X | | |
| Streptococcus pneumoniae | | | X | X |
| Streptococcus viridans | X | X | X | X |
| Candida albicans | | X | | X |

The Dot blot images were processed with a documentation system (Gel Doc ez, Bio-rad), and the different microbial antigens in different dilutions were compared with the positive anti-IgE controls.

**Results:** All patients have specific anti IgE to microbial antigens (see table below).

**Conclusion:** The presence of microorganism-specific IgE could explain, the relationship between the infections and / or microorganisms in CIU, as well, the urticaria control by Omalizumab, even when it has not been detected IgE sensitizations to common allergens. Finally, these findings, showed that the bacterial allergy could be one line of research to understand the unresolved etiology of urticaria.

## 1063 | Dermographism and sensitization to mites

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**Background:** Dermographism is the most common form of inducible urticaria. It shows itself as hives made by scratching or rubbing on the surface where it has been produced and with the same morphology. The pathogenesis has not been clarified nor has it been associated until now with the sensitization to allergens.

We have studied the relationship between the presence of dermographism and domestic mites sensitization.

**Method:** We have selected 95 patients older than 14 years old. All of them had symptoms compatible with dermographism at the moment of medical evaluation. At least one third of patients additionally showed rhinitis and/or asthma symptoms.

**We performed::** - Skin prick tests with our basic neumoalergens (mites *D. Pteronyssinus y Lepidoglyphus Destructo*r, pollen, molds, dog, cat and horse dander, latex and anisakis simplex).

- Determination of specific IgE levels for Dermatophagoides pteronyssinus, Lepidoglyphus destructor, and anisakis were measured in serum by using the ImmunoCAP (Thermo Fisher Scientific).

- Blood count, serum immunoglobulins, antithyroid antibodies, serine tryptase and proteinogram.

**Results:** Blood count, serum immunoglobulins, antithyroid antibodies, serine tryptase and proteinogram were normal.

We divided patient in different groups. First, patients with dermographism with negative skin test and IgE to mites (n = 29; *phenotype 1*). Second, patients with dermographism with positive skin test and/or IgE to Derp. Pteronyssinus and Lepidoglyphus destructor (n = 29; *phenotype 2*): 2.1 Both skin test and specific IgE positive (n = 15); 2.2: Negative skin test but positive specific IgE (n = 5); 2.3 Positive skin test and negative specific IgE (n = 9). And a third group of patients with dermographism with additional rhinitis and/or asthma symptoms (n = 37; *phenotype 3*): 3.1 Both skin test and specific IgE positive (n = 7); 3.2 Both skin test and specific IgE negative (n = 30).

**Conclusion:** In our patients with dermographism, a third are sensitized to house dust mites *D. Pteronyssinus and/or L. Destructo*r.

## 1064 | Urticaria as a presenting symptom of a patient with carcinoid tumor

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**Background:** Typical carcinoid syndrome is characterized by flushing, abdominal pain and diarrhea occurring in lower than 10% of all patients. Very rarely, initial signs include skin manifestations. Our purpose is to highlight cutaneous manifestations in the diagnosis and assessment of atypical gastric carcinoid tumor.

Case presentation: 66 year old male patient had chronic urticaria and angioedema for 1 year. There was no typical triggering factor. His urticaria activity score (UAS) 7 was calculated as 28. Laboratory findings showed anemia, diminished iron, ferritin, and vitamin B12, with increased serum gastrin and anti-gastric parietal cell antibody (anti-GPC: 1/40 titer positive) levels. Gastric endoscopy showed submucosal lesions with the diameter of 5 mm, and 3 nodular areas similar to neuroendocrine tumor in gastric corpus. Gastric biopsy was positive with synaptophysin, chromogranin and CD56. Ki67 index was found 0% which was confirmed with grade 1 neuroendocrine tumor. Serum gastrin level [575 pg/mL (13-115)] and chromogranin A level [225.9 mg/mL (<94)] were elevated. Serum autoantibodies, total and specific IgE levels were detected in normal ranges. Abdominal computerized tomography (CT), oncologic FDG PET-CT and gallium 68 PET-CT scan did not show any other neuroendocrine tumor (NET) lesions except gastric NET. His urticaria lesions were non-responsive to maximal doses of antihistaminic tablets and steroid-dependant. Therefore, omalizumab therapy was prescribed. After the third dosage of omalizumab, his urticaria has been faded away. His NET has been following by endocrinology department every six months as far as the patient has no other symptoms except urticaria.

**Conclusion:** In literature, limited number of urticaria and angioedema cases have been reported as the only presenting symptom of carcinoid tumors. Carcinoid tumors with upper gastrointestinal localisations secrete histamines, that is why we expect these cases would respond to oral H1-antagonist tablets. Interestingly, our patient was non-responsive to antihistamines. In conclusion, physicians should consider the possibility of existence of neuroendocrine malignancies, specifically gastric carcinoids when evaluating patients presenting with chronic urticaria, iron deficiency anemia, elevated anti-parietal cell antibody and serum gastrin levels.

Consent: Written informed consent was obtained from the patient.

Conflict of interest: Authors declare no conflict of interest.

## 1065 | Evaluation of efficacy and tolerance of an anti-pruritic spray in subjects with chronic urticaria

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**Background:** Urticaria results from the appearance of pruritic papules and/or erythematous plaques caused by substances from mastocytes present in the skin, notably histamine. Chronic urticaria is defined as flare-ups that occur at least two or three days per week over a six-week period. In addition, affected subjects are often prone to an atopic or auto-immune profile that promotes urticaria [1].

The association of polyphenols (ambora, green tea) and the soothing active ingredients slow down the itching biological process from the outset by reducing the release of pruritic mediators (e.g. histamine, cytokines, etc.) of immune cells such as mastocytes and lymphocytes, involved in urticaria.

In this context, the purpose of the study was to evaluate the efficacy and the tolerance of an anti-pruritic spray containing the polyphenols and the soothing ingredient. The tested product aims to quickly calm the itching in subjects with chronic urticaria.

**Method:** A prospective, observational, non-comparative and multicentre study was conducted on 30 subjects with chronic urticaria aged over 18 years old in Poland. The product was used as often as necessary during 21 days (D21). The efficacy and the quality of life (Skindex) were evaluated on D0 and D21. The tolerance and the cosmetic properties were assessed on D21.

**Results:** On average, the product was applied 2.3 times per day with a significant decrease of 5D-pruritus scale (-35%) and sensations of itching (-58%) between D0 and D21. In terms of quality of life, a significant decrease of the Skindex score was observed (-48%). The product soothed the pruritus within 60 seconds for all subjects and the anti-pruritic effect lasts at least 2 hours for 80% of subjects. The product also showed very good cosmetic properties and was well tolerated; no intolerance case was reported.

**Conclusion:** In conclusion, this study confirms the interest to use an anti-pruritic spray in subjects with chronic urticaria.

## 1066 | A case of chronic spontaneous urticaria developing resistance to omalizumab with good clinical response to a subsequent trial of re-treatment

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**Background:** Most patients with chronic spontaneous urticaria (csu) show a rapid response to add-on treatment with omalizumab. Time to response varies between 1 & 24 weeks. Despite progress, our knowledge regarding the mechanism of action of omalizumab is incomplete. To date only a few patients with csu developing resistance to omalizumab have been reported. We present a patient with severe csu and initial response to omalizumab, who developed resistance to treatment but subsequently showed an excellent response to a trial of re-treatment.

**Method:** A 46 year old patient presented with a 5 year history of csu with angioedema and delayed pressure urticaria. Previous treatments consisted of desloratadine 20 mg/d, fexofenadine 540 mg/d, ebastine 40 mg/d rupatadine 40 mg/d, dapsone 50 mg/d and even high dose desloratadine combined with montelukast 10 mg/d which all had no effect. Prior to commencing treatment with omalizumab, wheals occured on a daily basis. Within 4 weeks of receiving the first dose of omalizumab in addition to rupatadine 40 mg/d, her csu showed near complete remission. In the week before omalizumab and for a few days after, her urticaria flared but on 3 of 4 weeks she was largely asymptomatic (UAS7 0-5). After 3 years of successful treatment she reported an increase in csu activity. No trigger factors could be identified. Add-on treatment with cyclosporine was refused, montelukast showed no, and prednisolone only transient benefit. Over a period of 2 months wheals occurred almost daily and a maximal score of 42 was achieved on UAS7. We replaced omalizumab with cyclosporine but this was subsequently discontinued due to side effects. 3 months later the patients' csu remained poorly controlled with up to 100 wheals occurring almost daily despite rupatadine 40 mg/d. Due to the good initial response to omalizumab and lack of good treatment alternatives, a trial of re-treatment was considered.

**Results:** Within 1 week of re-commencing omalizumab she once again achieved near complete remission of csu with UAS7 $\leq$ 3 on 3 of 4 weeks.

**Conclusion:** The mechanism of action of omalizumab and the development of resistance to it in csu, are incompletely understood. Our case shows that some csu patients developing resistance to omalizumab may benefit from a subsequent trial of re-treatment, particularly if treatment alternatives are poorly tolerated.

## 1067 | Information and communication technologies in patients with chronic urticaria: UCARE Project

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**Background:** Information and communication technologies (ICTs), are broadly defined as technologies used to communicate,

manipulate and store data by electronic means. This includes e-mail, SMS text messaging, video chat and online social media as well as all the different computing devices that perform a wide range of communication and information functions. A rapid increase in the use ICTs in recent decades is an enormous contributing factor in the development of a number of novel clinical and public health intervention strategies.

The aim of the present study is to assess the level of ICT use and to examine patterns of preferences among patients with chronic urticaria (CU).

**Method:** We will conduct an anonymous multicentre cross-sectional study, starting from January 2018, to investigate the use of ICTs in patients with CU, using a questionnaire as a survey method. This questionnaire will assess the frequency of use of social media and ICTs in patients, and their preferences for receiving and asking disease-related information. The survey will consist of 20 items, evaluating demographical information, time with disease, medication currently used, and additional aspects of social network use.

**Results:** We will use a chi-squared test to assess the association between Internet access or owning a cell or smartphone, and age, gender, type of urticaria, educational level and number of years since diagnosis. We will employ the same test to assess the association between the independent variables previously introduced and the frequency of use of each ICT type (short messaging service [SMS], Facebook, Twitter, YouTube, Email, Internet, LinkedIn and Skype) as well as agreement in receiving and seeking information (i.e. asking questions to the practitioner) through such ICTs. We will perform adjusted regression analyses between categories of age, gender, educational level, type of urticaria, years since diagnosis and the use and level of interest shown in communicating through ICTs.

**Conclusion:** A variety of ICT forms are revolutionizing healthcare and becoming mainstream tools to assist patients in self-monitoring and decision-making. Our study aims to fill the gap about frequency and preferences of ICTs among chronic urticaria patients. This knowledge could potentially lead to the development of new strategies to improve the outcomes of patients with chronic urticaria.

## 1068 | Update on latin American chronic urticaria registry (CUR)

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**Background:** Chronic urticaria was reported to have huge impact on quality of life.

Our aim is to report on remarkable findings from a registry of a large sample of patients, potentially providing clues for its approach and management.

**Method:** Restricted electronic on line registry, entering anonymous data of patients having chronic urticaria, including evaluations like UAS7 (Urticaria Activity Score in 7 days), quality of life (Chronic Urticaria Quality of life Questionnaire—CU-Q2oL), diagnostic lab tests and management variables.

**Results:** 285 patients with a median length of 14 months suffering from urticaria were registered, being 71% women; mean age 35.9 years. In 72% of patients no causal agent was identified.

Parasites were found in 9.3% and Thyroid Peroxidase Antibodies in 8.9%, while Autologous Serum Skin Test was positive in 47% and IgG to Mycoplasma in 42% of evaluations.

Two thirds of patients reported wheals on UAS7, with just 1/4 having concomitant angioedema. Almost 2/3 reported significant affection on quality of life because of itch by CU-Q2oL.

Just 14% of patients achieved total control on first anti-histamines provided, and less than half had good control of urticaria. Cetirizine was the first choice in 44%, followed by fexofenadine (15%) and first generation anti-histamines (16%).

**Conclusion:** Chronic urticaria affects quality of life in a significant proportion of patients. Causal factor is usually elusive, with a low frequency of parasites and TPO in our patients, having negligible control with conventional treatment in most of them.

An optimized approach and cost effective management in low-middle income settings is needed.

## 1069 | Questionnaire-based and polysomnographical evaluation and comparison of quality of sleep in cases of chronic urticaria

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**Background:** Urticaria is among the most commonly seen dermatological diseases. It has been demonstrated that severe disturbances in quality of life may develop in cases of chronic urticaria. In this study, we aimed to evaluate the quality of sleep in chronic urticaria cases with chronic urticaria quality of life questionnaire (CU-Q2ol), urticaria activity score 7 (UAS-7), Pittsburgh quality of sleep index (PSQI) and polysomnography (PSG), and, thus, to examine the association between chronic urticaria and sleep disturbance.

**Method:** Cases at 18-65 years of age which were being followed-up in our clinic with diagnosis of chronic urticaria and were not receiving any antihistaminic medication for last one month were

included in the study. CU-Q2ol, UAS-7, PSQI and PSG results of the patients were evaluated. Correlation of data with each other in regard to sleep disturbances was evaluated.

**Results:** 21 patients were included in the study. Patients' mean total score in CU-Q2ol was 36.25 ± 13.23. Patients' mean UAS-7 value was 16.71 ± 9.41. Mean total PSQI was 9.75 ± 3.92, the ratio of total scores ≥5 and those with poor quality of sleep was 87.5%. Mean Epworth sleepiness scale (ESS) score was 9.71 ± 2.05, with total score ≥10 in 52.4%. In PSG, mean apnea-hypopnea index (AHI) was 11.93 ± 12.6, with 44.4% of the patients having AHI ≥5. When patients having AHI<5 were compared with patients having AHI ≥5, no significant difference was determined in regard to total CU-Q2ol score, mean score for questions concerning status of sleep, UAS-7 and PSQI. When correlation analysis was performed between CU-Q2ol and total score for questions concerning status of sleep, a positive correlation was determined with PSQI ($P$ = 0.037).

**Conclusion:** It was demonstrated in our study that patients with chronic urticaria had poor quality of sleep and this disturbance was independent from AHI.

## 1070 | Clinical phenotype: CSU and diabetes mellitus type I, when therapeutic options are limited

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**Background:** The underlying causes and some of the mechanisms of mast cell degranulation in patients with CSU are described, however the more we know the more clinical questions appear. Individual approach is needed to every situation and the clinical phenotyping can be a start to bring answers to new horizons of the pathogenesis. Autoimmune comorbidities are already in focus.

**Method:** A case of 53-years old woman with the history of severe chronic urticaria over 1 year (weals and angioedema), accompanied with autoimmune conditions (Hashimotos thyroiditis, diabetes mellitus type I). The patient came through all steps of treatment from therapeutic dose of antihistamines, escalated doses, omalizumab 300 mg every 4 weeks. Injections of Dexamethasone and Prednisolone initially resolved the illness; however, when the glucocorticoids were decreased and urticaria emerged again and could not be controlled by any of the medications used. Moreover, the glycoprofile was unbalanced and the levels of blood glucose were uncontrolled by adapted basic treatment and reached extremely high levels. The patients refused to start the immunosuppressive therapy due its adverse events.

The treatment was monitored by UCT, UAS7 and AAS. Laboratory assessment: ESR 21 (N = 2-15), anti- IgG TPO 954 (0-50 ME/mL) with negative dynamic to 1304 ME/mL in 6 month, IgE -anti -TPO negative. C reactive -protein 18.66 mg/L (N- 0-6.00). ASST positive. Omalizumab was discontinued due to absence of improvement in CSU symptoms after three consecutive doses. The plasmapheresis without intravenous immunoglobulin replacement was initiated.

**Results:** The symptoms were relieved during the first procedure and the disease improved shortly thereafter. The following weeks the symptoms still occurred but with lower intensity and severity. (angioedema was gone). The second attempt with omalizumab was successful after this course (5 procedures of plasmapheresis).

**Conclusion:** So, theoretically this method removes medium to large molecular substances such as IgG and IgE from circulation. Approximately 40%-50% of patients with CU have functional IgG autoantibodies against either the high-affinity IgE receptor (FcεRIa) or IgE, or anti- IgG TPO with\without IgE -anti –TPO, but comorbid autoimmune conditions can have extra classes of autoantibodies that can be involved in the pathogenesis. (diabetes mellitus type I: ICA, anti-IA-2, anti-GAD, IAA and etc.)

## 1072 | Acute urticaria due to brimonidine

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**Case report:** Rosacea is a chronic skin disorder associated with flushing, erythema, dryness, burning and stinging, and inflammatory papules and pustules. New treatments available or in development target the inflammatory and erythematous components of the disease. These agents include the selective alpha-2 receptor agonist brimonidine. Allergic contact dermatitis to brimonidine is an unusual condition. In addition to this, urticarias due to brimonidine are rarely reported. We report on a 35-year-old woman who, immediately after apply a thin layer of brimonidine gel as preparation for a rosacea treatment on her face developed facial urticaria, which reverted in approximately four hours with systemic steroids. She had previously tolerated this product without any problems, but has not use it again ever since. Skin prick-tests with brimonidine (0.03 mg/mL) and latex were realized in the patient. Skin prick-tests with brimonidine were realized in eleven healthy control subjects.

**Results:** Skin prick-tests with latex was negative in the patient. Skin prick-tests with brimonidine were positive in the patient (9x5 mm). The prick-test with brimonidine was negative in teen healthy control subjects.

**Conclusions:** We report on a case of immediate urticaria due to brimonidine and triggered by an immediate, probably IgE-mediated, hypersensitivity mechanism. We highlight this case because it is the only case described in the literature with a positive prick-test.

## 1073 | Urticaria as a paraneoplastic syndrome: A case report

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**Background:** Urticaria is a complex disease with multifactorial etiology and it may be a warning of an underlying malignant condition.

**Report:** A 74-year-old male, retired factory worker, was referred to our department with a 4 month history of intensely pruritic migratory urticarial lesions, without angioedema nor any other signs or symptoms. No eliciting factors were evident. His past medical history as well as his family history was unremarkable. Skin prick tests with common inhalant allergens were negative. Hemogram, VS, standard chemistry, coagulation study, viral markers (HIV and HCV) and thyroid function were normal. However, a complete IgG / lambda monoclonal gammopathy of undetermined significance was detected. The myelogram did not present a characteristic phenotype of multiple myeloma. The skeleton X-ray were normal. The urticaria was resolved with antihistamine (Bilastine 20 mg/day) as well as moisturizer and he has remained asymptomatic.

**Clinical relevance:** The association of monoclonal gammopathy of undetermined significance (MGUS) in patients with chronic urticaria (CU) may have multiple isotypes and it may sometimes represent a variant of Schnitzler syndrome. In this patient, MGUS was diagnosed during the workup of another disease. It is difficult to differentiate a pathogenic relationship from a coincidental one. Nonetheless, MGUS is one of the most common pre-malignant disorders and therefore, appropriate follow-up with malignancy screening is warranted. Chronic urticaria associated with paraneoplastic syndromes is relatively rare but it is important to document these cases in order to increase their awareness.

MONDAY, 28 MAY 2018
TPS 27
SKIN AND MAST CELLS

## 1074 | Alteplase Induced Angioedema and urticaria: pathophysiology and treatment options

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**Background:** Orolingual angioedema associated with tissue plasminogen activator (tPA) administration in stroke patients is a rare, but potentially life-threatening side effect, with a incidence between 0.2% and 5.0%. It typically manifests as a mild, transient facial swelling, but may cause fatal airway obstruction in around 13% of those developing tPA-related angioedema. tPA activates plasminogen to plasmin, which in turn degrades fibrin but also converts factor XII into its active form. Thereby factor XIIa activates the plasma contact pathway and stimulates the production of bradykinin. Bradykinin increases vascular permeability potentially resulting in angioedema. Treatment with ACEi, blocking the degradation of bradykinin, is recognized as the main risk factor for occurrence of tPA-induced angioedema. However, no uniform guidelines exist on how angioedema in this setting should be treated or whether a relative contra-indication would be imperative in those with recent episodes of ACEi-induced-angioedema and a minor indication for thrombolysis.

**Case Report:** A 63-year-old male presented with sudden onset of vertigo, dysarthria and temporary loss of consciousness, since <1 hour. Home medications included Lisinopril. Clinical examination was normal, except an abnormal Romberg's test. Head CT scan and angiography were negative and tPA was administered for a potential stroke. A lip and tongue swelling was noticed 10 minutes after tPA. The infusion was stopped. Methylprednisolone, ebastine and tranexamic acid were administered. 15 minutes later, rapid progression towards orofacial angioedema, stridor and respiratory distress was observed, next to an urticarial rash. Epinephrine was administrated. However, collapse due to asphyxia occurred, necessitating an urgent tracheotomy and resuscitation. The angioedema resolved. The patient left 4 days later. From hindsight, the patient reported previous episodes of angioedema that was attributed to ACEi use. C1-esterase-inhibitor deficiency was excluded. Familial history was negative for angioedema. Serial serum tryptase levels were normal arguing against anaphylaxis.

**Conclusion:** A case of life-threatening angioedema after tPA, presumably bradykinin-mediated, is reported. Prior ACEi-induced-angioedema should be considered as a potential relative contra-indication for tPA and treatment guidelines for this reported severe side-effect, potentially including tranexamic acid, icatibant and C1-esterase-inhibitor, are mandatory.

## 1075 | What could be hidden by hypereosinophilia?

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**Background:** Hypereosinophilia is frequently a reactive condition due to infections, autoimmune disorders or allergic reactions, but in a minority of case is caused by hematologic disorders. A patient aged 72 years presented to our clinic complaining asthenia and weight loss of about 10 kg in the last two years. She had episodes of abdominal colicky pain and colonic diverticulosis. She also had proteinuria and stage 2 of chronic kidney disease (glomerular filtration rate of 79 mL/min) and severe osteoporosis. Due to clinical history, blood count alterations (anemia, lymphopenia, hypereosinophilia and thrombocytosis) and hepatosplenomegaly she carried out haematological evaluation.

**Method:** In the diagnostic assessment, it was decided to perform an bone marrow biopsy and blood samples were taken for genetic studies by next-generation sequencing.

**Results:** Bone marrow biopsy showed an increase in the myelopoietic and megakaryocyte series with regular maturation and distribution. In addition there was the presence of spindle-shape cells. Immunohistochemistry showed CD117 (c-KIT) positivity, highlighting the presence of aggregates of mast cells as well as individual mast cells, with the interposition of rare eosinophilic granulocytes with a predominantly trabecular location. For this reason the patient was tested for serum tryptase which was increased to 80 ng/mL. The search of C-Kit mutations on peripheral blood showed the presence of the D816V mutation with the co-occurence of JAK2 (V617F) mutation.

**Conclusion:** These findings appear compatible with the concurrent diagnosis of chronic myeloproliferative syndrome and systemic mastocytosis (systemic mastocytosis with an associated hematological neoplasm SM-AMENM). This condition had been very rarely reported in the literature, being associated with a severe prognosis. The patient is now on chronic therapy with Oncocarbide with discrete benefit on both conditions. It also was given anti-H2 antihistamine, adrenaline, 25-OH cholecalciferol therapy.

## 1076 | Role of pro-inflammatory cytokines in metabolic syndrome

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**Background:** Aim of this work was to investigate the role of the pro-inflammatory cytokines in metabolic syndrome (MetS) and their association with metabolic syndrome components.

**Method:** We have investigated serum concentrations of the pro-inflammatory cytokines such as, IL-6, IL-1β and TNF-α in 68 patients with metabolic syndrome compared to those 52 patients without MetS by ELISA kits from 2016 September to 2017 June. Metabolic syndrome was defined by the Harmonized definition of the MetS. Laboratory data and anthropometry parameters were measured. All data are expressed as mean ± SD.

**Results:** The initial socio-demographic characteristics of patients with and without MetS did not differ statistically. There was a significant increase of IL-6 ($P < 0.05$), IL-1β ($P < 0.01$), and TNF-α ($P < 0.001$) in MetS subjects compared to those without MetS. Among components of the MetS, abdominal obesity (AO) LDL-cholesterol and fasting glucose positively correlated with IL-6 ($r = 0.572$, $P = 0.035$; $r = 0.468$, $P = 0.041$; and $r = 0.417$, $P = 0.045$ respectively). Only AO ($r = 0.367$, $P = 0.032$) and LDL cholesterol ($r = 0.395$, $P = 0.040$) positively correlated with IL-1β. TNF-α was not correlated with SBP and DBP as IL-6 and IL-1β, however there were correlations TNF-α with AO ($r = 0.335$, $P = 0.034$) and Triglycerides ($r = 0.410$, $P = 0.043$) in MetS subjects.

**Conclusion:** Serum levels of pro-inflammatory cytokines were raised in MetS subjects compared to those without MetS. Among MetS components waist circumference is the most sensitive component to assess the patients pro-inflammatory state.

## 1077 | Pharmacokinetic profile of cetirizine in healthy young adults

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**Background:** Cetirizine, marketed as a racemic mixture is a specific long-acting H1 antagonist shown to be effective in allergic rhinitis and urticaria. In physiological pH it exists in the form of a zwitterion, resulting in low distribution volume, low serum concentration, low affinity for myocardium and high skin concentrations. Pharmacokinetic studies in specific populations pointed out significant differences with the normal population indicating the dose reduction in patients with renal and liver function impairments. Our study is focused on a group of young adults.

**Method:** The study was in accordance with the Helsinki Declaration and was previously approved by the National Comity of Ethics. This was a one dose study conducted on 16 fasting young healthy volunteers, of which 11 were females and five males. The mean age was 21 ± 1 years old and the body weight 61.13 + 9.44 kg and the body high 169 ± 7 cm. Blood samples were taken from the median cubital vein in a predefined schedule. The plasma concentrations of Cetirizine were measured with an HPLC method previously validated. For the non-compartmental analysis PK Solver-2.0 as Add-in of Microsoft Excel 2010 was used, and for the compartmental analysis; Monolix-4.3.2.

**Results:** After oral administration of 10 mg of Cetirizine the calculated values maximal concentration ($C_{max}$) was 393.05 ± 73.02 ng/mL, time of the maximal concentration ($T_{max}$) was 1.06 ± 0.46 hours, the elimination half-life ($T_{1/2}$) was 4.17 ± 0.74 hours, the area under the curve from zero to 24 hours ($AUC_{0\text{-}24}$) was 2735.79 ± 513.11 ng/mL*hours and the mean residence time (MRT) was 6.4 ± 1.03 hours. Compartmental analysis with the modeling software reveals the "model with oral administration with zero-order absorption, first-order elimination, two compartments and $t_{k0}$, alpha, beta, A and B parameters" as the model with less information loss.

**Conclusion:** This study brings data from a specific population group, healthy young adults aged 20-27 years old. The differences of some parameters with those of literature may be interpreted as consequences of differences in volumes of distributions in different age groups.

## 1078 | Rare cause of recurrent angioedema; Hereditary angioedema type three

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**Case report:** A 35-year-old woman is being followed without treatment with the diagnosis of hashimoto thyroiditis, vitiligo and prolactinoma. In 2009, she had a complaint of lip and face swelling during zona infection. In 2016, the complaint of swelling on the lips and eyelid during menstruation repeated. After going into and out of the sea in 2017, complaints of swelling on the lips were present. The patient did not complain of concurrent swallowing difficulty and shortness of breath. Patient referred to emergency room three times in the last four months with similar complaints. Therefore examinations for the cause of recurrent angioedema were done. In skin prick tests of the patient with respiratory and nutrient panel was detected negative. The values of C3, C4, ANA and IgA, IgM, IgG, IGE were normal in the patient whose other routine examinations were normal. C1 esterase inhibitor level and function of the patient without a family history were reported as normal (C1 esterase inhibitor level: 30.4 mg/dL (reference 22.0-38.0), C1 esterase inhibitor function:

99.8% (reference 70%-132%) .The factor 12 mutation was reported as homozygous positive. Patient who frequently referred to emergency room because of recurrent angioedema was diagnosed as hereditary angioedema type 3.

## 1079 | Pharmacodynamics study of Cetirizine in Albanian healthy young adults

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**Background:** Cetirizine is a potent H1-receptor antagonist indicated in the treatment of allergic rhinitis and urticaria. Cetirizine is widely used due to its potent antihistaminic effects in yielding strong and fast relief of itchy sensation, sneezy and rhinorrhea and its unlikely probability to manifest anticholinergic side effects in therapeutic doses. Histamine flare and wheal inhibition by anti-H1 are widely used as a standard to test and compare the effect intensity and duration. Our study aimed to test these effects of Cetirizine in young healthy adults.

**Method:** This was a double-blind, single dose study in healthy young adults, previously approved by the National Comity of Ethics. Eleven females and five males with a mean age 21 ± 1 years participated in this study. Histamine skin pricks were tested before and after they received a tablet of 10 mg Cetirizine as previously scheduled. Twenty minutes after each test flare and wheal were drawn in a transparent paper which was then scanned and measured with a software. Wilcoxon Signed Ranks Test two-sided with significance at 5% level was used to analyze the differences.

**Results:** Forty minutes and 1 hour after Cetirizine administration there was a significant inhibition of the wheal and the Flare respectively ($P < 0.001$). The mean time of the maximal effect for the wheal and flare was respectively 6.64 ± 1.4 hours and 9.4 ± 7.8 hours. As there was achieved a total inhibition of the wheal in all the subjects, none of them had a full inhibition of the flare. A significant inhibition of both wheal and flare was observed 29 hours post-dose ($P < 0.001$). No side effects were observed or reported during the study and thereafter.

**Conclusion:** This study brings pharmacodynamics data on Histamine flare and wheal inhibition by Cetirizine from a specific population group, healthy young adults aged 20-27 years old. The parameters measured and analyzed in this study were similar to those obtained from other studies.

## 1080 | Morbus adisson with coexisting asthma bronchialis, urticaria and chronic angioedema

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**Background:** To describe a clinic case; a female patient of 52 years old with asthma bronchialis, urticaria, chronic angioedema and Morbus Adisson.

**Results:** A female patient 52 years old with Adisson disease diagnosed 2 years ago came with urticarie, angioedema after use of NSAID. Further examination revealed patient suffered from asthma bronchialis. Skin test specific IgE were negative. Patch tests were positive for potassio bicromato and balsam of peru. Bodyplethysmographie revealed a generalized disventiator obstructive syndrome, mild and no reversibility against b2 agonist. Patient was treated with steroids.

**Conclusion:** Further examination and follow up need to be done in order to determine any correlation among this diseases. Steroids seems to improve clinical conditions of asthma bronchialis, angioedema urticaria and Addison disease.

## 1081 | Angioedema as presenting symptom for low grade B-cell lymphoma

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**Background:** Angioedema due to acquired deficiency of c1 inhibitor is rare and is known as Acquired angioedema. Rare but recognized associated with lymphoproliferative diseases. Due to expansion of B cell clones producing anti -C1 INH antibodies, anti C1q antibodies, due to the underlying disease.

Reduced or deficiency of c1 -inhibitor leads to activation of the classical complement path way leading to secretion of bradykinin which increases vascular permeability and induces angioedema.

**Case report:** A 65 year old female with asthma presented with first episode of lips an tongue angioedema. With no family history. No obvious trigger. On investigation lab results were normal including normal cell blood count liver enzymes, renal function test and erythrocyte sedimentation rate. Due to no response to antihistamine adrenalin and corticosteroid treatment, complement parameters were checked to rule out bradykinin induced angioedema. Presented with low C4 and low C1 esterase inhibitor activity including low C1q, suspecting antibodies production. Computed tomography scan of chest and abdomen was normal. Due to recurrent episodes of angioedema further investigation was preceded with bone marrow aspiration which revealed infiltration with B cell low grade lymphoma.

Repeated blood investigation showed appearance of hemolytic anemia with hemoglobin 8 g/dL a year after angioedema symptoms started .The patient was started treatment promptly.

**Conclusion:** Adult onset angioedema nonreactive to standard therapy should prompt physicians to suspect underlying lymphoproliferative disorder despite normal labs. One should order C1 esterase and C1q levels and if low precede further investigation including bone marrow aspiration.

## 1082 | Dealing with the itch associated with allergen skin testing without an antihistamine?

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**Background:** Patients and children in particular experience substantial discomfort during allergen skin testing. Alleviating the prominent symptom of "itching" may be a problem, as systemic and local antihistamines should not be applied so as to avoid interference with the test results. A liquid itch relieving preparation (IRP) is available on the market, which contains a mix of components, among which no antihistamine can be found. It uses a novel Skin Relief technology (containing Ambora and Green tea extracts) combined with a soothing dermatological active ingredient Enoxolone and supposedly blocks the itching signal at the targeted surface. The manufacturer claims that the preparation relieves itch within 60 seconds of its application. We performed a simple study to verify this claim.

**Method:** We used IRP in 20 consecutive subjects, 15 males, median age 12, range 6-49 years, whose workup implied AST. Their preliminary diagnoses were "asthma" (6 subjects), "allergic rhinitis" (10 subjects), "atopic dermatitis" (2 subjects) and "food allergy" (2 subjects). All of them had refrained from systemic antihistamines for at least one week. Standard skin prick tests (SPT) were applied as appropriate, including histamine controls to assess the level of their skin sensitivity. Subjects were asked to mark their sense of itch in the area of the skin to be tested on 100 mm visual-analogue scales (VAS) starting from "0"—"no itch" to "100"—"unbearable itch". VAS assessments were repeated 20 minutes after AST was done; then IRP was applied according to the manufacturer's instructions, and the VAS assessments were repeated after 60 seconds and 20 minutes.

**Results:** There VAS assessments are shown in table format: Table 1 IRP did not affect the wheal and flare of the histamine control, nor did it abolish positive SPT. No differences were outlined between subjects with different diagnoses.

**Conclusion:** The commercially available itch relieving preparation not containing defined pharmacological antihistamine is effecting in relieving itch associated with allergen skin testing.

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|---|---|---|
| **Before AST (1)** | **4.9 ± 2.6** | **vs (2) $P < 0.001$; vs (3) $P = 0.001$; vs (4) $P = 0.348$** |
| 20 min after AST (2) | 39.3 ± 5.1 | vs (3) $P = 0.006$; vs (4) $P < 0.001$ |
| 60 s after IRP (3) | 26.6 ± 4.9 | vs (4) $P = 0.001$ |
| 20 min after IRP (4) | 8.5 ± 3.0 | vs = versus |

## 1083 | Impaired endothelial function in patients with hereditary angioedema

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**Background:** Hereditary Angioedema due to C1-INH deficiency (C1-INH-HAE) or with normal C1-INH (FXII-HAE) is characterized by recurrent swellings due to altered generation of vasoactive mediators, among which bradykinin (BK) and other endothelium events are crucial. Through the binding and activation of the two human BK-receptors, Kinins may have dual beneficial and deleterious effects in vascular and inflammation physiopathology. The presence of coronary endothelial dysfunction, which can precede the formation of atherosclerotic plaques, was previously showed in C1-INH-HAE patients.

**Method:** We investigated the systemic endothelial function of patients affected by C1-INH-HAE, FXII-HAE and a group of healthy controls by flow-mediated dilation, using plethysmography-based probes placed on fingertips of the right hand (*Endopath).*

**Results:** We found a statistically significant difference in FMD of HAE patients compared to controls ($P < 0.0001$). No statistically significant differences were found comparing the FMD of C1-INH-HAE to FXII-HAE patients. A statistically significant correlation was revealed between FMD and patients' chronological age.

**Conclusion:** The coronary endothelial dysfunction previously shown in C1-INH-HAE patients involves the peripheral vessels as well. We observed a systemic endothelial dysfunction in HAE. Further investigations may clarify differences and similarities among the two disease subgroups and explore the effects of bradykinin receptors signaling on endothelial function. Being atherosclerosis linked to heart attacks, stroke and peripheral vascular disease, a regular cardiovascular follow-up should be implemented in these HAE patients

## 1084 | Bone pain and unexplained osteoporosis in a young patient

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**Background:** Systemic Mastocytosis (SM) is characterized by the accumulation of mast cells in tissues other than the skin. Bone involvement is frequent in patients with SM; 30% of patients have a low bone mass and 20% have fractures. At the same time, SM affects 10% of male patients with idiopathic osteoporosis and the risk of osteoporotic fractures is high. Routine measurements of bone mineral density and vertebral morphometry are warranted. The bone turnover markers indicate the involvement of complex bone metabolism in mastocytosis-related manifestations. Bisphosphonates (BP) represent the first-line treatment for osteoporosis-related mastocytosis. We report a case of SM with bone pain and with an area of osteolysis in the femur as first sign and symptom. We had to consider the risk of adverse reaction when we decided to treat the patient with BP, but the patient was under antihistaminic treatment and also we made a premedication to reduce the risk.

**Method and results:** A 32-year-old man was admitted to our Center in 2014 for recent onset of widespread, severe bone pain without clinical explanation. Serum tryptase level was high (49.6 μg/L), so it was decided to perform bone marrow biopsy to confirm the hypothesis of SM. In the 2014 the T-score was −2.4 for the Lumbar Spine and −1.8 at the Hip (osteopenia). In 2015 the condition worsened, leading to a diagnosis of osteoporosis (T-score Spine −2.6 and T-score Hip −2.2), so he was started on therapy with Zoledronic Acid (ZA) 4 mg every 28 days for four consecutive months in association with Paracetamol, Corticosteroids and Protonic Pump Inhibitor to prevent drug-induced reactions. The results were successful and in 2017 he was switched to therapy with ZA 5 mg/year, a more convenient mode of administration, that is being administered without adverse effect and with a good outcome and increase in bone density.

**Conclusion:** The patient responded well to BP first, with an improvement in bone mineral density and resolution of bone pain. According to what has been found in the literature, a single 5 mg ZA intravenous infusion in patients with osteoporosis secondary to indolent SM is associated with significant increases in spine and hip bone mineral density, and with decreases of bone turnover markers over at least 1 year. Yearly ZA might represent a therapeutic option for indolent SM-associated osteoporosis.

## 1085 | Hereditary angioedema—pancreatitis?—clinical case

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**Introduction:** Abdominal crises occur in 90% of cases of Hereditary Angioedema (HAE), in 21% are the only manifestation, hindering the differential diagnosis between abdominal crisis of HAE and acute abdomen of another etiology.

**Case report:** A 39-year-old female, with HAE type II diagnosis from the age of 25, with irregular therapy and follow-up in the Immunoallergology (IA) outpatient department. For several years, she presented crises of abdominal pain associated with vomiting, greater intensity in the premenstrual period. An evaluation in general practitioner with colonoscopy, upper digestive endoscopy and pelvic magnetic resonance, did not reveal alterations. After 9 years of absence in the IA outpatient department, she restarted treatment with Stanozolol 2 mg daily, with progressive improvement. A crises of intense abdominal pain took her to the Emergency Service of her residence area. Initially, acute surgical abdomen was excluded. She performed abdominal ultrasound, that showed globose and swollen pancreas with heterogeneous and hypoechoic structure, without other alterations. Analytically, C-reactive protein (CRP) was increased—17.3 mg/dL, with no other alterations in the remaining analytical parameters (hemogram, liver tests including lipase and amylase). She was treated with several analgesic drugs (Acetaminophen, Butylscopolamine, Metamizole and Tramadol) without improvement, complete improvement of pain occurred only after the administration of C1 inhibitor. The patient repeated abdominal ultrasound 24 hours after with visualization of the pancreas and spleen without anomalies and moderate amount of free fluid in the Morrison space and PCR was also normalized. 72 hours later, she was totally asymptomatic and was discharge with the diagnosis of abdominal crisis of HAE due to therapeutic failure.

**Conclusions:** Abdominal crises with pancreatic involvement are rare. Its pathophysiology is uncertain, but it is thought to be secondary to edema of the pancreatic duct or Vater's ampulla, followed by obstruction of the same. HAE should be considered as a possible cause of pancreatic edema/pancreatitis and C1 inhibitor/Icatibant may be a fast-acting therapeutic option. The authors describe 1 case of HAE crisis with exclusively pancreatic edema in which C1 inhibitor was an essential therapy.

## 1086 | Lack of influence of food in the pharmacodynamic profile of bilastine in humans

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**Background:** The pharmacokinetics (PK) and pharmacodynamics (PD) of the non-brain penetrating antihistamine bilastine are well understood and characterized by a population PK/PD model. An indirect response model with bilastine inhibiting the histamine wheal effect was established. This model has now been used to investigate the influence of food on the PD of bilastine, and concretely the temporal evolution of the wheal effect by using a modeling and simulation approach. The objective is to evaluate if the changes observed at a PK level have clinical relevance from a PD perspective.

**Method:** The PK/PD model available was informed by data from 12 clinical trials. The PD endpoint data was available from two studies and used to characterize the effect of bilastine on wheal and flare. Moreover, food effect had been characterized in 2 PK studies and the data was used to model the effect of food in the PK of bilastine. The PK parameters relative to the fed state were then used to simulate the temporal evolution of the wheal effect using the PK/PD model. All analyses were conducted by nonlinear mixed effect modeling (NONMEM v 7.2). Using the PK model developed (food effect model) and the PK/PD model already available, Monte-Carlo simulations for plasma concentrations and PD over time were performed for both the fed and the fasting states.

**Results:** . A reduced bioavailability (F) and a slow absorption constant characterized the PK of bilastine when administered concomitantly with food (F = 77% relative to the fasting state and Ka = 0.51 $hour^{-1}$, a 3-fold reduction compared to fasting conditions). The rest of the PK parameters remained unchanged. Onset of action was 1 hour for bilastine both in fed and fasted conditions. Maximum wheal inhibition occurred at 3.5 hours (fasted 78% and fed 77%). From 2 to 12 hours, the percentage reduction with bilastine for both fasted and fed was between 75% and 86% after the third day of treatment. A 50% inhibition in wheal effect was maintained during 23 hours for both conditions after the third day. The results of the simulations show that even if the PK is altered with food, the PD is maintained unchanged.

**Conclusion:** Even if a significant food effect was described for bilastine at a PK level, the difference is not translated directly into the PD. Therefore, the antihistaminic effect of bilastine remains unaffected by the concomitant administration with food. The results of these simulations will be further confirmed in a dedicated clinical trial.

## 1087 | Angioedema in patients with urticaria is associated with an increase in thrombin generation peak

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**Background:** Chronic urticarial (CU) is a widespread and recurrent disease characterized by the appearance of wheals is frequently accompanied by angioedema (AE). CU patients show increased activation of coagulation and fibrinolysis. Isolated cases of AE, as in HAE, show similar patterns with characteristic elevations during the attacks. Moreover, oral anticoagulants appear to be effective in the treatment of CU. The thrombin generation test (TGT) is a global coagulation test which quantifies the *in vitro* ability of plasma to generate thrombin.

**Aim:** To evaluate the thrombin generation in patients with CU with or without associated AE.

**Method:** We have analyzed thrombin generation in 68 patients with CU. Plasma from patients was incubated with a mixture of tissue factor (4 pM), fluorogenic substrate and CaCl2. Lag time (LT), endogenous thrombin potential (ETP), peak height (PK), time to peak (ttPK) and the pending of thrombin maximum generation (Vo): 5 parameters were analyzed. TGT parameters were related to the CU severity, the presence of AE and other clinical parameters.

**Results:** We also found no correlation between the different TGT parameters and other clinical and analytical parameters associated with UC (Table 1).

**Conclusion:** Patients with UC and a history of AE showed increased peak of thrombin generation compered to CU patients without AE, indicating the presence of a hypercoagulation state in these patients. These results further suggest that the TGT can be useful to evaluate the role of the coagulation cascade in diseases with inflammatory component. However, the clinical relevance of these findings is still under investigation. These results further suggest that the TGT can be useful to evaluate the role of the coagulation cascade in diseases with inflammatory component.

| | Pk (nmol/L) | ETP (nmol/L) | Vo (nmol/L/min) | LT | ttPK (min) |
|---|---|---|---|---|---|
| 28 UC with AE | 187.6 ± 53 | 1449 ± 326.9 | 46.45 ± 20.46 | 5.365 ± 1.067 | 10.33 ± 1.991 |
| 40 UC without AE | 164 ± 59 | 1499 ± 507.1 | 36.40 ± 21, 27 | 5.559 ± 1.382 | 10.86 ± 2.494 |
| Statistical significance | P = 0.0018 | P = 0.0686 | *P* = 0.0355 | P = 0.0120 | *P* = 0.0348 |

## 1088 | Antihistamine bioequivalence estimation through weal and flare inhibition, a Cetirizine study

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**Background:** The existence of lots of antihistamine generics in the pharmaceutical market, and the relatively low plasma concentrations that most of them yield in therapeutic doses, makes necessary exploration of alternative methods of bioequivalence evaluation. There is a clear evidence about the relation between doses, plasmatic concentration and Histamine wheal and flare inhibition in the case of cetirizine, adequately prescribed through the specific pharmacokinetic-pharmacodynamic models. This can be exploited to evaluate the possibilities for bioequivalence estimation through pharmacodynamic parameters, which is the main aim of our study.

**Method:** This is an open, one dose, randomized, crossover study, with two periods, two sequences and two treatments on fasting healthy volunteers. The study was in accordance with the Helsinki Declaration and was previously approved by the National Comity of Ethics. Sixteen volunteers with a mean age 21 ± 1 years old, of which 11 females participated in the study. Venous blood samples were taken in a predefined time schedule along with a Histamine skin test after which the flare and wheal surface was scanned and measured with a software. Cetirizine plasma concentration was measured with a previously validated HPLC method. Bioequivalence was evaluated in accordance with respective procedures and guidelines of FDA and EMA.

**Results:** Both cetirizine products have no differences in respect to the pharmacodynamic and pharmacokinetic parameters analyzed. The 95% confidence interval of the mean ratios of the $AUC_{0\text{-}24}$, $AUC_{0\text{-}inf}$, Cmax, $AUCE_{0\text{-}24}$, and $E_{max}$, between the test and the reference, were within the bioequivalence ranges (80%-125%) in both cases. No statistical difference was revealed when comparing the respective $T_{max}$ and $TE_{max}$ too.

**Conclusion:** The two cetirizine products tested were bioequivalent. The bioequivalence was evident even when tested with the pharmacodynamic parameters. There is strong evidence that supports the use of Histamine Skin Prick test for the bioequivalence evaluation of different cetirizine products.

## 1089 | Bradykinin-mediated angioedema associated with combination of angiotensin-converting enzyme and dipeptidyl peptidase IV inhibitors: a disproportionality analysis from the WHO database

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**Background:** Bradykinin-mediated angioedema (BMA) is a rare but potentially lethal adverse drug reaction of angiotensin-converting enzyme inhibitors (ACEi). Dipeptidyl peptidase IV inhibitors (DDP4i) are known to inhibit the degradation of bradykinin and substance P, involved in the pathogenesis of BMA. Concurrent use of vildagliptin and ACEi was associated with an increased risk of BMA. There is no data concerning the risk of BMA with others DPP4i in combination with ACEi, nor with DPP4i alone.

**Method:** We performed a disproportionality analysis using data from the WHO pharmacovigilance database by a case-noncase study, until the 14/12/2017. We extracted all individual cases safety reports (ICSRs) included in the high level term "angioedemas", according to the Medical Dictionary for Regulatory Activities classification. Given the absence of term "BMA", we selected only the ICSRs of angioedema without associated symptoms evoking another underlying mechanism, such as histamine angioedema (e.g. pruritus, urticaria, rash, etc.). Drug class exposure was "ACEi" and "DPP4i", considered suspect or concomitant, using the ATC classification. We calculated the reporting odds ratio (ROR) of angioedema with ACEi alone, DPP4i alone and combination of ACEi and DPP4i. A signal was considered to be significant if the lower bound of the confidence interval is superior or equal to 1. According to the interaction additive model, a ROR value for coexposure that exceeds the sum of the RORs estimated for each individual drug class support a potential drug-drug interaction.

**Results:** ACEi were associated with 22 827 ICSRs of angioedemas, DPP4i with 688 cases and combination of ACEi and DPP4i with 269 cases. The ROR was 6.67 (95% CI 6.58-6.77) for ACEi alone, 0.44 (95% CI 0.41-0.47) for DPP4i alone, and 27.64 (95% CI 23.76-32.16) for combination of both ACEi and DPP4i. No DDP4i was individually associated with a significant ROR for angioedema.

**Conclusion:** According to these results, combination of DPP4i and ACEi was associated with an increased risk of report of angioedema, but not with DPP4i alone. This result is consistent with previous study and supports a pharmacodynamic interaction. Further studies are needed to confirm this risk induced by the combination of ACEi and DPP4i. One of the major limitations is the absence of term "bradykinin-mediated angioedema".

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CLINICAL ASPECTS

## 1090 | Disease in the first 6 months of life and environmental factors associated with allergic rhinitis

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**Background:** Risk factors in relation to Allergic rhinitis (AR) have recently been of considerable interest. However, evidence supporting the risk factors of allergies is still unclear. The objective of this study was to investigate potential risk factors of AR.

**Method:** This was a case-control survey. 242 patients with AR and 258 healthy persons were enrolled. Questionnaires involved pre-pregnancy diseases and pregnancy medical disorders of the mothers, the conditions and disorders of the participants during the first 6 months of life,other related issues include family allergic history and home environmental factors. About 40 potential risk factors in relation to AR were investigated and analyzed using chi-square test and logistic regression.

**Results:** There was no correlation between mother's disorders such as periodontitis, rhinitis, diabetes etc. and the onset of AR ($P > 0.05$). A multivariate analysis showed, neonatal jaundice ($P < 0.001$), respiratory system infection ($P < 0.001$), diarrhea ($P < 0.001$), eczema ($P < 0.001$) in the first 6 months of life and home environmental factors (house decoration ($P < 0.001$), mold environment ($P < 0.001$), keeping flowers ($P < 0.001$), passive smoking ($P < 0.001$)) increased the risk of AR. Besides, there was no significant difference in current height and birth weight of the participants between AR and control group. However, AR group had significantly lower current weight ($P = 0.003$) and age ($P < 0.001$) compared with the control group. Paternal age and maternal age in the AR group were significantly higher than the control group ($P < 0.01$).

**Conclusion:** Diseases in the first 6 months of life and home environmental factors increased the risk of sequential AR. the older parents increased the possibility of AR in the offspring.

Table 1 - Four categories of AR potential risk factors

| Maternal conditions of pre-pregnancy | Maternal disorders during Pregnancy | Participant characteristics | Other conditions involved |
|---|---|---|---|
| Periodontitis | Periodontitis | Feeding patterns | Parental allergic history |
| Rhinitis | Rhinitis | Gestational age | House decoration |
| Pre-pregnancy diseases[a] | Ardent fever | Delivery manners | Living area |
| | Antibiotics | Neonatal jaundice | The second generation family allergic history |
| | Pregnancy complication[b] | Respiratory system infection | Mold environment |
| | Medication of pregnancy complication[c] | Diarrhea | keeping flowers |
| | | Eczema | Keeping animals |
| | | Kawasaki disease | Smoking |
| | | Anemia | |
| | | Candida albicans stomatitis | |
| | | Urticaria | |
| | | Urinary tract infection | |
| | | Antibiotics taken | |
| | | Drug allergy | |
| | | Food allergy | |

[a]Pre-pregnancy diseases including diabetes, abnormal thyroid function and hypertension.
[b]Pregnancy complication including diabetes, abnormal thyroid function, hypertension and intrahepatic cholestasis.
[c]Medication of pregnancy complication including hypoglycemic, hypotensor, thyroid related medicines and insulin injection.

Table 2 - General characteristics of enrolled subjects

| Characteristic | AR N = 242 | Control N = 258 | Statistic | *P* value |
|---|---|---|---|---|
| Gender | | | $\chi^2 = 0.555$ | $P > 0.05$ |
| Male | 130 | 128 | | |
| Female | 112 | 130 | | |
| Age (y) | 12.26 ± 5.39 | 14.01 ± 5.72 | $z = -3.692$ | $P < 0.001$ |
| Height (m) | 1.47 ± 0.169 | 1.48 ± 0.16 | $z = -3.692$ | $P = 0.707$ |
| Weight (kg) | 41.64 ± 15.79 | 44.83 ± 12.69 | $z = -2.943$ | $P = 0.003$ |
| Birth weight (kg) | 3.36 ± 0.36 | 3.32 ± 0.21 | $z = 1.242$ | $P = 0.214$ |
| Paternal age (y) | 28.87 ± 4.84 | 27.23 ± 2.16 | $z = 4.052$ | $P < 0.01$ |
| Maternal age (y) | 26.20 ± 4.27 | 24.56 ± 2.10 | $z = 4.596$ | $P < 0.01$ |

The data of general Characteristics of participants were statistic analysis by *z* text analysis.
*Significance at $P < 0.05$.

Table 3 - Variables with an association with AR in the univariate analysis

| | AR | | control | | | |
|---|---|---|---|---|---|---|
| Associated factors | Yes | No | Yes | No | χ2 | *P* |
| Maternal conditions of pre-pregnancy | | | | | | |
| Periodontitis | 11 | 231 | 0 | 258 | 11.99 | 0.001 |
| Rhinitis | 27 | 215 | 0 | 258 | 26.42 | 0.001 |
| Pre-pregnancy diseases | 1 | 241 | 1 | 258 | 0.001 | 0.97 |
| Maternal disorders during Pregnancy | | | | | | |
| Periodontitis | 8 | 234 | 0 | 258 | 6.70 | 0.10* |
| Rhinitis | 10 | 232 | 0 | 258 | 8.87 | 0.003* |
| Ardent fever | 18 | 224 | 1 | 257 | 18.12 | 0.00 |
| Antibiotics used | 10 | 232 | 1 | 257 | 0.14 | 0.004 |
| Pregnancy complication | 4 | 238 | 0 | 258 | 2.47 | 0.12* |
| Medication of pregnancy complication | 0 | 242 | 0 | 258 | 0 | >0.05 |
| Gestational age | | | | | | 0.002& |
| <37 weeks | 13 | | 2 | | | |
| 37-41 weeks | 229 | | 256 | | | |
| Feeding patterns: | | | | | | |
| breastfeeding | 129 | 0 | 145 | 0 | 4.535 | 0.10 |
| bottle feeding | 63 | 0 | 77 | 0 | | |
| Mixed feeding | 50 | 0 | 35 | 0 | | |
| Delivery manners: | | | | | | |
| Vaginal delivery | 160 | | 156 | | | 0.045 |
| Caesarean delivery | 98 | | 86 | | 0.322 | |
| Diseases in first 6 months | | | | | | |
| Neonatal jaundice | 73 | 169 | 11 | 247 | 59.94 | 0.00 |
| Respiratory system infection | 47 | 195 | 11 | 247 | 27.98 | 0.00 |
| Diarrhea | 57 | 185 | 10 | 248 | 41.67 | 0.00 |
| Eczema | 63 | 179 | 7 | 251 | 56.40 | 0.00 |
| Kawasaki disease | 1 | 241 | 0 | 258 | 0.001 | 0.97 |
| Anemia | 1 | 241 | 0 | 258 | 0.001 | 0.97 |
| Candida albicans stomatitis | 4 | 238 | 0 | 258 | 2.468 | 0.12* |
| Urticaria | 10 | 232 | 1 | 257 | 8.14 | 0.005 |

*(Continues)*

(Continued)

| Associated factors | | AR Yes | AR No | control Yes | control No | χ2 | P |
|---|---|---|---|---|---|---|---|
| Urinary tract infection | | 0 | 242 | 0 | 258 | 0 | >0.05 |
| Antibiotics consumption | | 60 | 181 | 24 | 234 | 22.96 | 0.00 |
| Drug allergy | | 21 | 221 | 1 | 257 | 21.55 | 0.00 |
| Food allergy | | 42 | 202 | 4 | 254 | 37.34 | 0.00 |
| Direct relatives allergy | | | | | | | |
| First degree relatives allergy | Maternal allergy | 37 | | 2 | | 68.95 | 0.00# |
| | Paternal allergy | 33 | | 10 | | | |
| | Parents allergy | 7 | | 1 | | | |
| | No allergy | 165 | 0 | 245 | | | |
| Second degree relatives allergy | | 37 | 205 | 0 | 258 | 43.85 | 0.00 |
| Living condition | | | | | | | |
| Living area | city | 167 | | 142 | | 16.00 | 0.00 |
| | Rural | 40 | | 82 | | | |
| | Urban-rural fringe | 35 | | 34 | | | |
| House decoration | | 83 | 159 | 25 | 233 | 41.13 | 0.00 |
| Mold contamination | | 62 | 179 | 2 | 256 | 69.38 | 0.00 |
| Keeping flowers or plants | | 90 | 152 | 33 | 225 | 40.08 | 0.00 |
| Keeping animals | | 41 | 201 | 16 | 242 | 14.26 | 0.00 |
| Parents Smoking | | | | | | | |
| Active smoking | | 4 | | | | 19.56 | 0.00# |
| Passive smoking | | 114 | | 79 | | | |
| No smoking | | 124 | | 179 | | | |

#Exact: Monte Carlo method.
*Pearson $\chi^2$ Continuity Correction.
&Ridit.
The others: Person $\chi^2$.

Table 4 - Variables with an association with AR in the multivariate logistic regression

| Associated factors | β-value | Exp (B) | 95% CI for Exp (B) Lower | upper | P-value |
|---|---|---|---|---|---|
| Maternal conditions of pre-pregnancy | | | | | |
| Periodontitis | −19.39 | 0.00 | 0.00 | | 0.998 |
| Rhinitis | −20.59 | 0.00 | 0.00 | | 0.997 |
| Maternal disorders during Pregnancy | | | | | |
| Periodontitis | −20.74 | 0.00 | 0.00 | | 0.998 |
| Rhinitis | −18.55 | 0.00 | 0.00 | | 0.998 |
| Ardent fever | −1.79 | 0.17 | 0.01 | 2.26 | 0.18 |
| Antibiotics consumption | 2.45 | 11.55 | 0.40 | 337.27 | 0.16 |
| Gestational age | −1.52 | 0.22 | 0.03 | 1.59 | 0.13 |
| Feeding patterns | | | | | 0.80 |
| Bottle feeding | −0.27 | 0.76 | 0.32 | 1.79 | 0.53 |
| Mixed feeding | −0.26 | 0.78 | 0.32 | 1.88 | 0.57 |
| Delivery manners | | | | | 0.24 |
| Vaginal delivery | −15.83 | 0.00 | 0.00 | | 1.00 |
| Difficult labour | −16.42 | 0.00 | 0.00 | | 1.00 |

*(Continues)*

(Continued)

| Associated factors | | β-value | Exp (B) | 95% CI for Exp (B) Lower | upper | *P*-value |
|---|---|---|---|---|---|---|
| Diseases in the first 6 months: | | | | | | |
| Neonatal jaundice | | −1.80 | 0.17 | 0.07 | 0.40 | 0.00* |
| Respiratory system infection | | −2.06 | 0.13 | 0.04 | 0.41 | 0.001* |
| Diarrhea | | −1.37 | 0.26 | 0.10 | 0.68 | 0.007* |
| Eczema | | −1.48 | 0.23 | 0.08 | 0.68 | 0.008* |
| Candida albicans stomatitis | | −13.34 | 0.00 | 0.00 | | 0.999 |
| Urticaria | | −1.78 | 0.17 | 0.01 | 2.01 | 0.16 |
| Antibiotics consumption | | 0.49 | 1.63 | 0.62 | 4.29 | 0.33 |
| Drug allergy | | −2.25 | 0.11 | 0.007 | 1.69 | 0.11 |
| Food allergy | | −1.19 | 0.31 | 0.07 | 1.30 | 0.11 |
| Direct relatives allergy: | | | | | | 0.59 |
| First degree relatives allergy | | | | | | |
| | Maternal allergy | 0.50 | 1.65 | 0.23 | 11.70 | 0.62 |
| | Paternal allergy | 0.57 | 1.77 | 0.58 | 5.37 | 0.31 |
| | Parental allergy | 1.26 | 3.52 | 0.21 | 60.31 | 0.39 |
| Second degree relatives allergy | | −20.65 | 0.00 | 0.00 | | 0.997 |
| Living condition: | | | | | | |
| Living area | | −0.22 | 0.80 | 0.52 | 1.23 | 0.31 |
| House decoration | | −0.95 | 0.39 | 0.19 | 0.80 | 0.01* |
| Mold contamination | | −3.41 | 0.03 | 0.007 | 0.15 | 0.00* |
| Keeping flowers or plants | | −1.26 | 0.28 | 0.14 | 0.57 | 0.00* |
| Keeping animals | | −0.75 | 0.47 | 0.19 | 1.20 | 0.11 |
| Smoking: | | | | | | 0.01* |
| Active smoking | | 21.64 | 2505222863.10 | 0.00 | | 0.999 |
| Passive smoking | | 0.90 | 2.45 | 1.36 | 4.41 | 0.003* |

Abbreviations: OR, odds ratio; CI, confidence interval.
*Multivariate logistic regression, Significance at $P < 0.05$.

## 1091 | A cross-sectional prevalence survey of allergic rhinitis in Argentina: The para study

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**Background:** In Argentina, according to the ISAAC phase III study, 27.9% of patients between 6-7 years old and 37.6% between 13-14 years old are affected by allergic rhinitis (AR). Neffen et al. demonstrated that 3.5% of adult and children had a physician diagnosis of AR using another questionnaire. The aim of this study was to determine the prevalence of AR in Argentina in a population of 5-44 years old using a self-reported symptom questionnaire, and to evaluate demographic characteristics.

**Method:** A National cross-sectional prevalence study to detect self-reported signs and symptoms compatible with AR was used. Subjects between 5 and 44 years old from urban areas more than 100 000 inhabitants in Argentina were included. The information was collected using a validated telephone questionnaire (Mancilla Hernandez et al. Rev Alerg Mex 2015;62:196-201). Informed consent was recorded verbally.

**Results:** 3200 subjects were surveyed: 51.8% were females; age 5-19 years old (37.6%) and 20-44 years old (64.2%). About level of education, 69.8% of study responders completed secondary or higher education. About Healthcare coverage, 22.8% had no coverage. Most frequent symptoms were sneezing (58.5%) and nasal congestion (51.4%). 44.3% of participants had family history of allergy such as Asthma, AR, Urticaria, Food Allergy, Drug Allergy, Insect Bites Allergy and Atopic Dermatitis. Global prevalence of AR symptoms was more frequent in females (24% vs 16.7%, $P = 0.0001$). The overall prevalence for all age groups was 20.5%. Regarding the distribution by age of the disease, similar percentages of AR were found among age-groups evaluated: 21.1% for 5-12 years old, 23.1% for

the group aged 12-19 years old and 19.4% for 20-44 years old ($P$ = NS). Stratifying by both, sex and age, only subgroup of male adults has less prevalence than others ($P < 0.0001$)

**Conclusion:** Findings of this first national cross-sectional survey have confirmed a high prevalence of self-reported symptoms of AR in adults and children in Argentina, especially in females. Male adults has less prevalence than others subgroups.

## 1093 | Strong association of sinus occupancy and loss of smell severity in asthma patients

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**Background:** Symptom-based diagnosis of CRS, with the support of nasal endoscopy and sinus CT scan, constitute the basis of international guidelines. However, an overuse of CT scan indications for CRS diagnosis and follow-up has been detected.

**Objective:** To investigate the correlation of loss of smell with sinus occupancy in asthmatic patients.

**Method:** From a cross-sectional prospective study in asthmatics (N = 492), 181 patients with NAR (n = 19, 10.5%), AR (n = 43, 23.5%), CRSsNP (n = 42, 23.2%), CRSwNP (n = 73, 40.3%), or without sinonasal disease (n = 4, 2.2%) were evaluated for: a) loss of smell severity (VAS, 0-100 mm) and prevalence of anosmia (VAS >70 mm); and b) sinus occupancy by CT scan according to Lund&-Mackay score (LMS, 0-24, median [25-75 IQR]. A logistic model was used (OR, Odds ratio [95% CI].

**Results:** Anosmia was more frequent in CRS than in rhinitis (28.1% vs 3.9%, $P < 0.001$) and in CRSwNP than in CRSsNP (40.6% vs 13.4%, $P < 0.001$). LMS was higher in CRS than in rhinitis (8 [4-15] vs 0 [0-0], $P < 0.001$) and in CRSwNP than in CRSsNP (10 [6-18] vs 5 [1-7], $P < 0.001$). In addition, LMS was associated with loss of smell in patients with hyposmia (OR = 2.66 [1.27, 5.53], $P = 0.009$) but mainly with anosmia (OR = 16.67 [4.43, 62.67], $P < 0.0001$).

**Conclusion:** Sinus occupancy by CT scan showed a clear association with loss of smell, mainly with anosmia. Therefore, the routine assessment of loss of smell in daily clinical practice may help the diagnosis and follow-up of CRS in asthmatic patients while potentially reducing the overuse of CT scans.

## 1094 | Berberine reduces the inflammatory reaction in chronic sinusitis with nasal polyps

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**Background:** Chronic sinusitis with nasal polyps (CRSwNP) is a common nasal disease globally and in China that is histologically characterized by persistent inflammation and irreversible structural remodeling in the sinonasal mucosa. Current treatment strategies involve surgery. However, recurrence remains a major challenge and is largely mediated via the inflammatory reaction. Berberine (BER), a traditional Chinese herb, is used in the treatment of infection, allergies, and cancer. Therefore, in this study, we investigated the effects of BER on the regulation of inflammatory responses in CRSwNP for the purpose of determining whether BER could be used to prevent relapse.

**Method:** Sixty-four patients who had been diagnosed with CRSwNP were enrolled in the study initially (n = 33 in the treatment group and n = 31 in the placebo group). None of the patients had received any prior treatment for CRSwNP. Patients in the treatment group received oral BER 0.3 g at each time, twice per day for 30 days before surgery and did not use intranasal corticosteroids, oral or topical antihistamines, or oral glucocorticoids during the study period. Polyp tissues were collected at the time of diagnosis and after surgery. Histologic staining, reverse transcription polymerase chain reaction, flow cytometry, western blotting, and enzyme-linked immunosorbent assays were performed to detect the levels of cytokines and immune cells.

**Results:** BER reduced the expression of the cytokines interleukin IL-4, IL-33, IL-25, IL-5, IL-13, IL-22, CCL-11, and CCL-24 in polyp tissues of patients in the treatment group compared with levels in tissues of patients in the placebo group ($P < 0.05$). In addition, the eosinophil distribution was reduced significantly in polyp tissues of patients in the treatment group ($P < 0.05$). Overall, recurrence was detected in 9% (3/33) of patients in the treatment group compared with 32.3% (10/31) of patients in control group during a 10-month follow-up.

**Conclusion:** The results of this study suggest that BER may be an effective therapeutic agent for preventing the recurrence of CRSwNP.BER on the regulation of inflammatory responses in CRSwNP for the purpose of determining whether BER could be send to prevent relapse.

## 1095 | Clinical and molecular investigation on osteitis in chronic rhinosinusitis

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**Background:** The evidences of osteitis are frequently observed in the patients with chronic rhinosinusitis (CRS), especially in the recalcitrant cases. However, the studies focusing on biological markers of osteitis are limited, and it is still not clear whether the osteitis is differently associated with the various phenotypes of CRS.

**Method:** Patients with CRS without nasal polyps (n = 27) or CRS with nasal polyps (CRSwNP, n = 47) and control (n = 9) were enrolled. Clinical information and CT scores, histologic phenotypes were investigated. The clinical parameters (Global osteitis score) and molecular marker of bone remodeling, receptor activator of nuclear factor kappa-B ligand (RANKL) are analyzed in each type of CRS. CRS mice models was tested using anti-RANKL.

**Results:** Global osteitis score (GOS) was significantly higher in all CRS vs control. GOS in non-eosinophilic CRSwNP was higher compared to eosinophilic CRSwNP. Osteitis was dominant in maxillary sinus of non-eosinophilic CRS vs in ethmoidal sinus of eosinophilic CRS. Moreover, high GOS in non-eosinophilic CRSwNP was associated with high score of postoperative endoscopic findings. Bone remodeling marker RANKL was upregulated in CRS and mRNA expression was positively correlated with Lund-Mackay CT score and GOS. A potent RANKL inducer IL-22 and neutrophils-associated markers (MPO and CXCL2) was associated positively with RANKL protein level in CRS. In mouse CRSwNP model, anti-RANKL treatment abrogated neutrophil recruitment in nasal mucosa.

**Conclusion:** Clinical osteitis is present in CRS and CRSwNP, with more clinical significance in non-eosinophilic CRSwNP. RANKL is well-correlated with clinical osteitis and disease severity in CRSwNP. These findings shed light on the importance of RANKL as a potential biomarker of CRS and a key player in CRS pathogenesis.

## 1096 | The analysis and study of allergen features in chronic rhinosinusitis with or without polyps

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**Background:** Allergen features were compared in the two subtypes of CRS: chronic rhinosinusitis with nasal polyps(CRSwNP) and chronic rhinosinusitis without nasal polyps(CRSsNP). To study the distribution features and clinical significance of allergens in patients with chronic rhinosinusitis(CRS) and chronic rhinosinusitis with polyps(CRSwNP).

**Method:** The Allergen features were compared in the two subtypes of CRS. To study the distribution features and clinical significance of allergens in patients with chronic rhinosinusitis(CRS) and chronic rhinosinusitis with polyps(CRSwNP).The analysis was performed in 187 cases of CRS and CRSwNP. Differences of allergens features of CRS were analyzed, and they were compared to the allergens of 65 patients with allergic rhinitis(AR).

**Results:** The total allergen positive rate in CRS was 49.8%. The allergen positive rate, distribution proportion of inhaled and food allergens, distribution proportion of allergens subsets, distribution proportion of single and multiple allergens between two subtypes of CRS had no significant difference($P > 0.05$). The major allergens of CRS were single inhaled allergens(72.3%). Some CRS patients were allergic to food allergen (8.6%). The minority allergens of CRS were a mixture of inhaled and food allergens (7.2%). Compared to AR, the distribution proportion of inhaled and food allergens ($\chi 2 = 17.81$, $P < 0.001$), the distribution proportion of allergens subsets ($\chi 2 = 15.51$, $P < 0.001$), and the distribution proportion of single and multiple allergens($\chi 2 = 9.727$, $P < 0.001$) had significant difference.

**Conclusion:** The allergen positive rate of CRS is much higher than the prevalence of allergic diseases in general population, suggesting that allergic factors may be closely correlated to the pathogenesis of CRS. The clinical features of allergens are similar in the two subtypes of CRS, while there are significant differences in allergen distribution between CRS and AR patients. The detection of allergens may be helpful in prevention and treatment of CRS.

## 1097 | MP-AzeFlu for management of allergic rhinitis symptoms in patients ≥65 years: A post hoc efficacy and safety analysis from three pooled phase 3 trials

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**Background:** Allergic rhinitis (AR) is common among older adults, and medication efficacy and tolerability may vary with age due to comorbidities and interaction with other medications. Intranasal MP-AzeFlu (azelastine hydrochloride [AZE] and fluticasone propionate [FP]) has proven to be an effective treatment for AR. This post hoc analysis compared efficacy and safety of MP-AzeFlu in improving AR symptoms in patients 18-64 years vs ≥65 years.

**Method:** Data were pooled from three phase 3 multi-center, randomized, double-blind trials of subjects ≥12 years with moderate/

severe AR (Carr W, et al. *J Allergy Clin Immunol*. 2012;129:1282-9). Subjects in this post hoc analysis received MP-AzeFlu (137 μg AZE/50 μg FP) twice daily for 14 days and recorded individual nasal and ocular symptom scores (rated absent to severe [0-3]). The total nasal and ocular symptoms (TNSS; TOSS) were calculated. Maximum daily scores were 24 (TNSS) and 18 (TOSS). Analyses assessed change from baseline in TNSS and TOSS over 14 days (ANCOVA). Safety was monitored via adverse events (AEs).

**Results:** Of the 3043 subjects in the intent-to-treat population (ages 18-83 years), 760 received MP-AzeFlu. Regardless of age, subjects who received MP-AzeFlu experienced significant mean improvements over baseline in overall TNSS and TOSS symptoms. Both TNSS and TOSS improvement scores were slightly higher for the ≥65 years age group (n = 19) compared with the 18-64 years age group (n = 741) (mean [SD] change from baseline for TNSS: −7.2 [4.4] vs −5.7 [5.3] and TOSS: −4.2 [3.6] vs −3.2 [4.0]). Symptom improvement scores were slightly higher for the ≥65 years age group compared with the 18-64 years age group for all categories of TNSS (mean change from baseline for congestion: −1.8 vs −1.3; nasal itch: −1.8 vs −1.3; runny nose: −1.6 vs −1.4; sneezing: −2.0 vs −1.7) and TOSS (watery eyes: −1.6 vs −1.1; eye itch: −1.5 vs −1.2; red eyes: −1.0 vs −1.0). AEs were reported by 17.6% (18-64 years) and 14.8% (≥65 years) of subjects. The most frequent AEs for subjects aged 18-64 years also occurred at similar rates in subjects ≥65 years (dysgeusia: 4.2% vs 3.7%; headache: 2.3% vs 3.7%; epistaxis: 2.2% vs 0%), and no AE was reported by >1 (3.7%) subject in the ≥65 years group.

**Conclusion:** MP-AzeFlu improved AR symptoms to a similar extent, and had a similar safety profile, among older and younger adults.

## 1098 | Aspirin exacerbated respiratory disease: Role of periostin in Brazilian patients with chronic rhinosinusitis and nasal polyps

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**Background:** Aspirin exacerbated respiratory disease, also known as AERD, is a condition characterized by eosinophilic chronic rhinosinusitis, nasosinusal polyps, asthma and hypersensitivity to Aspirin and other non-steroidal anti-inflammatory drugs. A higher expression of the biomarker Periostin has been described in serum, nasosinusal tissue, extracellular matrix and nasal polyps among patients with AERD.

**Objectives:** To evaluate serum levels of Periostin in Brazilian patients with AERD and compare to levels among patients with Perennial Allergic Rhinitis (PAR) and healthy individuals.

**Method:** Twenty-nine patients diagnosed with AERD (20F/9M) were selected from those attending the Allergy and Otolaryngology Clinics. Patients were submitted to confirmatory exams including Oral Provocation Test with Aspirin. Nasal polyps were removed by Functional Endoscopic Sinus Surgery and eosinophils in this tissue were quantitated. Eosinophil counts in peripheral blood was obtained. Serum Periostin was measured by ELISA and total IgE was determined using ImmunoCAP. As control groups, 12 (9F/3M) patients with PAR and 23 healthy subjects (14F/9M) were selected. Samples of nasal tissue and blood were collected from these subjects during elective surgery for correction of anatomical variations, and compared with the patients with AERD.

**Results:** Patients with AERD were older (median 54 years, range 22-60) than PAR patients (median 30 years, range 19-57, $P = 0.0001$) and healthy controls (median 29 years, range 19-53; $P = 0.0001$). Blood and tissue eosinophils in patients with AERD were higher than in PAR patients and in healthy controls. Blood eosinophil counts showed median values of 640 eos/mm$^3$, range 100-5100; median 200 eos/mm$^3$, range 100-500; and median 100 eos/mm$^3$, range 100-400 in patients with AERD, PAR and control individuals, respectively ($P = 0.0003$ and $P = 0.01$). Media tissue eosinophils were 113.3 cells/High Power Field HPF; 2.5 cells/HPF and 0.7 cells/HPF, respectively ($P = 0.003$ and $P = 0.017$). Serum Periostin was higher in patients with AERD as compared to healthy controls (median 602 ng/mL, range 290.7-1055.1 ng/mL vs 496.7 mg/mL, range 327.4-713.4 ng/mL, $P = 0.01$). No significant differences were observed for total IgE levels within the three groups.

**Conclusion:** In a subset of Brazilian patients with AERD, we observed elevated blood and tissue eosinophils and higher serum Periostin, as compared to patients with PAR and healthy individuals.

## 1099 | Association between obesity and refractoriness of chronic rhinosinusitis with nasal polyp

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**Background:** It is well known that obesity is associated with asthma, particularly severe and uncontrolled asthma. However, there are few studies about the relationship between rhinosinusitis and obesity. The aims of this study are to determine whether obesity is associated with surgical outcome for chronic rhinosinusitis with nasal polyp (CRSwNP) and to elucidate differences in cytokine profiles according to body mass index (BMI).

**Method:** A total of 338 patients (151 obese and 187 non-obese) with CRSwNP who underwent endoscopic sinus surgery (ESS) between Jan. 2014 and Apr. 2017 were enrolled in this study. Preoperative demographic data, computed tomography (CT, Lund-

Mackay score), endoscopic findings (modified Lund-Kennedy score), and sinonasal quality of life questionnaire (sinonasal outcome test 22 [SNOT-22]) scores were analyzed. When performing surgery, sinonasal tissues and blood were collected. Levels of leptin, adiponectin, and common cytokines were analyzed for 119 nasal polyps (54 obese, 65 non-obese) and plasma samples of 40 patients (18 obese, 22 non-obese). Protein levels were measured by Multiplex cytokine analysis kits and ImmunoCap®. Comparative analysis was performed according to the presence or absence of obesity (BMI $\geq$ 25 kg/m$^2$) and the classification of eosinophilic nasal polyp (ENP) or non-eosinophilic nasal polyp (NENP).

**Results:** There was no significant difference in tissue eosinophilia, preoperative CT score, endoscopic score, and SNOT-22 scores between the obese and non-obese group. However, SNOT-22 scores were worse in the obese group at 3 and 6 months after ESS ($P$ = 0.037, 0.005 respectively). In plasma, BMI positively correlated with leptin, IL5, and IL10 and negatively correlated with adiponectin. The level of leptin and CCL11 in nasal polyp tissue was elevated in the obese group compared to the non-obese group. Leptin, CCL11, and IL5 were elevated while adiponectin, CXCL1, and CXCL2 were decreased in the obese group compared to the non-obese group in NENP, but not in ENP.

**Conclusion:** Obese patients with CRSwNP had worse quality of life after ESS. These worse outcomes might be associated with an increased level of eosinophilic mediators in NENP.

## 1100 | Correlation between treatment for allergic rhinitis and the use of asthma medication

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**Background:** Evidence exists to suggest a correlation between the occurrence of allergen-driven upper and lower airway inflammation, and exacerbation of one may lead to exacerbation of the other. For example, patients with allergic rhinitis (AR) are often also diagnosed with asthma, and among these individuals, untreated AR is associated with poorly controlled asthma and higher rates of asthma-related exacerbations and emergency department (ED) visits. In contrast, treatment of AR is associated with fewer exacerbations and ED visits. This retrospective cohort study examined the correlation between the use of medications to treat AR and the concomitant use of asthma medication.

**Method:** Individuals were identified from the Danish National Prescription and Patient Registries who, during the pollen seasons April-July of 2013-2015, received a first-time prescription for topical fixed-combination azelastine hydrochloride plus fluticasone propionate (MP-AzeFlu), intranasal corticosteroids plus oral antihistamine in combination (INCS+OAH; prescriptions within $\leq$7 days of each other), or INCS followed by add-on OAH (prescriptions >7 days apart). Patients were included in the analysis if they also received a prescription for asthma $\leq$15 months prior to the first AR prescription. The primary endpoint was change in asthma prescriptions during the 15 months following the first AR prescription (analyzed using $t$ test). The correlation between specialist consultations and asthma prescriptions was also examined.

**Results:** Of the 6733 individuals who met all inclusion criteria, 161 received MP-AzeFlu, 1583 received INCS+OAH combination, and 1176 received INCS and add-on OAH. In the 15 months following the initial AR prescription, prescriptions for asthma in the MP-AzeFlu cohort increased nonsignificantly by 0.8 (95% confidence interval [CI]: −0.1-1.7; $P$ = 0.082). Conversely, asthma prescriptions in both the INCS+OAH and INCS/add-on OAH cohorts increased, respectively, by 2.3 (95% CI: 2.0-2.5; $P < 0.001$) and 1.9 (95% CI: 1.6-2.3; $P < 0.001$). No correlation was observed between specialist consultations and change in asthma prescriptions. Findings were similar when the data were analyzed by individual year.

**Conclusion:** Treatment with MP-AzeFlu was associated with a substantially smaller increase in asthma prescriptions than treatments with INCS and OAH. These findings suggest that MP-AzeFlu may provide better control of AR, contributing to improved control of asthma.

## 1101 | Berberine treatment reduces symptoms of allergic rhinitis: A randomized double-blind clinical trial

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**Background:** Allergic rhinitis (AR) is a common nasal disease worldwide and in China specifically, and although it is not a fatal disease, the symptoms can be severe and greatly diminish patients' quality of life, possibly by even negatively impacting behavior, learning, and memory. The current standard therapy includes intranasal corticosteroids, oral and topical antihistamines, and an oral glucocorticoid. Unfortunately, these pharmacological treatments only control the symptoms of AR temporarily and have low therapeutic effectiveness for many patients with resistance. Moreover, long-term use of these agents can result in serious side effects. Therefore, the development of a new herbal drug for AR treatment would be of great benefit to patients. The aim of this study was to assess the effectiveness of berberine (BER) against the symptoms of AR in patients.

**Method:** Ninety-three patients were enrolled in this double-blind, randomized clinical trial study (n = 47 in the treatment group and n = 46 in a placebo control group). Patients in the treatment group received oral BER 0.3 g at each time, twice daily for 4 weeks. The efficacy of the drug with respect to alleviating AR symptoms (rhinorrhea, sneezing, nasal obstruction and itchy nose) was evaluated through patient-provided visual analog scale (VAS) scores (range, 0-10) before administration and at the end of the treatment period. Serum IgE levels were checked at the time of diagnosis and the end of intervention. The collected information was analyzed statistically using SPSS software.

**Results:** AR symptoms were significantly improved in the treatment group compared with the control group (76.6% (36/47) vs 21.7% (10/46); $P < 0.05$). Furthermore, the mean total VAS score for patients in the treatment group was reduced from 6.21 ± 1.83 before treatment to 1.36 ± 1.51 after treatment ($P < 0.05$). Moreover, the reduction in free IgE levels was greater in the treatment group than in the control group.

**Conclusion:** The results of this study suggest that the Chinese herbal medicine BER may be effective for improving the symptoms of AR. A multicenter clinical trial is needed to confirm this finding.

## 1102 | Tropomyosin sensitization in house dust mite allergic patient—preliminary results

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**Background:** House dust mite allergy is the main cause of perennial allergic rhinitis in Poland. Tropomyosin is a minor allergen in house dust mite, but main allergen in shrimp and a known cause of cross sensitisation. The aim of this work is to establish the frequency of shrimp allergy to different allergen components in house dust mite allergic patients.

**Method:** Preliminary results are available for 46 patients (23 women and 23 men, aged 18-65) with a positive house dust mite allergy diagnosis and declared shrimp related symptoms (research group). 30 patients with a negative allergy diagnosis were included in the control group. In all patients the allergen-specific IgE concentration to Dermatophagoides pteronyssinus, Dermatophagoides farinae and shrimp allergen extracts were measured (ImmunoCap). Specific IgE levels to allergen components Der p 10 (Dermatophagoides pteronyssinus tropomyosin) and Pen a 1 (shrimp—Penaeus aztecus tropomyosin) were also measured with the use of the ImmunoCap method.

**Results:** As predicted, most patients were sensitized to Dermatophagoides pteronyssinus—32 (70%). 28 patients (60.8%) were sensitised to Dermatophagoides farinae. Shrimp allergens (Immunocap) sensitised 29 patients (63%). Only 10 patients had elevated level of IgE specific to shrimp tropomyosin (21.7%) and house dust mite tropomyosin (21.7%). Only 34.5% of shrimp allergic patients were sensitised to shrimp tropomyosin. It is worth to emphasize that the correlation between concentration of IgE Der p 10 and IgE Pen a 1 was close to 100%, what may suggest strong cross reactivity.

**Conclusion:** Those preliminary results suggest that sensitisation to tropomyosin is not the most important cause of shrimp sensitisation in patients allergic to house dust mite. Further research is required to identify other sensitising allergen component of shrimp in this important group of patients.

## 1105 | Functional features of the nasal mucosa in patients with chronic polypoid rhinosinusitis

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**Background:** Functional changes in nasal mucosa and paranasal sinuses may be a cause of irreversible changes, such as metaplasia, more common in chronic polypoid rhinosinusitis.

The aim of the study was to investigate the physiological features of the nasal mucosa and paranasal sinuses in different types of chronic polypoid rhinosinusitis.

**Method:** We examined 120 patients between 15-80 years old who were hospitalized in the ENT department with the diagnosis of chronic polypoid rhinosinusitis at the 3rd clinic of Tashkent Medical Academy from 2013 to 2017. All patients underwent clinical and functional examination of nose, including pH determination using by a special indicator, saccharin test to the transport function, determination of the suction function with 1% atropine and excretory function using cotton swab.

**Results:** In patients with "eosinophilic" polypoid rhinosinusitis, mucociliary transport was 35.2 ± 0.80 minutes, pH 7.4 ± 0.01, suction—88.6 ± 6.5 minutes, excretory—57.9 ± 0.9 mlg and in patients with "neutrophilic" polypous rhinosinusitis, mucociliary transport was 34.5 ± 0.65 minutes, pH 7.3 ± 0.01, suction—76.2 ± 5.0 minutes, excretory—54.9 ± 0.8 mL. The study showed that disruption of the transport function, changing the concentration of hydrogen ions (pH), reduction the absorption function and an increase the nasal excretory function.

**Conclusion:** Identification of the functional changes of nasal mucosa can contribute to determine the process of polypoid rhinosinusitis and choosing treatment tactics of chronic polypoid rhinosinusitis.

## 1106 | Evaluation of potency of local and systemic corticosteroid therapy in chronic rhinosinusitis with nasal polyps through the allergological parameters

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**Background:** Rhinosinusitis is a significant health problem which seems to mirror the increasing frequency of allergic rhinitis and results in a large financial burden on society. Chronic rhinosinusitis (CRS) with and without nasal polyps represent different stages of one chronic inflammatory disease of the mucosa of the nasal cavity and paranasal sinuses. The cause of nasal polyp disease remains controversial. The aim of our study is to understand the role of eosinophil cationic protein (ECP), serum tryptase, total and specific IgE (phadiatop) in assessing of different therapies of nasal polyposis.

**Method:** The study included 70 patients, who were diagnosed with chronic rhinosinusitis with nasal polyps. All patients consulted by allergologist. The patients were split into two groups. The first group (35 patients) received only intranasal corticosteroid sprays, and the second group (35 patients) received intranasal corticosteroid sprays combined with intramuscular corticosteroid injections. All patients were under observation for 80 days, during which the clinical status of the patients was evaluated, and in the end, laboratorial tests were retaken.

**Results:** In the first group, there was a decline in TIgE in 12 patients. (34.2%, $P < 0.01$), Tryptase in four patients (11.4%, $P < 0.01$), ECP—11 patients (31.4%, $P < 0.01$) while Phadiatop was not altered in any patient. In the second group, there was a decline in TIgE in 22 patients (62.8%, $P < 0.01$), Tryptase—14 patients (40%, $P < 0.01$), ECP—18 patients (51.4%, $P < 0.01$) and Phadiatop—6 patients (17.1%, $P < 0.05$).

**Conclusion:** We concluded that the patients who were received both intranasal corticosteroid spray and systemic intramuscular corticosteroid therapy showed better clinical improvement than the patients who were received only intranasal corticosteroid spray therapy. The same results were shown by lab tests. Our data indicate that ECP, Tryptase, TIgE and Phadiatop are reliable markers to evaluate the efficacy of the treatment of patients with chronic rhinosinusitis with nasal polyps.

## 1108 | Endoscopic sinus surgery with two different middle turbinate treatment methods: Impact on olfaction

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**Background:** To evaluate differences in olfactory function of CRS patients after Endoscopic Sinus Surgery (ESS) with two different middle turbinate treatment methods.

**Method:** This prospective controlled study was carried out on CRS patients underwent ESS. Patients participating in the study were divided into two groups-group 1: partial middle turbinectomy (n = 22) and group 2: partial middle turbinectomy and middle turbinate fenestration (n = 23). Objective assessment of olfactory function using the University of Pennsylvania Smell Identification Test (UPSIT) and subjective assessment of symptom using visual analogue score (VAS) were performed before and 3 months after surgery.

**Results:** There were significant improvement comparing postoperative and preoperative UPSIT in both group 1 (35.23 ± 2.96 vs 32.23 ± 2.54, $P = 0.000$) and group 2 (36.09 ± 2.35 vs 32.04 ± 2.64, $P = 0.000$). The VAS were also significantly improved postoperatively compared to preoperatively in both group 1 (5.77 ± 0.75 vs 6.73 ± 1.08, $P = 0.000$) and group 2 (5.13 ± 0.81 vs 6.78 ± 1.28, $P = 0.000$). Patients undergoing partial middle turbinectomy and middle turbinate fenestration were more likely to show improvements in UPSIT (4.00 ± 1.20 vs 3.00 ± 1.11, $P = 0.014$) and VAS (1.59 ± 0.21 vs 0.95 ± 0.15, $P = 0.000$) compared to those with only partial middle turbinectomy.

**Conclusion:** Partial middle turbinectomy and middle turbinate fenestration during ESS is an effective method for improving postoperative olfactory function.

## 1109 | Nasal irrigation for the alleviation of nasal symptoms in pregnant women with allergic rhinitis

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**Background:** Allergic rhinitis (AR) is a common nasal disease in China, and symptoms include sneezing, nasal obstruction, smell disturbance as well as rhinorrhea. AR has a severe impact on the quality of life of patients, especially females during pregnancy. Medications for AR, such as intranasal corticosteroids, cannot be used during pregnancy. Therefore, in the study, we investigated the effectiveness of nasal irrigation with normal saline for reducing the symptoms of AR in pregnant patients.

**Method:** Female patients with AR symptoms were collected through the Ear, Nose, and Throat and Gynecology Departments. Serum IgE and allergen levels were detected in all patients. Endoscopy was performed to observe the nasal mucosa. Pregnant patients who had been diagnosed with AR received nasal irrigation treatment with normal saline, twice daily for 30 days. Nasal resistance was examined before and after 30 days of treatment. The efficacy for alleviating AR symptoms (rhinorrhea, sneezing, nasal obstruction, and itchy nose) was evaluated through patient-reported visual analog scale scores (from 0-10). The Quality of Life Questionnaire was administered on the final day of treatment.

**Results:** Fifty pregnant women who had been diagnosed with AR were enrolled in the study. All patients (100%) in the treatment group experienced symptom relief during the study period. Fifteen patients (30%) reported mild symptom relief, 20 patients (40%) reported moderate symptomatic relief, and 15 patients (30%) reported significant relief. Improvement of nasal resistance was detected in 30 patients (80%).

**Conclusion:** Nasal irrigation may alleviate AR symptoms in pregnant patients and thereby improve their quality of life. The optimized contents of the nasal irrigation solution require further investigation to achieve further improved efficacy.

MONDAY, 28 MAY 2018
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IMMUNE MECHANISMS OF INFECTION

## 1110 | Specific IgE production against bacterial pathogens in cystic fibrosis patients

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**Background:** Chronic pulmonary colonization with facultative pathogenic bacteria such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenza*, *Escherichia coli* and *Pseudomonas aeruginosa* is common among cystic fibrosis patients. Specific IgE directed against these pathogens has not been comprehensively studied in these patients but might contribute to pulmonary disease course.

We sought to determine specific IgE responses to bacterial pathogens in sera from cystic fibrosis patients and analyze their kinetic during disease course.

**Method:** Sera from patients (0-52 years) with cystic fibrosis, asthma or healthy controls were analyzed regarding the prevalence of bacterial pathogen specific IgE detected by immunoblotting (bacterial extracts) or DELFIA (dissociation-enhanced lanthanide fluorescence immunoassay) (*H. influenzae* (P6), *S. pneumoniae* (PsPC) and *P. aeruginosa* (ExoA)). In order to delineate kinetics of pathogen specific IgE responses in sera from consecutive blood draws of subgroup of 38 cystic fibrosis patients (1-23 years old) were determined.

**Results:** Patients with cystic fibrosis produced specific IgE against several facultative pathogenic bacteria known to colonize their airways. The majority of the 38 cystic fibrosis patients showed specific IgE directed to *S. pneumoniae* in at least one sample of consecutive blood draws, whereas IgE directed to *P. aeruginosa* was detected in less of those samples. Kinetics of sensitization to both pathogens did not correlate with each other. Sensitization pattern to bacterial pathogens changed with time suggesting a possible association to the course of disease.

Immunoblots revealed distinct IgE patterns in cystic fibrosis patients compared to sera from other patient groups possibly attributable to different sensitization routes.

**Conclusion:** Our data provide evidence, that cystic fibrosis patients are sensitized to different bacterial pulmonary pathogens and correlation with clinical data will provide insight into the clinical relevance of this currently not comprehensively studied immune response.

## 1111 | Genotopic (sequence) analysis of mycobacterium tuberculosis, isolated from patient with pulmonary TB

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**Background:** The main purpose of the scientific work is to carry out a scientific analysis of the molecular-genotypic properties of tuberculosis infection in the Republic of Azerbaijan, mainly of drug resistant tuberculosis, on the clinical course and treatment outcomes of the disease, laboratory findings, and also on socio-economic characteristics of the illness.

**Method:** The mycobacteria samples collected from the 75 patients involved in the study were studied by molecular—genetic methods: as well as DNA extraction from microbacteria and DNA sequencing was also performed. Examples for a more thorough investigation of the genome chain were sent to the BROAD (US) laboratory. Pathological material was collected from the 75 patients involved in the study, clean culture was obtained, DNA was extracted from tuberculosis mycobacteria, DNA was sequenced for further genetic analysis. Among the isolated samples, were identified strains with different genetic characteristics. The frequency of stamming among the selected samples based on their genetic characteristics is as follows: Beijing strain—58 patients (77%), T1-9 (12%), H3-4 (6%), LAM9-3 (4%), T5-RUS1-1 (1%). Based on the sequencing results of the investigated specimens, Beijing strain prevailed over all—58 patients (77%).

**Results:** Based on the results of recent chemotherapy due to tuberculosis, samples collected for sequencing were analyzed for genetic characteristics among TB patients registration groups based on DST. The relationship of the drug resistance characteristics with the genetic feature of selected samples (75) is shown in Table 1.

**Conclusion:** 1. The frequency of stamming among the selected samples (75 patients) based on their genetic characteristics is as follows: Beijing strain -58 patients (77%), T1-9 (12%), H3-4 (6%), LAM9-3 (4%), T5-RUS1-1 (1%). Based on the sequencing results of the investigated specimens, Beijing strain prevailed over all—58 patients (77%).

2. Based on the data obtained from the analysis of the drug resistance characteristics of the selected samples (75), Beijing strain prevailed over of each type of resistance: Sensitive - 10 patients - 8

Beijing (80%), Monoresistance - 1 patient- 1 Beijing (100%), Polyresistance - 1 patient- 1 Beijing 1 (100%), MDR- 56 patients-41 Beijing (73%), XDR-7 patients-6 Beijing (86%).

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The relationship of the drug resistance characteristics with the genetic feature of selected samples

| | Beijing | H3 | LAM9 | T1 | T5-RUSI |
|---|---|---|---|---|---|
| MDR | 41 | 4 | 3 | 8 | 0 |
| Sens. | 8 | | | 1 | 1 |
| XDR | 6 | 1 | | | |
| MonoDR | 1 | | | | |
| PoliDR | 1 | | | | |

## 1112 | Polymorphisms of interleukin -2 and interleukin-4 genes are associated with recurrent pulmonary tuberculosis in the intensive phase of chemotherapy

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**Background:** To study the influence of gene polymorphism (*IL-2* and *IL-4*) and cytokines in patients with recurrent pulmonary tuberculosis (RPTB)

**Method:** The study comprised 130 individuals: including 100 patients with RPTB(1st group) and 30 healthy donors (2nd group).- Serum levels of cytokines IL-2 and IL-4 were evaluated by ELISA(pg/L). Measurements on serum samples of patients were conducted prior or during first days after admission to the hospital and after 2 months on standard anti-TB therapy. The method of investigation of gene polymorphism of cytokines (for the sets real-time)-an allele-specific PCR using intercalating coloring Sybr Green. Two polymorphic variants were examined: T-330G promoter region of *IL-2* (rs2069762) and C-589T-*IL-4* (rs2243250) genes

**Results:** In the 1st group the levels of IL-4 and IL-2 were 9.5 ± 0.2 and 39.4 ± 0.7, while in 2nd group these values were 29.9 ± 1.2 and 21.6 ± 0.8, respectively ($P < 0.05$). Among patients with RPTB the heterozygous genotype was most prevalent; TG-74.0 ± 4.3%(N = 74) for *IL-2* and CT-61.0 ± 4.8%(N = 61) for *IL-4* genes ($P < 0.05$). The homozygous genotype was accordingly less common: GG-26.0 ± 4.3% (N = 26) and TT-39.0 ± 4.8%(N = 39), of which 18.0 ± 3.8%(N = 18) and 21.0 ± 4.0%(N = 21) of patients had mutation and remaining had normal homozygote genotype, i.e., TT-8.0 ± 2.7%(N = 8) and CC-18.0 ± 3.8%(N = 18) for *IL-2* and *IL-4* genes, respectively. In contrast, most of healthy donors had normal homozygous genotype with TT-60.0 ± 8.9%(N = 18) and CC-56.6 ± 9.0%(N = 17) with low frequency of mutations; GG-16.6 ± 6.8%(N = 5) and TT-23.3 ± 7.7%(N = 7) and heterozygous genotype TG-23.3 ± 7.7%(N = 7) and CT-20.0 ± 7.3%(N = 6) for *IL-2* and *IL-4* genes, respectively. Following a 2 month treatment, there was a significant reduction of cytokine levels in the IL2-29.5 ± 0.5 and increased in the IL4-16.6 ± 0.4, when compared to the beginning of therapy and after 2 months ($P < 0.001$)

**Conclusion:** Compared to healthy controls patients with RPTB had significantly lower levels of serum IL-4 and high-IL-2. This coincided with greater frequency of heterozygous polymorphism C-589T and T-330G of *IL-4* and *IL-2* genes. Further studies are warranted whether higher rate of RPTB has a causal immunogenetic relationship to allelic polymorphism of genes encoding for *IL-2* and *IL-4*. Standard 2-month anti-TB therapy results in reversal of inflammation characterized by decrease in IL-2 and increase of IL-4 to the levels comparable to healthy donors. IL-4 and IL-2 are immune correlates of treatment outcome and can help to identify better strategy for TB management

## 1113 | Changes in some cytokines of patients with relapse and multidrug-resistant pulmonary tuberculosis receiving anti-tuberculosis chemotherapy

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**Background:** Select cytokines in patients with relapse and multidrug-resistant pulmonary tuberculosis (MDR-TB) receiving anti-tuberculosis chemotherapy were compared to the levels in healthy individuals in order to assess the balance between inflammatory and anti-inflammatory responses.

**Method:** We observed 55 patients with infiltrative pulmonary tuberculosis. Cytokines, IL-2, IL-10 and IFN-γ, were examined by quantitative ELISA (pg/L) in patients with relapse MDR-TB (1st group; N = 41), patients with relapse tuberculosis (2nd group; N = 15) and healthy individuals (3rd group; N = 30). All patients received standard anti-tuberculosis drugs: Isoniazid (0.3 g); Rifampicin (0.6 g); Pyrazinamide (2 g); Ethambutol (1.2 g) and/or Streptomycin (1 g).

**Results:** At baseline the 1st group had serum levels of IL-2 (43.6 ± 0.8) pg/L; IL-10 (34.8 ± 0.8) pg/L and IFN-γ (108.2 ± 1.1) pg/L; 2nd group had IL-2 (39.6 ± 1.5) pg/L; IL-10 (38.6 ± 1.2) pg/L and IFN-γ (103.3 ± 1.4) pg/L vs IL-2 (21.6 ± 0.8) pg/L; IL-10 (50.2 ± 1.2) pg/L; IFN-γ (63.8 ± 2.2) pg/L in the control group. After 2 months, there was a significant decrease in pro-inflammatory cytokine levels

in the 1st (IL-2: 35 ± 0.9; IFN-γ: 75.6 ± 1.9) pg/L and 2nd group (IL-2: 28.6 ± 1.3; IFN-γ: 66.7 ± 3) pg/L, respectively. Conversely, IL-10 increased in 1st and 2nd groups to 41.9 ± 0.9 pg/L and 46.0 ± 1.7 pg/L ($P < 0.05$).

**Conclusion:** Prior to the study initiation patients with tuberculosis had higher IL-2, IFN-γ and lower IL-10 content than healthy controls. Two-month chemotherapy produced significant reduction in pro-inflammatory cytokines and increase in anti-inflammatory IL-10, with levels approaching those of healthy controls. Thus, tuberculosis drugs appear to have the anti-inflammatory effect in tuberculosis patients, which was predictive of positive clinical outcome.

## 1114 | Antibiotic resistance: ligands of innate immunity take the challenge

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**Background:** The antibiotic resistance propagation in a microbial community represents a global threat to human health. By 2050, mortality from antibiotic resistant strains of bacteria is projected to increase to 10 million people per year, which will exceed the death rate from cancer. Mutations in bacteria occur faster than new antibacterial drugs are marketed. In search of effective protection against infections, new strategies and approaches are being developed, one of which is the use of activators of innate immunity combined with etiotropic chemotherapy. By 2050, mortality from antibiotic resistant strains of bacteria is projected to increase to 10 million people per year, which will exceed the death rate from cancer. Mutations in bacteria occur faster than new antibacterial drugs are marketed. In search of effective protection against infections, new strategies and approaches are being developed, one of which is the use of activators of innate immunity combined with etiotropic chemotherapy.

**Method:** Muramyl peptides that are part of the peptidoglycan cell walls of all known bacteria, and regularly formed in the body during the decay of microflora are the natural regulators of immunity.

**Results:** When interacting with intracellular receptors of innate immunity, they trigger a signaling cascade of reactions that induces the expression of a large number of genes, in particular, the genes of pro-inflammatory cytokines (IL-1, IL-2, IL-6, IL-8, IL-12, tumor necrosis factor alpha, interferon), acute phase proteins, inflammatory enzymes (NO synthase and cyclooxygenase), molecules of the main histocompatibility complex. The result of the activation of the receptors of innate immunity is the body's reaction, manifested in the enhancement of the antimicrobial function of neutrophils, monocytes and macrophages, increasing the cytotoxic activity of macrophages, natural killers (NK cells) and T-killers, which eventually leads to the elimination of the pathogen. Muramyl peptides induce the synthesis of colony-stimulating factors and thus activate leukopoiesis, restoring the disturbed balance of blood cells.

**Conclusion:** Thus, muramyl peptides are involved in stimulating all forms of anti-infective protection of the body: phagocytosis, cellular and humoral immunity, as well as hemopoiesis, regulating all links of the immune system. The report discusses clinical studies of drugs based on muramyl peptides in the treatment of immune disorders, allergy, infectious and oncological diseases.

## 1116 | The effect of respiratory syncytial virus infection on the accumulation of nuocytes in lung tissue of allergic mice

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**Background:** IL-33 extend their effect on the innate lymphoid cells type II—nuocytes. Nuocytes produce IL-5 and IL-13 which play an important role in allergic bronchial asthma (BA). Previously we showed that IL-33 expression was increased in lung tissue of mice infected with respiratory syncytial virus (RSV) and in mice with RSV-induced BA exacerbations. The aim of the study was to assess changes in nuocytes amount using the mouse model of RSV-induced BA exacerbations.

**Method:** Female BALB/c mice were divided into four groups: mice with induced BA (1st group), mice with RSV-induced BA exacerbations (2nd group), mice with RSV infection (3rd group) and intact mice (4th group). BA was induced by i.p. injections of ovalbumin allergen (OVA) mixed with aluminum hydroxide on days 0, 14, 28, followed by i.n. OVA challenge on days 42-44. During induction of BA mice were infected with RSV strain A2 in dose of $5 \times 10^6$ $TCID_{50}$ on day 40. Third group of animals was treated with RSV only. IL-33 gene expression and viral load in lungs were evaluated by qPCR. Airway hyperreactivity (AHR) was measured by non-invasive plethysmography. Accumulation of nuocytes were assessed in lungs and spleens by flow cytometry.

**Results:** All three groups demonstrated significant increase in AHR compared to intact mice. RSV infection was confirmed by qPCR, allowed to detect 2-7 $\times 10^6$ viral genome copies/1 μg of total RNA isolated from lung tissue. Histological analysis revealed predominantly eosinophil infiltration after OVA sensitization and lymphocyte infiltration in animals treated with RSV only. The mice received OVA followed by RSV infection demonstrated both eosinophil and lymphocyte infiltration into the lungs. IL-33 gene expression in lung tissue measured by qPCR was significantly increased (1.5-1.7-fold) in the lungs of infected mice (groups 2 and 3). Despite that, these groups did not show increased numbers of nuocytes in lung and

spleen. However, we shown 2-fold and 3-fold increased accumulation of nuocytes in lungs and spleens of mice with experimental BA, respectively. In addition, the levels of activated nuocytes were elevated in lungs and spleens of mice with BA only.

**Conclusion:** We didn't confirm the hypothesis that nuocytes are activated under RSV infection. A significant increase in the number and proportion of activated nuocytes in the lungs and spleens was observed in mice with BA phenotype. Supported by RSF No 14-15-00894.

## 1117 | Comparison of IP-10 production induced by ex-vivo stimulation with Respiratory Syncytial Virus (RSV) and the TLR3 agonist Poly I:C in human and non-human primate lung tissues

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**Background:** Human Respiratory Syncytial virus (HRSV) is a major cause of respiratory disease young children and is known as a risk factor for asthma. HRSV and the viral mimic Poly I:C activate toll-like receptor 3 (TLR3), initiating an innate response with release of immune mediators, e.g. interferon gamma-induced protein 10 (IP-10). In this work, we aimed to perform an ex vivo HRSV infection in precision-cut lung slices (PCLS) from human, rhesus, and cynomolgus macaques, comparing whenever possible the response with the viral surrogate poly I:C.

**Method:** PCLS containing airways were prepared from lung sections of human, rhesus, and cynomolgus macaques. The slices were inoculated with HRSV-A2 $10^6$ IU/mL, UV-inactivated HRSV, or vehicle control for 48 hours. Macaque slices were also incubated with Poly I:C 100 μg/mL with and without the immunosuppressive dexamethasone 50 μg/mL. Viral replication, tissue viability, and immune response assays were assessed in supernatants, lysates, or slices.

**Results:** The inoculum infectivity of $10^6$ IU/mL as well the UV-inactivation were confirmed by plaque-assay on Hep-2 cells. Immunofluorescence staining using a FITC-labeled anti-RSV showed the presence of infected macrophages in PCLS, but not in mock infected samples. HRSV stimulation slightly decreased tissue viability, as seen by Live/DEAD staining and LDH assay. The viral infection increased IP-10 production in PCLS of human, rhesus, and cynomolgus macaques, reaching respectively 13.3, 3.4, and 1.7 fold-increase in comparison to the vehicle controls. Poly I:C stimulation caused IP-10 response comparable to HRSV in rhesus and cynomolgus PCLS. The IP-10 production ratio comparing HRSV/Poly I:C was 1.1 in rhesus and 0.9 in cynomolgus PCLS.

**Conclusion:** HRSV infects ex vivo PCLS of human and non-human primates, inducing the release of the pro-inflammatory chemokine IP-10. This response is comparable to the viral surrogate poly I:C. In the future, these systems can be used to further investigate host response to HRSV, especially in the context of asthma development.

## 1118 | Mycoplasma infection and wheezing in children

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**Background:** Aim of our study was to evaluate rate of implication of *M. pneumoniae*, *M. hominis* in wheezing in children with community-acquired pneumonia (CAP).

**Method:** The study included 330 children aged 7 years and younger suffering from CAP. The presence of *M. pneumoniae*, *M. hominis* infection was confirmed by specific *ELISA* serologic diagnosis.

**Results:** 162 patients completed study group with *Mycoplasma*-positive infection (110 patients with *M. pneumoniae* and 52 patients with *M. hominis*) and control group - 168 children without *Mycoplasma* infection (*Mycoplasma* - negative group). The analysis based on the serotype of *Mycoplasma* infection showed that wheezing was more frequently reported among children with *M. hominis* infection —88.5%, 95% CI: 76.6-95.6, and with *M. pneumoniae* infection—84.4%, 95% CI: 76.2-90.6. These results slightly differ from those obtained in the control group in which obstructive bronchitis was detected in 79.2%, 95% CI: 72.2-85 of cases; $\chi^2$=2.9, $P > 0.05$. Bronchial obstruction occurred 1.3 times more often in the *Mycoplasma*-positive group. The pulmonary system involvement is often associated with atypical flora. *Mycoplasma* can trigger wheezing in children with genetic predisposition or with preceding immunological changes.

**Conclusion:** *Mycoplasma* respiratory infection (*M. pneumoniae*, *M. hominis*) play an important role in appearances of wheezing in children with acute bronchopulmonary pathology.

## 1119 | Peculiarities of the epstein-barr virus prevalence among patients with pollen allergy

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**Background:** About 90% of the total population of the planet is infected by Epstein-Barr virus (EBV). In genetic defects of the immune response latent EBV-infection can be reactivated, causing clinical manifestations, including allergic pathology.
Purpose is to determine the prevalence of activated EBV infection in patients with pollen allergy.

**Method:** 362 persons with clinical and laboratory manifestations of pollen allergy were examined, 53.1% females, 46.9% males, age 22.6 ± 2.4 years. SPT (Diater, Spain), total and specific IgE by ELISA. DNA EBV by PCR, Rotor Geen 6000.

**Results:** Based on specific allergic studies, pollen allergy was confirmed in 355 (98.0%) patients: in 241 (67.8%)—polysensitization, in 114 (32.2%)—monosensitization. According to molecular genetic studies, activated EBV infection was detected in 291 (81.9%) cases: in 102 (35.0%) - monoinfection, in 189 (65.0%) - combined infection and in most 101 (53.4%) EBV+HHV6.

**Discussion:** In the human body, viruses of herpes live in the form of latent infection. Reducing general and local immunity for any reason is a potential EBV activator in the body. According to numerous studies, the association of EBV with a number of oncologic, lymphoproliferative, autoimmune diseases, secondary immunodeficiencies and other. However, a relatively small number of reports are related to the association of EBV with allergic diseases, in particular atopic ones.
We found that among patients with activated EBV infection, polysensitization was found to be 2.2 times more frequent, chest syndrome was 1.32 times more common and hyper-IgE syndrome occurred 1.5 times more frequently. In most of these patients, atopy was not detected in medical history.

**Conclusion:** The prevalence of activated EBV infection among patients with pollen allergy was 81.9%. The presence of EBV infection can act as a potential trigger for the formation of polysensitization and hyper-IgE syndrome, even in patients without atopy medical history.

**Keywords:** pollen allergy, EBV, hyper-IgE syndrome, atopy.

## 1120 | Do previous human bocavirus and coronavirus infections cause atopy in children?

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**Background:** Human bocaviruses (HBoV) and coronaviruses (CoV) are some of the important causes of both upper and lower respiratory tract infections in children. However, it is not clear yet that one of these two virus infections may cause atopy in children. We designed our study to determine whether if the children who were infected with HBoV or CoV, developed atopy later.

**Method:** We evaluated the laboratory test results of five boys (45.4%) and six girls (54.6%), 11 children (6 with HboV and 5 with CoV). Their average age at the study time was 59.2 ± 45 months. Nasal swab specimens were taken from these patients who admitted to our hospital with respiratory symptoms between 2015-2016. Patients are recalled after an average of 21 ± 2.5 months. ISAAC questionnaire and skin prick test to common inhalated allergens were performed.

**Results:** Only one patient had family history of atopy. Forty percent of the patients with CoV and 50% of the patients with HboV developed rhinitis. One patient with CoV and one patient with HboV developed recurrent wheezing. One patient with CoV developed atopic dermatitis. All skin prick tests were negative. It was noteworthy that 72.7% of the patients were passive smokers.

**Conclusion:** HboV and CoV may be associated with rhinitis but there is a need for more patient groups for a clear result.

## 1123 | Assessment of gene expression of immune cells during interaction with structural components of Streptococcus pneumoniae

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**Background:** *Streptococcus pneumoniae* can cause invasive forms of disease, including meningitis, pneumonia, and bacteremia. Reaction of immune cells in response to exposure to *S. pneumoniae* was assessed including Toll-like receptors (TLRs) which are involved in mediation of signal transduction.

**Method:** *E. coli* lipopolysaccharide (LPS) and heat-inactivated whole celled *Streptococcus* were used to activate peripheral blood mononuclear cells (PBMC) and dendritic cells (DC) from 20 healthy volunteers. CD86, MD - 2, CD 14, CD- 6, CD- 8, TLR-2, TLR-6, TNFgene expression total RNA of stimulated PBMC and DC was isolated using Tri-Reagent with RT-PCR performed.

**Results:** The expression of eight genes significant to immune system was impacted by Streptococcus and their components with increased expression of genes for CD86, MD - 2, CD 14, CD- 6, CD-8, TLR-2, TLR-6, TNF ($P < 0.05$ for the t-test).

**Conclusion:** Increased expression of genes whose products are involved in response to the presence of a microorganism or their structural components was seen including those whose expression depends on activation of TLR including pro-inflammatory cytokines and chemokines; molecules involved in apoptosis of eukaryotic cells;

and antimicrobial peptides. These activated TLRs are directly involved in the activation and differentiation of dendritic cells, and B and T lymphocytes. A systematic approach to evaluate genomic interactions may provide new therapeutic targets for microbial diseases.

## 1124 | Influence of synbiotics on the t cell response of grass pollen-allergic individuals in vitro

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**Background:** Seasonal allergic reactions to airborne allergens such as grass pollen are triggered by Th2 cells that can differentiate from naive $CD4^+$ T cells upon stimulation by allergens. As sensing of the intestinal microbiota by the host mucosal immune system is important to induce protective immune responses, modification of the gut microbiota might be able to support health and to prevent or treat allergies. Hence, we aimed to investigate the effects of synbiotics on the differentiation of human immune cells in the context of grass pollen allergy.

**Method:** Peripheral blood mononuclear cells from grass-pollen allergic patients and healthy controls were stimulated in vitro with grass-pollen extract and supplemented with different synbiotics. T helper cell subset differentiation was examined by flow cytometry and the measurement of cytokines in culture supernatants.

**Results:** In contrast to non-allergic controls, in grass pollen-allergic individuals, stimulation with grass pollen extract induced proliferation of Th2 cells. The addition of synbiotics, containing different probiotic strains of *Lactobacillus*, *Bifidobacterium* and fructooligosaccharides as prebiotic supplement, regulated the immune response of allergic individuals on the T helper cell level. A shift from an allergic Th2-driven immune response towards a Th1 immune phenotype was observed. This effect was mediated directly by synbiotics as well as indirectly by "only" culture supernatants of the probiotic bacteria.

**Conclusion:** Taken together, the presence of synbiotics showed an immune-modulating capacity via suppression of Th2-type inflammation in peripheral blood mononuclear cells of grass pollen-allergic individuals. Hence, these effects of synbiotics on the host immune response might implicate a potential approach to modify allergic immune responses. Further studies might give an insight into the regulatory mechanisms of specific compounds derived from probiotics, which suppress the Th2-driven immune-phenotype.

## 1125 | 16S rRNA profiling of the dermatophagoides farinae core microbiome: Enterococcus and bartonella

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**Background:** It is important to study the microbiome of the house dust mite owing to its potential immunomodulatory effects on allergic disease development. A 16S rRNA amplicon analysis using high-throughput sequencing technology was performed to determine the core microbiome of the house dust mite *Dermatophagoides farinae*.

**Method:** In this study, 16S rRNA amplicon analysis using high-throughput sequencing technology, 16S rRNA cloning, cultivation of mite homogenates, and several different stains were performed.

**Results:** The genera *Bartonella* and *Enterococcus* occupied almost 99% of the microbiome of *D. farinae*; these findings were supported by 16S rRNA cloning, cultivation of mite homogenates, and several different stains. Based on staining results, the genus *Enterococcus* was distributed throughout the intestinal lumen and stool and the genus *Bartonella* was detected in the hemocoel of mites.

**Conclusion:** *Bartonella* and *Enterococcus* were identified as core microbiome of *D. Farinae*. These bacteria in the house dust mite have potential immunomodulatory roles in allergic diseases.

## 1126 | TLRs ligands and chemokines role in tumor cells migration and expression of innate immunity factors

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**Background:** The influence of innate immunity factors on tumor formation has been actively studied in recent decades, but the possibility of activation of metastasis by stimulation of TLRs has not been studied so the aim of this work was to study the chemotaxis of healthy and tumor cells towards TLRs ligands and CXCL12.

**Method:** The investigated material-line K562; mononuclear cells (MNCs) from healthy donors and patients with myelomonoblastic leukemia. Chemoattractants used were: CXCL12 (ThermoFisher, USA), synthetic ligands DNA_lig (ccg-gtc-cac-aag-ggg-ggc-ca) and

RNA_lig (ccg-agg-aug-cga-ggc-uug-uu). To study chemotaxis in vitro, a Boyden96 chamber was used - WellFiltrationPlateMultiscreenTM - MIC with a pore size of 8 μm (Millipore, USA). Chemotaxis was studied in dynamics after 10, 60 minutes and a day using the above ligands. As control, RPMI-1640 medium without glutamine was used (PanEco, Russia). The statistical analysis was carried out using the computer statistical program BioStat2009 5.8.3.0, as well as the MicrosoftExcel 97-2003 program.

**Results:** In patients with myelomonoblast leukemia, both spontaneous and induced (under the influence of CXCL12), the migration activity was reduced 7-fold during the whole experiment of the migration, but after using of chemotherapy, the migration activity was partially restored. There is a blocking of inducible expression of TLR4 and EGFR receptor genes in cells with myelomonoblastic leukemia. Chemokine CXCL12 leads to a twofold increase in the chemotaxis of MNCs in healthy donors and TLR-mediated induction of expression of the genes of the chemokine receptors CCR4 and EGFR is observed in these cells.

**Conclusion:** CXCL12 reduces the chemotaxis of tumor cells in patients with myelomonoblastic leukemia and also the expression of EGFR and TLR4, leading to tumor regression, as a decrease in chemotaxis leads to a decrease in metastasis, and a decrease in expression of the epidermal growth factor receptor and TLR4 leads to a decrease in proliferation. The role of DNA and RNA ligands in the MNC of healthy donors is twofold: on the one hand, inhibition of chemotaxis, on the other hand activation of the expression of innate immunity factors.

## 1127 | Differential maturation of TLR7/8-mediated responses between atopics and non atopics

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**Background:** Age-dependent changes of innate cytokine production have been reported, including molecules implicated in antiviral responses. Furthermore, several studies suggest that the postnatal development of these responses might be modified by the presence of atopy and this might be linked to an enhanced susceptibility to infections. Nonetheless, most of the recent research focuses on changes occurring early in life and there are rare data on differences in responses between allergic and non allergic subjects.

**Method:** We aimed to evaluate i) the maturation trajectory of the TLR7/8 antiviral pathway ii) if this trajectory varies between atopics and non atopics. Peripheral blood mononuclear cells (PBMCs) were isolated from otherwise healthy atopic and non-atopic subjects, aged 0-45 years. Atopy was assessed by medical history and skin prick testing to eight common aeroallergens and egg white. Selected cytokines involved in antiviral TLR7/8 response were measured by Luminex multiplexing technology in 24 hours culture supernatants of R848-stimulated PBMCs. Data were analyzed by estimating the non-parametric correlation between age and cytokine expression in atopics and non atopics. A sub-analysis was performed for ages 0-20 years in both groups.

**Results:** The analysis comprised data from 39 atopic and 39 non atopic patients (mean age 10.8 years, age range 0-45 and mean 10.3 years, range 0-43.3, respectively). Significant age-related increases in the production of IL-1β, TNF-α, MIP-1β were found only in non atopics. Significant age-related increase in the production of IFN-α2 and IL-12 was found only in the non-atopics 0-20 years-old. Significant maturation of antiinflammatory IL-10 production was observed in both groups and different age ranges.

**Conclusion:** Age-related increases in cytokines implicated in innate antiviral responses were observed mostly for non atopics. Atopy was associated with suboptimal Th1- proinflammatory cytokine and interferon type I responses, in the context of the TRL-7/8 pathway postnatal maturation. Differences in the developmental pattern of those cytokines between atopics and non atopics may contribute to the reported increased susceptibility of atopics to infections.

## 1128 | The experimental reprogramming of phenotype of subpopulation of neutrophilic granulocytes IFNa/ßR+IFN?R+TLR4+ of healthy persons

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**Background:** Neutrophilic granulocytes (NGs) are important cells in realization of antiviral defence, but viruses can arm the antiviral functions of NG. NGs express IFNα/βR, IFNγR, TLR4 receptors, which recognize viral RNA, DNA, PAMP.

**Method:** We studied NGs of 16 healthy persons of both sexes, aged 20-55 years. IFNα/βR, IFNγR, TLR4 receptors were tested by flow cytometry method.

**Results:** NGs of healthy persons express IFNαβR1, CD119, TLR4. The number of IFNαβR$^+$NG was 1.50% [0.85; 1.90]. The numbers of IFNγR$^+$NG and TLR4$^+$NG were different: group A—IFNγR$^+$NG - 2.20% [1.33; 5.15] and group B—% of IFNγR$^+$NG -20.90 [18.65;

39.25] ($P \leq 0.001$). In group C: TLR4$^+$NG was 5.05%[1.65; 8.15] and in group D TLR4$^+$NG was 32.05% [21.95; 42.78] ($P \leq 0.001$). The action of dsRNA was different: IFNaR$^+$NG increased to 2.80% [1.80; 3.40]($P \leq 0.005$); in group A: IFN$\gamma$R$^+$NG increased to 11.30% [9.68; 21.30]($P1 \geq 0.001$), in group B: IFN$\gamma$R$^+$NG decreased to 11.30% [9.68; 21.30] ($P \leq 0.002$) vs control. In group C: TLR4$^+$NG increased from 5.05% [1.65; 7.53] in control to 43.37% [31.20; 61.80] ($P \leq 0.001$). In group D: TLR4$^+$NG increased from 32.27% [21.95; 46.50] to 41.10%[36.25; 50.70] ($P \leq 0.05$). rIFNa2b wasn't changed IFNaR$^+$NG ($P \geq 0.05$). In group A and group B rIFNa2b was not changed the number of IFN$\gamma$R$^+$NG vs control ($P1 \geq 0.05$; $P2 \geq 0.05$). rIFNa2b increased TLR4$^+$NG in group C: from 5.05% [1.65; 7.53] in the control - to 27.20% [9.93; 42.10] ($P \leq 0.002$). In group D: the level of TLR4$^+$NG was not changed vs control ($P \geq 0.05$). Combine use of dsRNA and rIFNa2b increased IFNaR$^+$NG vs control ($P \leq 0.001$) and vs effects of rIFNa2b ($P \leq 0.01$). The combine use of dsRNA and rIFNa2b to increase IFN$\gamma$R$^+$NG in group A—up to 6.95%[3.20; 9.25] ($P \leq 0.05$) vs intact control and to decrease IFN$\gamma$R$^+$NG vs dsRNA effect ($P \leq 0.002$). In group B dsRNA and rIFNa2b to increase IFN$\gamma$R$^+$NG—to 33.88% [19.10; 39.45] vs of dsRNA effect −11.30%[9.68; 21.30] ($P \leq 0.002$). In group C dsRNA and rIFNa2b to decreased TLR4$^+$NG to 8.30% [2.45; 17.20] vs rIFN$\alpha$ ($P \leq 0.05$) and dsRNA effects ($P \leq 0.003$). In group D the high level of TLR4$^+$NG didn't changed after combine use of dsRNA and rIFNa2b and influence of dsRNA vs intact control ($P1 \geq 0.05$; $P2 \geq 0.05$), but was decrease vs mono- rIFNa2b effects ($P \leq 0.002$).

**Conclusion:** We demonstrated that dsRNA, rIFNa2b and their combine use transformed phenotype of subpopulation IFN$\alpha/\beta$R$^+$ IFN$\gamma$R$^+$ TLR4$^+$ NG in a different manner.

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## 1129 | Immediate allergic reaction with eosinophilia due to Carbapenems

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**Case report:** Our patient is a 45-year-old Caucasian man with a history of hypertension and cholangiocarcinoma that required Roux-en-Y Gastric Bypass. Due to ulterior infections he was treated with Meropenem, presenting in less than 8 hours after the initial infusion, a generalized exanthema and progressive eosinophilia (1.01 mil/mmc). There were no other organs affected. It slowly ended disappearing after the suspension of the antibiotic. Due to the evolution of the infection, Meropenem was substituted by Piperacillin-Tazobactam and other non-beta-lactams which were well accepted. The patient had a positive evolution, showing a correlation between the recovering from the infection and the analytical data. Two weeks later, due to a new abdominal infection, he was prescribed Imipenem, presenting a very similar generalized cutaneous exanthema and higher eosinophilia (2.02 mil/mmc). After interruption of the treatment, he experienced full recovery in the next two days. Afterwards, he tolerated Cephalosporins.

**Method:** A complete physical examination was firstly done, followed by Hemogram, amplified biochemistry with liver parameters, kidney function test and consecutive triptase determination. Four weeks later, allergologic study was carried out, including cutaneous test and tolerance test.

**Results:** The protocol of Beta-lactams was completed, having a total negative result to prick and intradermocutaneous -ID- test (BPO-PPL, MDM, Penicilina G-Na, Ampiciline and Amoxicillin, both 2 mg/mL and 20 mg/dL). It was amplified with both prick and intradermo test to Cefazoline, Cefotaxime, Ceftazidime, Piperaciline-Tazobactam (all doses: 200 mg/dL), Imipenem and Meropenem (doses: 10 mg/mL) and ID 20 mg/mL with negative results. An oral challenge to therapeutical dose of Penicilin, Penicillin G Benzathine Intramuscular and Amoxicillin confirmed the tolerance, no clinical or analytical change was observed during the test. No tolerance challenge was done with Carbapenem due to the highly suggestive history of allergy and the risk of a major complication.

**Conclusion:** With all the data provided, a drug induced hypersensitivity was diagnosed. We present a case of immediate allergic reaction with eosinophilia due to Carbapenems, with tolerance to other beta-lactams antibiotics.

## 1130 | Hypersensitivity reaction to metronidazole in a patient with Sjögren Syndrome

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**Background:** According to the literature, patients with Sjögren Syndrome, especially anti-Ro positive patients have significantly more prevalent drug allergy and skin contact allergy. However, so far none of the cases of metronidazole hypersensitivity reaction has been reported in Sjögren Syndrome patient.

**Case report:** A 67 year old female was diagnosed with primary Sjögren Syndrome in March 2015 based on ocular and oral symptoms and signs, positive minor salivary gland biopsy with positive antinuclear antibodies and anti-Ro antibody. Initially she was treated with corticosteroids and antimalarials.

In May 2015 she was admitted to the Clinic for Pulmonary Diseases, Clinical Centre of Serbia due to fever, fatigue, right rib cage pain and fainting. According to laboratory findings consistent with inflammation (elevated procalcitonin levels 1.33 μg/L, erythrocyte sedimentation rate 116 and C reactive protein level 281.3 mg/L) and Chest X ray she was diagnosed with right sided upper lobe pneumonia and treated with combined antibiotics (ceftriaxone, ciprofloxacin and metronidazole). The next day she developed maculopapular rash that was latter depicted as a toxic allergic exanthema. Previous treatment was therefore discontinued, and meropenem was introduced with corticosteroids and antihistamines. Skin lesions resolved within few following days.

In August 2015 our patient was admitted to the Clinic of Allergology and Immunology, Clinical Centre of Serbia where the metronidazole graded dose oral drug challenge was performed with 400 mg of metronidazole. Three hours after its completion, itchy rash consistent with diffuse erythema on her face, chest, hands and feet was noticeable. With intensive corticosteroid, antihistamines (prescribed by an allergist) and topical treatment (prescribed by a dermatologist) skin lesions resolved within a few days. Due to the positive drug challenge, metronidazole was discontinued from further use. Later on, drug challenges were performed with doxycycline, azithromycin, gentamicin and all of them were negative.

**Conclusion:** Although metronidazole hypersensitivity reactions are rarely described, there are individual cases of localized or generalized itchy exanthema related to metronidazole use. Due to low sensitivity of cutaneous testing, oral drug challenge remains the gold standard for the diagnosis of both early and delayed hypersensitivity reactions.

## 1131 | Hypersensitivity reactions in treating multiple sclerosis: two case reports

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**Background:** Treatment for multiple sclerosis (MS) has been changed in the last years due both to new drugs either to pharmacological modification of known molecules.

We report two clinical cases of MS patients with cutaneous immediate hypersensitivity reactions to interferon beta1a in its modified pegylated formulation and to dimethylfumarat.

**Case 1:** A 25 years old lady affected by MS started in August 2017 subcutaneous pegINF beta1a administered every 15 days. A few hours after the second injection she developed a itching skin rush involving the trunk, abdomen and arms. Constantly relapsed after the next three doses despite antihistamines. PegINF beta1a was tested with SPT and ID test from a concentration of 1:10 000 and increasing 10 fold at 30 minutes intervals. SPT Histamine 10 mg/mL and ID saline 1/1 were used as positive control. Patch test with undiluited pegINF beta-1a was negative. An immediate positive reaction with a 10 mm wheal and erithema developed at 1:10 000 and 1:1000 ID. The test was negative in two healthy subjcts.

**Case 2:** A 43 years old man with MS since 2010 had a negative allergic history apart from an erithema due to cosmetics. Treatment with corticosteroids and INF was well tolerated. After a few days he started dimethylfumarate (DMF) 240 mg 2 times daily, he developed a itching skin rush and urticaria localized to the trunk and face responsive to antihistamins. SIDAPA patch test were negative as for DMF 0.01% in vaseline. SPT 1/100 with DMF resulted positive with a wheal within 20 minutes. Two control subjects were tested as negative.

Written informed consent of patient has been obtained in the two cases.

**Discussion:** The first case shows cutaneous immediate hypersensitivity response to INFbeta1a. Literature reports a few cases of urticaria and anaphylaxis but this is the first for the pegylated formulation. Polyethylene glycol (PEG) confers to a drug modified pharmacokinetics, solubility and immunogenicity. Immediate reaction to PEG (macrogol) have been described when combinated in vaccines or drug pils.

DMF is a known cause of contact dermatitis related to footwear, wallets and furniture. Flushig is a reported side effect of DMS in MS managed with dose reduction. This case shows the possibility to immediate sensitization to DMF. As the armamentarium to treat MS now combines immunomodulatory and biologic drugs, the avaliability of diagnostic and desensitization protocols for hypersensitivity reactions must be keeped in mind.

## 1132 | Dress syndrome to phenytoin and allopurinol: Case reports

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**Case report:** Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon but serious hypersensitivity drug reaction, manifested with rash, fever, lymphadenopathy and visceral organ involvement.

Case 1: An 27-year old man presented to our department with skin redness and generalised itching, swelling of the lips, ears, hands and feet, and dysphagia. He had started treatment with phenytoin after an experience of post-traumatic generalized epileptic shock. Blood tests revealed eosinophilia, hepatic involvement, and previous infection of viral B hepatitis (see table). Drug withdrawal and prednisolone treatment leaded to attenuating of mentioned skin symptoms within 2 days, associated by occurrence of a exfoliative dermatitis. One week after admission, the patient developed fever that lasted for 4 days with enlarged lymph nodes on submandibular, paracervical, axillar and inguinal regions. A preventive antibiotic therapy is started and 2 weeks later, the lymph nodes were not palpable and the skin got the normal appearance. Corticoid therapy is reduced gradually according to symptoms resolvement.

Case 2: A 56-year old woman presented to our department with a 6-day history of pruritic, macular rash, periorbital swelling, cheilitis and fever. She had started some weeks ago the allopurinol for asymptomatic hyperuricemia, had longer history for treatment of arterial hypertension and type-2 diabetes mellitus (olmersartan, nitrendipine, methyldopa, furosemide, regular and glargine insulin), and experienced nephrectomy and cholecystectomy. The patient was febrile, while blood tests revealed eosinophilia, increased seric creatinine/urea levels (due to nefrectomy), and severely-altered liver parameters (see table). The allopurinol withdrawal, topical and systemic corticoid therapy, and the liver protectors attenuated serologic transaminases levels and patient's skin lesions within few days, followed by substantial improvement of laboratory findings one week after therapy start. The treatment dosage was gradually tapered and finally stopped within a period of 2 months in accordance with attenuating and complete resolvement of the clinical and laboratory abnormalities.

Our case demonstrated that DRESS syndrome is a severe drug reaction, but the immediate introduction of treatment and supportive measures can improve disease's outcome even after a temporary exacerbation or severe affection of internal organs.

| | | | | | | |
|---|---|---|---|---|---|---|
| CASE 1 | Parameters/(normal ranges) | Day 1 | Day 3 | Day 7 | Day 14 | Day 20 |
| | AST (U/L)/(0-32) | 84 | 63 | 1218 | 49 | 62 |
| | ALT (U/L)/(0-31) | 26 | 204 | 1466 | 557 | 188 |
| | GGT (U/L)/(9-39) | - | 1103 | 849 | 688 | 318 |
| | ALP (U/L)/(64-306) | • | 482 | 371 | 229 | - |
| | Eosinophils/$mm^3$/(2-500) | 2540 | - | - | 444 | - |
| | Leukocytes/$mm^3$/(4.0-10.0)×$10^3$ | 12.7 × $10^3$ | - | 29.8 × $10^3$ | 11.1 × $10^3$ | 10.5 × $10^3$ |
| CASE 2 | Parameters/(normal ranges) | Day 1 | Day 4 | Day 8 | Day 10 | Day 60 |
| | AST (U/L)/(0-32) | 211 | 39 | 27 | 27 | 25 |
| | ALT (U/L)/(0-31) | 1119 | 363 | 168 | 86 | 27 |
| | GGT (U/L)/(9-39) | - | 288 | - | 120 | 30 |
| | LDH (U/L)/(140-280) | 612 | 482 | 425 | 371 | 289 |
| | Urea(mg/dL)/(10-40) | 112 | 110 | 109 | 98 | 94 |
| | Creatinine(mg/dL)/(0.6-1.3) | 1.6 | 1.6 | 1.4 | 1.4 | 1.4 |
| | Eosinophils/$mm^3$/(2-500) | 1358 | - | - | 420 | 120 |

## 1133 | Multiple drug hypersensitivity syndrome: Clinical case

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**Introduction:** Drug hypersensivity reactions affect >7% of the general population, representing an important public health problem. Multiple drug hypersensivity syndrome (MDHS) is a peculiar clinical condition characterized by a propensity to react against different chemically unrelated antibiotic or non-antibiotic drugs (tow or more). The origin of MDHS is still unclear but recent studies place severe cutaneous adverse reactions, particulary DRESS, at high risk of inducing multiple sensitizations and thus they increase the understanding of, at least, a part of the spectrum of MDH pathways.

**Case report:** 54 years-old woman, nurse, with a past medical history of multiple myeloma, chronic renal failure on regular hemodialysis, type II diabetes mellitus, asthma, and hypertension. She was referred to the Immunoallergology (IA) outpatient department because of a DRESS after treatment with vancomycin, amikacin and piperacillin-tazobactam—several long-term treatment with antibiotics due to febrile syndrome. She also described one episode of a pruritic maculopapular generalized exanthema on the 2th day of treatment with meropenem for febrile neutropenia. In order to do an allergologic evaluation, all antibiotics involved were tested - skin prick tests (SPT) and intradermal (ID). Piperacillin-tazobactam, amikacin and daptomycin SPT an ID were negative in immediate and late reading. ID with vancomycin and meropenem were positive in late reading. To evaluate beta-lactams allergy, beta-lactam-specific IgE were performed and negative, SPT and ID with major (PPL) and minor (MDM) determinants and penicillin, clavulanic acid and cephalosporins were also negative in immediate and late reading. Amoxicillin ID positivity was observed at 48 hours. The diagnosis of delayed hypersensitivity reaction to vancomycin, meropenem and aminopenicillins was established.

**Conclusion:** The number of hypersensitivity reactions to antibiotics described is increasing and consequently the MDHS diagnosis. It should be emphasized that patients with MDHS present a risk of reaction to a new drug far superior to the general population and for that it is essential take steps to avoid or prevent infections and thereby minimize the need for antibiotic therapy. The authors describe a case of a clinical condition still uncommon: delayed hypersensitivity to vancomycin, meropenem and aminopenicillins where the prompt recognition of this entity was essential for rapid diagnosis and therapeutic alternatives.

## 1134 | Delayed hypersensitivity reaction to isoniazid

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**Background:** Isoniazid (isonicotinic acid hydrazide) is a first-line antituberculous drug, useful as monotherapy or a part of combination therapy for tuberculous and nontuberculous mycobacterial infections. Despite its wide use, hypersensitivity reactions to isoniazid are infrequent and allergy workup is not performed in most communications.

**Materials and methods:** We report the case of a 30 years-old woman with history of severe psoriasis with no satisfactory response to methotrexate, cyclosporine and phototherapy, so that she would start anti-TNFα treatment. Preliminary study showed a tuberculin

skin test positive, therefore the patient was started on treatment with isoniazid and pyridoxine (vitamin B6) 300/50 mg/day for latent tuberculosis infection. Four weeks later, she presented a pruritic generalized maculopapular exanthem with erythematous and scaly patches, with no facial involvement or fever, as well as normal blood count parameters.

The treatment was discontinued and the eruption regressed in the days after.

**Results:** One month after, during a lesion-free period, skin prick test were performed with isoniazid (60 mg/mL) and pyridoxine (150 mg/mL). Both drugs were also tested by closed patch test (20% petrolatum). Reading delayed prick test at 48 hours was positive only to isoniazid (15 × 8) and at 96 hours (30 × 25). Patch test to isoniazid also revealed positive reactions on day 2 and day 4 (+++), while prick and patch test to pyridoxine were negative.

Prick test with delayed reading and patch test with isoniazid were negative in five healthy controls, excluding the possibility of irritant skin test reactions. Delayed-hypersensitivity to isoniazid was diagnosed and its usage was forbidden.

**Conclusion:** We present a case of a maculopapular eruption resulting from treatment with isoniazid, and according to our experience, we can affirm that prick test with delayed reading and patch test with isoniazid are useful in the diagnosis of delayed hypersensitivity reactions to isoniazid.

## 1135 | Multiple sensitization to parenteral contrast media

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**Introduction:** Hypersensitivity to iodinated contrast media (ICM) can present as immediate or nonimmediate reactions and their evaluation should include skin tests (ST), in vitro methods and drug challenge test (DCT). In case of sulphur hexafluoride (macrogol 4000, used as excipient), a second-generation ultrasound contrast agent used in ultrasound, a 0.4% rate of severe adverse events has been observed, including three cases of death.

**Case report:** A 40-years-old woman, diagnosed of ischemic cardiopathy, developed an anaphylactic shock 5 minutes after the administration of 2 mL sulphur hexafluoride intravenous during an echocardiogram. She was treated in emergency room with a total recovery. 2 months earlier, she had developed an extensive erythematous-maculopapular rash converging in plaques in relation with adhesive dressings which had been placed during a hospitalization due to thoracic pain. An allergic contact dermatitis was suspected and recommendations thereon were given. Interestingly, an arteriogram with iodixanol (ICM) was carried out one week before skin reaction with good immediate tolerance.

**Methods:** Blood test: Blood count and serum chemistry were done during both reactions to contrast media. Serum tryptase level was not measured during the anaphylaxis, but its baseline level was quantified later.

Skin Tests: skin prick-tests (SPT) and intradermal test (IDT) with sulphur hexafluoride, macrogol 4000, iodixanol, iohexol and ioversol, with immediate and delayed reading. Patch-test with TRUE TEST© and serial acrylates with 48-96 hours readings.

In vitro test: basophil activation test (BAT) with sulphur hexafluoride and macrogol 4000.

DCT with intravenous ioversol (100 cc), according our department protocol and with no premedication.

**Results:** IDT with sulphur hexafluoride was positive on immediate reading. Macrogol 4000 and controls were negative. SPT and IDT with iodixanol were both positive on delayed reading. All the other ST and controls were negative. Patch-tests were all negative.

Blood tests results were normal with a serum tryptase level of 4 KU/L. BAT was negative.

Ioversol used in DCT was tolerated.

**Conclusions:** We present a patient with a double sensitization to parenteral contrast media: an anaphylactic shock due to sulphur hexafluoride and an atypical delayed exanthema related to iodixanol, and diagnose was obtained with ST in both cases.

This is the first documented case with a positive immediate ST to sulphur hexafluoride.

## 1136 | Late hypersensitization to inhaled budesonide

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**Introduction:** Budesonide is a glucocorticoid used in treatment of many pathologies, for example asthma and rhinitis. Reactions to budesonide have been described occasionally and used to be late reactions.

**Clinical case:** Female patient, 59 years old, with moderate to severe persistent rhinitis with 10 years of evolution, had been medicated with inhaled fluticasone furoate 27.5 μg. She had started a new inhaled therapeutic (budesonide 150 μg + formoterol 4.5 μg), due to a 6 months evolution clinical condition of persistent cough and recurrent wheezing. One week later, 4 hours after last administration, presented an episode of dyspnea and oropharyngeal burn that developed to uvula edema. After 20 mg of prednisolone and 5 mg of levocetirizine without improvement, she gave entrance in the Hospital and had a complete resolution of clinical condition after administration of intravenous anti-histamines and corticosteroids.

The patient was referred to our department, did a spirometry (mild bronchiolar obstruction with reversibility on bronchodilation test); skin prick test to aeroallergens (negative); standard battery of Portuguese Group of Contact Dermatitis-(positive to budesonide 0.1% at 96 hours) and epicutaneous tests with patient usual medication and other glucocorticoids (positive for budesonide 160 μg + formoterol 4.5 μg at 96 hours). Six healthy patients controls showed negative results when tested with epicutaneous tests for the aforementioned glucocorticoids and patient usual medication.

The patient had indication to avoid all products with budesonide and started inhaled therapeutic with fluticasone 250 μg + salmeterol 25 μg, which had been negative in epicutaneous test and was tolerated.

**Discussion:** It was then established the diagnosis of late hypersensitization to inhaled budesonide on a patient with mild persistent asthma and moderate to severe non allergic rhinitis. Besides all symptoms that patient had presented (dyspnea, oropharyngeal burn and uvula edema) seem hypersensitization type I, positive epicutaneous tests demonstrated hypersensitization type IV to budesonide.

**Conclusion:** Although epicutaneous tests with glucocorticoids aren't standardized, they allowed us to diagnose this patient with late hypersensitization to inhaled budesonide, mediated by T cells and choose an alternative therapeutic.

## 1137 | Behcet's disease mimicking drug hypersensitivity

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**Background:** Erythema nodosum (EN) is a delayed-type hypersensitivity reaction which occurs secondary to drugs, inflammatory bowel disease, malignancy, sarcoidosis, pregnancy, and other conditions. We present an uncommon case mimicking drug hypersensitivity presenting with recurrent EN.

**Case presentation:** A healthy 32 year old female patient was receiving a standard dose of oral levofloxacin for acute sinusitis in 2015. On the 7th day of treatment, she developed oral and genital aphthous ulcers and plantar erythema nodosum. The lesions were treated by oral steroid therapy. In 2016, cefaclor tablets were prescribed due to upper airway infection, after receiving the second oral cefaclor, plantar erythema nodosum occured again which disappeared in a month without any medication. In 2016, she received oral clarithromycin due to the upper airway infection, on the second day of clarithromycin, oral and genital aphthous ulcers, acneiform erupsions on back and chest, and right axillary lymphadenopathy occured. Patient was referred to our clinic with the suspicion of drug hypersensitivity. On the physical examination, acneiform lesions on her back and erythema nodosum lesion on the dorsum of hand were detected. Laboratory tests were in normal ranges. Drug patch tests with the culprit drugs mixed with 10% and 30% petrolatum resulted negative. Patient was suspected to have Behcet's disease, and consulted to rheumatology department. Oral colchicum dispert twice a day was prescribed. Afterwards, patient achieved to take oral amoxicillin-clavulanate for a week without any hypersensitivity; and has been following by oral colchicum dispert maintenance therapy since then.

**Conclusion:** Behçet's disease is characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, gastrointestinal involvement, neurologic disease, vascular disease, or arthritis. Skin manifestations may include acneiform lesions, papulo-vesiculo-pustular eruptions, pseudofolliculitis, nodules, and erythema nodosum. In our case, it is remarkable that the patient had drug induced reactions with different kinds of antibiotics, all of the reactions were late onset but her lesions were different from delayed onset maculopapular erupsions. In conclusion, Behcet's disease should be suspected as the major reason of erythema nodosum.

Written informed consent was obtained from the patient.

Authors declare no conflict of interest.

## 1138 | A case report of eczematous drug eruptions due to recombinant human erythropoietin alfa

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**Introduction:** Cutaneous reactions caused by erythropoietin injection (including preservative and stabilizer) have been discussed in previous researches. This case report is a patient who has experienced eczematous drug eruptions due to the injection of erythropoietin alfa but become successful in the injection of erythropoietin beta.

**Case report:** A 50-year-old-male, draftsman with no previous history of atopic disease was prescribed subcutaneous injection of recombinant human erythropoietin alfa for the treatment of anemia due to chronic kidney disease. About 2-3 weeks after the injection of erythropoietin alfa, he developed itchy rashes on body and limbs. Drug discontinuation was suggested due to the suspicion of delayed allergic reaction to erythropoietin alfa. Skin prick, intradermal test and patch test were applied. After 10 days of the subcutaneous injection of erythropoietin alfa (once a week), the itchy rashes reoccur. The diagnosis was allergic to erythropoietin alfa. The skin biopsy revealed suppurative folliculitis. After skin recovery, patch test with the different kinds of erythropoietin including preservative and stabilizer were performed. Another kind of erythropoietin was selected

(Erythropoietin beta). After drug administration to the therapeutic level, found no adverse effects.

**Conclusion:** Erythropoietin can cause drug eruption as found in this case report. The patient developed skin eruptions due to the injection of erythropoietin alfa, but become successful in injection of erythropoietin beta. In summary, the patients who are allergic to erythropoietin alfa can use other kinds of erythropoietin.

| Agent | Prick | Intradermal test (0.02 mL) 48 h | 96 h | Patch test (96 h) undiluted |
|---|---|---|---|---|
| Positive control (Histamine) | Positive | NT | NT | NT |
| Negative control (Normal saline) | Negative | NT | NT | Negative |
| [1]EPO-a | Negative | Negative | Negative | Negative |
| [2]EPO-a | Negative | Negative | Negative | Negative |

| Agent | Patch test 48 h | 96 h | 168 h |
|---|---|---|---|
| [1]EPO-a | Negative | Negative | Negative |
| [2]EPO-a | Negative | Negative | Negative |
| [3]EPO-b | Negative | Negative | Negative |
| [4]5% Polysorbate-80 | Negative | Negative | Negative |
| Sodium citrate | Negative | Negative | Negative |

## 1139 | Case report of severe anaphylaxis induced by morphine and tramadol

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**Background:** Opioid is a class of drugs composed by natural, semi-synthetic or synthetic compounds that specifically binds to opioid receptors and have similar properties to the endogenous opioids. Some opioids trigger direct histamine release from mast cells, but anaphylactic reactions are rare.

**Method:** We report a case of a 51-year-old woman referred for investigation of perioperative anaphylaxis. She was diagnosed with colon adenocarcinoma and laparotomy with colectomy was indicated. Five minutes after anesthetic induction with propofol, fentanyl, ketamine, cisatracurium, morphine and bupivacaine, she had hypotension, bradycardia, urticaria and bronchospasm, culminating in a cardiorespiratory arrest that was reversed. In the diagnostic investigation, skin tests for latex and drugs were performed: propofol, fentanyl, ketamine, cisatracurium, morphine and bupivacaine. The prick and intradermal tests were positive for morphine. Skin test and oral challenge with 50 mg of tramadol were performed. Immediately after administration of 20% of the total dose, patient had bronchospasm and urticaria. The diagnosis of mastocytosis was ruled out. She was referred to the oncologist with recommendations against the use of opioids during anesthetic induction and analgesia and the diagnosis of morphine as the probable culprit drug of her severe perioperative anaphylaxis.

**Conclusion:** The reported patient had one anaphylactic perioperative reaction to morphine and another anaphylactic reaction to tramadol during her diagnostic investigation. Remain the question if this patient had two allergic anaphylactic reactions with cross-reaction between morphine and tramadol, or two non-allergic anaphylaxis due to "hypersensitive" mast cells.

## 1140 | Hidden Allergen—Drug allergy, a clinical report

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**Background:** The suspicious of drug allergy is common in the population, the diagnosis is not always easy. A wide range of clinical manifestations can occur affecting different organ systems. In patients taking multiple drugs, particularly those admitted in hospitals who undergo different therapeutics and procedures finding the etiology for the drug reaction can be difficult.

**Clinical report:** 44 years old female with allergic rhinitis and anemia was admitted to the Infectious Diseases Department of a tertiary hospital for fever of unknown origin. Other associated symptoms were sore throat, metacarpo-falangic and right knee arthritis and evanescent non-pruritic rash (accentuated during fever spikes). Workup revealed leukocytosis, neutrophilia and C-reactive protein 14 mg/dL. Cultural exams were negative. She was started on antibiotics—Ceftriaxone, gentamicin, clindamycin and doxycycline- and naproxen but maintained fever. At day 12 of ceftriaxone, gentamicin and doxycycline, day 7 of clindamycin and day 1 of naproxen a generalized pruritic maculopapular rash appeared accompanied by agranulocytosis. After administration of G-CSF there was normalization of the hematologic disorder. Further workup revealed high ferritin levels and 28% glycosylated ferritin. The patient was diagnosed with Adult Onset Still's disease and medicated with indomethacin with significant improvement. She was referenced to a Drug allergy outpatient department.

Immunoallergologic evaluation revealed: specific IgE for penicillin, amoxicillin and cephalosporin were negative; skin prick, intradermal and epicutaneous tests were negative for immediate and late reactions (Penicillin, amoxicillin, ampicillin, cefuroxime, cefepime, ceftriaxone, gentamicin, clindamycin, doxycycline, naproxen, minor determinant mix and penicilloyl polylysine). She was submitted to

drug challenge with the suspected drugs, all of them were negative except for clindamycin—24 hours after administration of clindamycin the patient developed a pruritic rash on the torso, cervical area and upper limbs, no further symptoms developed.

**Conclusion:** Clindamycin allergy is rare and can be associated with immediate or late reactions. Apart from cutaneous exanthema is usually associated with acute generalized exanthematous pustulosis and toxic epidermal necrolysis.

## 1141 | Unusual presentation of amoxicillin hypersensitivity: Case report

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**Case report:** Drug-induced cutaneous disorders frequently display a characteristic clinical morphology. Fixed drug eruption (FDE) describes the development of one or more annular or oval erythematous patches as a result of systemic exposure to a drug; these reactions usually resolve with hyperpigmentation and may recur at the same site or at other sites with re-exposure to the drug. Patch testing on the previously involved location and provocation challenges have been used to identify the suspected agent and check for cross-reactivity to medications. Overall, FDE may account for as much as 16%-21% of all cutaneous drug eruptions. Most cases involve sulfonamide antibiotics, tetracyclines, nonsteroidal anti-inflammatory drugs, and, less frequently, penicillins.

We describe the case of a 34-year-old man with asthma, allergic rhinitis and nasal polyposis which on two separate occasions was given amoxicillin/clavulanic acid. The patient reported on both occasions the development of well defined, purple, itchy patches (approximately 3-4 cm) on the palm of the left hand and left forearm on the second day. The lesions persisted for 5 days after the drug was stopped and faded thereafter. There were no other drugs involved.

Skin tests to PPL, MDM, amoxicillin, clavulanic acid, cefuroxime and benzylpenicillin were negative. An oral challenge test with amoxicillin was performed; 2 hours after the last dose, the same lesions were observed at the left forearm. A subsequent challenge test with intravenous benzylpenicillin was negative. As a result, an alert for amoxicillin was entered into the patient's electronic record to prevent further reactions.

In this patient, FDE was suspected based on the emergence of characteristic, recurrent lesions after administration of amoxicillin/clavulanic acid. Challenge tests confirmed the diagnosis of FDE due to amoxicillin hypersensitivity. Cross-reactivity within the beta-lactams group was excluded. This case highlights amoxicillin as an infrequent causative agent for FDE.

## 1142 | Basophil activation test in a patient with cetuximab-induced anaphylaxis

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**Background:** Cetuximab is EGFR targeting mAb used for treatment of metastatic colorectal cancer. Severe systemic hypersensitivity reactions to cetuximab occur in 3% of patients and a possible reason is IgE sensitation to alpha-gal. In such cases, panitumumab treatment is alternative.

**Case presentation:** A 61-year-old female was diagnosed with rectal adenocarcinoma. One year after radical surgery, progression with pulmonary metastasis was shown. In first line of systemic therapy she received premedication with pantoprazole, metoclopramide, clemastine and dexamethasone, followed by cetuximab infusion. During first minutes of infusion, grade 4 anaphylactic reaction occurred. A reaction started with generalized pruritus, urticaria, rhinitis, followed by hypotension, bradycardia and loss of consciousness. She was treated with fluids, clemastine and methylprednisolone. Next day she received same premedication followed by panitumumab. During first 30 minutes she had grade 1 reaction with generalized urticaria. The third day she had generalized urticaria 10 minutes after metoclopramide application. Skin prick tests with cetuximab (5 mg/mL) were negative, but intradermal test were positive in concentrations 1:100 and 1:10. Intradermal tests with 4% succinylated gelatin were also positive. Other skin tests were negative (panitumumab, pantoprazole and metoclopramide). Laboratory tests revealed normal basal tyrptase and positive sIgE to alpha-gal (1.45 kIU/L). To confirm the clinical relevance of cetuximab and alpha-gal sensitization we performed basophil activation test (BAT). BAT response was highly positive for both cetuximab and alpha-gal, with comparable values and dose response curves. Thus, we showed 70%, 63%, 58%, 35% and 4% of CD63 positive basophils for stimulation with cetuximab (500-0.1 μg/mL), and 67%, 40%, 17%, and 1% for stimulation with alpha-gal (33.3-0.033 ng/mL). BAT response to panitumumab was negative (<5%; 500-0.1 μg/mL). Drug provocation with panitumumab was negative and patient received treatment with panitumumab.

**Conclusions:** Our result suggest BAT is useful approach for risk assessment of cetuximab-induced anaphylaxis. We demonstrated hypersensitivity reaction was related to highly positive cetuximab and alpha-gal BAT response. Further studies are needed to evaluate if BAT can distinguish between alpha-gal sIgE-positive individuals who are clinically tolerant from those at risk for anaphylaxis after cetuximab.

## 1143 | Allergy to povidone-iodine: a case report

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**Background:** A 53 year old patient with macular edema in receiving treatment of intravitreal injections of Aflibercept as follows: a monthly injection for the first three doses, followed by an injection every two months.

The first cycle (of three injections) are administered and there is nothing untoward as a result, however, on starting the second cycle of treatment, from the first dose, there is lower palpebral edema, with itchiness in the lacrimal 24 hours after administering lasting 4 days and stopping suddenly, although it did have to be treated with an ointment the last time there was a reaction which the patient does not remember the name of the ophthalmologist holds the ophthalmologic ointment Aureomicina responsible for the reaction, but in the following cycles, Tobrex is administered and there is a similar reaction.

In the operating theatre, the skin is disinfected using povidone-iodine and pupil dilation is carried out with Tropicamide (showing no immediate reaction in the surgery).

**Method:** As we are dealing with a late cutaneous reaction, the study of the medicine involved is carried out by means of epicutaneous medicine testing.

In order to do the study of Aflibercept, we wore gowns, two sets of gloves, a mask, eye protection and in a containment hood in the outpatients hospital.

**Results:** Epicutaneous:

Povidone-iodine: Positive (++)

Aflibercept, lidocaine, atropine, cyclopentolate 1%, phenylephrine 10%, tropicamide 1%, flou test: oxibuprocaine+fluorescence, anesthetic eye drops: tetracaine, tobramicine, auromicine, double anesthetic eye drops: tetracaine+oxibuprocaine: negative

True-test: negative

Cutaneous testing (prick and intradermal): lidocaine, tropicamide,auremicine, tobramicine, tetracaine: negative

Controlled conjunctival provocation: tropicamide, tobramicine, auromicine and anesthetic eye drops: negative

Controlled cutaneous povidone iodine provocation: well tolerated.

**Conclusion:** The patient diagnosed himself with dermatitis when in contact with Povidone-iodine and despite the fact that the cutaneous provocation was negative, it is known that when there is surgery involved, there needs to be moistness and occlusion for it to show up clinically.

The application of this antiseptic seems to lose its irritation and allergic properties when it dries on the skin and therefore tends to give a negative result in these patients, but this does not mean that they are not allergic to this antiseptic.

## 1144 | Immediate hypersensibility reaction to ranitidine

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**Background:** Ranitidine is a widely used H2 receptor antagonist (H2RA) usually used for gastroduodenal ulcer, gastroesophageal reflux disease, ulcer bleeding and prophylaxis, chronic urticaria and even for anaphylaxis management. It is generally safe and a well tolerated drug; nevertheless there are very few cases of immediate hypersensitivity reactions described in the literature.

We report the case of a 60 year old man who experienced erythema and pruritus immediately after an intravenous injection of ranitidine and hyoscine butylbromide given for gastric pain treatment.

**Method:** Investigations included a combination of skin prick test (SPT), intradermal test (IDT), oral provocation test and basophil activation test (BAT).

**Results:** SPT and IDT were performed for ranitidine (10 mg/mL and 0.01 mg/mL respectively) and hyoscine butylbromide (0.5 mg/mL and 0.005 mg/mL respectively) being exclusively positive for ranitidine at IDT dose with a $15 \times 25$ mm papule (histamine control $23 \times 35$ mm). Oral provocation test for hyoscine butylbromide was negative. BAT for ranitidine and famotidine were carried out, being negative for both drugs.

**Conclusion:** Skin tests for H2RA are the best option when studying a suspected reaction to H2RA and are also useful for assessing cross-reactivity between other H2RA. The sensitivity for BAT in diagnosis of drug allergy is about 50%, and the specificity up to 93%, although these percentages make reference to the common drugs studied (beta-lactams, quinolones, pyrazolones, etc). Specific studies for H2RA are still to be done. In our case we had a negative result for the BAT test, although we proved ranitidine was responsible for the reaction.

An alternative treatment was not studied as our patient already tolerated omeprazole, and H2RA are currently rarely used in our country.

## 1145 | The importance of an exhaustive allergologic study

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**Background:** The most common drugs responsible for allergic reactions prior and during surgery are muscle relaxants and antibiotics. Latex also accounts for a significant number of incidents. Allergologic studies are important, especially in life threatening reactions, as results can determine the drug responsible for the reaction, and therefor avoidance and precautionary measures can be established.

We report the case of a 78 year old man, with no history of previous allergic reactions, which experienced an anaphylactic shock during an intravenous injection of cefazolin and gentamicin prior to anesthetic induction for hip surgery.

**Method:** Investigations encompass a combination of skin prick test (SPT), intradermal test (IDT), specific IgE, basophil activation test (BAT) and provocation test.

**Results:** Serum tryptase at the time of the reaction was elevated (21.60 μg/L), being normal at baseline (6.97 μg/L). SPT and specific IgE for latex were negative. Specific IgE for penicilloyl g, penicilloyl v, ampicillin, amoxicillin and cefaclor were all negative. SPT and IDT were performed for beta-lactam antibiotics including cefazolin, being all negative, followed by SPT for aminoglycosides (gentamicin and tobramycin), being positive for gentamicin at SPT concentration of 40 mg/mL. BAT supported our suspicions as it gave a positive result for gentamicin, being negative for cefazolin. Finally intravenous provocation test with cefazolin was performed, being well tolerated by the patient.

**Conclusion:** Gentamicin is an aminoglycoside antibiotic used systemically for septicemia and as prophylaxis during surgery. Immediate type allergy (type I) to gentamicin is rarely reported. Since 2016, approximately only five cases have been reported in literature. In our case, initial theories were pointed towards cefazolin as beta-lactams report a higher rate of allergic reactions. After an exhaustive allergological study, results disproved our initial theory indicating gentamicin as the responsible drug.

## 1146 | Anaphylaxis due to a solution of macrogol (polyethylene glycol) in a laxative solution, probably ige-mediated

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**Background:** Polyethylene Glycol (otherwise known as Macrogol or PEG) is a polymer with a wide application as an excipient, solvent and dispersing agent in food, cosmetic and pharmaceutical industry. It presents distinct length polymer chains with a molecular weight from 200 to 10 000 000 g/mol conferring them specific properties.

Macroglol with a molecular mass between 3500 and 4000 g/mol is commonly used as osmotic laxative previously to colon endoscopy and radiologic examinations. After the introduction, anaphylactic reactions to Macroglol are rarely reported, considering it safe and well tolerated.

**Method:** We report a case of 65-year old woman, with no previous history of atopy, currently followed by the department of General Surgery and Digestive with the diagnosis of a colon carcinoma.

Just after the intake of an evacuant solution containing PEG, in the context of a colonoscopy preparation, she experienced paresthesia and oedema of lips, malaise, generalized itching, hives, dyspnea and aphonia. The arterial pressure was 88/55 and oxygen saturation 95%, needing treatment with corticosteroids and antihistamines, with quickly improving.

She had no taken any other drug that day and no other cofactors were identified in that episode. She reported various episodes of immediate cutaneous reactions after taking different drugs in the past with a negative allergologic study.

**Results:** Prick test with the same involved laxative undiluted solution (Macroglol 4000) was positive.

Prick test with another trade name of evacuant solution with same molecular weight of Macroglol was positive. Prick test with both solutions were negative in six control patients. Basophils Activation Test (BAT) with the two solutions of Macroglol 4000 was positive. Administration of an alternative laxative solution without PEG was tolerated. Subsequently we advised the patient to check the excipient listed for all kinds of drugs and cosmetics.

**Conclusion:** We present a case of anaphylaxis due to a laxative solution of Macrogol (4000 g/mol) with in vivo (skin prick test) and in vitro (BAT) positive test, suggesting an immediate hypersensitivity reaction Ig-E mediated, probably promoted by the increased absorption due to the loss of mucosal integrity of the colon. We have no found, in the published literature, another case of IgE-mediated hypersensitivity to PEG demonstrated by a BAT positive response.

## 1147 | Contact urticaria due to a benzyl-indazole drug

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**Case report:** Benzyl-indazole drugs are usually well tolerated, and there are scarce reports of allergic reactions in our environment.

Benzindamine is the most frequently used drug of this group. It is widely used both in everyday life and in the nursing care.

It is a locally-acting nonsteroidal anti-inflammatory drug with local anaesthetic and analgesic properties.

We report on a 56-year-old man who, immediately after of the topical application of benzindamine in left inferior limb developed acute urticaria in this limb, which reverted in approximately 2 hours with systemic steroids.

She had previously tolerated this product without any problems.

Skin prick-tests with benzindamine (0.06 mg/mL) and latex were realized in the patient.

Skin prick-tests with benzindamine were realized in eleven healthy control subjects.

**Results:** Skin prick-test with latex was negative in the patient.

Skin prick-test with benzindamine was positive in the patient (6 × 5 mm).

The prick-tests with benzindamine were negative in eleven healthy control subjects.

**Conclusions:** We report on a case of contact urticaria due to benzindamine and triggered by an immediate, probably IgE-mediated, hypersensitivity mechanism.

Some of the drug used in daily clinical practice can cause allergic contact urticaria and should therefore be borne in mind.

## 1148 | Delayed hypersensitivity reaction caused by rivaroxaban in a patient with atrial fibrillation

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**Background:** The use of new oral anticoagulants which act as direct inhibitors of activated factor X is constantly increasing, due to lower rates of serious and fatal bleeding events than warfarin/acenocoumarol. Rivaroxaban, the first commercialized drug in this group, is the most used for prevention of thromboembolic events. However, <10 cases of hypersensitivity reactions have been described so far, most of them delayed and severe. To present a case of delayed hypersensitivity to rivaroxaban, diagnosed by a positive LTT (lymphoblastic transformation test).

**Method:** A 79 year old woman with hypertension and chronic atrial fibrillation (AF) was referred to our clinic for suspected drug allergy. She reported that 2 months before, for AF she was started on oral amiodarone and rivaroxaban, presenting on the seventh day with both of them generalized erythema, pruritus, micropapular rash and facial angioedema. No oral or other mucosal were observed, neither pustules, vesicles or blisters. Blood eosinophilia, enlarged lymph nodes, renal and hepatic injury were discarded in Emergency, where the new drugs were discontinued and replaced by acenocoumarol. The rash subsided one week later, with oral antihistamines. Before and after the episode the patient also has been taking losartan and hydrosalurethyl, with good tolerance. She denied other adverse reactions. In Allergy department we performed skin prick tests and intradermal tests with amiodarone (0.05 mg/mL and 0.5 mg/mL) and rivaroxaban (0.1 mg/mL and 1 mg/mL), and a LTT with both drugs, 3 months after the reaction.

**Results:** Cutaneous tests with immediate and delayed readings (48 and 96 hours): negative; mild erythema without papule or pruritus occurred 24 hours later in the higher concentration of rivaroxaban intradermal test (interpreted as probably irritant). LTT resulted positive for rivaroxaban and negative for amiodarone. Posteriorly, the patient was restarted on amiodarone with good tolerance.

**Conclusion:** As the use of new oral anticoagulants become more extensive, given their efficacy, safety and comfort of posology, is probable that more hypersensitivity reactions might occur in the future. To the best of our knowledge, this is the first reported case of hypersensitivity to rivaroxaban in which the implication of this drug has been documented by a positive LTT. The LTT could be a useful diagnostic tool of delayed hypersensitivity reaction caused by rivaroxaban, especially in more severe cases, in which in vivo tests are contraindicated.

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## 1149 | De-labelling of beta-lactam hypersensitivity: A 2-year experience from a tertiary hospital allergy service

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**Background:** Patients with history of beta lactam allergy, often self-reported, are commonly encountered in the hospital setting. This frequently leads to increase use of broad spectrum and more expensive antibiotics that may be unnecessary or even less efficacious at times due to fear and concerns about potential disastrous outcomes. Nonetheless, with increasing awareness, many patients are now being referred to Allergy Service for formal evaluation. We aim to look at patients who underwent evaluation for beta-lactam hypersensitivity and determine the number of patients that were successfully de-labelled.

**Method:** A retrospective analysis was conducted with patients referred for evaluation of questionable beta-lactam allergy to the Allergy Service in our institution from the years 2016-2017. Initial evaluation process included a thorough history to determine the type of hypersensitivity reaction and suitability for further testing. Patients underwent skin prick test (SPT) and intradermal (IDT) with either (a) both major and minor determinants of penicillin, benzyl penicillin, amoxicillin and ampicillin, and/or (b) the culprit drug itself. If skin testing was negative, oral or intravenous (IV) drug challenge was then performed after informed consent. Clinical details and reactions were documented. Patients were also contacted post challenge to ensure no delayed reaction had occurred.

**Results:** A total of 130 patients were evaluated for beta-lactam allergy in the 2 year period, of these 80 were females and 50 were males. 107 of the referred patients had presumed penicillin group allergy and 29 had cephalosporin group allergy (3 patients had both penicillin group+cephalosporin allergy). 95 cases (73%) were successfully de-labelled. Beta-lactam allergy was confirmed in 26 patients (20%); identified by positive SPT in two patients, positive IDT in six patients and positive drug challenge in 18 patients (15 patients developed rash/urticaria, 1 had respiratory symptom and 2 patients developed anaphylaxis). 14 patients were referred before any drug allergy labelling was done, out of which 10 were confirmed not to have beta-lactam allergy.

**Conclusion:** In our study, 80% of patients were confirmed not to have true beta-lactam allergy. We were able to successfully remove beta-lactam allergy label from the electronic record for 73% of the patients.

## 1150 | Descriptive analysis of diagnostic Methods in betalactams hypersensitivity in our allergy unit

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**Background:** Betalactams (BL) are the compounds most frequently involved in drug reactions mediated by specific immunological mechanisms. We describe our experience in the methods used to confirm the diagnosis of BL hypersensitivity.

**Method:** Between 2015 and 2017, BL allergy was confirmed in 80 subjects. To reach the diagnosis, *in vivo* (skin prick and intradermal tests) and *in vitro* tests (basophil activation test, *BAT*, and radio allergo sorbent test, *RAST*) were performed. When necessary a drug provocation test (DPT), the diagnostic *gold standard*, was also carried out.

**Results:** A total of 66% referred amoxicillin-clavulanic acid (AX-CLV) as trigger for the hypersensitivity reactions (HRs), followed by AX (21%), penicillin (6%) and cephalosporins (5%). Almost 80% of HRs were immediate (<60 minutes). Positivity of skin tests was observed in 65% subjects, of BAT in 61% and of RAST in 68%. In 67% of individuals a DPT was necessary to establish the diagnosis. Patients with immediate HR displayed a positive DPT with a median dose of 20 mg (5-500 mg) of penicillin and 287 mg (5-500 mg) of AX, whereas non-immediate reactors developed positivity after a full therapeutic dose and during the home treatment course. Finally, 44% subjects were diagnosed of selective allergy to AX, 32% of selective allergy to CLV, 22% of allergy to all BL and 2% of selective allergy to cephalosporins.

**Conclusion:** Patients with selective allergy to AX and CLV are clearly increasing, probably due to the broad use of these drugs, whereas hypersensitivity to other BL is decreasing. Therefore, in patients with story of AX-CLV/AX reactions the performance of a combination of *in vivo* and *in vitro* test followed by DPT when necessary is crucial to obtain an accurate diagnosis and to perform safely the DPT.

## 1151 | Analysis of results of penicillin allergy evaluation

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**Background:** Unverified penicillin allergy leads to adverse downstream clinical and economic sequelae. Penicillin allergy evaluation can be used to identify true, IgE-mediated allergy.[1]

Beta-lactam antibiotics are the drugs that most frequently produce adverse reactions mediated by a specific immunological mechanism.[2] Within these, penicillins are the group most involved and best studied. Currently, amoxicillin, probably due to its high consumption, has displaced benzylpenicillin in terms of the number of reactions.[3]

**Method:** We have evaluated 90 patients with reported penicillin allergy referred to our hospital in the last seven months, performing penicillin allergy histories, penicillin skin testing and drug challenges under medical observation to distinguish true allergy. In addition, we have analyzed, based on positive results, who had personal or atopy family history, who had an immediate reaction, who had a dubious skin prick test with intradermal positive and who was evaluated with an oral challenge with the drug involved and who with an alternative.

**Results:** We have obtained a positive result 17 patients out of 90 with reported penicillin allergy (18.88%). Of these, they have a family history of atopy the 35.29% and a personal history of atopy the 17.65%. Most of the patients with positive results have had an immediate reaction (64.71%). In two patients skin prick test was doubtful, so we performed intradermal test with positive result. Moreover, one of them was positive patch test. In 23.53% of patients skin tests were negative, so it was conducted oral challenge with the suspect drug, with positive result in all of them. More than half of patients (64.71%) was carried out oral challenge with an alternative drug, with negative results in all of them.

**Conclusion:** In our study of penicillin allergy evaluation, 5.88% of our patients were positive with skin prick test, 64.71% with intradermal test, 5.88% with patch test and 23.53% with oral challenge. We have obtained a positive result in the 18.88%, data similar to others described in the literature. One of them shows us that only 19% of the suspected cases of reported beta lactams allergy were confirmed, emphasizing the importance to refer patients to an Allergy Centre for investigation.[4]

## 1152 | A retrospective analysis of the outcomes of penicillin challenge in patients with syphilis and self-reported penicillin allergy

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**Background:** Penicillin allergy is self-reported in 10% of the UK population. Syphilis is a sexually transmitted infection caused by *Treponema pallidum* for which penicillin is the first line treatment. Since 2012 syphilis diagnoses have increased by 97% and an epidemic is ongoing. Untreated infection can lead to acute or long-term neurological and cardiovascular sequelae. The current British Association for Sexual Health and HIV (BASHH) guidelines for the management of syphilis recommend desensitisation for patients with penicillin allergy. In order to improve care of patients with confirmed syphilis and self-reported penicillin allergy, a referral pathway from sexual health to immunology services for rapid assessment and treatment has been developed.

**Method:** A retrospective evaluation was carried out looking at a cohort of patients referred urgently from the sexual health clinic to investigate suspected penicillin allergy. All the patients had a diagnosis of syphilis that required prompt treatment. Two of the three patients had a history of rash following penicillin. The third patient had been diagnosed with penicillin allergy based on positive skin tests in China but could not recall an adverse reaction following penicillin. The patients all underwent blood, skin and graded challenge testing to penicillin. Following challenge the patients were given a full treatment course of penicillin for syphilis.

**Results:** The patients all had negative allergen specific IgE (penicillin panel), normal mast cell tryptase, negative skin prick and intradermal testing (standard panel of penicillins and the penicillin chosen for challenge—either amoxicillin, benzathine penicillin or procaine penicillin). All patients assessed tolerated penicillin and subsequently received first line curative treatment. Clinical and serological follow up was carried out in the sexual health clinic to ensure treatment had been curative.

**Conclusion:** Rapid assessment for penicillin allergy improves outcomes in patients with syphilis by allowing appropriate rapid use of first line antibiotic therapy. With the ongoing increase in syphilis diagnoses nationally, clinical services need to be responsive to treatment challenges posed. We present our pathway for rapid assessment of penicillin allergy in urgent cases with syphilis.

## 1153 | Penicillin allergy in elderly patients

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**Background:** Penicillin allergy remains the most common drug allergy. There are a large number of patients labelled as allergic to drugs commonly used in clinical practice without having been studied. This creates a major health resource problem, having to use alternative antibiotics.

**Method:** A retrospective review of medical records was performed in patients over 60, studied by adverse reactions to penicillin for a period of 12 years. Diagnosis was supported by in vivo testing including skin test such as prick and intradermal test. Whether skin tests were negative a single-blind challenge or Drug Provocation Test was performed under medical surveillance to establish or exclude the diagnosis of penicillin allergy and, in selected cases, to provide alternative drugs for the patient in need. A total of 804 patients over 60 were studied for penicillin allergy, during a period of 12 years.

**Results:** The results of the study show 106 positive cases (13.18%) of penicillin allergy. This percentage is similar to those obtained in studies conducted in general population. Most positive cases were detected by skin tests (n = 78). Benzylpenicillins were the betalactam group most frequently involved in adverse reactions studied (33%, n = 265), contrary to current consumption pattern.

**Conclusion:** The label of penicillin allergy is quite often erroneous. This involves using of more expensive and less effective therapeutic alternatives, which also facilitate the emergence of multi-resistant micro-organisms. Hence the importance of confirming the diagnosis of allergy. Finally, we did not find differences in the study of penicillin allergy in patients older than 60 years compared with the general population.

## 1154 | Epidemiology of severe cutaneous adverse reactions (SCARs) in Latin America

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**Background:** Severe cutaneous delayed drug reactions (toxic epidermal necrolysis -TEN-, Stevens-Johnson syndrome -SJS-, acute generalized exanthematous pustulosis -AGEP- and drug reaction with eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome -DRESS/DiHS-) among others, are a rare but potentially fatal complications of drug treatment. Although its epidemiology has been described in different latitudes, it is unknown in Latin America. Our aim was to describe the epidemiological characteristics of severe cutaneous reactions to drugs in countries of Latin America.

**Method:** An online questionnaire was designed to report new and old cases (since 2013). It was a modified and adapted version of ENDA questionnaire for drug allergy interesting group. Sociodemographic data, type of reaction (TEN, SJS, DRESS-DiHS, AGEP), culprit drug (s), treatment, complications, mortality and sequelae, were described. Three centers from Colombia, one from Argentina, one from Brazil and one from Paraguay were included. An Excel database was created, in which cases were recorded and analyzed.

**Results:** Thirty seven cases were reported. 24 (65%) were women. The median age was 47 years. 19 (51%) had DRESS/DIHS, 6 (16%) TEN, 3 (8%) SJS, 3 (8%) AGEP, 3 (8%) other not classified SCARs, and 1 (2.7%) overlapping TEN/SJS. The main culprit drugs were aromatic anticonvulsants in 17 cases (46%), beta lactam antibiotics in 6 (16%), non-beta lactam antibiotics in 3 (8%) and allopurinol in 2 (5.4%). In 100% of the patients the suspect drug was withdrawn. Thirty one patients (83.7%) received systemic corticosteroids. Complications occurred in 17 cases (49%) and death in one patient (2.7%). Seven patients (19%) had some type of sequelae.

**Conclusion:** In this preliminary study of SCARs in Latin American countries, DRESS/DIHS was the most frequently reported clinical entity, and the anticonvulsants were the main triggers. Complications were frequent, but mortality was low.

## 1155 | Drug-induced cough: analysis of nationwide spontaneous reports in Korea over ten years

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**Background:** Many drugs can cause cough by various mechanisms. While angiotensin-converting enzyme (ACE) inhibitors are known as the most common cause of cough, the number of cough-inducing drugs are increasing with the introduction of new drugs into the market. The study aimed to assess the causative drugs of cough and the characteristics of the subjects with drug-induced cough using nationwide spontaneous reports in Korea.

**Method:** Cases of drug-induced cough were recruited from the spontaneously reported pharmacovigilance data, which has been recorded in the Korea Institute of Drug Safety & Risk Management-Korea Adverse Event Reporting System database (KIDS-KAERS database) over recent 10 years (from Jan 2006 to Dec 2015). The ingredients of drugs were classified according to Anatomical Therapeutic Chemical code (ATC code). Adverse drug reactions were defined

using WHO-Adverse Reaction Terminology (WHO-ART) indicative of cough.

**Results:** From 856 524 cases of spontaneously reported adverse drug event cases, a total of 9003 cases (4.5%) were identified as drug-induced cough. Most cases occurred in adults (93.4% of the subjects) and females were more common than males (54.9% vs 45.1%). Regarding severity, only 629 cases (7.0%) were classified as serious based on WHO criteria. The most common causative drug category was antineoplastic and immunomodulating agents (24.8%), followed by cardiovascular drugs (24.2%). The most common causative drugs were ACE inhibitors including perindopril and ramipril.

**Conclusion:** In the nationwide spontaneous reports of adverse drug events, many cases of drug-induced cough have been reported so far. Much attention is needed to find new causative drugs of cough in the future.

## 1156 | Perioperative reactions in our allergy unit: retrospectively analysis in the last 4 years

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**Background:** Allergological assessment to determine the mechanism of the perioperative reaction and to identify the agent responsible and recommendation of a range of drugs or agents likely for future surgery is essential, but it often poses a significant challenge. In this study, we analyze our experience in the investigation of adverse reactions during anesthesia in the last 4 years.

**Method:** A total of 15 patients who attended our Allergy Unit with suspected perioperative reactions between January 2014 and December 2017 were reviewed retrospectively.

The severity of the perioperative allergic reactions was graded according to Ring and Messmer system.

All potential culprits were tested. The allergological evaluation included serum-specific IgE, skin testing (skin prick test and intradermal test) and supervised oral challenge. However, the tests was adapted according to the clinical history of each patient.

| Patient | Gender/ Age | Time interval between reaction and assessment (months) | Severity (Ring y Messmer) | Tryptase test (ug/ L) | Culprit drug | Cross-reaction test | Remark |
|---|---|---|---|---|---|---|---|
| 1 | F/46 | 1 | III | 18 (1) | Cefazolin (ID 20 mg/mL) | ß-lactam with the same ring structure R1CH2 | Tolerated: ß-lactam with different ring structure R1CH-NH2 |
| 2 | M/35 | 12 | III | 2.43 (B) | Latex positive (skin prick test, serum specific IgE, molecular diagnosis, Use test) | Vegetables food (LTP) | In treatment with sublingual allergen specific immunotherapy with Latex extract |
| 3 | F/83 | 3 | III | 34.3 (1)<br>12.3 (B) | Patent Blue V (ID 25 mg/mL) | No | — |
| 4 | F/30 | 3 | ND | 1.78 (B) | Vecuronium (ID 0.1 mg/mL)<br>Cisatracurium (ID 0.002 mg/mL) | Non depolarizing neuromuscular blocking agent | Tolerated: Deporarizing neuromuscular blocking agent |
| 5 | M/56 | 7 | I | 4.01 (B) | Ranitidine (ID 1 mg/mL) | H2-receptor antagonist | — |
| 6 | F/69 | 5 | III | 22.5 (1)<br>7.56 (B) | Patent Blue V (ID 25 mg/mL) | No | — |
| 7 | F/53 | 4 | III | 7.92 (1)<br>3.51 (2)<br>1.91 (B) | Gelatin (4 mg/mL) | Gelatin plasma expander (Colloid) | Tolerated: Crystalloid solutions |
| 8 | M/33 | 1 | II | 3.22 (B) | Cefazolin (ID 20 mg/mL) | ß-lactam with the same ring structure R1CH2 | Tolerated: ß-lactam with different ring structure R1CH-NH2 |
| 9 | F/72 | 4 | III | ND | Amoxicillin (ID 20 mg/mL) | Aminopenicillins | Tolerated: Cephalosporins with ring structure OCH3 |

M: Male, F: Female. 1: First. 2: Second. B: Baseline. ND: not described. ID: intradermal. LTP: lipid transfer protein.

**Results:** Grade III, II and I reactions were observed in 9, 1 and 3 patients, respectively. In 2 patient we didn't know the reaction suffered. Tryptase measurements were available for 11 patients. Of those, 3 and 4 patients had elevated and normal levels respectively and suffered grade 3 reaction.

IgE mediated reactions was diagnosed in 9 patients (60%): 3 for ß-lactam antibiotics (33.3%), 2 for Patent Blue (22.2%), 1 for neuromuscular blocking agents-NMBAs (11.1%), 1 for latex (11.1%), 1 for colloids (11.1%) and 1 for ranitidine (11.1%). Cefazolin was the ß-lactam antibiotics causing the largest number of reactions.

Non-IgE-mediated reactions was diagnosed in 6 patients (40%). The allergy tests were negative and tryptase levels were normal.

**Conclusion:** In our series, among the 9 patients who suffered allergy reactions during anaesthesia and the cause was subsequently identified, ß-lactam antibiotics were the most common causative agent (33.3%), followed by Patent Blue (22.2%), NMBAs, latex, colloids and ranitidine (11.1% each agent). In contrast, data from other authors indicated that NMBAs were the most common cause of anaphylaxis, followed by latex, hypnotics, antibiotics, plasma substitutes and opioids.

These differences might be due to the small size of our study, which was limited to our centre over the last 4 years and thus may not be representative.

## 1157 | Why allergist does not use drug provocation test in China: Epidemiology of drug allergy in China

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**Background:** Drug Allergy(DA) is a common clinical symptom, as the standard for DA diagnosis. Drug Provocation Test (DPT) has become an international consensus. However, this diagnostic method has not been used in China.

Drug Allergy(DA) is a common clinical symptom, as the standard for DA diagnosis. Drug Provocation Test (DPT) has become an international consensus. However, this diagnostic method has not been used in China.

**Method:** Questionnaire on two versions, in paper and online. Papers for each head of allergy department who participated at the 2015-2017 annual academic conference in China, the online version for general allergist who cannot attend the meeting, and two versions are exactly the same.

**Results:** A total of 1582 allergists participated in the questionnaire, 352 questionnaires uncompleted, and 1230 were analyzed. Among the respondents,

1. The allergist has worked just for short years: 65.55% doctors have worked *less than 3 years*, and they have consulted the whole allergic patient *less than 50 people per month* (34.45%).
2. There are fewer patients *(less than 10 people)* for out-patient 52.54% and for in-patient 51.23% of DA. The main symptom is *Immediate skin/mucosal reaction* (out-patient 62.26%, in-patient 41.26%). Usually, the patient would visit allergist *after suggestion by other department* (62.12%) and they would arrive *in the first 3 months after the onset* (88.32%). The main categories of DA were *the antibiotic* (out-patient 83.12%, in-patient 85.42%), and *Penicillin* (out-patient 75.23%, in-patient 51.63%) was the primary cause in antibiotics.
3. The allergists were *lack of experience and without standard procedure of DPT in China* (31.17%). That was the main reason of not use DPT in clinical. Therefore, they thought *avoidance is better than firm diagnosis* (46.12%) in currently medical environment in China. That's why most allergists are *satisfied* (45.57%) with their diagnosis for DA. However, many allergists still hope through *academic conference* (51.63%) to learn more about *test in vivo* (54.21%) in DA.

**Conclusion:** Allergology is still a young discipline in China. Most allergists are lack of experience and standard procedure of DPT, which lead to the delay of DA test in vivo. For the same reason, many allergists are worry about the accident and dispute between doctor and patient caused by DPT, is also important reason for unwilling to carry out DPT.

## 1158 | Nocebo effect during drug provocation tests

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**Background:** The diagnosis of drug hypersensitivity is based in the medical history, in skin testing with the suspect drug and in drug provocation tests (DPT). The latter are considered the gold standard for diagnosis of drug hypersensitivity. DPTs may represent potential risk to the patient, however sometimes they're the only resource available for confirmation/exclusion of hypersensitivity. Placebo-controlled challenge (PCC), which is a provocation test with an inert substance, can help to establish the correct diagnosis in these patients. The nocebo effect, less studied, is defined as an unpleasant response to placebo, felt by the patient.

**Method:** From 2002 to 2017, 67 patients with possible drug hypersensitivity but with subjective presentation were also submitted to a PCC at our day-hospital, in addition to the remaining

diagnostic evaluation. All patients signed an informed consent. We made a retrospective analysis of their clinical records and excluded 11 patients whose records were missing or incomplete. It was analyzed each patient's medical history (focusing allergic disease) and clinical reaction to the suspect drugs. Signals/symptoms at PCC were characterized. We also studied the variation of the DPT's results when it was performed after a PCC.

**Results:** In a total of 56 patients, 54 were female, middle age 51. Nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics were the most frequently suspected class of drugs (22/18); 17 patients reported symptoms with multiple drugs. There were 20 patients with urticaria and/or asthma and 15 had a previous anaphylactic reaction to drugs. We counted 251 challenges: 189 DPT and 62 PCC. The latter were mostly positive and oral challenges (32/52 respectively). The clinical presentation at PCC was subjective in 27 patients (pruritus in 10, paresthesias in 6, heat/sweating in 5) and objective in 8 (urticaria in 2, erythema in 2). In 14 patients who had a positive/inconclusive DPT and repeated DPT with the same culprit drug after PCC, the final outcome was not reproducible in 10 patients.

**Conclusion:** When clinical presentation is subjective, a PCC can be a decisive factor to the final result, taking in consideration that: a DPT may be difficult to classify, a positive PCC doesn't imply a negative DPT and an objective presentation is also possible in a PCC. It would be important to have guidelines on the interpretation of DPT and the use of PCC on drug hypersensitivity, as they exist in food allergy.

## 1159 | Qualitative and quantitative evaluation of the drugs prescribed in allergy provocation testing in planning compounding needs

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**Background:** Our centre has a dedicated drug allergy testing program that generates a high volume of procedures including skin and drug provocation tests. To ensure efficient and quick access we created operating procedures that streamlined the evaluations. Over 800 drug prescriptions are currently filled by pharmacy annually and the volume is increasing. A major change from the previously existing program was a reduction in testing doses per visit. To assess the impact of the new operating procedures, we required a study of our drug and pharmacy resource utilization.

**Aim:** To define and quantify the ongoing pharmacy needs in sustaining a large drug allergy assessment program.

**Method:** A retrospective review of pharmacy files was used to identify and quantify the drugs and dosages most frequently used and to determine prescription trends within the allergy testing program over the last 3 years.

**Results:** The two categories of drugs most consistently prescribed were antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). B-Lactam derivatives (Penicillin V and Amoxillin) accounted for 40%-50% of all testing requests, either in single dose or in graded challenges. While 4 compounded dosages were available for each of the drugs, the 10% and 100% dose were most often prescribed. Next in frequency among the antibiotics, was Ciprofloxacin, accounting<5% of prescriptions. In decreasing order the most tested of the NSAIDs were Ibuprofen, ASA, Celecoxib and Naproxen, altogether corresponding to less than 10% of all prescriptions.

**Conclusion:** The present retrospective evaluation allowed pharmacy to define the nature and volume of the drugs needed for the allergy testing program. Penicillin V and Amoxillin were mostly prescribed at 10% and 100% of the dose. These were the only 2 drugs identified that justified bulk compounding, and offered as floor stock.

## 1160 | Wrong diagnosis of penicillin-anaphylaxis: Jarisch-herxheimer reaction by spirochetal lysis

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**Background:** Syphilis, caused by Treponema pallidum, remains a global problem, with >12 million infections estimated per year.

In accordance with current treatment guidelines, patients should receive a single intramuscular injection of benzathine penicillin G. A substantial proportion of patients may develop Jarisch-Herxheimer reaction (JHR): a transient immunological phenomenon syndrome manifesting clinically with short term constitutional symptoms, such as abrupt fever, chills, myalgias, tachycardia, vasodilatation with flushing or hypotension.

The overall rate of JHR for syphilis is estimated to be 10%-25% and an increase in the incidence may be expected as high as 50% among patients co-infected with HIV and other spirochetal infectious diseases.

**Method:** A 28-year-old HBV-positive man with previous history of gonorrhoea, presented in July 2017 a red ulcered lesion with gummy consistency in genitals confirming syphilitic chancre after serology results IgG Treponema pallidum +. RPR+1/8. Consequently, he received Penicilin G benzatyn 2400 U IM, describing after 2-3 hours worsening headache, dizziness, shivering, arthralgia, drowsiness and fever (39°C).

On examination in the emergency department he showed tachycardia and hypotension 90/60 mm Hg with no rash or respiratory distress.

His symptoms resolved within 20 minutes after Dexclorfeniramine, corticoids and Acetaminophen IV.

**Results:** Initially, this reaction was thought to be a result of a drug allergy, but upon further review and the onset of fever, we determined that it met the diagnostic criteria of JHR.

His twin brother was diagnosed with penicillin and betalactamic allergy. Neutrophilia 83% was to be underlined in the blood test.

After this, drug oral challenge with PENICILLIN was performed, ruling out penicillin allergy.

**Conclusion:** It is not uncommon to confuse drug allergy with JHR.

JHR should be an anticipated reaction to early doses of antibiotic treatment for treponemal diseases, such as syphilis.

Antibiotic treatment should be continued; it is not a warrant to stop treatment.

Clinicians should be aware and anticipate JHR as a potential complication to early doses of antibiotic for spirochetal diseases such as syphilis or Lyme, leptospirosis.

## 1162 | Ibuprofen pastille related fix drug eruption

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**Case report:** Fixed drug eruption (FDE) is a distinctive type of cutaneous drug reaction. It is characteristically recurs in the same locations upon reexposure to the culprit drug. FDE is rare condition of drug related skin eruptions. Acute FDE usually presents with a single or a small number of dark red or violaceous plaques that resolve leaving hyperpigmentation. Diagnosis is made based on patient's history. The medication history should be taken in great detail and include all types of medications and routes of administration, since patients may overlook medication. In this case report we present a pastille related FDE. 41 years old man attended to our outpatient clinic complaint with red-brown skin eruptions.

In May 2017 he took ibuprofen+pseudoephedrine pills and ibuprofen pastilles because of cold. One day later red pruritic 3-4 cm diameter round eruptions raised his right dorsal hand and two eruptions on his right side of lumbar area. Desquamation in oral mucosa, hyperemia and pruritus in his eyes accompanied with this symptoms. One month later second and third reactions appeared on the same area and same form, but he said that he didn't take ibuprofen+ pseudoephedrine pills. Then the fourth reaction more generalized and recovered leave scars. In his detailed history he took ibuprofen pastilles for sore throat in all reactions. His routine laboratory blood tests were in normal limit, total IgE level was 504 IU/L.

Skin patch test performed with ibuprofen, 72 hours later hyperemia and edema appeared on the back skin. It was approved positive drug reaction.

FDE is rare condition of drug related skin eruptions. Diagnosis is made based on patient's history. The medication history should be taken in great detail and include all types of medications and routes of administration, since patients may overlook medication. If FE overlooked recurrent exposure to the culprit drug the reactions cause severe mucosal desquamative lesions and may be life threaten.

## 1163 | Fixed eruption

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**Background:** 80 years old man with episodes of erythematous-purplish injuries in extremities that improve with oral corticosteroids and leave residual injury. No mucosal lesions. Not neither pruritus nor pain. No trigger factor. The patient does not have precedents of interest. He only realizes treatment with paracetamol for pains.

**Method:** Patch test with paracetamol negative at 48-96 hours. Exposure test with paracetamol immediate negative. After 2 days the patient presented the same skin injuries in legs(multiple oval erythematous purple spots) that we treated with corticosteroids. Oral prednisone to 1 mg/kg of weight (diminishing dose). No biopsy done because of the refusal of the patient.

**Results:** Fixed eruption due to paracetamol.

**Conclusion:** Paracetamol may be the reason of skin lesions. If mucosal involvement we need to exclude a Steven Johnson syndrome. Every toxicodermia, for more defenseless that it could seem, has the potential risk of evolving to a serious form, for what the retreat of all drugs is essential. Usually the remove of the drug produces improvement and treatment. When necessary antihistamines and oral corticosteroids can be added. A detailed medical history and physical exploration is essential.

## 1164 | Bullous fixed drug eruption with ciprofloxacin

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**Case report:** Fixed drug eruption of cutaneous drug reactions are rarely reported due to the use of ciprofloxacin. We will present here a case of bullous fixed drug eruption of ciprofloxacin.

**Case:** 39-year-old female patient. In May-2017, erythema and bullous rash on the hand had appeared 30 minutes after oral ingestion of ciprofloxacin tablets. She stated that the same symptoms had developed twice on the same place and in the same manner after the use of the drug which she had not remembered the name of drug. A typical bullous fix was evaluated as a drug eruption with the patient's history and examination findings. After drug therapy local complaints with corticosteroids and oral antihistamines improved.

The patient was unresponsive in oral drug provocation tests with amoxicillin-clavulanic acid, clarithromycin and trimethoprim sulfamethoxazole for 6 months. The patient could use these drugs.

**Discussion and Conclusion:** In rare cases, eruption of the bullous fix can be followed by ciprofloxacin. These patients can tolerate easefully antibiotics without quinoline.

## 1165 | Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome due to vemurafenib

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**Background:** DRESS syndrome is a severe, idiosyncratic reaction to a drug. It is characterized by a prolonged latency period and distinct clinical manifestations (fever, exanthema, lymphadenopathy, eosinophilia, visceral involvement). The reaction is potentially life-threatening.

**Method:** Case report of a patient diagnosed with DRESS Syndrome due to vemurafenib, a B-Raf enzyme inhibitor used for the treatment of late-stage melanoma.

**Results:** Forty-two year old female patient, with Stage IVc melanoma with BRAF (+) mutation, started on therapy with Vemurafenib. Nine days later, presents to the emergency room with fever (39°C), lymphadenopathies, erythrodermia, hematologic (Platelets 109 000/L, lymphopenia) and metabolic dysfunction (alanine aminotransferase 54 UI/L, aspartate aminotransferase 99 UI/L, glomerular filtration rate 54 mL/minutes, C-reactive protein 11.11 mg/dL, lactate dehydrogenase 638 UI/L). Systemic infection was ruled out and diagnosis of DRESS syndrome according to RegiSCAR criteria was established. The skin biopsy showed discrete and focal vacuolization of the basal membrane, a superficial and perivascular lymphocytic infiltrate and eosinophils. IgM serology to human herpes 6 virus was positive. Vemurafenib was stopped and treatment with high dose corticosteroids was initiated. Progressive normalization of internal organ and skin involvement occured in the next 3 weeks. The patient was later started on dabrafenib and trametinib with good tolerance.

**Conclusion:** DRESS syndrome is a delayed type of drug hypersensitivity that should be ruled out in patients who present with fever and exanthema, in the context of a recent drug introduction. Its diagnosis requires a high level of clinical suspicion and a systematic evaluation to rule out systemic symptoms in patients with cutaneous adverse reactions. We report the 5th case of DRESS syndrome due to therapy with Vemurafenib. This case suggests the possibility of using dabrafenib as an alternative in patients with a previous severe drug reaction induced by vemurafenib. Written informed consent was obtained from the patient to present this case.

## 1166 | Amoxicillin depend nonsteroidal anti-inflammatory drugs intolerance

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**Background:** Nonsteroidal anti-inflammatory drugs (NSAIDs) induce a wide variety of adverse reaction. The mechanism for inducing drug hypersensivity reaction is related to the capacity for inhibiting cyclooxygenase enzymes or to their recognition inducing immunoglobulin E response. Although, NSAIDs have been reported to be the cause of co-factor enhanced Food Allergy. No cases of NSAIDs enhanced drug allergy have been reported to date. The aim of this study was to examine the relationship of amoxicillin intake and allergy symptoms induced by NSAIDs.

**Method:** A 48 years old woman was referred to Allergy section after an adverse reaction consisted of generalized urticaria 10 minutes after taking amoxicillin, acetylcysteine and mefenamic acid. Specific IgE (Pharmacia FEIA CAP System), Basophiles Activation Test and Penicillin standard skin tests (prick and intradermal reaction) were negative. Simple blind challenges with amoxicillin, acetylcysteine, AAS and mefenamic acid were negative.

One year later, the patient reported two adverse reactions consisted of generalized urticarial, facial angioedema and dyspnea 30 minutes after amoxicillin, colchicine and etoricoxib intake. The second reaction consisted of generalized urticarial 30 minutes after taking amoxicillin and dexketoprofen. Since these episodes she has tolerated amoxicillin without NSAIDs intake on several occasions and paracetamol without amoxicillin.

A new allergologic research included simple blind challenges with dexketoprofen, paracetamol and the combination of these with amoxicillin. During the test, serum levels of triptase and specific IgE to penicillin were monitored.

**Results:** Challenge test with amoxicillin: negative. Challenge test with combination of amoxicillin and NSAIDs (dexketoprofen and paracetamol, respectively): both positive. Serum levels of triptase and specific IgE to penicillin during the reactions were negative.

**Conclusion:** We reported a case of drug hypersensivity to amoxicillin intake together with NSAIDs. Serum levels of IgE to penicillin remain negative during the reactions; hence NSAIDs enhanced penicillin allergy is unlikely. Underlying mechanism of this reaction could be interference by the NSAIDs in the arachidonic acid metabolism pattern, as previously reported. The lack of in vitro tests makes the diagnosis depends exclusively on drug challenge. The precise role of the amoxicillin in the development of the reaction remains unknown.

## 1167 | Adverse reaction to rifampicin: a case report

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**Case report:** Rifampicin is a critically important drug in anti-mycobacterial therapy that is usually well tolerated. Hypersensitivity reactions are uncommon in immuno-competent patients.

A 53 year old HIV-sero-negative male, previous long term South African resident, with a significant TB exposure history presented with mediastinal lymphadenopathy which revealed necrotic granulomas on histology. He was commenced on quadruple therapy with Rifater® (isoniazid, rifampicin, pyrazinamide) and ethambutol with pyridoxine. He developed hepatotoxicity within a few days of commencing therapy with ALT rising from 80 to 166 U/L. Treatment was stopped with improvement in his liver function test within a few weeks with a view to individual drug introduction, according to NICE TB guidelines. One month later, 30 minutes after restarting rifampicin 300 mg, ethambutol 1300 mg and pyridoxine 10 mg, he developed a severe generalised pruritic erythematous rash associated with conjunctival injection and dizziness. He was remote from the hospital at this time, so blood tryptase, FBC and liver function tests could not be performed. He was advised to take no further treatment. A diagnosis of rifampicin induced red man syndrome was postulated. He improved after oral antihistamines and was referred for allergy tests.

Skin prick test (SPT) to rifampicin 60 mg/mL and rifabutin 150 mg/15 mL at a dilution of 1:100 and neat concentrations, respectively were negative. Immediate intradermal skin test (IDT) to rifabutin at a 1:100 dilution was negative. However, immediate IDT to rifampicin at a 1:1000 dilution from the SPT dilution, was positive (weal 12 mm and flare >30 mm) in keeping with an IgE-mediated hypersensitivity.

Oral challenge with rifabutin 150 mg, followed by 300 mg an hour later, was tolerated and he has continued without problem on therapeutic doses of rifabutin together with isoniazid, pyrazinamide, ethambutol and pyridoxine over subsequent months with no development of hepatotoxicity or further rashes.

This case highlights IgE-mediated allergic reaction to rifampicin, masquerading as red-man syndrome due to systemic histamine release. Martinez *et al*., 1999 demonstrated that non-adherence to anti-mycobacterial therapy and previous rifampicin exposure, are amongst the risk factors for IgE-mediated reactions to rifampicin. Skin testing with rifampicin and rifabutin are helpful to diagnose rifampicin allergy. Rifabutin is an alternative anti-mycobacterial in severe rifampicin allergy.

MONDAY, 28 MAY 2018
TPS 32
LABORATORY VALIDATION AND CANCER TREATMENT

## 1168 | An 7-color panel for detection of Human Innate Lymphoid Cells by flow cytometry

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**Background:** Innate lymphoid cells (ILC) play an important role in innate immunity, lymphoid organogenesis and tissue remodeling. They form an heterogeneous population that can be categorized into 3 groups (i.e. ILC1, ILC2 and ILC3) based on their phenotype and/or distinct patterns of cytokine production. The detection and enumeration of different blood ILC subsets is important to understand immune regulation in pathological conditions, such as allergy, oncology and inflammation diseases. Flow Cytometric analysis of ILCs in human blood is challenging as frequencies may range below 0.1% of white blood cells, thus requiring considerably elevated sample volumes and/or cell-enrichment.

**Method:** Due to the lack of specific markers for ILCs definition, multiple antibodies are required including a lineage channel to remove most of the leukocytes population. Based on current knowledge in human ILC biology, we have evaluated the expression and association of several ILC markers to design an optimized dry and ready-to-use 15 antibodies/7-color panel (CD294/Lineage/CD117/Nkp46/CD127/CD161/CD45) for flow cytometry.

**Results:** The panel in dry DURAClone format allows for the detection of all ILCs subsets in whole blood samples or peripheral blood mononuclear cells (PBMCs).

**Conclusion:** This panel is an easy to use approach with minimized pipetting and results variabilities providing a well suited solution for longitudinal and multi-sites studies.



## 1169 | Expression of immune system genes by the Daudi cell line

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**Background:** Daudi cells are B-lymphocyte-like culture of human cells originating from Burkitt's lymphoma characterized by Epstein-Barr virus (EBV) latency. Immunopathogenesis of infections caused by EBV is directly related to clonal expansion of B-lymphocytes caused by changes in cytidine deaminase (CDA) gene expression with alteration of the expression of a number of immune system genes.

**Method:** Immune system gene expression was studied in the Daudi cell line (RRPCEM, Belarus). As a control, mean gene expression was assessed in peripheral blood mononuclear leukocytes (PBMC) cell cultures from 12 healthy individuals. Total RNA was isolated from mononuclear leucocytes in peripheral blood using Tri-Reagent (Sigma, USA). cDNA was synthesized and labeled from total RNA using Superscript cDNA Synthesis Kit (Invitrogen, CA). The labeled cDNA was hybridized to the Discover Chip™ (Arrayit, USA). DNA-arrays were scanned on Innoscan 700 (Carbon, France).

**Results:** Human Discover Chip™ used to study gene expression showed that the Daudi line was characterized by expression of 18 genes not expressed in 12 control PBMC cultures: CCNB1, MYB, MYC, FUBP1, CCND3, PRKDC, STAT5A, MAN2B1, VAMP, EGR1, IL12RB2, ITGAE, E2F1, SLC22A2, CXCR2, MTHFR, SOD1, PLK. A characteristic feature of expression of the Daudi cell line immune system genes, compared with PBMC cultures, is increased expression ($P < 0.05$) of groups of genes (n = 8) associated with activity of cyclin-dependent kinases with Daudi B lymphocytes characterized by specific expression of cyclin B1 genes and D3, not detectable in uninfected PBMC. Enhanced expression of cyclin-dependent kinases 4 and 5 (CDC 4, CDC 5) genes from the Daudi line was 3 fold greater than in uninfected PBMC.

**Conclusion:** Identification by DNA-array of features of EBV latency associated with the activity of cyclin-dependent regulation genes can be used to create a diagnostic test based on PCR expression.

## 1170 | Cryopreservation alters the absolute levels of immune responses but does not change the response profiles of circulating immune cells

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**Background:** Freshly isolated peripheral blood mononuclear cells (PBMCs) are seldom used in immune cell analyses in cohort studies, as the use of fresh cells is usually laborious and impractical due to logistical and scheduling reasons. Several challenges may also hinder the interpretation of the results i.e. alterations in data acquired during different periods of time and, in multicenter studies, the differences in instrumentation and technical personnel. Analysis performed in one center in one batch using cryopreserved PBMCs is widely used answer to these challenges. Few studies, however, have published data concerning the effect of freezing on PBMCs. In this study, we investigated whether cryopreservation affects immune

responsiveness of PBMCs and whether freezing affects functional properties of circulating antigen-presenting cells, namely dendritic cells (DCs) and monocytes.

**Method:** We stimulated fresh and cryopreserved PBMCs of adults (N = 6) with different antigens (PI, POLY(I:C), and 3 doses of LPS) for 18 hours. Expression of functional markers CD80 and ILT4 on circulating myeloid DCs (mDCs), plasmacytoid DCs (pDCs) and monocytes was analyzed by flow cytometry. Cytokine production of PBMCs (IL-1β, IL-10, IL-12/IL23p40, IL-13, IL-17, TNFα, IFNγ) was analyzed by multiplexed ELISA method.

**Results:** The overall response profiles induced by different stimuli were similar in fresh and frozen cells, but the intensity of the responses varied in some extent. Some immune responses were slightly weaker in frozen cells than in fresh cells (PI, POLY(I:C) and LPS stimulated expression of CD80 in mDCs, POLY(I:C) stimulated expression of CD80 and LPS stimulated expression of ILT4 in monocytes ($P < 0.05$)). The response to increasing doses of LPS was lower in frozen cells, measured as the percentage cells expressing CD80. Cytokine data are in line with the cellular data, although some cytokines seem to be more sensitive to cryopreservation and thawing than others.

**Conclusion:** Based on the results, it can be concluded that cryopreservation does not have a critical effect on the response profile of cells, and thus cryopreserved cells can be used in cohort studies reliably. The study suggests, though, that when interpreting and comparing the results of different studies, the possible effects of freezing on the absolute levels of immune responses should be taken into account.

## 1171 | Immune characteristics of inflammatory and non-inflammatory forms of chronic abacterial prostatitis

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**Background:** Features of the pathogenesis of inflammatory and non-inflammatory forms of chronic abacterial prostatitis (CAP) were assessed including assessing immune parameters in the pathogenesis of CAP.

**Method:** 42 patients with chronic abacterial prostatitis were examined. 30 healthy men were the control group. Production of cytokines in the blood and ejaculate was determined by an enzyme immunoassay.

**Results:** Chronic abacterial inflammation of the prostate gland was accompanied by a significant increase in concentration of SLPI, IL-8, TNF-α, IL-17 in the seminal plasma and serum concentration, and a decrease in the concentration of IL-6 and TGF-β1 compared to healthy men ($P < 0.05$). There was no statistically significant difference between SLPI, IL-8, TNF-α, IL-23, IL-17, and TGF-β1 in the ejaculate of patients with inflammatory and non-inflammatory forms of CAP ($P < 0.05$). The concentration of IL-6 in ejaculate of patients with inflammatory forms of CAP was significantly greater than in patients with non- inflammatory form of CAP ($P = 0.01$).

**Conclusion:** The inflammatory and non-inflammatory forms of CAP are pathologically similar with changes in the concentration of the studied cytokines except for IL-6 in both forms with signs of inflammation. The terms "leukocytic" vs "non-leukocytic" chronic abacterial prostatitis are more correct than "inflammatory" and "non-inflammatory" when describing chronic abacterial prostatitis.

## 1172 | Assessment of safety and tolerability of dendritic cell immunotherapy in patients with pancreatic cancer

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**Background:** Pancreatic cancer (PC) in Belarus has an incidence of 8-9 cases per 100 thousand people. This study assesses the safety and tolerability of immunotherapy with autologous DC injected into patients with PC.

**Method:** 6 patients with PC received at least 5 subcutaneous injections of autologous DC loaded with tumor-cell-lysate and WT-1/Muc-1 peptides. DC were obtained from monocytes using 6-day (GM-CSF/IL-4) protocol, pulsed with the antigens on day 7. A skin test was performed before the first injection of cells to prevent possible allergic reactions. The suspension of DC was injected subcutaneously in the forearm. After injection of the DC, all patients had clinical examination, evaluation of the injection site, thermometry and subsequent general laboratory tests done 24 hours after DC injection.

**Results:** The status of all patients after DC immunotherapy was evaluated as satisfactory. Heart rate, blood pressure in patients remained within the age norm. Skin had normal color without rash or peripheral edema. There were no local or systemic allergic reactions. The body temperature after the injection did not exceed 37°C. Regional lymph nodes were not detected by palpation. The number of erythrocytes and hemoglobin level of blood remained within the normal range without anemia or thrombocytopenia. No changes in WBC profile associated with inflammatory or allergic diseases occurred. No transient increase in the level of transaminases and bilirubin occurred. General urine analysis showed absence of proteinuria and ketonuria with no adverse effect on renal function.

**Conclusion:** This study showed no significant adverse impacts on 6 PC patients undergoing DC immunotherapy with absence of allergic reactions, flu-like symptoms, anemia, thrombocytopenia, renal dysfunction and liver function changes indicating good tolerability and safety of the vaccine based on autologous DC in patients with PC.

## 1174 | Importance of laboratory medicine in the diagnosis of Langerhans cell histiocytosis (LCH) associated macrophage activation syndrome (MAS)

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**Case report:** Langerhans cell histiocytosis (LCH) is rare disease. LCH is due to abnormal proliferation of Langerhans cells, which can often be regarded as reactive lesions. LCH is rarely reported in association with macrophage activation syndrome (MAS) even more. MAS is characterized by high-, therapy-resistant fever, elevated triglyceride, ferritin, D-dimer values, decreased fibrinogen level, and pancytopenia in particular. MAS may directly leads to life-threatening multi-organ failure. The recognition and characterization of LCH associated MAS is a very complicated, especially in persistent bacterial or viral infection or in presence of immunodeficiency. The laboratory medicine has crucial role in this diagnostic and therapeutic decision making.

Four years old boy with extremely poor clinical conditions was hospitalized in December 2016. He had continuous, therapy-resistant fever, dermatitis, vasculitis and perianal abscesses requiring multiple surgical treatment. Procalcitonin results were in the normal range despite highly elevated CRP level (over 100 mg/L). The level of serum IgG and IgM remained in the lower range of reference values despite the inflammation. LDH was permanently over 1000 U/L. According to the flow cytometric analysis the number of $CD3^+$/$CD69^+$ T cells, and $CD3^+$/HLA-$DR^+$ T cells are between 20% and 37%, reflecting to the early and late T cell activation. Phagocytotic index was in the normal range but increased fluorescence intensity can be observed due to *E. coli* and PMA stimulation. Half year later some bone lytic area was appearing on the skull and CT scan showed a tissue mass of unknown origin in his right orbit. Histopathological examination revealed histiocytosis (LCH). At this time the relevant clinical chemistry parameters were following: se. ferritin >8250, CRP: 290 mg/L, D-dimer: 6708 ng/mL, fibrinogen: 1.9 g/L, ASAT: 173 U/L, ALAT: 72 U/L, se. cholesterol: 7.7 mmol/L, se. triglyceride: 4.02 mmol/L, se. LDH: >3000 U/L, S100: 22.83 μg/L (ref. value: 0-0.105!!). Reduced $CD4^+$ and total B cell count with permanently low immunoglobulin levels (despite infection) suggest severe immune dysfunction. According to the clinical course and the laboratory findings autoimmune/auto-inflammation associated LCH and MAS are likely to be present. As a result of LCH-III protocol supplemented long-term steroid and antibiotics the patient is in a good clinical condition, and the laboratory parameters returned to the normal range.

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HEREDITARY ANGIOEDEMA AND MYELOID CELLS

## 1176 | Bone marrow mast cell burden influences the severity of periodontal disease, in mastocytosis

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**Background:** Mastocytosis encompasses a heterogeneous group of rare diseases characterized by an accumulation of clonal mast cells in different tissues and organs, such as the skin, bone marrow and the gastrointestinal tract, among other locations. Periodontal disease is an inflammatory condition that affects the tissues surrounding/supporting the teeth—gums, cementum, periodontal ligament and alveolar bone. It is broadly classified as gingivitis, or periodontitis, when alveolar bone loss is present. Here we investigated the impact of mastocytosis on the severity of periodontal disease.

**Method:** A cross sectional study was conducted with 67 mastocytosis patients, aged 18-69 years (median: 45 years, interquartile range: 20). Medical data was collected via a short questionnaire and clinical records, and included: diagnostic category of mastocytosis, duration of disease, bone marrow mast cell burden (BMMC%) as assessed by flow cytometry, associated bone disease and bone mass index, basal serum tryptase levels, multilineage involvement of hematopoiesis by KIT mutation, atopy, cardiovascular risk factors - diabetes mellitus, arterial hypertension and obesity - and toxic habits - alcohol consumption and tobacco smoking. Periodontal examination included: measurement of periodontal pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP).

**Results:** For CAL, the best-fitting model emerging as the most significant predictor resulted in an adjusted $R^2$ of 0.55 and included diagnosis of diabetes mellitus (1.097, $P = 0.001$), diagnosis of periodontal disease according to the CDC/AAP classification (0.758, $P < 0.001$), plaque index (0.862, $P = 0.045$), BMMC% (0.082, $P = 0.048$) and age (0.024, $P = 0.001$). For PPD, the best-fitting model emerging as the most significant predictor resulted in an adjusted $R^2$ of 0.44 and included plaque index (0.629, $P = 0.011$), daily consumption of alcoholic beverages (0.576, $P = 0.001$), diagnosis of diabetes mellitus (0.519, $P = 0.005$), osteoporosis (0.435, $P = 0.001$) and age (0.009, $P = 0.022$).

**Conclusion:** These results show, for the first time, that among mastocytosis patients, besides the already known periodontal disease risk factors that include diabetes, age, osteoporosis and alcohol consumption, the bone marrow mast cell burden is also associated with increased periodontal disease severity.

## 1177 | Metformin inhibits aryl hydrocarbon receptor-mediated mast cell activation

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**Background:** Recent preclinical and clinical studies have suggested a potential anti-inflammatory effect of metformin, an anti-diabetic drug, beyond its glucose-lowering activity. We have recently found that the aryl hydrocarbon receptor (AhR, a cellular chemical sensor)-ligand axis is critical in modulating mast cell response via, in part, the induction of ER/mitochondrial stress response. However, the potential regulatory effect of metformin on mast cell function and allergic responses remains unknown. We aimed to test a hypothesis that metformin may play a role in modulating AhR-mediated activation of mast cells with or without the combined stimulation with cross-linkage of antigen and IgE.

**Method:** Varying doses (1 μM-1 mM) of metformin was evaluated for its effect on AhR-mediated mast cell degranulation as measured by the level of hexosaminidase release, cytokine levels (TNF-a and IL-13) by ELISA and intracellular calcium by measuring the ratio of Fluo-4 vs Fura red fluorescent dyes in murine bone marrow-derived mast cells (BMMCs) with or without the stimulation in vitro by cross-linkage with ovalbumin (OVA) and anti-OVA IgE Abs and in vivo by assessing the level of passive cutaneous anaphylaxis (PCA).

**Results:** Metformin at relatively low doses (1-10 μM) was shown to mildly suppress IgE-mediated responses, including degranulation (34% reduction, $P = 0.0135$), TNF-α (23% reduction, $P = 0.0139$) and IL-13 (38% reduction, $P = 0.0015$) secretions in BMMCs. Importantly, metformin at the same doses potently inhibited mast cell responses in all parameters (100% reduction, $P < 0.0001$ for degranulation; 87% reduction, $P < 0.0001$ for TNF-α; 90% reduction, $P < 0.0001$ for IL-13) in mast cells treated with an AhR ligand, 5,11-dihydroindolo[3,2-b]carbazole-6-carbaldehyde (FICZ). Mechanistically, its inhibitory effect was mediated through the suppression of FICZ-induced MAPK activation, intracellular calcium release and ROS generation. Metformin also blocked AhR-mediated PCA in vivo (90% reduction, $P < 0.0001$).

**Conclusion:** Metformin, a common anti-diabetic agent, was shown to exert inhibitory effect on AhR-mediated mast cell activation in vitro and in vivo, suggesting its potential utility as a newer form of therapy for asthma and allergic diseases; this is particularly relevant when considering the adverse effect of the exposure to environmental polycyclic aromatic hydrocarbons.

## 1178 | An engineered IgE-Fc variant inhibits basophil degranulation ex vivo

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**Background:** Allergen-specific IgE plays a major role in the development of allergic reactions. It binds with high-affinity to the primary IgE receptor FcεRI on basophils and mast cells. Upon exposure to the cognate allergen IgE-loaded cells immediately degranulate and release soluble mediators causing allergic symptoms. The therapeutic anti-IgE antibody Omalizumab is known to neutralize free IgE and to prevent binding of IgE to basophils and mast cells. Recently, we have reported that Omalizumab actively desensitizes basophils at high concentrations. Furthermore, we have provided evidence that a mutated IgE-Fc variant, which is resistant to Omalizumab binding, may be used to actively replace the IgE-repertoire on the surface of primary human basophils when co-applied with Omalizumab. This combination treatment significantly increased inhibition of antigen-mediated basophil activation ex vivo. Here, we aim to further investigate the exact mechanism of basophil inhibition for the mutated IgE-Fc variant.

**Method:** Human primary basophils were isolated from whole blood donations of grass-pollen allergic individuals and treated with wild-type IgE-Fc or mutated IgE-Fc variants alone or in combination with Omalizumab. Subsequently, cells were challenged with a grass-pollen allergen mix. Basophil activation was measured by flow cytometry.

**Results:** Interestingly, the mutated IgE-Fc variant alone diminished basophil activation in a competition-independent manner, while the wildtype IgE-Fc variant showed no effect. Furthermore, the IgE-Fc variant showed synergistic and dose-dependent inhibition already at low concentrations when used in combination with Omalizumab.

**Conclusion:** Our data indicate that the mutated IgE-Fc variant might engage an inhibitory receptor on the surface of basophils. However, further studies are required to confirm this hypothesis. The IgE-Fc variant could potentially be used as an efficient add-on treatment to the current Omalizumab therapy.

## 1179 | Development of a LC-MS/MS Method for the quantification of eicosanoids in myeloid cell supernatant

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**Background:** Eicosanoids are oxygenated lipid mediators derived from polyunsaturated fatty acids like arachidonic acid. Through different (non-) enzymatic pathways a diverse group of metabolites can be synthesized that are highly diverse in their actions. Because of its specificity and sensitivity liquid chromatography—mass spectrometry (LC-MS/MS) has enabled a comprehensive analysis of lipid mediators. Herein we present the development of a method for the quantification of 52 oxylipins and its application in zymosan-stimulated polymorphonuclear leukocytes (PMN).

**Method:** PMN were isolated from fresh whole blood of 6 healthy volunteers via centrifugation on a density gradient. PMN were treated with zymosan, a yeast cell wall component, or left untreated (control). After 24 hours all PMN were incubated with the $Ca^{2+}$ ionophore A23187, supernatants were harvested and stored in 50% methanol (MeOH) at −80°C until further processing.

Five different solid phase extraction (SPE) methods were compared for their precision and accuracy. Based on these parameters, Strata-X single columns were selected as the extraction method of choice. Samples were diluted to a MeOH content of 10% before SPE. Eluates were evaporated and reconstituted in MeOH:$H_2O$ for LC-MS/MS analysis. Concentrations were calculated using a calibration curve.

**Results:** SPE using Strata-X columns showed the most accurate and reproducible results for the eicosanoid extraction from cell culture medium. Of the 52 metabolites included in the LC-MS/MS panel only 11 or 13 were detectable in the samples from PMN stimulated with ionophore or zymosan/ionophore, respectively. 9- and 15-hydroxyeicosatetraenoic acid (HETE), as well as, prostaglandin (PG) $E_2$ and $PGF_{2\alpha}$ were detectable only after zymosan stimulation, while leukotriene (LT) $D_4$ and 12-oxoETE were only present in control samples.

The concentration of 5-lipoxygenase (5-LO) metabolites, $LTB_4$, $LTC_4$, $LTD_4$, $LTE_4$ and 5-HETE was higher in ionophore compared to zymosan/ionophore stimulated PMN. Zymosan treatment led to an increase of the cyclooxygenase (COX) metabolites thromboxane $B_2$ and $PGE_2$.

**Conclusion:** The described method allows the quantification of up to 52 lipid mediators. Zymosan stimulation of human PMN led to the secretion of COX metabolites, while 5-LO metabolites were more abundant in control PMN, which is in line with the current literature. The established method can be used to quantify lipid mediators in a variety of (patho-) physiological settings.

## 1180 | Raised basal mast cell tryptase concentrations in a large British cohort

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**Background:** Serum mast cell tryptase (MCT) ≥11.5 ng/mL has previously been reported in 900/15 298 (6%) subjects in an Austrian cohort with immediate and delayed allergy on a background of multisystem disease. Dominantly inherited *TPSAB1* gene allele duplications and triplications (alpha-tryptasemia) have recently been identified as an underlying cause of a baseline MCT ≥8.0 ng/mL in 35 American and British families. The aim of this survey was to determine the prevalence of baseline MCT above ≥8.0 ng/mL and associated clinical phenotype in a large British cohort.

**Method:** We retrospectively surveyed anonymized baseline MCT in a cohort of patients referred to the Greater Manchester Immunology Service in the five-year period from 2012 to 2017. Patients with a clinical history of acute allergic reactions/anaphylaxis and duplicate samples were excluded.

**Results:** 4283 blood samples were analysed from patients with a median age 38 (range 0-96) years, 60% of whom were female. 195 (5%) (median age 52 (range 0-86) years, 50% female) had a baseline MCT ≥8.0 ng/mL. 87 (45%) patients had been labelled as having a "mast cell disorder- not further defined", 72 (37%) patients had repeat baseline MCT measured one week or more following an allergic reaction and 24 (12%) had atopic disease or chronic idiopathic urticaria/angioedema.

**Conclusion:** One in twenty subjects in our British cohort, nearly half of whom had been labelled with undefined mast cell disorders had a MCT ≥8.0 ng/mL. Genetic testing for alpha-tryptasemia in these patients might provide an underlying genetic cause for a proportion of their high MCT and clinical features.

## 1181 | Value of long-term prophylaxis of hereditary angioedema: a review of physicians' recommendations

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**Background:** Hereditary angioedema (HAE) is a rare autosomal dominant disorder stemming from a deficiency or dysfunction of C1-inhibitor (C1-INH), and results in recurrent episodes of angioedema. These debilitating attacks, which lead to poor quality-of-life (QoL) and can be fatal, may be treated using on-demand therapy and/or long-term prophylaxis (LTP). Physicians' opinions differ on criteria for starting LTP and on the choice of LTP regimen. The objective of this literature review was to describe and summarize international physicians' opinions on these issues.

**Method:** In Embase® and PubMed, a targeted search was conducted for peer-reviewed articles published between 2002 and 2017. Publications were included if they discussed physicians' opinions on appropriate criteria for starting LTP and/or the choice of LTP regimen. Publications were excluded if they were not guidelines, consensuses, comments, letters, reviews, or editorials, or only included pediatric patients. The reference list of each publication was assessed for eligible papers not found in the databases.

**Results:** Of 367 articles identified in the databases, 40 were included in the review, and another 7 were included based on reference mapping. Of the 47 articles, 28% were guidelines, 26% were expert consensuses, and 45% were international articles (others were country-specific). Most (68%) were published after 2011. The most recent expert consensus documents and guidelines were less likely to recommend number of attacks as the only criterion for starting LTP and more likely to recommend a broader range of criteria, including QoL impact, location of attacks, access to resources, and inadequate control with on-demand therapy. Due to limitations associated with antifibrinolytics (lack of efficacy) and attenuated androgens (severe adverse events), the majority of recent guidelines recommend either that LTP treatment selection be customized according to individual risk factors or that plasma-derived C1-INH (pdC1-INH) be the preferred first-line LTP treatment in all patients.

**Conclusion:** Recent publications recommend a broad range of criteria for starting LTP, including HAE impact on patients' QoL, location of attacks, access to resources, and inadequate control with on-demand therapy. With regard to regimen, most recent publications recommend that LTP should either be individually customized or that all patients should receive first-line treatment with a pdC1-INH.

## 1182 | Prophylaxis with subcutaneous C1-Esterase inhibitor (C1-INH [SC]) reduces symptom days and severity of symptoms in patients with Hereditary Angioedema (HAE): Results from the COMPACT study

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**Background:** Subcutaneous C1-esterase inhibitor (C1-INH [SC]) at 60 IU/kg was approved in June 2017 by the US Food and Drug

Administration as routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescents and adults, based on the pivotal Phase III COMPACT trial. This study demonstrated a 95% reduction in the median attack rate with C1-INH (SC) relative to placebo. The effect of prophylactic therapy on the number of days with HAE symptoms and/or the severity of symptoms may be a more relevant measure of efficacy for patients with HAE. This analysis examines the efficacy of C1-INH (SC) in terms of its impact on the number of HAE symptom days and the severity of symptoms, based on patient-reported data in the COMPACT study.

**Method:** Patients self-administered C1-INH (SC) or placebo twice weekly in a double-blind, crossover manner over 2 consecutive 16-week treatment periods. The time-normalised number of days of HAE symptoms and the sum of severity scores per patient were exploratory endpoints. Each day, patients entered in an eDiary whether they experienced HAE symptoms (yes/no). For every day of recorded HAE symptoms, the patient graded the severity of each symptom as mild = 1, moderate = 2, or severe = 3. The following parameters were calculated per patient: (a) time-normalised number of days of HAE symptoms, (b) time-normalised number of consecutive HAE symptom days, (c) sum of symptom severity scores, and (d) sum of symptom severity scores combined with rescue medication use. Days with missing entries for HAE symptoms were considered symptom-free days.

**Results:** C1-INH (SC) reduced the time-normalised number of HAE symptom days overall and consecutive HAE symptom days relative to placebo. The mean (SD) time-normalised number of HAE symptom days per month was 1.61 (4.39) with C1-INH (SC) 60 IU/kg and 7.51 (5.59) with placebo. The mean (SD) time-normalised number of consecutive HAE symptom days was 0.84 (1.37) per month with C1-INH (SC) 60 IU/kg and 5.00 (2.66) per month with placebo. The sum of symptom severity scores was also lower with C1-INH (SC) 60 IU/kg compared with placebo (0.07 vs 0.45) as was the sum of symptom severity scores combined with rescue medication use (0.09 vs 0.73).

**Conclusion:** Based on analysis of patient-reported data, prophylaxis with C1-INH (SC) 60 IU/kg increases the number of symptom-free days relative to placebo in patients with HAE and reduces the severity of HAE symptoms.

## 1183 | A family with type III hereditary angioedema and the c.9886A>G mutation in the plasminogen gene

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**Background:** Hereditary angioedema is a life-threatening disease characterized by recurrent episodes of subcutaneous and mucosal swelling and abdominal cramping. Corticosteroids and antihistaminic drugs that are used in case of acute histamine-induced angioedema are ineffective in case of an acute hereditary angioedema. Making the correct diagnosis is crucial for patients with this disease. Based upon family history, we were able to identify a family with hereditary angioedema manifesting in adulthood, with a fatal case of a 19-year old female member of the family. Laboratory and genetic diagnostics of C1-INH and F12 genes were completely normal, indicating a hitherto unknown mutation responsible for angioedema in this family.

**Method:** We evaluated clinical data, family history, and routine laboratory parameters and performed Sanger sequencing of exon 9 of the PLG gene.

**Results:** In one of affected family members, we were able to identify the c.9886A>G mutation in the plasminogen (PLG) gene that was recently described to be associated with hereditary angioedema. This mutation leads to a missense mutation with an amino acid exchange p.Lys330Glu in the 3rd kringle domain of plasminogen. There is no direct relationship between the earlier described cases with this mutation and the family we report here. In all affected members of the family, the symptoms manifested in early adulthood, with swelling of the face, the tongue and the larynx. The frequency of attacks was variable, between once in a year to once in a month. In one of the three family members, we found a slightly decreased level of coagulation factor XII and of plasminogen. Icatibant proved to be very effective for the treatment of acute attacks in the affected family.

**Conclusion:** The occurrence of the same c.9886A>G (p.Lys330Glu) mutation in the PLG gene in many families with no or only unknown distant relationship suggests that the disease might have been inherited through the generations without being purged from the population. The mutated amino acid exchange appears to be significant for the function of plasmin or plasminogen. We found a decrease in plasma levels of coagulation factor XII and plasminogen, which may be beneficial markers for diagnosis and monitoring of this disease.

## 1184 | Involvement of the coagulation system in hereditary angioedema

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**Background:** Coagulation parameters are altered during angioedema (AE) attacks in C1 inhibitor deficiency hereditary angioedema. Several biomarkers are useful in the diagnosis (fibrin degradation products (FDPs), D dimer (DD), and fragments of prothrombin 1 + 2). Also, a correlation between the levels of biomarkers and activity phases of the disease has been detected.

Alterations in coagulation parameters have an etiopathogenic role in the AE attack, but have not been considered as biomarkers of activity phases.

TGT is a global coagulation test which quantifies *in vitro* the ability of plasma to generate thrombin and estimates alterations in coagulation parameters.

The objective is to assess the usefulness of the thrombin generation test (TGT) to characterize patients with hereditary angioedema (HAE).

**Method:** Seventeen HAE patients from Hospital La Fe were recruited to obtain blood samples in remission and during AE attacks. None of them experienced thromboembolic events.

Plasma was collected in citrate tubes to obtain platelet rich plasma.

Hemostatic parameters were analyzed:.

TGT was conducted using a Calibrated Automated Thrombogram (CAT) method and a Fluoroskan Ascent as a reader. Results were analyzed via Thrombinoscope v5.

Citrated plasma was incubated with calcium, tissue factor, phospholipids and a fluorogenic substrate.

A thrombin generation curve is generated, obtaining parameters: latency time (Lagtime), thrombin generation maximum speed (Vo), maximum peak of thrombin generated (Peak), time to generate the maximum peak of thrombin (ttPeak), total quantity of generated thrombin (ETP), and the end time of thrombin generation (StartTail).

TGT parameters from 322 healthy donors were used as controls.

**Results:** Thirty-eight samples were collected from seventeen HAE patients (58.8% female). Fifteen (39.5%) samples were collected during AE attacks.

TGT parameters and FDPs were significantly higher in HAE patients compared with controls ($P < 0.0001$), although no significant differences were found in TGT between acute attacks and remission.

| | Controls | AEH patients | Acute attack | Remission |
|---|---|---|---|---|
| Lagtime (min) | 5.62 | 4.59 | 4.72 | 4.47 |
| ETP (nM*min) | 1266.83 | 1638.92 | 1526.63 | 1751.21 |
| Peak (nM) | 103.39 | 190.43 | 162.43 | 218.43 |
| ttPeak (min) | 12.23 | 9.75 | 10.11 | 9.39 |
| Vo (nmol/L/min) | 17.59 | 42.66 | 34.42 | 50.9 |
| StartTail (min) | 36.93 | 29.29 | 29.76 | 28.82 |

| | Reference values | AEH patients | Acute attack | Remission |
|---|---|---|---|---|
| D-Dimer ng/mL | (20-240) | 3509 | 6738 | 280 |
| Fibrinogen mg/dL | (170-437) | 398 | 412 | 385 |
| Platelets $10^3/\mu L$ | (150-400) | 286 277 | 301 454 | 271 100 |
| PT sec | (14.2-19) | 13.4 | 13.03 | 13.77 |
| APTT sec | (23-35) | 26.51 | 25.14 | 27.89 |
| C3 mg/dL | (90-180) | 117 | 115.9 | 118.23 |
| C4 mg/dL | (10-40) | 5.9 | 4.8 | 7 |
| C1-inh mg/dL | (21-39) | 7.15 | 6.8 | 7.5 |
| FVIII % | (68-156) | 145 | 149.63 | 140.46 |
| FXI % | (69-154) | 129.1 | 125.31 | 132.9 |
| FXII % | (57-163) | 119.98 | 114.65 | 125.32 |

**Conclusion:** HAE patients showed increased thrombin generation capacity.

A decrease trend in TGT is observed in AE attacks.

FDPs were increased during AE attacks, but normalized at remission periods.

These results support the involvement of coagulation in the pathophysiology of HAE, although no increase in prevalence of thrombosis is observed during acute attacks.

## 1185 | C1-Esterase inhibitor (C1-INH) functional activity of subcutaneous C1-INH for the prevention of Hereditary Angioedema (HAE) attacks: Pharmacokinetic comparison in adolescent and adult patients

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**Background:** Subcutaneous C1-esterase inhibitor (C1-INH [SC]) at 60 IU/kg was approved by the US Food and Drug Administration in June 2017 as routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescents and adults, based on the Phase III COMPACT study. We compared C1-INH functional activity in adolescents and adults to determine the effect, if any, of age on the pharmacokinetics (PK) of C1-INH.

**Method:** In the COMPACT study, patients self-administered C1-INH (SC) or placebo twice weekly in a double-blind, crossover manner over 2 consecutive 16-week treatment periods. Blood samples were drawn for assessment of C1-INH functional activity at screening; at weeks 3, 5, 8, 11, and 14 of each treatment period; and at the end-of-study visit. Observed C1-INH functional activity was plotted against time and stratified by age group (≤17 years and

>17 years). In addition, PK parameters derived from a population PK analysis of the COMPACT study were evaluated.

**Results:** Similar C1-INH functional activity over time was observed in patients ≤17 years and >17 years. Mean C1-INH functional activity after administration of C1-INH (SC) 60 IU/kg ranged from 52.9% to 64.9% in adolescents and from 63.9% to 69.4% in adults, well above the critical threshold of 40%. Population PK analysis in subjects with HAE showed that within the age range analysed (12-72 years), age did not have a clinically relevant effect on the PK of C1-INH functional activity after SC administration.

**Conclusion:** Overall, these analyses demonstrate similar PK of C1-INH functional activity after administration of C1-INH (SC) in adolescents and adults.

## 1186 | Efficacy of Prophylaxis With Subcutaneous C1-Esterase Inhibitor (C1-INH [SC]) in Female Patients With Hereditary Angioedema: Subgroup Analysis From the COMPACT Study

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**Background:** Women with hereditary angioedema (HAE) due to deficiency in C1-esterase inhibitor (C1-INH) often present with more severe symptoms and more frequent attacks than men and may, therefore, derive particular benefit from routine prophylactic therapy. Prophylactic therapy with intravenous C1-INH (C1-INH [IV]) replacement therapy requires repeated venous access, and prophylaxis with attenuated androgens may be associated with virilisation and menstrual irregularities, side effects that can be significant for female patients. Subcutaneous C1-INH (C1-INH [SC]) at 60 IU/kg was approved in June 2017 by the US Food and Drug Administration as routine prophylaxis to prevent HAE attacks in adolescents and adults, based on the COMPACT trial, which demonstrated a 95% reduction in the median attack rate with C1-INH (SC) relative to placebo. In this analysis, we evaluated the efficacy of C1-INH (SC) 60 IU/kg in female patients treated in the COMPACT study.

**Method:** Patients self-administered C1-INH (SC) or placebo twice weekly in a double-blind, crossover manner over 2 consecutive 16-week treatment periods. The primary efficacy endpoint was the time-normalised number of HAE attacks and a key secondary endpoint was the percentage of responders (ie, patients with ≥50% reduction in the time-normalised number of attacks). Subgroup analyses by sex were performed for these 2 endpoints.

**Results:** Of the 45 patients randomised to treatment with C1-INH (SC) 60 IU/kg, 32 (71.1%) were female. Among female patients, the time-normalised median number of attacks per month was 0.29 with C1-INH (SC) 60 IU/kg vs 4.06 with placebo. The median attack rate was reduced by 93% relative to placebo. Of the 27 female patients included in the responder analysis, 24 (89%) had ≥50% reduction in attacks and were classified as responders, 22 (82%) had ≥70% reduction in attacks, and 14 (52%) had ≥90% reduction in attacks. With C1-INH (SC) 60 IU/kg, 12 of 32 female patients (38%) were attack free. Subgroup results by sex for the time-normalised number of HAE attacks and the percentage of responders were similar to the overall analysis results.

**Conclusion:** Prophylactic treatment with C1-INH (SC) reduced the median attack rate by 93% relative to placebo in female patients with HAE, with 89% of patients experiencing ≥50% reduction in attacks. For female patients with HAE, prophylactic C1-INH (SC) is a convenient, effective alternative to C1-INH (IV) and attenuated androgen therapy.

## 1187 | On-demand vs prophylactic subcutaneous C1-esterase inhibitor for the management of hereditary angioedema: A benefit-risk assessment of the COMPACT study data

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**Background:** Subcutaneous C1-esterase inhibitor (C1-INH [SC], 60 IU/kg) for routine prophylaxis to prevent hereditary angioedema (HAE) attacks was recently approved in the United States. Benefits and risks of prophylactic C1-INH [SC] plus possible on-demand treatment as compared to on-demand treatment alone was quantitatively assessed based on the COMPACT study data (NEJM 2017; 376:1131-1140) for patients with at least 4 or more HAE attacks (requiring acute treatment, medical attention or causing significant functional impairment) over a consecutive 2-month period.

**Method:** Key benefit and risk outcomes relating to prevention of HAE attacks, control of HAE symptoms, global assessment of response to therapy (GART) and treatment emergent adverse events (TEAE) were identified. Using data from the COMPACT study, a double-blind crossover trial, the proportion of patients with each benefit/risk outcome was determined for the approved dose. Risk differences (RD) for each outcome were calculated per 100 patients as proportion of prophylactic C1-INH [SC] plus on-demand treated patients minus proportion of on-demand treatment alone patients.

**Results:** Using the intent-to-treat population (N = 45), RDs for reduction of HAE attacks to <1 per month was 75.6% (95% Confidence Interval [CI] = 62.2%-88.9%) and free of any attack or laryngeal attack was 40.0% (95% CI = 25.7%-54.3%) and 18.0% (95% CI = 6.6%-29.0%) respectively. Proportion of subjects with investigator graded "none/mild" attacks (RD = 56.0%, 95% CI = 40.5%-70.6%), no days with HAE symptoms (RD = 40.0%, 95% CI = 25.7%-54.3%), or no attacks treated with intravenous medication(s) (RD = 53.0%, 95% CI = 36.0%-70.0%) were higher for prophylactic C1-INH [SC] plus on-demand than for on-demand alone treatment. Results were similar for good/excellent subject (RD = 53.3%, 95% CI = 35.9%-70.8%) and investigator (RD = 77.8%, 95% CI = 64.8%-90.8%) GART. In the safety population, no significant differences between prophylactic C1-INH [SC] and placebo were observed for TEAE incidence.

**Conclusion:** Benefits of treatment options to prevent HAE attacks favors prophylactic C1-INH [SC] plus on-demand treatment while risks are comparable to on-demand treatment alone in patients with an average of 2 or more attacks per month.

## 1188 | Prevention of Hereditary Angioedema (HAE) attacks by anatomical location with subcutaneous C1-esterase inhibitor (C1-INH [SC]) treatment: Results from the phase III COMPACT study

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**Background:** Hereditary angioedema (HAE) is characterised by recurrent episodes of swelling of the face, limbs, trunk, and genitourinary and respiratory tracts. Laryngeal attacks pose the greatest risk, as airway obstruction can lead to asphyxiation. Subcutaneous C1-esterase inhibitor (C1-INH [SC]) at 60 IU/kg was approved by the US Food and Drug Administration in June 2017 as routine prophylaxis to prevent HAE attacks in adolescents and adults, based on the COMPACT study. In this study, the median attack rate was reduced by 95% with C1-INH (SC) 60 IU/kg relative to placebo. We examined the effects of C1-INH (SC) on the HAE attack rate by anatomical location.

**Method:** In the COMPACT study, 45 patients self-administered C1-INH (SC) 60 IU/kg body weight or placebo twice weekly in a double-blind, crossover manner over two 16-week treatment periods. The primary endpoint (time-normalised number of HAE attacks) was analysed by anatomic location of HAE attacks (facial, peripheral, laryngeal, thoracic, abdominal, genitourinary, other).

**Results:** During prophylaxis with C1-INH (SC), both the number of patients experiencing HAE attacks as well as the number of HAE attacks was lower relative to placebo at each anatomic location. Treatment with C1-INH (SC) 60 IU/kg effectively reduced the number of patients with HAE attacks at all anatomic locations relative to placebo: abdominal (18 vs 39), peripheral (14 vs 38), genitourinary (2 vs 22), facial (3 vs 6), and laryngeal (0 vs 9) regions. The number of HAE attacks by location was markedly lower with C1-INH (SC) 60 IU/kg than with placebo: abdominal (43 vs 243), peripheral (27 vs 207), genitourinary (3 vs 56), and facial (3 vs 8) regions. No laryngeal attacks occurred during treatment with C1-INH (SC) 60 IU/kg vs 12 with placebo. The majority of attacks that occurred during treatment with C1-INH (SC) 60 IU/kg were of mild or moderate intensity. Only 9% of patients experienced a severe attack with C1-INH (SC) 60 IU/kg, compared with 69% of patients on placebo. C1-INH (SC) was well tolerated, with no related serious adverse events.

**Conclusion:** Prophylaxis with C1-INH (SC) 60 IU/kg is effective in reducing the rate of HAE attacks at all anatomic locations. No patient experienced a laryngeal attack during treatment with C1-INH (SC) 60 IU/kg.

## 1189 | Onset of effect of prophylactic treatment with subcutaneous C1-esterase inhibitor (C1-INH [SC]) for prevention of Hereditary Angioedema (HAE) attacks: Findings from the phase III compact study

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**Background:** Subcutaneous C1-esterase inhibitor (C1-INH [SC]) at 60 IU/kg was approved by the US Food and Drug Administration in June 2017 as routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescents and adults, based on the Phase III COMPACT trial. This study demonstrated that the median attack rate was reduced by 95% with C1-INH (SC) relative to placebo. We explored the onset of the preventive effect of C1-INH (SC) after treatment initiation.

**Method:** In the COMPACT study, patients self-administered C1-INH (SC) or placebo twice weekly in a double-blind, crossover manner over 2 consecutive 16-week treatment periods. Per study design, the first 2 weeks of each treatment period were excluded in the primary analysis (time-normalised number of HAE attacks) to account for possible wash-in/wash-out effects, a methodological aspect of

any crossover trial. In the present post-hoc analysis, we evaluated results from the first 2 weeks of treatment to determine how early the preventive effect of C1-INH (SC) could be observed.

**Results:** In the first 2 weeks of treatment, 10/45 patients (22%) experienced attacks with C1-INH (SC) 60 IU/kg vs 34/45 patients (76%) with placebo. A total of 14 attacks occurred (none severe) during the first 2 weeks of therapy with C1-INH (SC) 60 IU/kg vs 70 attacks with placebo (17 severe). Population pharmacokinetic models indicate that C1-INH functional activity exceeds the critical threshold of 40% after the second dose of C1-INH (SC) ($C_{max}$ = 60.7%, $T_{max}$ = 58.7 hours, $C_{trough}$ = 48%).

**Conclusion:** The preventive effect of C1-INH (SC) is already evident in the first 2 weeks of switching from on-demand treatment, as evidenced by less severe and fewer attacks during prophylaxis.

## 1190 | May oxidative stress play a role in hereditary angioedema?

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**Background:** Hereditary Angioedema due to C1-INH deficiency (C1-INH-HAE) or with normal C1-INH is characterized by recurrent swellings due to uncontrolled production of vasoactive mediators, among which bradykinin (BK) is crucial. Oxidative stress is the result of an imbalance between endogenous production of free reactive oxygen species and reduced antioxidant defense mechanisms that can worsen inflammation and injury conditions by enhancing pro-inflammatory cytokines release and altering enzymatic functions. Through the binding and activation of the two human BK-receptors, Kinins may have dual beneficial and deleterious effects in vascular and inflammation physiopathology. We assessed the serum concentrations of AGEs and AOPPs in patients affected by HAE.

**Method:** The blood samples were collected to measure the serum concentrations of AGEs and AOPPs by spectrofluorimetric and spectrophotometric methods in patients affected by C1-INH-HAE and FXII-HAE during remission.

**Results:** The circulating levels of AOPPs observed on control group (0.94 (0.36) nmol/mg) were significantly lower than those observed on the C1-INH-HAE group (1.68 (0.47) nmol/mg; $P$ = 0.002) and FXII-HAE (1.50 (0.27) nmol/mg; $P$ = 0.001). The circulating levels of AGEs were significantly higher in C1-INH-HAE group (211.58 (151.05) AU/g; $P$ = 0.02) than the FXII group (141.48 (89.59) AU/g), thus demonstrating a state of heightened oxidative stress.

**Conclusion:** Our observations show additional underlying events involved in HAE and are of central importance for further investigations of differences in bradykinin receptors signaling among the two disease subgroups, that may result in the differences here preliminary demonstrated in oxidative stress markers.

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## 1191 | Updated safety analysis of a high-dose hypoallergenic 6-grasses pollen allergoid from clinical trial data

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**Background:** Subcutaneous high-dose hypoallergenic allergen immunotherapy (AIT) using a 6-grasses pollen allergoid has been well-established for decades in grass-pollen specific immunotherapy of allergic rhinitis and asthma. Recently performed new clinical trials prompted a reappraisal of the overall safety data pool from clinical trials.

**Method:** 1023 patients diagnosed for grass pollen allergic rhinoconjunctivitis (+/-) asthma were included in 5 randomized, controlled trials. The pooled active safety set (PASS) comprised all patients receiving active AIT via the standard dose escalation scheme (7 injections) either as preseasonal or perennial treatment for a maximum of 3 years. Adverse events (AE), adverse drug reactions (ADRs) as well as routine biochemical and hematological laboratory safety parameters were analysed. The Medical Dictionary for Regulatory Activities (MedDRA 19.0) terminology was used throughout for coding with recoding of AE terms from lower MedDRA versions where appropriate. All codes were assessed to their primary system organ class (SOC).

**Results:** 495 (254 female, 241 male) patients with a mean age of 32.8 years and a mean duration of allergic rhinoconjunctivitis of 12.1 years where included in the safety analysis. 98 (19.8%) Patients were diagnosed for having bronchial asthma at study entry. More than 40% if treatment emergent AEs were observed in the following SOCs: General disorders and administration site conditions (n = 240) as well as infections and infestations (n = 219). 4.4% of patients (n = 22) had systemic reactions. 1 treatment related serious adverse event (anaphylactic reaction) was observed. The most frequent drug related adverse events (ADRs) were injection site reactions like swelling (reported for 31.1% of patients, n = 154), pruritus (25.3%, n = 125), and erythema (18.2%, n = 90). No notable differences in changes of laboratory measurements following AIT compared to placebo were observed.

**Conclusion:** The updated overall analysis of safety data from randomized, controlled clinical trials confirmed previous analyses of clinical trial data and was found in accordance with the long-term experience from the use of the high dose hypoallergenic 6-grasses pollen allergoid in the market.

## 1192 | Monitoring change in ige/igg4 ratio has predictive significance for estimating efficacy of allergen-specific immunotherapy (ait) and enhances rendering clinical decisions during treatment

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**Background:** Clinicians administering AIT need improved monitoring of its effects and as objective as possible evaluation of its efficacy. Determining IgE and IgG4 levels before initiating treatment, and 1 and 3 years into treatment, allows monitoring its effects. Monitoring the changes in the IgE/IgG4 ratio and dynamics of this change which correlates with a clinical improvement may serve to predict efficacy.

**Method:** The repeated measures design study included 108 patients in two groups: the SLIT group, 63 patients—67 follow-ups per allergen (P), and the VIT group, 45 patients—54 P. The SLIT group had patients treated for HDM (41 P), and patients on pre-co-seasonal pollen AIT (grass 11 P, ragweed 10 P, birch 5 P). The VIT group had 28 patients on rush protocol (18 for bee and 9 for wasp) and 18 patients on conventional protocol (9 bee, 2 wasp, and 7 for both). The IgE and IgG4 levels were measured by the ImmunoCAP method. The Friedman test was used to compare data.

**Results:** Connecting the clinical improvement with the change in serological parameters and their ratio over time, three desirable patterns of IgE change have been identified. They share IgG4 increase and a decrease in the IgE/IgG4 ratio: (a) IgE decrease in 24% of SLIT patients, and in 35% of VIT patients; (b) moderate IgE increase after 1 year, with a decrease to the level below the baseline after 3 years in 13% of patients in both groups; (c) a marked IgE increase after 1 year with a decrease to the level below the baseline after 3 years in 13% of patients in both groups. There was a 59%decrease in the IgE/IgG4 ratio mean after 1 year compared to the baseline in the SLIT group, i.e. 91% in the VIT group. No statistically significant difference in IgE levels after 1 and 3 years compared to the baseline was found in all patients except those on the VIT rush protocol (a statistically significant difference). A statistically highly significant difference was determined regarding a decrease in the IgE/IgG4 ratio after 1 and 3 years when compared to the baseline in both groups, which is of predictive significance for estimating the efficacy of immunotherapy.

**Conclusion:** A decrease in the IgE/IgG4 ratio in patients on AIT realistically predicts establishing of allergen tolerance. Routinely monitoring changes in this ratio can contribute significantly to understanding clinical improvements and help in making clinical decisions on stopping or modifying AIT.

## 1193 | The clinical and immunological effect of vitamin d supplementation combined with grass-specific slit in children with allergic rhinitis

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**Background:** An important issue in sublingual immunotherapy (SLIT) is how to improve efficacy. The aim of the study is to compare the clinical and immunological efficacy of SLIT: with vitamin D supplementation to placebo in children with allergic rhinitis.

**Method:** Fifty children aged 5-12, sensitive to grass pollen, with allergic rhinitis (8 patients had concomitant asthma) participated in 5 month prospective, randomized, double-blind, placebo-controlled trial. Children received Oralair 300 IR tablet with either vitamin D 1000 IU daily supplementation, or placebo. Primary endpoints included symptom-medication score and lung function. The secondary endpoint was the immunological efficacy measured by the following $CD4^+$ $CD25^+$ $Foxp3^+$ cells, TLR4, interleukin (IL)-1, IL-6, TNF, IL-10 and transforming growth factor beta1 levels in cell culture supernatants.

**Results:** When compared to placebo group, SLIT+vitamin D group therapy was more effective in the reduction of nasal symptoms ($P = 0.04$), asthma symptoms ($P = 0.001$) and combined symptom-medication score ($P = 0.001$); there was no significant difference between groups in medication and ocular scores. We observed a significant improvement of FEV1 (vitamin D group $P = 0.014$, placebo group $P = 0.015$) and FEV1%VC levels (vitamin D group $P = 0.004$, placebo group $P < 0.001$), within both groups, between visits. FENO results did not differentiate statistically significantly the study participants in terms of receiving SLIT along with vitamin D or placebo.
Significant increase in the percentage of $CD4^+$ $CD25^+$ $Foxp3^+$ and in TLR positive cells in children receiving SLIT+ vitamin D was observed compared to placebo group. Increase in $CD4^+$ $CD25^+$ $Foxp3^+$ induction, and in TLR positive cells recruitment were independently associated with better clinical effect of SLIT in children.

**Conclusion:** We demonstrated the clinical and immunological effect of vitamin D supplementation on SLIT. Reduction in symptom-medication score and improvement in lung functions as well as significant increase in the percentage of $CD4^+$ $CD25^+$ $Foxp3^+$ and TLR positive cells in children receiving SLIT+ vitamin D was observed compared to placebo group
Vitamin D supplementation combined with SLIT provides an effective and well-tolerated new immunotherapy modality for treating children with allergic rhinitis.

## 1194 | Safety profile of cluster allergen specific immunotherapy (AIT) in ash pollen allergic patients

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**Background:** Among tree pollen the ones from ash are sometimes underestimated as cause for allergic symptoms. The objective was to evaluate retrospectively diagnostic results of patients with allergic symptoms during spring time for sensitization to ash pollen as well as the safety of allergen specific immunotherapy (AIT).

**Method:** Patients with positive anamnesis and allergic symptoms during spring time were tested for ash pollen sensitization in skin prick test (SPT) and nasal provocation test (NPT). In case of positive results, AIT (CLUSTOID Esche) was prescribed and the safety profile of the cluster schedule (0.2 + 0.5 mL with an interval of 15 minutes on the first treatment day, followed by monthly maintenance injections of 0.5 mL) was documented (according to Pfaar et al. 2009).

**Results:** 30 patients with allergic symptoms during spring time also had positive SPT results for ash pollen (wheal diameter ≥3 mm), of these 15 patients showed additionally positive results in NPT. These patients received specific AIT using the cluster schedule. So far, 97 injections were analysed, all local reactions were of grade 0 (wheal diameter <5 cm). No systemic reactions were observed.

**Conclusion:** Overall, AIT with a high-polymerized ash pollen extract was well tolerated. As ash pollen are supposed to be an important allergen during spring time, it is recommended to include SPT and NPT with ash pollen in the test panel for allergological diagnostic. Additionally, determination of ash pollen specific IgE could be applied. Furthermore, appropriate AIT should be considered for ash pollen allergic patients.

## 1194A | Impact of sublingual immunotherapy with a five-grass pollen tablet on grass pollen allergic rhinitis and asthma: A real-life, long-term analysis in France

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**Background:** Data on the fulfilment of prescriptions of symptomatic medications in patients with grass pollen allergy were

analysed to evaluate the long-term effectiveness of sublingual immunotherapy (SLIT) on allergic rhinitis (AR) and asthma.

**Method:** By using data in the Lifelink™ Treatment Dynamics database (IQVIA, Paris, France), we compared two cohorts of patients with AR: a group treated with Oralair® (Stallergenes Greer, Antony, France) SLIT tablets (n = 617), and a matched control group having received symptomatic medications only (n = 10 990). Oralair®'s effectiveness was assessed as the change in symptomatic medication fulfilments between the pre-index period (before the initiation of SLIT) and the follow-up period (after SLIT), and as the onset of asthma or the progression of pre-existing asthma (based on fulfilments of prescriptions for asthma medication). The number of fulfilments per year was calculated for each patient and each period.

**Results:** In line with prescribing guidelines, the mean duration of treatment with Oralair® was 6.3 months per season for either 2 seasons or 3 seasons. The mean number of symptomatic medications for AR fulfilled per patient and per year in the pre-index period was 6.7 ± 5.9 in the SLIT tablet group and 9.6 ± 7.7 in the control group. In the follow-up period, this value fell for the SLIT tablet group (to 2.6 ± 4.2) but did not change significantly in the control group (8.6 ± 8.1). When considering individuals not taking any asthma medications in the pre-index period, asthma onset during the treatment period was observed in 12.1% of those in the SLIT tablet group and in 15.8% of those in the control group. The corresponding values for the follow-up period were 1.2% in the SLIT tablet group and 5.8% in the control group. When considering individuals already taking asthma medications in the pre-index period, the mean ± SD number of asthma medication fulfilments in the pre-index period was lower in the SLIT tablet group (4.7 ± 4.6) than in the control group (8.1 ± 7.9). The corresponding values for the treatment period were 4.1 ± 5.4 and 10.2 ± 9.5, respectively. In the follow-up period, the number of asthma medication fulfilments fell more in the SLIT tablet group (to 2.3 ± 4.1) than in the control group (7.2 ± 9.0).

**Conclusion:** A real-world analysis of data on symptomatic medication prescriptions in patients with grass pollen allergy showed that Oralair® tablets have long-term effectiveness by relieving allergic rhinitis and slowing a progression to asthma.

## 1194B | A real-life, retrospective analysis evidencing slower long-term progression of asthma in grass pollen allergy patients treated with sublingual immunotherapy tablets

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**Background:** To assess the long-term effectiveness of sublingual immunotherapy (SLIT) on the occurrence and progression of asthma, we analyzed data on the fulfilment of prescriptions of symptomatic medications in patients with grass pollen allergy.

**Method:** Using the Lifelink™ Treatment Dynamics database (IQVIA, Paris, France) of data on prescription fulfilment by 7300 pharmacies across France, we compared two cohorts of patients with grass-pollen-induced allergic rhinitis (AR): a "SLIT tablet" group of 1099 patients having received Oralair® and/or Grazax® SLIT tablets, and a control group of 27 475 patients. The analysis focused on asthma onset in patients not having received asthma medications during the reference (pre-index) period, and on the progression of asthma in patients having already received asthma medications during the pre-index period.

**Results:** 37.6% (n = 413/1099) of the SLIT tablet group and 39.2% of the control group (n = 10 776/27 475) had asthma at the index date. Among the initially non-asthmatic patients, asthma onset was observed during the treatment period in 12.1% of the patients in the SLIT tablet group and in 12.3% of the patients in the control group. During the follow-up period, the frequency of asthma onset was three times lower in the SLIT tablet group (n = 11/603, 1.8%) than in the control group (n = 782/14 645, 5.34%). After adjustment for age, the risk [95% CI] of asthma onset in the SLIT tablet group during the follow-up period was found to be 63.7% [31.5%; 80.7%] lower than in the control group ($P = 0.0018$). In patients with asthma in the pre-index period, fulfilments of asthma medications fell by 40% in the SLIT tablet group (when comparing the pre-index and follow-up periods) and increased by 20% in the control group. When compared with the control group after age matching, the regression coefficient [95% CI] for the risk in the SLIT tablet group was -0.61 [-0.76;-0.46] ($P < 0.0001$).

**Conclusion:** A retrospective analysis of the fulfilment of prescriptions of symptomatic medications shows a significant reduction in anti-asthma treatment deliveries for RA patients with associated asthma and suggests that worsening of allergy (the occurrence of asthma) is less frequent 2 or 3 years after the initiation of treatment with SLIT tablets.

## 1195 | An examination of the reasons for treatment discontinuation and non-compliance to allergen immunotherapy

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**Background:** Allergic rhinitis (AR) patients treated with subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) may be non-compliant or discontinue treatment too early, which can negatively impact efficacy. Therefore, understanding the reasons for non-compliance and treatment discontinuation is vital to help improve compliance, persistence and thus outcomes. This study reported reasons for treatment discontinuation to SCIT and SLIT and non-compliance to SLIT in patients with AR in published real-world studies.

**Method:** A literature review was conducted in Embase, MEDLINE, EBM reviews, PsycInfo and EconLit (1998-2017) using key search terms for allergic rhinitis, SCIT, SLIT, non-compliance and non-persistence. Across all studies, ~20% of patients were non-compliant, and 1-year drop-out rates ranged from 23% to 74%. Reasons for non-compliance and treatment discontinuation in this subset of patients were stratified according to the WHO dimensions for adherence (patient-related, treatment-related, or socio-economic).

**Results:** From the 428 publications identified, six studies reported reasons for non-compliance to SLIT (n = 3) or treatment discontinuation (n = 3) to SCIT or SLIT, and the results were grouped for analysis. The majority of patients cited treatment-related factors as the primary reason for discontinuation (66% for SLIT, 50% for SCIT). Common reasons were a length of treatment for SLIT and frequency of injections for SCIT. 45% of patients discontinued SCIT due to patient-related factors such as travel to doctors and waiting time for administration. Only 24% of SLIT patients discontinued due to patient-related factors. Socio-economic reasons for discontinuation were low for both therapies (10% SLIT and 5% SCIT). Conversely, for non-compliance to SLIT, socio-economic factors were the most frequently cited reasons (50%), and included taking time off work and financial concerns.

**Conclusion:** Of patients who discontinued therapy, treatment-related factors were the most cited reasons for SCIT and SLIT, reflecting concerns with administration and treatment length. Non-compliant SLIT patients cited socio-economic factors as common reasons for non-compliance, suggesting financial concerns over a long treatment course. Differences in reasons for non-compliance and treatment discontinuation may be due to patients assigning differing importance for compliance (a day-to-day decision) compared to the long-term decision to discontinue treatment.

## 1196 | Prediction of efficacy of sublingual immunotherapy in children with pollen-food allergy syndrome associated with birch pollen allergy

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**Background:** The high prevalence of seasonal allergic rhinoconjunctivitis (ARC) and pollen-food syndrome (PFAS) demonstrate the significance of the study of predictors of sublingual immunotherapy (SLIT) efficacy in these patients.

To study the possibility of prediction of SLIT efficacy among children with ARC and PFAS with different sensitization profiles.

**Method:** The study included 101 children (5-18 years old) with ARC and PFAS. The sIgE levels to birch pollen and to recombinant component-resolved allergens (CRA) (Bet v1, Bet v2, Bet v4, Bet v6) were identified using Immuno Cap analyzer. Children received 2 courses of SLIT by standardized commercial birch pollen extracts. The ADO scale was used for evaluation of SLIT clinical efficacy.

**Results:** 53% of patients had monosensitization to rBet v1 component. The rest 47% had combinations IgE to rBet v1 and IgE to one, two or even three minor allergens (35%, 10%, 2% accordingly).

After 2 courses of SLIT by standardized pollen extracts symptoms of ARC and PFAS decreased in 90% and 63% patients accordingly.

In group 54 patients with monosensitization to rBet v1: 49 patients had a reduction of ARC (85% had 3-4 degree by ADO); 41 patients had reduction of PFAS. 3 patients hadn't finished treatment due to allergic reactions.

Among 26 patients with sensitization to rBet v1/v6: 24 patients had a reduction of ARC (75% - 3 to 4 degree by ADO); 17 had reduction of PFAS. 1 patient hadn't finished treatment due to allergic reactions.

In 9 patients with sensitization to rBet v1/v2: 7 patients had a reduction of ARC (57% - 3 to 4 degree by ADO); 3 had reduction of PFAS. 10 patients with sensitization to rBet v1/v2/v6 showed the similar results: 10 patients had a reduction of ARC (57% - 3 to 4 degree by ADO); 3 had reduction of PFAS.

2 patients had sensitization to all CRA, and only 1 patient who also received SLIT with grass allergens had reduction of ARC only (2 degree by ADO).

**Conclusion:** As the result of the study it was identified that beneficial effect of SLIT is highest in patients with monosensitization to rBet v1. The increase of sIgE sensitization profiles to minor birch allergens caused less efficacy of SLIT treatment.

## 1197 | Clinical response to subcutaneous Dermatophagoides pteronyssinus immunotherapy is independent of sensitization to Blomia tropicalis among children with allergic rhinitis and asthma

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**Background:** House dust mite *Dermatophagoides pteronyssinus* (DP) and *Blomia tropicalis* (BT) are the dominant mites inducing allergic diseases in the tropics. It is not known if DP subcutaneous immunotherapy (SCIT) is of benefit for patients sensitised to both DP and BT.

**Method:** 95 children (5-17 years old) with allergic rhinitis and asthma sensitised to both DP and BT received 3 years DP-SCIT. Clinical symptom and medication scores, serum specific IgE and specific $IgG_4$ were evaluated during DP-SCIT. In order to investigate whether the treatment outcome was dependent on the sensitisation pattern between DP and BT, patients were further grouped into DP and BT co-sensitisation and cross-reaction, according to positive or negative IgE against BT major allergen (BTMA) Blo t 5 and Blo t 21. BTMA+ group, with specific IgE to either Blo t 5 or Blo t 21, was defined as the co-sensitized group; BTMA- group, with no detectable IgE to both Blo t 5 and Blo t 21, was defined as the cross-reactive group in this study.

**Results:** All the recruited 95 patients completed 1 year of DP-SCIT, 74 (78%) patients completed 3 years of treatment. After 3 years of DP-SCIT, compared to baseline, all patients had significant reduction in symptom and medication scores. Lung function ($FEV_1$) was significantly improved as well. 65% of the patients were free of medication use and asthma symptoms, 3% of them were free of rhinitis symptom, and the $FEV_1$% in all patients were higher than 95% of predicted. DP-SCIT induced significant increases in DP and BT specific $IgG_4$. In 50% of patients, DP specific $IgG_4$ increased more than 67 fold and BT specific $IgG_4$ increased more than 2.5 fold. Further investigation in BTMA groups showed moderate correlation (spearman $r$ = 0.48, $P$ = 0.004) between specific IgE against DP and BT in the BTMA- group (n = 34), indicating specific IgE cross-reactivity. No specific IgE correlation (spearman $r$ = 0.03, $P$ = 0.82) was found in the BTMA+ group (n = 61) indicating co-sensitisation to both DP and BT. The two groups showed almost identical change in clinical responses. DP and BT specific IgG4 significantly increased during DP-SCIT, no difference was found between the two BTMA groups.

**Conclusion:** DP-SCIT can induce specific IgG4 cross-reacting with BT allergens. Patients with specific IgE sensitisations to both DP and BT may have clinical benefit from DP-SCIT treatment. Moreover, the clinical benefit of SCIT was independent of IgE cross-reactivity or co-sensitisation to DP and BT.

## 1198 | Shortened updosing schedule for allergen products for subcutaneous allergy immunotherapy: Design of a safety and tolerability trial

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**Background:** The duration of updosing for subcutaneous allergy immunotherapy (SCIT) is important for patient acceptance and convenience. To shorten the updosing schedule of two SCIT products (ALK, Denmark) a clinical trial was initiated in 2017 to demonstrate safety and tolerability of up-dosing schedules with 7 injections (three allergens: grass, birch and house dust mite), all compared with the established 11-injection schedule for grasses.

**Method:** The phase II partly-randomised (only the two grass arms were randomised), controlled, open-label trial is being conducted in Germany and Spain (EudraCT No. 2017-000971-97). A total of 320 subjects with allergic rhinoconjunctivitis to grass, birch or house dust mites (with or without asthma, aged 12-65 years) are allocated to 1 of 4 treatment arms (1:1:1:1) with updosing of the grass-, birch- or house dust mite SCIT product to 100.000 SQ-U as maximum dose by either 7 (all allergens) or 11 weekly injections (grass only, serving as control group). Subsequently, all patients receive the first two maintenance injections with 2- and 4 week-intervals respectively, thus the total treatment lasting 12 or 16 weeks.

**Results:** The primary endpoint is the number of treatment-related adverse events. Secondary endpoints include number of local and systemic reactions (immediate and delayed), number of serious adverse events, discontinuations due to adverse events, as well as change in vital signs and peak expiratory flow (pre and post injection).

**Conclusion:** With this trial design it is possible to generate safety data for a new short updosing schedule for 3 allergens at the same time. If the trial shows acceptable safety and tolerability of the 7-injection updosing schedule, updosing of SCIT for these 3 allergens may become feasible with 4 injections to a dose of 10.000 SQ-U and with 3 additional injections to 100.000 SQ-U. Results of the trial are expected in the end of 2018.

## 1199 | The effects of house dust mite sublingual immunotherapy in allergic rhinitis children

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**Background:** We often face allergic rhinitis patients who are poly-sensitized aside from house dust mite. The aim of this study is to evaluate the effects of house dust mite sublingual immunotherapy (SLIT) in allergic rhinitis children and compare the effects of house dust mite SLIT in poly-sensitized allergic rhinitis children with mono-sensitized allergic rhinitis children.

**Method:** We investigated 16 allergic rhinitis children who were basically sensitized to house dust mite and received house dust mite SLIT for 1 year and 6 months. Among 16 patients, 9 patients were mono-sensitized to house dust mite (Group 1) and 7 patients were poly-sensitized aside from house dust mite (Group 2). We also assigned another 7 allergic rhinitis children who were only treated by medication as control group. Nasal symptoms (rhinorrhea, sneezing, nasal obstruction, nasal itching, sleep disturbance) and anti-allergic medications use were assessed at every 6-month visit.

**Results:** The symptoms of allergic rhinitis started to improve after 6 months of SLIT and significantly improved after a year and a half in group 1 and group 2 compared with control group. There was no significant difference between group 1 and group 2. Anti-allergic medication use in group 1 and group 2 significantly decreased after a year and a half compared with control group and there was no significant difference between group 1 and group 2.

**Conclusion:** House dust mite SLIT was more effective than treatment only by medication. The effect of house dust mite SLIT was similar between mono-sensitized and poly-sensitized allergic rhinitis children. House dust mite SLIT could also be recommended to poly-sensitized allergic rhinitis children.

## 1200 | Subcutaneous cluster immunotherapy (SCIT) with a high-polymerized grass pollen extract is safe and effective in a DBC clinical trial

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**Background:** The objective of this study was to evaluate the safety and efficacy of subcutaneous immunotherapy (SCIT) with different concentrations of a high-polymerized allergen extract (cluster allergoid) of timothy pollen in patients suffering from allergic rhinitis/rhinoconjunctivitis to grass pollen.

**Method:** A prospective, randomized, double-blind, controlled, multicenter phase II study was conducted with four different concentrations of cluster allergoid CLUSTOID Wiesenlieschgras (group 1: 2000 TU/mL; group 2: 10 000 TU/mL; group 2: 30 000 TU/mL; group 4: 50 000 TU/mL). Out of 103 patients screened, 83 grass pollen allergic patients (18-59 years) were randomized. The cluster build-up phase was followed by four monthly maintenance injections of 0.5 mL. The efficacy was evaluated by the change of the threshold concentration step needed to induce a positive reaction in a titrated nasal provocation test (tNPT) before start and after end of the study (pre-post analysis). The safety profile was assessed for each treatment group by analyzing treatment-related adverse events.

**Results:** Overall, 77 patients (45 male, 32 female) were evaluable with pre and post data for the tNPT, group 1: n = 20 patients; group 2: n = 19; group 3: n = 20; group 4: n = 18. Significant differences in increased dosing steps in tNPT were detected for groups 2 (2.00) and 4 (1.67) compared with group 1 (0.80), but not for group 3 (1.35). A significant improvement was shown for groups 2 (89.5% of the patients), 3 (85.0%) and 4 (100.0%), compared with group 1 (45.0%), while the highest extent of improvement (≥3 steps) was observed in 8 patients in group 2. Local reactions (LR) increased from group 1 to 4 (13, 31, 79 and 79, respectively), and were significant between group 1 and groups 3 and 4. In groups 1 and 2 all LRs were of grade 0. No LRs > grade 2 were observed at all. Unspecific (e.g. headache) or mild (e.g. rhinorrhea) systemic reactions (5, 6 and 9) were reported in group 2, 3 and 4, respectively. No serious adverse event occurred during the study.

**Conclusion:** Treatment of patients suffering from allergic rhinitis/rhinoconjunctivitis to grass pollen was effective and well tolerated at different concentrations with a satisfying risk-benefit profile for the concentration of 10 000 TU/mL of grass pollen cluster allergoid.

## 1201 | Impact of grass pollen sublingual immunotherapy tablets on allergic rhinitis and asthma: Methodological aspects of a real-life, retrospective database analysis performed in France

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**Background:** We performed a real-life, retrospective study of the long-term effectiveness of a tablet formulation of grass pollen sublingual immunotherapy (SLIT) in allergic rhinitis (AR).

**Method:** Using the Lifelink™ Treatment Dynamics database (IQVIA, Paris, France), we analyzed prescription fulfilment data from 7300 pharmacies in France between March 2012 and December 2016. Two cohorts of patients aged 5 years or over with AR (defined as those having fulfilled at least one prescription for an antihistamine and/or a nasal corticosteroid during the pollen season before the index date) were selected: a "SLIT tablet" group of patients having received Oralair® and/or Grazax® for at least two seasons, and a control group having received symptomatic medications only (at least 2 deliveries per season). Patients with severe asthma were excluded.

**Results:** Out of a total of 44 963 patients having received SLIT tablets, 1099 were analyzed after selection for the index year, the duration of follow-up, and other criteria: 37.6% had had received asthma medication, 90% were aged between 5 and 45, 56.1% had received Oralair®, 39.9% had received Grazax®, and 3.9% had received both tablets. Of the 193 628 control patients, 27 475 were selected. 39.2% of the latter had received asthma medication. Given that the control group was older than the SLIT tablet group (only 30% of the controls were aged between 5 and 45), we selected a subgroup of 10 990 age-matched control patients. The criterion that excluded the largest number of patients (apart from the requirement for treatment initiation) was the need for two successive courses of treatment. The primary endpoints were the progression of AR (assessed as the change in fulfilment of prescriptions for symptomatic medications between the pre-index and follow-up periods) and the onset of asthma in individuals who were not initially receiving asthma medication. A secondary endpoint was the progression of asthma in patients already receiving asthma medications.

**Conclusion:** The long-term effectiveness of SLIT tablets in grass pollen allergy can be assessed by a retrospective analysis of fulfilments of prescriptions for allergic rhinitis and asthma medications in a selected cohort of patients.

## 1202 | Investigating the real-world differences in patient compliance to allergen immunotherapies

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**Background:** Allergen immunotherapy relies on the consistent administration of allergen extract, therefore compliance to these treatments (subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) tablets and drops) is vital for efficacy. As SCIT is administered as an injection by a healthcare professional, and SLIT is self-administered, compliance to SCIT may be perceived as superior. Therefore, a review of real-world studies investigating compliance to SCIT, SLIT-tablets or SLIT-drops was conducted. Real-world studies, instead of clinical trials, were included in this review as they are more likely to reflect actual clinical practice and patient compliance.

**Method:** A literature review was conducted in Embase, MEDLINE, EBM reviews, PsycInfo and EconLit (1998-2017) using key search terms for AR, SCIT, SLIT-tablets and SLIT-drops, and real-world compliance. Compliance was reported according to ISPOR Medication Compliance and Persistence Work Group definitions.

**Results:** From the 428 publications identified, eight studies (seven SLIT [one SLIT-tablets, two SLIT-drops, four unspecified], one both SCIT+SLIT-tablets) reported compliance rates and were included in the analysis. Real-world compliance rates ranged from 80% to 81% for SLIT administration and 83% for SCIT administration. Only one study compared compliance of SLIT to SCIT, with similar rates reported over three years (81% and 83% respectively). Three studies reported "good" compliance (physician-reported or patients consuming >60% of allergen extract) to SLIT-drops or SLIT-tablets. The good compliance rates were higher for SLIT-drops (90%-99%) compared to SLIT-tablets (77%-80%). Observed compliance to SLIT-drops or SLIT-tablets did not vary by country or geographical region. The percentage of patients defined as having "good" compliance to SLIT-tablets or SLIT-drops did not vary by study length or patient population.

**Conclusion:** Whilst compliance to SCIT may be perceived as superior to SLIT-tablets and SLIT-drops, comparable compliance rates between SCIT, SLIT-tables and SLIT-drops were identified across real-world studies. Differences between perception and real-world results may be explained by a lack of direct comparisons between SCIT and SLIT administration. Limitations included discrepancies in definitions of compliance, as well as methodology between studies. However, these are common to reviews analysing compliance, regardless of therapy area.

## 1203 | Clinical effects of sublingual immunotherapy in comparison with medication in the allergic rhinitis: An interim report of 3-year case-control study

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**Background:** Recently there have been couple of Korean reports demonstrating the superiority of sublingual immunotherapy(SLIT). In this study, the clinical effects of 3-year results were compared and analyzed dividing allergic rhinitis patients into the two groups of "SLIT group(patient)" and "medication group(control)".

**Method:** Recently there have been couple of Korean reports demonstrating the superiority of sublingual immunotherapy(SLIT). In this study, the clinical effects of 3-year results were compared and analyzed dividing allergic rhinitis patients into the two groups of "SLIT group(patient)" and "medication group(control)".

**Results:** Total of 474 patients were registered, and SLIT was performed with 126 patients (mean age, 20 [4-50]; M:F = 68:58; adults: children = 74:52). SLITone® was performed with 407 patients, SLITone® switched to Staloral® was 43 patients, newly start Stalorl® was 51 patients, Staloral® to Actair® was 17 patients, newly start Actair® was 11 patients. Among 126 patient group, 36 patients were missed and 66 patients (52%) were maintained treatments after 3-year follow-up. At the point of the end of the treatment, symptom scores were as followings: nasal discharge, 3.1-1.7; nasal obstruction, 3.1-2.1; sneezing, 2.0-1.4($P < 0.05$). Rescue medication were decreased from 12.2 for pre-treatment into 2.8 for post-treatment ($P < 0.05$). Control group was included 32 patients(mean age, 23.1 [4-46]; M:F = 20:12; adults:children = 21:11). At the point of the end of the follow-up, mean symptom scores were as followings: nasal discharge, 3.6-3.0; nasal obstruction, 3.4-3.1; sneezing, 3.1-2.6 ($P < 0.05$).

**Conclusion:** In the allergic rhinitis patients, successful compliance for 3-year SLIT compared with control was approximately 52%.

## 1204 | An IgG inhibition ELISA to measure the stability of alum-adsorbed grass pollen allergoids

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**Background:** An IgG inhibition ELISA was developed for the stability determination of alum-adsorbed grass pollen allergoids. Despite the complex nature of allergoid products, this assay allows to study the stability of the allergoid Drug Product by means of allergoid specific IgG.

**Method:** *IgG inhibition ELISA*: Rabbit IgG antibodies specific for grass allergen allergoids are pre-incubated with different concentrations of alum-adsorbed grass pollen allergoid. The mix is added to an allergoid coated microtiter plate. Unbound IgG will bind to the allergoid coat and is subsequently incubated with anti-IgG HRP labeled conjugate and stained with TMB. Results are expressed as percentage inhibition relative to the uninhibited value. The concentration of alum-adsorbed allergoid that is required to inhibit 50% IgG is used as read-out. *Circular Dichroism*: Far-UV CD spectra (190-260 nm) were recorded on a J-815 Spectropolarimeter. A cuvette with a stirring compartment was used to keep the suspension homogeneous during measurement.

**Results:** The IgG inhibition ELISA assay is specific for grass pollen allergoids (not for other allergen allergoids), has a good inter- and intra-assay precision and is robust for assay variation. Thermally stressed alum-adsorbed grass pollen allergoids were used to show that the IgG inhibition assay can be used as a stability indicating method. Severe thermal stressing resulted in a higher 50% inhibition value, indicating a loss of IgG epitopes. Furthermore, far-UV CD analyses showed that there is a close relation between the decreasing IgG binding capacity (50% inhibition values) and the loss secondary protein structures by unfolding (CD-ratio 207/222 nm values).

**Conclusion:** The IgG inhibition assay was demonstrated to be a valuable method to determine the stability of alum-adsorbed grass pollen allergoid preparations. In addition, a relation was shown between the IgG binding capacity and the change in secondary protein structures.

## 1205 | Design of a pivotal phase III trial of allergen specific immunotherapy (AIT) using a high-dose house dust mite (HDM) allergoid in patients with allergic bronchial asthma

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**Background:** Until now there is limited evidence on asthma therapy with allergoids. Recently, AIT with either high or low allergoid doses was performed in a dose-finding trial (EudraCT-No.: 2011-002248-29), showing promising results. The minimal inhalation corticosteroids (ICS) dose required to achieve asthma control was reduced significantly in all AIT dose groups compared to placebo. The current clinical trial is carried out to confirm efficacy and safety in a larger number of subjects for the considered optimal dose.

**Method:** 1038 male and female outpatients (age 12-65 years) asthmatics allergic to HDM are enrolled. During the baseline phase, the patient's minimal dose of ICS required to achieve asthma control will be assessed. After the baseline period, approx. 446 patients will receive double-blind placebo-controlled treatment for approx. 8 months, followed by a 2nd period of 16 weeks to assess the minimal ICS dose and further 2 months of observation for the assessment of asthma exacerbation. Based on the results of the dose finding study regarding the efficacy endpoints and the safety profile, the optimal allergoid dose is considered to be 5400 PNU.

**Results:** Competent Authorities and Ethic Committees in all participating 12 EU countries, Serbia, Russia and Ukraine approved the study design. The primary endpoint of the trial is the change in predefined dose steps of the minimal daily ICS dose required to achieve asthma control after approximately 8 months of subcutaneous AIT. All efficacy data will be determined using daily questionnaires and the ACQ6 by e-diary for 4 months from October to January.

**Conclusion:** The aim of this clinical trial is to demonstrate efficacy and to evaluate safety of AIT with an allergoid preparation of major allergens of *Dermatophagoides pteronyssinus* in patients suffering from allergic bronchial asthma caused by house dust mites. Asthma increases the burden of allergic disease and health care costs, especially when uncontrolled. With the development of a high-dose preparation we intend to treat asthmatic patients highly efficiently.

## 1206 | Smoking history negatively affects allergen specific immunotherapy efficacy

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**Background:** Specific Immunotherapy (SIT) is the only causal treatment in patients allergic to airborne allergens. It has been proven to be widely effective in allergic populations, but individual patients vary in terms of response to the therapy. The aim of the study was to assess the factors that might affect the efficacy of SIT.

**Method:** Patients treated with SIT for grass pollen or house dust mites were included. The efficacy of SIT was assessed with the use of Allergy Control Score (ACS), performed before and at least after one year of SIT. The following variables were assessed as potential risk factors for a poorer response to SIT: age, gender, type of allergy, type of allergen, type of vaccine, type of SIT and smoking history.

**Results:** The study group consisted of 148 subjects. SIT was effective in the entire group, lowering the ACS result from 22.31 to 14.35 points ($P < 0.0001$). No differences in efficacy in terms of assessed risk factors were found, except for smoking history (ACS change from 21.8 to 18.1 points; $P = 0.09$, OR=0.323 (CI 0.11-0.88); $P = 0.02$).

**Conclusion:** Smoking history affects SIT outcomes.

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## 1208 | Satisfaction of Immunotherapy in patients and physician; multicenter study

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**Background:** Specific immunotherapy (SIT) is a suitable treatment option for asthma and allergic rhinitis (AR), but it is not commonly used in Korea. In the achievement of the treatment, it is important that immunotherapy is applied with ideal dose and regular intervals and it is essential for the patient compliance. The aim of this study is to investigate evaluate compliance with immunotherapy protocols of patients who were treated with SIT in clinic and their satisfaction of the treatment.

**Method:** We performed a multicenter, cross-sectional survey using a specially designed questionnaire that was given to allergy specialists and patient in Korea. A member of the trained research group conducted face-to-face questionnaire interviews with each respondent.

**Results:** Most of the respondents considered AR with asthma (n = 229) and allergic asthma (n = 85) as the most suitable indications for SIT. Of all respondents, 69.1% of patients were satisfy with SIT and physician's satisfy in 84.4%. The highest allergen-positive rate in patients were associated with house dust mites. Compliance of subcutaneous immunotherapy was very high in both patients and physician.

**Conclusion:** This study shows that most patients are AR with asthma. In our study SIT compliance and satisfy are found to be high in both groups.

## 1209 | Immediate adverse reactions during SCIT in combined allergic rhinitis and asthma syndrome

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**Background:** **A**ims to evaluate the immediate adverse reactions in Combined Allergic Rhinitis and Asthma Syndrome (CARAS)patients who underwent allergen-specific subcutaneous immunotherapy (SCIT).

**Method:** We reviewed the adverse reactions data of 113 CARAS patients who underwent SCIT at our hospital during 2015 -2017.

**Results:** (a) Immediate local and systemic reactions were occurred in 90 (79.65%) and 13(11.5%) patients respectively, and incidence of immediate local and systemic adverse reactions in single injection were 39.32% and 0.50%, respectively; (b) The frequency of immediate local reactions were ascend with the increasing of SCIT dosage; (c) Compared with girls (≤14 years), boys seemed more likely to occur immediate local reactions; and females seemed to be more likely to occur systemic reactions; (d) The prevalence of immediate local reactions in children (≤14 years) were significantly higher than those in adults; while the prevalence of immediate systemic reactions had no difference between different ages; (e) Immediate systemic reactions of some patients may happened after the immediate large local reactions.

**Conclusion:** Immediate local reactions are common during SCIT, while immediate systemic reactions are rare. Furthermore, boys are more likely to take place immediate local reactions, female and large local reactions are risk factors for the development of immediate adverse reaction.

## 1210 | Application of allergen immunotherapy and the fear of recourse claims

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**Background:** Allergen immunotherapy is a cost intensive therapy and usually covered by patients' health insurances. Bur recourse claims for physicians are possible. Research on recourse frequency and impact on immunotherapy prescription is rare.

**Aim:** To identify the frequency of regress claims in a dermatological setting and to assess its impact on general prescription behaviour and immunotherapy.

**Method:** All physicians of the Psoriasis-Praxisnetz Süd-West e.V. (n = 222) were invited to participate in a web based questionnaire study on the topics of dermatology and medical law. The survey was separated into two sub-polls which were carried out after a first poll deciding whether the topic of medical law is of any interest for the dermatological practice. The topic of interest was located in the second poll.

**Results:** Overall, 66 dermatologists participated in this study. Most participants were form Bavaria, Baden-Wuerttemberg or Rhineland-Palatinate and had more than 10 years of experience as a dermatologist. Out of the 66 participating physicians 28.8% (n = 19) already experienced a previous regress claim. Of these, 73.7% (n = 14)

stated, that the experienced regress claim changed their prescription behaviour. Half of these participants (n = 8) further stated, that the fear of a possible recourse affects their prescription behaviour, whereas only 4 out of the 47 other participants declared a possible influence. Missing values excluded, this leads to a substantial hesitation in physicians who experienced a prior recourse (50.0% vs 16.7%). Nevertheless, this seems not to affect the usage of allergen immunotherapy, as all 19 physicians who already experienced a regress claim, stated to use allergen immunotherapy.

**Conclusion:** The fear of a possible regress can change physicians' prescription behaviour but does not seem to have an effect on the prescription of allergen immunotherapy. Therefore, the topic should be addressed from another perspective such as providing trainings on relevant regulations for physicians who experienced a prior recourse claim. This approach could also improve patient centred care related to modern treatments.

## 1211 | Sublingual immunotherapy in patients with seasonal allergic rhinitis and SCUAD phenotype

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**Background:** An important subpopulation in seasonal allergic rhinitis (SAR) is represented by polysensitized patients with moderate to severe form of disease inadequately controlled by drug treatment according to generally accepted guidelines. Most of these patients are unsatisfied with pharmacological therapy (PhT) and belong to severe chronic upper airway disease (SCUAD) phenotype. We evaluated in real-life clinical practice the effectiveness of sublingual allergen immunotherapy (SLIT) added to PhT in polysensitized SAR patients unresponsive to drugs.

**Method:** The prospective (randomized and controlled) study covered 13 adolescent and adult subjects, aged 16-45 years with moderate to severe SAR with/or without seasonal allergic asthma, induced by hypersensitivity to different ragweed pollen, with poor answer to PhT and indication to SLIT. The experimental group was composed of 7 patients subjected to precoseasonal SLIT (antiallergic biologically standardized vaccines in the form of sublingual drops (Ragweed pollen extract) and PhT, while 6 adequate matched patients on PhT only served as controls. Clinical effects of SLIT was evaluated by the SAR symptom-drug (diary card) score (SDS) measurement, symptom (visual analogue scale) score (VAS) measurement (control of SAR), severity of SAR measurement (according to ARIA guidelines) and nonspecific bronchial hyperreactivity (NBH) measurement (methacholine bronchial provocation test) before initiation of SLIT and 1 year later.

**Results:** The SDS were significantly reduced in patients subjected to SLIT ($P < 0.01$) 1 year after the onset it. VAS also was significantly reduced ($P < 0.05$) with satisfied control of SAR and the same time with translation from moderate-severe to mild-moderate SAR, after SLIT. NBH was also significantly reduced ($P < 0.05$) 1 year after the onset SLIT. In patients receiving PhT only, SDS, VAS and severity of SAR did not change and significantly higher ($P < 0.01$) from the value obtained in the experimental group. NBH also remained unchanged and significantly higher ($P < 0.05$) then in experimental group.

**Conclusion:** Precoseasonal SLIT added to PhT shows short-term beneficial clinical effects in polysensitized patients with SAR and SCUAD phenotype.

## 1212 | Efficiency and safety of allergen immunotherapy in patients with sensitization to molds: A systematic review

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**Background:** Allergen immunotherapy (AIT) with mold extracts has been performed for many years but the final demonstration of its clinical efficacy is still missing, due to the small number of studies and the inconsistency of results. Our aim was to systematically review efficacy and safety of AIT for the treatment of respiratory allergies to molds.

**Method:** Computerized bibliographic searches of Medline, Web of Science and the Cochrane Library (through September 2017) were supplemented with manual searches of reference lists. Randomized and non-randomized studies of intervention comparing AIT to placebo or pharmacotherapy were included. The end points were reduction of symptoms and medication use in patients treated with AIT compared to controls. The strength of the evidence was graded based on the risk of bias, consistency and magnitude of effect, according to the GRADE Working Group's guide.

**Results:** Ten studies (248 children, 99 adults; median sample size, 28) met the inclusion criteria. The risk of bias was moderate to high in all but one studies. Low strength evidence supports the assumption that AIT is effective in reducing symptoms and medication use, with only 5 out of 10 studies reporting higher benefit in the AIT group vs comparator group. Subgroup analyses of studies sharing similar characteristics did not explain inconsistency. Safety does not appear was not major concern for *Alternaria* AIT.

**Conclusion:** This is not enough strength of evidence to suggest that mold AIT is efficacious for the treatment of respiratory allergies. High-quality studies with an adequate sample size are needed.

## 1213 | Tolerability of a two week rush up-dosing with modified trees, modified grasses or modified grasses/trees mixture in pollen allergic subjects in the day-to-day practice

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**Background:** Two Phase IV studies with modified grass and birch pollen, respectively, have led to the authorization of a subcutaneous Rush up-dosing scheme (3 injections in 2 weeks for adults). In the course of a non-interventional study (NIS) the tolerability was tested in the day-to-day practice. In the Phase IV study with modified grass pollen 92.8% of patients and in the study with modified birch pollen 98.4% reached the maintenance dose of 0.5 mL.

**Method:** The prospective NIS was performed in 116 doctor's offices in Germany. The Rush up-dosing with 3 injections (0.1, 0.3 and 0.5 mL) was documented in patients getting a subcutaneous immunotherapy with modified tree or grass pollen or a mixture of those. After each injection with the patients documented in a diary any side effects within 24 hours after the injection. By using an electronic case report form (eCRF) every participating doctor's office documented a total of four injections per patient.

**Results:** Data from 1040 patients undergoing one therapy were evaluable, thereof 449 (43.2%) undergoing treatment with Trees, 435 (41.8%) with Grasses and 156 (15%) with a mixture of Grasses and Trees. Of the patients with a complete documentation of the Rush up-dosing (n = 964) the highest dose of 0.5 mL was reached by 98.8% (n = 414) of 419 patients being treated with Trees, 97.5% (n = 385) of 395 patients being treated with Grasses and 96% (n = 144) of 150 patients being treated with the mixture of Grasses and Trees. Based on available data for early (n = 1019) and late (n = 1006) local reactions (ELR, LLR) as well as systemic reactions (ESR, LSR) the following breakdown could be made (number of patients with at least one reaction) (see Table)

Severe systemic reactions (grade III and IV) did not occur.

**Conclusion:** In total 97.8% of the patients reached the highest dose of 0.5 mL. The tolerability of the single therapies with modified Trees, Grasses and the Grasses/Trees mixture were similar. In daily practice the Rush up-dosing has proven itself.

## 1214 | Trial design for safety evaluation of an accelerated dose escalation schedule with one strength of a 6-grasses pollen allergoid

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**Background:** Subcutaneous specific immunotherapy (SCIT) with a hypoallergenic grass pollen allergoid is an effective and tolerable treatment method. This study investigates the safety and tolerability of an accelerated dose escalation scheme with only one strength of the preparation.

**Method:** 13 sites in Germany, Poland, Spain and Russia will recruit patients (18-65 years) with a positive skin prick test to grass pollen allergens, specific IgE [>0.70 kU/L] and symptoms of rhinoconjunctivitis on grass pollen exposure documented in the medical history. The safety and tolerability of an accelerated dose escalation scheme (3 injections with strength B) will be compared with the standard escalation scheme (7 injections with strength A+B) of a hypoallergenic grass pollen in a multicentre phase II clinical trial. Both groups will receive 2 additional maintenance doses. All adverse events will be recorded. Patients and investigators will assess the tolerability of the therapy using a 5-point Likert scale.

**Results:** The study design has been approved by Competent Authorities and Ethic Committees in all participating countries. Approximately 100 male and female outpatients, aged 18-65 years, will be screened. It is planned to randomize 70 patients, 35 patients in each active treatment group.

The use of an alternative dose escalation schemes with less injections is common in daily practice. The current trial investigates a treatment scheme with 3 dosing escalation steps with one strength in a controlled environment. We expect these are the minimal number of injections for a dose escalation of an allergen immunotherapy with the 6-grasses pollen allergoid.

**Conclusion:** The advantage of this new one strength high-dose allergen immunotherapy (AIT) option is that administration of less injections is comfortable and minimizes the risk to confuse vial A with vial B. For the patients it is convenient to get less injections and to have less visits their physicians. Also less absence from jobs are favorable for the patients.

## 1215 | Pilot study of tolerance of a cluster initiation schedule of immunotherapy with an allergenic extract of mites absorbed in aluminium hydroxide

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**Background:** Native extracts used in immunotherapy have the disadvantage that their initiation schedules are very long in time compared with the allergoid ones.

Objective: We have evaluated the tolerance to a new cluster schedule during the dose-increase phase using an extract of mites absorbed in aluminum hydroxide and standardized in IR/mL.

**Method:** We pooled our patients in two groups based on weight: less than 40 kg and equal or more than 40 kg. The schedule using the highest concentration vial consisted in 3 days of cluster: day 1, day 8 and day 22. On the first day were administered two doses of 0.1 mL separated by 30 minutes in the group of less weight and 0.10 + 0.20 mL in the other group. The second day, separated by 30 minutes, patients with least weight was administered 0.2 and 0.3 mL and 0.3 and 0.5 mL in the greater weight. Finally, the third day, both groups were given directly their maintenance dose according to their weight: 0.5 and 0.8 mL respectively. Finally the third day all received the maintenance dose that was directly 0.50 mL for the <40 kg group and 0.80 mL for the ≥40 kg.

**Results:** Total patients: 61. In the <40 kg group we included 28 patients of whom only 11 presented mild local reactions. In the ≥40 kg group we included 33 patients and we could observe 10 mild local reactions and 3 intense local reactions. These three patients continued the maintenance doses with 0.50 mL instead of 0.80 mL. Nobody presented systemic reactions in any of the two groups.

**Conclusion:** We present a new cluster schedule during immunotherapy dosing-increase phase with a native extract of mites absorbed in aluminum hydroxide with good tolerance.

## 1216 | Study the effect of allergen rush immunotherapy on allergic rhinitis

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**Background:** Allergen Immunotherapy is an effective treatment for allergic rhinitis. Routine immunotherapy requires at least 6-5 months to reach the maintenance dose, but rash immunotherapy reduces build up phase. Although the safety and efficacy of this method are still under discussion. The aim of this study was to evaluate the efficacy of subcutaneous rush immunotherapy in patients with permanent allergic rhinitis after one year of treatment.

**Method:** Immunotherapy was performed with Weed Mix extract on 15 patients with permanent allergic rhinitis aged 15-50 years who were susceptible to salsola and pig weed. Before and after one year of rush immunotherapy specific anti-weed mix (salsola, pig weed) Measured by ELISA in patients.

**Results:** Specific IgE against salsola before immunotherapy (35.79 mean =) and after one year of immunotherapy (2.82 mean =) with $P < 0.022$. Specific IgE against pigweed before immunotherapy (5.37 mean = (and after one year of immunotherapy) 0.47 mean = (with $P < 0.005$).

**Conclusion:** Rush Immunotherapy is an effective therapeutic method for patients with allergic rhinitis. It seems that in cases requiring faster response to treatment, this immunotherapy can be considered as a substitute for conventional immunotherapy.

## 1217 | Design of a pivotal phase III allergen immunotherapy study to assess the efficacy and safety of subcutaneously administered tyrosine adsorbed modified birch allergen+MPL

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**Background:** In previous clinical trials were have shown that a modified birch allergen subcutaneous immunotherapy (SCIT) product (1.0 mL) with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants achieving a cumulative dose of 27 300 SU was shown as the most effective dose without added safety signals. The current pivotal Phase III study aims to confirm the safety and efficacy of this cumulative dose compared to placebo in patients with moderate to severe seasonal allergic rhinoconjunctivitis due to birch-pollen with or without mild asthma.

**Method:** This multi-center (59 clinical study centers in 4 European countries) randomized, double-blind, placebo-controlled, and parallel-group study was initiated 2017. The start and stop of the birch pollen season in the different regions was predicted using historical pollen data provided by the European Aeroallergen Network. The primary outcome of this pivotal Phase III study is the difference in

the EAACI recommended total Combined Symptom and Medication Score (CSMS; Pfaar 2014), collected once daily and averaged over the peak birch pollen season of 2018, between the 27 300 SU and placebo treatment groups. The linguistic validity of the sponsor-developed CSMS questionnaire was ensured via intensive expert review and cognitive debriefing sessions with panels of allergy patients.

**Results:** The design of this study, including sample size and primary and secondary endpoints, will be discussed based on prior experience gained in two dose finding studies. In addition, the number of patients screened and randomized will be presented by country, gender and/or age and screen failures will be categorized.

**Conclusion:** This pivotal Phase III study is designed to establish the efficacy and safety of a cumulative dose of 27 300 SU birch MATA MPL SCIT product. The achievement of its aim will be an important milestone in the development of an efficacious and safe state-of-the-art birch SCIT.

## 1218 | The SQ tree SLIT-tablet induces clinically relevant treatment effect on moderate to severe allergic rhinoconjunctivitis (ARC)

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**Background:** The SQ tree SLIT-tablet is in development for treatment of ARC induced by pollen from the birch homologous group, e.g. birch, alder and hazel. Clinical efficacy of the treatment was investigated in a phase III, randomised, DBPC trial (EudraCT 2015-004821-15). Here we present findings illustrating the clinical relevance of the treatment effect.

**Method:** The trial included 634 subjects (12-65 years) with moderate-severe ARC despite symptomatic treatment. Subjects were randomised to SQ tree SLIT-tablet (12 DU) or placebo for at least 16 weeks prior to the alder/hazel pollen season and until the end of the birch pollen season (BPS). The primary endpoint was the ARC total combined score (TCS) in the BPS, i.e. the sum of daily symptom score (DSS) and the daily medication score (DMS). Secondary endpoints supporting the clinical relevance for the patients, included mild days (defined as days without intake of antihistamine tablet/eye drops and only mild symptoms, DSS $\leq$ 1, i.e. no more than minimal awareness of symptoms), severe days (days with DSS$\geq$6 and at least 2 moderate or 1 severe symptom), and ARC quality of life measured by RQLQ.

**Results:** The primary analysis showed an absolute difference in TCS between placebo and 12 DU of 3.02 (40%, $P < 0.0001$). The odds of experiencing a severe day during the BPS were approximately doubled in the placebo group compared to the 12 DU group (OR = 2.12, $P < 0.0001$) and the odds of experiencing a mild day were halved (OR = 0.52, $P < 0.0001$). Similar results were seen for the tree pollen season (TPS), covering both alder, hazel and birch pollen seasons. The total RQLQ score was improved for 12 DU compared to placebo during the BPS and TPS ($P < 0.05$, except for the last week of the TPS), with the most pronounced effects during week 2-5 of the BPS (absolute difference: 0.47-0.58, $P < 0.0001$). Treatment was well tolerated. The most frequent adverse reactions were mild or moderate local reactions related to the sublingual administration. No deaths were reported and no serious adverse events were assessed as related to the SQ tree SLIT-tablet.

**Conclusion:** Treatment with the SQ tree SLIT-tablet improved ARC symptoms and need for symptomatic treatment. The 12 DU group had less "severe days" and more "mild days" during the pollen seasons. The quality of life was similarly improved. These findings substantiate the clinical relevance of the SQ tree SLIT-tablet for patients with ARC induced by pollen from the birch homologous group.

## 1219 | A prospective single arm study to assess efficacy & safety of pidotimod in management of recurrent acute respiratory tract infections in Indian paediatric patients

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**Background:** Hypo-responsive immune system plays an important role in recurrent Acute Respiratory Tract Infections (ARTIs) in children. Pidotimod, a synthetic dipeptide, with potential stimulant activity on adaptive and innate immunity has shown positive clinical outcomes in management of ARTIs in children. This study evaluates the efficacy, safety and cost analysis of Pidotimod in management of recurrent ARTIs.

**Method:** This prospective, single arm study enrolled children of 2-12 years suffering from recurrent ARTIs. All subjects received Pidotimod therapy (800 mg daily for 15 days, followed by 400 mg daily for 45 days) as add-on to routine therapy. The clinical characteristic of all ARTI episodes (frequency, duration, need of antibiotics & hospitalization) in 6 months prior to enrolment was compared to those episodes occurring during 6 month follow-up period post-enrolment. The average cost incurred in treatment of ARTIs, school days & workdays (of parent) lost due to these episodes were evaluated additionally. An explorative assessment of T- & NK- cells markers in peripheral blood before & after therapy was performed.

**Results:** Total n = 57 subjects (mean age 4.6 ± 2.09 years, 61.4% males) completed entire study. The mean incidence of ARTIs reduced from 7.7 ± 2.34 episodes at baseline to 1.4 ± 1.23 ($P < 0.001$), with 31.6% subjects not suffering from any episode. The mean duration

of episodes reduced from 8.2 ± 3.58 to 2.5 ± 1.23 days ($P < 0.001$). 64% of episodes (vs 95% at baseline, $P < 0.05$) required antibiotics for mean duration of 2.3 ± 0.98 days (vs. 6.6 ± 1.76 days, $P < 0.001$). None of ARTI episodes in follow-up period required hospitalization as against 22.8% episodes, (mean duration 5 ± 2.06 days; $P < 0.05$) before pidotimod therapy. The number of school days lost & work days lost showed reduction of 3.6 ± 5.34 days($P < 0.001$) & 0.1 ± 4.07 days($P = 0.871$) respectively. The average expenses incurred in treatment of ARTIs shows significant reduction of Rs. 13 193 ± 1541 ($P < 0.001$). 11 adverse events were reported in 8 (14%) subjects, which were mild in nature. A statistically significant increase in absolute counts of T- & NK cells was seen in explorative assessment of immune markers.

**Conclusion:** The study shows Pidotimod to be well-tolerated effective therapy in reducing the incidence and severity of recurrent ARTIs, thereby providing additional benefit of reduction in discomfort & healthcare cost due to recurrent ARTIs. Thus, Pidotimod can be considered as potential therapeutic option for treatment of recurrent ARTIs in children.

## 1221 | Comparing the efficacy of 1-Grass and 5-Grass pollen slit tablets in the same patient: A case report

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**Background:** Two registered sublingual immunotherapy (SLIT) products are available to treat grass-pollen induced rhinoconjunctivitis, consisting of the 1-grass (Phleum pratense) and the 5-grass pollen tablets. No study of direct comparison of the efficacy of the two products was performed. We report the case of a patient who was treated in different years with the 5-grass or the 1-grass tablets with contrasting efficacy.

**Method:** The patient was a 18-year old woman suffering from 3 years of grass pollen induced rhinoconjunctivitis. In 2015 SLIT was started with the 5-grass pollen tablets, but in 2016, due to unavailability of the product, SLIT was performed by the 1-grass pollen tablets. In the third year of treatment SLIT with the 5-grass pollen tablets was resumed. For the 5-grass tablets SLIT was initiated before the pollen season and stopped after 7 months of treatment, while for the 1-grass tablets the treated was prescribed to be continuous. The efficacy of SLIT was evaluated by symptom-medication scores as reported in diary cards by the patient during the month of May, when the grass pollen usually reach the higher concentration in the atmosphere in Lombardy, where the patient lives.

**Results:** The mean symptom-medication score in the first year of treatment (5-grass tablets) was 4.35, compared with a mean score of 7.2 in the second year (1-grass tablets). The patient was unsatisfied of the symptoms control and asked to resume for the last year of SLIT the 5-grass tablets. The mean symptom-medication score in such year was 0.77. No clinically relevant adverse event was reported with any SLIT product.

**Conclusion:** Based on the momentary unavailability of the 5-grass pollen tablet, it was possible to assess in a same patient the clinical outcome associated to either of the two registered SLIT products. A significantly different efficacy of SLIT with the 5-grass tablets compared with the 1-grass tablets was observed.

## 1222 | Fusion proteins consisting of Bet v 1 and Phl p 5 form IgE-reactive aggregates with reduced allergenic activity

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**Background:** Bet v 1 and Phl p 5 representing major allergens in birch and grass pollen, occur as monomeric proteins with high allergenic activity as assessed by clinical provocation testing in patients.

**Method:** Hybrid molecules consisting of Phl p 5 and Bet v 1 either fused directly (hybrid 1) or separated by a short linker (hybrid 2, hybrid 3) were expressed in *E.coli* and purified. A biochemical and biophysical characterization was performed by SDS-PAGE, size exclusion chromatography (SEC), dynamic light scattering (DLS) and circular dichroism (CD) spectroscopy. Hybrid 1 was further studied by negative stain electron microscopy. Antisera raised against Phl p 5, Bet v 1 and peptides thereof were used to test hybrid 1 for IgG reactivity. IgE reactivity and basophil activation of hybrid 1 was studied by quantitative dot blotting and basophil activation tests.

**Results:** Unlike the isolated monomeric allergens, SEC and DLS showed that the hybrid formed stable, soluble high molecular weight aggregates which could be visualized by negative stain electron microscopy. CD-based secondary structure prediction of the hybrid indicated a loss of a-helical content compared to the equimolar mix of Phl p 5 and Bet v 1. The hybrid reacted as well as the monomeric allergens with Bet v 1- and Phl p 5-specific rabbit IgG antibodies but showed lower reactivity with peptide-specific IgG antibodies. Interestingly, the hybrid exhibited significantly stronger IgE binding than the equimolar mix when tested with sera of patients sensitized to Bet v 1 but not with sera of patients sensitized to Phl p 5. However, the hybrid elicited a 10-100-fold reduced basophil activation for all

tested patient sera when compared to the equimolar mix of the parental allergens.

**Conclusion:** The Phl p 5-Bet v 1 hybrid is the second known example of a protein which despite increased IgE reactivity to Bet v 1 exhibited strongly reduced allergenic activity due to formation of high molecular weight aggregates. The reduction of allergenic activity of the IgE-reactive high molecular weight allergen aggregates may be explained by altered orientation of IgE epitopes of Bet v 1 in the hybrid architecture.

## 1224 | The effects of local heating on hymenoptera venom allergenicity: Could high temperature change the natural history?

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**Case report:** Hymenoptera venoms contain vasoactive and proinflammatory mediators that cause local pain and swelling. In sensitized individuals, venom-specific IgE binds to IgE-binding epitopes, triggering an allergic reaction. The epitopes on major hymenoptera allergens are almost entirely discontinuous and conformation-dependent. Food allergy studies show that native conformational epitopes can be destroyed, and new epitopes appear during heating, the effect on protein allergenicity depending on the temperature and duration.

Hymenoptera allergy may cause large local reactions (LLRs) at the sting site and systemic reactions. Individuals who have previously experienced LLR often have LLRs to subsequent stings, and up to 10% have a systemic reaction. The treatment of LLRs is symptomatic, including cold compresses, antihistaminic, analgesic medication, and even a short course of glucosteroids.

Recently, I was stung on my foot by a wasp while walking barefoot at the edge of the sea. I felt intense pain at the sting site, and within minutes, abdominal cramps, with tachycardia and cold sweat. Fearing anaphylaxis, I ran through the very hot sand for 3-4 minutes to seek help. As, during this time, the pain decreased considerably and the other symptoms almost disappeared, I kept my foot in hot sand for 30 minutes, after which there was only mild swelling and erythema at the sting site, which persisted for the next two days.

I also describe the cases of 3 children with a history of LLR after insect sting, who attended the local hospital emergency department 5-15 minutes after being stung on the hand. They were all in good general condition, with no swelling in the affected hand. They were immediately placed with the sting site in water at temperature of 45-55°C for 1 hour, and remained asymptomatic. After 2 hours they were discharged and presented no symptoms after 12, 24, 72 hours, without further treatment.

**Conclusion:** These experiences suggest that exposure to local high temperature (depending on individual tolerance), immediately after a sting, could reduce venom-protein allergenicity and the severity of adverse reactions. To the best of my knowledge the effect of heating on venom-protein allergenicity has not been reported. *In vivo* (sting challenges with application of different supportable temperatures) and *in vitro* research (immunoblot with denaturized venom protein at different temperatures and for different times) is indicated.

## 1225 | The danger of bee sting therapy

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**Introduction:** Use of bee venom (BV) as a therapeutic agent for the relief of joint pain dates back to Hippocrates. Also known as apitherapy, this technique is widely used in Eastern Europe, Asia, and South America. Beneficial effects of bee stings can be attributed to melittin, an anti-inflammatory agent, known to be hundred times stronger than cortisone. Recent studies have reported that BV has anti-nociceptive and anti-inflammatory effects. It is used to treat disease such as rheumatoid arthritis, cancer, and neurodegenerative disorders (such as Alzheimer's and Parkinson's diseases). Unfortunately, certain substances in the BV trigger allergic reactions which can be life threatening in a sensitized individual.

**Case report:** We present a 60 year old woman who developed facial angioedema, tongue swelling and generalized urticaria 20 minutes after the fourth bee sting during a session of bee sting therapy (BST). Symptoms resolved with intramuscular methylprednisolone in less than one hour.

She had undergone 15 sessions of BST in the last year because of joint pain and chronic pruritus. In each session, she received 5-6 stings in her back, developing local reaction that usually resolved without treatment in less than 24 hours.

She did not suffer more hymenoptera stings after the last reaction. One bee sting several years before BST resulted in no reaction. She has no symptoms with honey, vegetable or other food ingestion.

**Methods:** Total IgE and specific IgE were determined using InmunoCAP system (Thermofisher, Scientific Inc).

Skin tests (both prick and intradermal) with ALK-Abelló extracts of Apis, Vespula and Polistes (Hørsholm, Denmark) were also performed.

**Results:** Total IgE was 40.4 KU/L, and basal triptase 4.23 μg/L, both of them within normal limits.

Specific IgE was positive for Apis 6.59 KUA/L and rApi m1 (Phospholipase A2) 1.07 KUA/L; and negative for Vespula spp, Polistes spp, Ves v1 (Phospholipase A1), Ves v5, and rPol d5.

Prick tests showed negative results for all extracts tested. Intradermal skin tests were positive for Apis at 1 μg/mL, but negative for Vespula and Polistes.

Our patient was diagnosed of anaphylaxis due to Apis venom, thus BST was contraindicated and an epinephrine autoinjector was prescribed. She rejected hymenoptera venom immunotherapy.

**Conclusion:** To our knowledge, this is the first case of anaphylactic reaction after bee sting therapy.

Bee sting therapy should be considered a risk factor for anaphylaxis.

## 1226 | Specific immunotherapy with aeroallergens: Indicated in a patient with serious persistent asthma?

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**Case report:** Treatment of uncontrolled persistent bronchial asthma is based on the use of corticosteroids (ICS) and bronchodilators, leukotrienes, and anticholinergics or other biological treatments such as Omalizumab. In the case of bronchial asthma of allergic origin must be consider the ITA (aeroallergens immunotherapy specific)

46 year old woman with allergic severe persistent uncontrolled asthma and positive skin test to epithelium horse and pollen grass (negative to other airborne allergens as mites, fungi and other pollens). It is recommended to avoid contact with horses, but the patient denies the possibility of avoiding exposure to the allergen (immediate family dedicated to working with horses), so etiological treatment is posed with ITA with a horse epithelium standardized extract (units S.Q.)

Patient initiates ITA in cluster schedule reaching maximum maintenance dose in 2 weeks with good tolerance. After 6 months presents less bronchial symptoms and needed only once rescue bronchodilator. FEV1 was 1.80 (72.8%) (basal 1.36%-53.3%) on spirometry and ACT was 29 (basal 11).

Patient reported good control of their disease, improved their quality of life, tolerating contact and exposure to numerous horses as well as contact with clothes of people who had been exposed.

Although ITA is absolute contraindication on uncontrolled asthma with a degree of evidence Ia, our case had only "transitory" contraindication and reported subjective clinical improvement and objetive in questionary of quality of life and reduced their maintenance medication.

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## 1227 | Importance of nPol d 1 in the diagnosis of allergy to wasps venom

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**Background:** In Mediterranean region, *Polistes* and *Vespula* are clinical relevant wasps. A panel of major vespid venom allergens was used to establish the sensitization to each vespid. We evaluated the importance of using Pol d 1 in the diagnosis of allergy to vespids venom.

**Method:** Patients who suffered an allergic reaction after a vespid sting were included. Specific IgE (sIgE) to natural *Vespula* (Ves v 1, Ves v 5) and *Polistes* (Pol d 1, Pol d 5) were detected using ADVIA Centaur system with ALK natural antigens. sIgE to total *Vespula* and *Polistes* venom were determined by ImmunoCAP. IgE levels >0.10 kU/L were considered as a positive result

**Results:** 69 patients were studied; 58.6% male, mean age 45.5 years (IQR 34.7-56 y). sIgE positivity to Vespula venom reached 81% using ImmunoCAP and 85.5% when using native allergens. Polistes sIgE positivity percentage was 81% using ImmunoCAP and 79.7% using main allergens. The study was negative in three patients. Double sensitization was diagnosed in 27 patients (39.13%). Phospholipases were more relevant allergens than antigen 5 in this study. The inclusion of nPol d1 in the panel of allergens implied a change of the diagnosis in 33 patients (47.8%)

**Conclusion:** The use of native allergens improves the diagnosis of patients with vespid allergic reactions. It has allowed the diagnosis when sIgE against the complete venom was not detected. Phospholipase A1 (Ves v 1 or Pol d 1) is the predominant vespid allergen in our area. In most of the cases it defines patient sensitization. The omission of nPol d 1 in the panel of allergens leads to a mistaken diagnosis in almost half of the cases

| Insect sensitization | With nPol d1 (%) | Without Pold1 (%) | Difference |
|---|---|---|---|
| Negative | 3 (4.3) | 8 (11.5) | 5 (7.2) |
| Vespula | 21 (30.4) | 42 (60.8) | 21 (30.4) |
| Polistes | 18 (26.1) | 7 (10.1) | −11 (−16) |
| Double | 27 (39.1) | 12 (17.4) | −15 (−21.7) |

| | CAP Vespula | nVes v 1 | nVes v 5 | CAP Polistes | nPol d 1 | nPol d 5 |
|---|---|---|---|---|---|---|
| % positivity | 82.1 | 72.4 | 47.8 | 81.1 | 68.1 | 55 |

## 1228 | Differences of Pol d 3 and Ves v 3 induced basophil activation between Spanish and German insect venom allergic patients

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**Background:** The two predominantly allergenic species in Spain are *Polistes dominula* and *Vespula* spp. In Germany *Polistes dominula* is virtually not present. Recently, Pol d 3 was identified as major allergen of *Polistes dominula* venom. It is a homologue of the prominent dipeptidyl peptidase IV allergen Ves v 3 from yellow jacket venom with a protein sequence identity of 76.1% and showed cross-reactivity in the basophil activation test (Schiener M et al. Sci Rep 2018, accepted). It was the aim of this analysis to compare the area under the dose-response curve (AUC) as combined parameter for basophil sensitivity and reactivity in insect venom-allergic patients from Spain and Germany with a positive result in Ves v 3 and Pol d 3 induced basophil activation.

**Method:** A basophil activation test (Flow CAST®) with different concentrations of Ves v 3 and Pol d 3 was performed in 28 insect venom allergic patients, 14 patients from Spain (Barcelona) and 15 patients from Germany (Munich).

**Results:** 8 out of the 14 Spanish patients showed a positive result to Ves v 3 and/or Pol d 3. 2 patients reacted only to Ves v 3, 3 patients only to Pol d 3 and 4 to both allergens. 9 out of the 15 German patients showed a positive result to Ves v 3 and/or Pol d 3. 4 patients reacted only to Ves v 3, 1 patient to only Pol d 3 and 4 to both allergens. The mean AUC for Pol d 3 was significantly higher ($P < 0.05$) in double-positive patients from Spain compared to the mean AUC for Ves v 3 from the same patients. Mean AUCs for Pol d 3 and Ves v 3 of the German double-positive patients showed no significant differences between the two allergens.

**Conclusion:** Cross-reactivity between Ves v 3 and Pol d 3 was found in 4 patients from Germany with no significant difference of

the AUC. Double-positive patients (n = 4) from Spain showed higher AUC-values to Pol d 3 compared to Ves v 3. The higher activation of the basophils by Pol d 3 might reflect the primarily sensitizing insect in Spain, but further investigations with a higher number of patients are needed.

## 1229 | Comparison of the three available tests: ImmunoCAP, Polycheck, and EUROLINE in Hymenoptera venom allergy

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**Background:** Differential allergy diagnostics using molecular components is a powerful tool in venom allergy. Immuno CAP is one of the gold standard tests for accuracy and reliability for quantitative IgE testing in venom allergy. Other tests, which are worldwide used, are based on multiparameter systems which streamline the diagnostic procedure by delivering a comprehensive and detailed patient profile in a single test. Two strip-shaped tests, the multiplex EUROLINE DPA-Dx Insect Venoms Profile 2 and Polycheck insects/CCD are used for monitoring and diagnosis.

**Aim of study:** To compare agreement between three available tests in Hymenoptera venom allergy.

**Method:** Sera from 59 patients with venom allergy were used in the study. 56 children were treated with specific immunotherapy (11 with bee venom and 45 with wasp venom). At the same point time from the serum of each patient, all 3 available tests—Immuno CAP (i1, i3, i208, i209, i211, i217), EUROLINE DPA-Dx Insect Venoms Profile 2 and Polycheck insects/CCD were done. Based on the results percent agreement with kappa value was calculated between all systems.

**Results:** Percent agreements and kappa value between EUROLINE and ImmunoCAP among wasp allergen components—i3, i209, i211 were 88%; 0.5, 90%; 0.6 and 68%; 0.4 respectively and honey bee allergen components—i1, i208, i217 were 95%; 0.9, 93%; 0.7 and 97%; 0.9 respectively. Agreement between Polycheck and ImmunoCAP i1 and i3 allergen components were 85%; 0.7 and 66%; 0.3 respectively. Agreement between Polycheck and EUROLINE i1 and i3 allergen component were 86%; 0.7 and 61%; 0.2 respectively. Based on wasp and bee components in all three systems, sensitization pattern was analyzed. Similar test results were found between EUROLINE and ImmunoCAP systems.

**Conclusion:** The comparative studies carried out showed a markedly higher compliance of results with the EUROLINE tests compared to Polycheck with the ImmunoCAP system. Percent agreement was extremely high and kappa value was substantial or almost perfect in the case of bee venom allergy between EUROLINE and ImmunoCAP system. Results of agreement and kappa value found between Polycheck and another test, especially in the case of wasp allergy, was unsatisfactory.

## 1230 | Contribution of molecular diagnosis of bee venom allergic patients with systemic reactions during venom immunotherapy

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**Background:** Bee venom (BV) allergy is one of the most common causes of severe anaphylaxis in adults. Venom immunotherapy (VIT) is considered the most effective treatment, but systemic reactions (SR) can occur during it. Molecular diagnosis can improve diagnostic accuracy, but no correlation was identified with SR during VIT.

**Aim:** Characterize the sensitization profile by molecular components of pts with anaphylactic reactions to BV under VIT and investigate if SR during VIT are related to different patterns of sensitization.

**Method:** Prospective study including 30 pts under VIT for at least 1 year. We considered a group of pts reacting during the ultra-rush (Group A) that was compared with the group with no reactions (Group B). Serum specific IgE (sIgE) for BV (i1) and recombinants: rApi m1, rApi m2, rApi m3, rApi m5 and rApi m10 were evaluated before and after 1 year of VIT by ImmunoCAP (Thermofisher Scientific, Uppsala, Sweden). A value >0.35 kUA/L was considered positive. All statistical tests were performed with Graph-Pad Prism v5.01.

**Results:** 80%-male, mean age-45 years old (14-70). Group A-10 pts; Group B-20 pts. 4 pts (2 -group A and 2-group B) were drop out during first year of VIT. Before VIT, sIgE to rApi m1 was detected in 86.7%, rApi m2-46.7%, rApi m3-16.7%, rApi m5-43.3% and rApi m10-70%. Positive results to at least one bee venom allergen were detected in 100%. 80% of pts were sensitized to >1 allergen and 13.3% to all allergens. Characterization profile of both groups - median and interquartile range (IQR25/75) before and 1 year after VIT are represented in table 1. There was no statistically significant differences in the profile of both groups before VIT, however we found a significant decrease: $P = 0.045$, $P = 0.017$, $P = 0.021$ to i1, Api m3, Api m10 respectively, in group B 1 year after VIT.

**Conclusion:** These data showed that 1 year after VIT there was a significant decrease of Api m3 and Api m10 in pts without reactions during VIT, however there was not found association between pts with SR during VIT and there sensitization profile. Nevertheless is important to study a greater number of pts.

| | Group A | | | | Group B | | | |
|---|---|---|---|---|---|---|---|---|
| | Median+ | IQR25/75+ | Median* | IQR25/75* | Median+ | IQR25/75+ | Median* | IQR25/75* |
| i1 | 8.58 | 2.52/26.68 | 7.37 | 1.62/65.88 | 10.05 | 2.53/24.93 | 5.14 | 1.92/17.10 |
| rApi m1 | 3.65 | 0.85/15.94 | 2.55 | 0.95/28.91 | 1.87 | 0.45/11.11 | 2.01 | 0.42/6.66 |
| rApi m2 | 0.74 | 0.02/3.46 | 0.63 | 0.05/9.25 | 0.03 | 0/1.61 | 0.11 | 0/0.70 |
| rApi m3 | 0.17 | 0.02/1.14 | 0.08 | 0.02/2.45 | 0.03 | 0/0.23 | 0.02 | 0/0.08 |
| rApi m5 | 0.29 | 0.02/2.85 | 0.85 | 0.03/3.39 | 0.16 | 0/2.25 | 0.13 | 0.01/1.43 |
| rApi m10 | 1.98 | 0.20/2.80 | 1.116 | 0.21/5.30 | 0.43 | 0.11/5.28 | 0.45 | 0.07/1.98 |

## 1231 | Hymenoptera venom allergy: Re-stings reactions

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**Background:** Hymenoptera venom immunotherapy (VIT) is the only effective treatment in hymenoptera venom allergy (HVA).

**Objective:** To analyze hymenoptera re-sting reactions in patients with indication for VIT.

To evaluate differences in the severity of reactions of re-stings between patients who underwent VIT or not.

**Method:** A medical records review of patients proposed for VIT between 2005 and 2016 in a Clinical Allergy Department of a University Hospital, followed by a structured telephone interview.

**Results:** A total of 113 patients were included; 80 (71%) males, with a mean age of 38 (±15) years; 23 (21%) beekeepers, 25 (23%) were atopic, 4 (4%) had asthma, 14 (13%) rhinitis and 18 (16%) cardiovascular disease, and 14 of these patients were on ACE/beta blockers. VIT with honeybee was proposed in 73 (64%), wasp 38 (34%) and P*olistes* 2 (2%).

The mean duration of VIT was 45 (±16) months. However, 23 completed less than 36 months. Of the total, 28 patients (25%) were not treated with VIT.

Eighty-eight patients (78%) participated in the telephone interview: 49 completed VIT (56%), 15 were still on VIT (17%) and 24 did not undergo VIT (27%). Of those who completed VIT, 14 (29%) were re-stung and 3 went to the emergency department (ER). Twenty-four patients (36%) were stung while still on VIT. Of those never on VIT, 12 (50%) were re-stung and 9 went to ER.

The severity of the reactions according to Mueller of the patients who completed VIT (mean follow-up time was 45 months (1-110 months)) and were stung again was: local reaction in 11 (79%), grade I in 1 (7%); grade III in 1 (7%). One had a toxic reaction after multiple stings. In those who were stung during VIT, 20 (87%) had local reactions, 1 (4%) grade I and 2 (9%) grade III. Of those who were not treated and were re-stung: 3 (25%) had grade I, 4 (33%) grade III and 5 (42%) grade IV. In this series, the patients who did not undergo VIT presented a greater number of systemic reactions when re-stung as well as more severe reactions ($P < 0.01$).

**Conclusion:** In this group with indication for VIT, the reactions of the re-stings were less severe in the patients who had completed or who were on venom immunotherapy, as expected. Three quarters of those who did not undergo treatment had severe anaphylactic reactions when they were stung again. This study reinforces the importance and the efficacy of immunotherapy in the treatment of hymenoptera venom allergy.

## 1232 | Insurance systems and geographic location influence differences in practice of hymenoptera venom allergy management in Europe

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**Background:** The influence of insurance systems and geographic location on Hymenoptera venom allergy (HVA) management in Europe is not well known.

**Method:** Structured questionnaire was sent on-line to one practicing doctor for each of the EAACI countries. Data were collected between November 2016 and November 2017.

**Results:** Response rate was 83% (30/36 countries). Countries belonged to either of the following three categories based on insurance systems: (a) One national insurer (ONI) providing free or partially free medical service, (b) Multiple national insurers (MNI) with different co-payments, and (c) Multiple national and regional insurers (MNRI). In 50% of all responding countries, health cover for children was different from that of adults. Patients in MNRI countries waited a median 5 weeks (Q1-Q3: 3-12) compared with ONI (median 3 weeks; Q1-Q3: 1-10) for investigations. GPs carried out initial investigations in MRI countries compared with ONI (75% vs 44%). VIT procedure is free of charge in most (60%) of ONI compared with 25% MNRI countries. Adrenaline autoinjector (AAI) is free of charge in 19% of ONI countries, 25% of MNRI countries, whereas patients are partially charged in all MNI countries. The cost of AAI for patients is higher in MNI countries (mean = €75.5 (±30.2)), compared with MNRI countries (mean = €51.25 (±8.7)).

Geographically 11/30 countries were in southern Europe, 13 were mid-European and 6 were in the north. Patients waited longer in the north for diagnostic tests (median 7 weeks, Q1-Q3: 2-18w) compared with the south (median 2 weeks; Q1-Q3: 0-4w). VIT procedure is mostly free of charge in north (73%) vs 30% in south. The density of specialists was the highest in the middle of Europe (median 1:32 000 population, Q1-Q3 = 1:62 000-1:20 000) and lowest in the north (median 1:123 000, Q1-Q3 = 1:434 000-1:67 000).

**Conclusion:** There are considerable variations in the management of HVA and in access to care across Europe based on the insurance systems and geographic location of the country.

## 1233 | Presence of Icarapin (Api m 10) in honeybee venom immunotherapy Anallergo

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**Background:** Reactions to honeybee stings range from small local reactions to large local reactions, up to anaphylaxis. The efficacy and safety of honeybee venom immunotherapy (VIT) are often problematic: VIT with honey bee venom (HBV) is less well tolerated and less efficacious than other Hymenoptera. Recently it was demonstrated (Blank 2011, Köhler 2014 and Frick 2016) that honeybee VIT may be less efficacious because of the absence of Icarapin (Api m 10), perhaps lost during processing of the venom extract.

The aim of the study was to characterize the allergens in the venom preparation marketed by Anallergo (Italy) for diagnosis and immunotherapy and particularly to demonstrate that Api m10 is present in therapeutic Anallergo VIT.

**Method:** Venom was digested with trypsin. Aliquots of venom was analyzed by UHPLC-ESI-MS/MS (ThermoFisher Scientific).

**Results:** Shotgun proteomics analysis demonstrated that Anallergo venom contained major allergens Api m1 Api m2 e Api m4; besides the analysis revealed the presence of Api 3 Api m5 e Api m10 too.

**Conclusion:** The study demonstrated that therapeutic preparation bee venom Anallergo contain all the relevant allergens and in particularly Api m10.

## 1234 | Protein identification in polistes dominula in anallergo extract for diagnosis and immunotherapy by shotgun proteomics approach

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**Background:** Reactions to Hymenoptera stings range from small local reactions to large local reactions, up to anaphylaxis. *Polistes* genus is widely spread in Europe and in the rest of the world. *Polistes dominulus*, *Polistes gallicus* and *Polistes nimphus* are common in the Mediterranean area, where they are responsible for hymenoptera venom allergy.

Until 1996, the only commercially available extract for diagnosis and immunotherapy (VIT) was a mixture of venoms from American species (*Polistes annularis*, *Polistes fuscatus*, *Polistes metricus and Polistes exclamans*), which are not represented in Europe, and are, at least in part immunologically different. First it was demonstrated an increased reactivity to *Polistes dominulus* and *gallicus* vs American species, involving intradermal test, skin prick test, RAST assay and RAST inhibition, clearly (Severino 2006). Several studies demonstrated the presence of a specific serine-protease in European *Polistes* especially in *Polistes dominulus* (Sanchez 1995, Hoffman 1998, McNairy 2000 and Winningham 2004). Bilò et al (2005) and Bonadonna et al (2007) showed that not using *Polistes dominulus* extract would have misdiagnosed the nature of anaphylactic reactions and delayed the initiation of VIT.

**Method:** Venom was digested with trypsin. Aliquots of venom was analyzed by UHPLC-ESI-MS/MS (ThermoFisher Scientific).

**Results:** Shotgun proteomics analysis demonstrated that Anallergo venom contained major allergens such as Antigen 5, phospholipase A1; the analysis revealed the presence of serine-protease too.

**Conclusion:** The study demonstrated that therapeutic preparation Polistes dominulus Anallergo contain all the relevant allergens and in particularly serine protease.

## 1235 | Intradermal tests for hymenoptera venom allergy in dogs—Preliminary Study

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**Background:** Every year dogs are stung by hymenoptera and show allergic reactions. To our knowledge, there are only a couple of studies regarding hymenoptera allergy and diagnose in dogs. In human patients, intradermal tests are widely used to confirm allergic sensitization to suspected allergens.

**Objective:** To evaluate both the diagnostic yield and safety of intradermal tests in dogs suspected of hymenoptera venom allergic reactions.

**Method:** Intradermal tests using three distinct venoms (*Apis melífera*, *Vespula spp*. and *Polistes spp*.) were performed in ten dogs suspected of hymenoptera venom allergic reaction according to clinical history and in a control group of dogs with no history of reactions. Each concentration of the three venoms was tested simultaneously and in sequence as described before for humans. Venom increasing concentrations (0.05 mL of 0.0001, 0.001, 0.01, 0.1, 1.0 μg/mL) were administered to the skin in 15 minutes intervals between injections.

If a positive reaction was observed the patient was considered sensitized and the subsequent concentration of that venom was not administered. The highest concentration used was 1 μg/mL. Histamine (0.0275 mg/dL) and phenol buffered saline solution (0.5%) with human serum albumin (0.03%) were used a positive and negative control respectively. The tests evaluation was made according intradermal tests criteria.

**Results:** Eight dogs had positive reactions to *Apis melifera* venom, five to *Vespula* spp. and four to *Polistes* spp. The reactions were obtained for venom concentrations between 0.01 and 1 μg/mL. Only one dog with suspected hymenoptera venom allergic reaction was not sensitized. The control group didn't show any reaction to the tested concentrations. All patients tolerated the test without any side effects.

**Conclusion:** The results of this preliminary study reveal that intradermal testing is both efficient, safe to use and helpful in the diagnosis of hymenoptera venom allergy in dogs. Correct diagnosis could allow allergen-specific immunotherapy in high-risk dogs. Although dogs did react to the main hymenoptera sting suspect, some of them also tend to be double positive to other venoms. In dogs, it's yet to be seen what contribution, if any, cross-reactivity plays in this type of tests.

## 1236 | Allergic reactions from hymenoptera in our emergency room for 2015-2016 divided by severity

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**Background:** Stings by Hymenoptera insects are relatively common in the population and may lead to a range of reactions from mild and local symptoms to life-threatening anaphylaxis. In Europe mainly honeybee and wasp are responsible for those incidents. There are also several uncommon and delayed types of reactions that may develop after Hymenoptera stings. According to data from European studies, insect stings are one of the main triggers of anaphylactic shock in adults. The objective of this study was to evaluate the prevalence of Hymenoptera sting allergy and the types of anaphylactic reactions that followed the stinging in the population of Tirana, Albania.

**Method:** This is a retrospective, descriptive study of cases diagnosed with "*Hymenoptera venom allergy*", admitted to the Emergency Department of University Hospital Center Mother Teresa from January 2015 till December 2016. Data for our study were obtained from the Hospital Patient Registries and were organized in a database. The analysis included the date and time of the sting, age and sex of the patient, the provoked symptoms, the time of stinging. Anaphylactic reactions were classified according to the Mueller classification and Ring & Messmer classification.

**Results:** This study included 512 patients. Of these, 297 (58%) patients were men and 215 (42%) women, with an average age of 39.1 years (range 12-95 years). The patients in the age category 20-40 years were stung the most often. August was the month with most stings, followed by July and September. According to Mueller classification, 468 (91.4%) were scored with a grade I reaction, 14 (2.7%) with a grade II reaction, 16 (3.1%) with a grade IV reaction. According to Ring & Messmer 470 (91.7%) had skin manifestations, 14 (2.7%) had gastrointestinal manifestations, 16 (3.1%) had respiratory and cardiovascular manifestations. 16 patients were reported as anaphylactic shock. There were no fatal reactions to hymenoptera stings.

The prevalence of Hymenoptera sting allergy in the adult population of Tirana was 0.09%.

**Conclusion:** The prevalence of Hymenoptera sting allergy in the adult population of Tirana was 0.09%. From 512 cases, only 33 of them needed in our clinic.

| Clinical manifestations based on mueller | n | % |
|---|---|---|
| Urticaria | 468 | 91.4 |
| Urticaria with gastrointestinal symptoms | 14 | 2.7 |
| Anaphylactic shock | 16 | 3.1 |

| Clinical manifestations based on ring and messmer | n | % |
|---|---|---|
| Cutaneous | 470 | 91.7 |
| Gastrointestinal | 14 | 2.7 |
| Respiratory and cardiac | 16 | 3.1 |

## 1237 | Wasp sting challenge tests in hornet allergic patients

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**Background:** Hornets (Vespa crabro) and wasps (Vespula germanica) belongs to Vespidae family. Their venoms show marked cross-reactivity. Majority of patients who had experienced severe systemic hypersensitivity reaction after hornet sting are sensitised with wasp venom. As there is a concern, that they may react with severe reaction also after wasp sting, they are treated with specific immunotherapy with wasp venom.

In hornet allergic patients there is a subgroup of patients with a history of wasp sting tolerance. Question arises whether in geographic environment with low frequency of hornet stings these patients really benefit from specific immunotherapy with wasp venom.

**Method:** We present the results of patients with hornet sting anaphylaxis and history of wasp sting tolerance. Immunological analysis

was performed (wasp and hornet sIgE, recombinant rVes v1 and rVes v5, BAT with wasp and hornet venom) and after that the wasp sting challenge test.

**Results:** In our selected group of 4 patients (3 men), aged 29-48 years all experienced anaphylaxis grade IV after hornet sting and tolerated former wasp stings. Three had detectable wasp sIgE and two detectable hornet sIgE. Two patients had positive, but low sensitive BAT with wasp venom. BAT with hornet venom was performed in three patients and was negative in all of them. In all 4 patients wasp sting challenge was negative.

**Conclusion:** All 4 patients with anaphylaxis grade IV after hornet sting and low sensitive wasp venom BAT tolerated wasp sting challenge. It seems that in patients with low sensitivity in BAT a large quantity of allergen (venom) is required to trigger anaphylactic reaction. That is the reason that they only react after hornet but not after wasp sting.

Considering the low probability of future hornet sting this subgroup of patients do not necessary benefit from specific immunotherapy with wasp venom. Avoidance of sting and adrenaline autoinjector seem sufficient prophylactic measures.

## 1238 | Ultra-rush protocols for hymenoptera venom immunotherapy in mastocytosis: What about tolerance?

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**Background:** Allergen immunotherapy (AIT) is recommended in anaphylaxis with hymenoptera venom. While anaphylaxis with hymenoptera venom may be particularly severe in mastocytosis, few studies are available on AIT toxicity in patients with mastocytosis. We present data from patients suffered from systemic mastocytosis (MS) who underwent venom immunotherapy using ultra-rush protocol.

**Method:** Data were issued from the reference centre in mastocytosis of Toulouse University Hospital. MS diagnosis was determined using World Health Organization diagnostic criteria. Hymenoptera venom immunotherapy was performed with an ultra-rush protocol (Table).

**Results:** Seven patients were included (4 women, 3 men), median age 47 years old. During the anaphylactic reaction, cutaneous signs missed in all cases. The reaction was most often severe: grade 2 (n = 1), grade 3 (n = 5), grade 4 (n = 1). Three patients suffered from digestive symptoms and one from respiratory manifestations. Basal tryptase in serum reached 10.1-41.7 μg/L. Hymenoptera venom specific IgE were low (0.11-1.51 kUI/L) except for one patient (35.6 kUI/L). AIT was initiated with Vespula venom in 3 patients, Polistis in 1 patient, Apis mellifera and Vespula in 1 patient, Vespula and Polistis in 2 patients. No reaction was observed during AIT. Four restringing accidents led to increase the cumulative dose to 150 μg and 200 μg in 2 patients. In these patients, the diagnosis of mastocytosis was made due to the resting.

**Conclusion:** Hymenoptera venom AIT using ultra-rush protocol seems well tolerated in patients with systemic mastocytosis. Specific studies are necessary to determine the real tolerance profile of this protocol. Collaboration with reference centres for mastocytosis should be considered for all patients with mastocytosis associated to hymenoptera venom allergy.

| | Injection | Dose (μg/mL) |
|---|---|---|
| Time of injection | | |
| Day 1 | | |
| 0′ | 1 | 0.1 |
| 30′ | 2 | 1 |
| 60′ | 3 | 10 |
| 90′ | 4 | 20 |
| 150′ | 5 | 30 |
| 210′ | 6 | 40 |
| Booster injection | | |
| Day 15 | | |
| 0′ | 1 | 50 |
| 30′ | 2 | 50 |
| Day 45 | | |
| 0′ | 1 | 100 |

## 1239 | The prevalence of Api m10 sensitization and a protocol of preparation modification during maintenance phase of VIT

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**Background:** Molecular diagnosis gives us a unique insight into the pathophysiology of allergy. The paper by Frick et al. (JACI 2016) showed the role of Api m10 in bee venom allergy. Additionally one of the preparations used in bee venom allergy displayed a lack of Api m10 which can result in lower efficacy of immunotherapy. We realized that part of our patients treated with venom allergy receive the preparation which can result in lack of efficacy.

The aim of the study was to analyze the number of patients with positive Api m10. Secondly we prepared the algorithm which we used in modifying the medication used.

**Method:** Api m10 was analyzed in 47 patients treated without Api m10. In patients with positive Api m 10 and 3 subjects with high risk of insect stings (bee keepers) regardless of the Api m10 result, the treatment was modified according to the protocol.

**Results:** Api m10 was analyzed in 47 patients, the positive result was found in 31 (65%) of patients. The mean result was 3.9 (range 0-48.3). In all 50 patients we change the medication to the one containing the Api m10. The dose used in immunotherapy was decreased to 50% of the last injection. Second dose, which was used further in maintenance treatment was injected after 3 weeks. We did not observe the side effects during the treatment.

**Conclusion:** Specific IgE to Api m10 is prevalent component in bee venom allergic patients. The protocol used was safe in all studied.

## 1240 | Basophil reactivity induced by venom immunotherapy

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**Background:** Venom immunotherapy (VIT) can be life saving for patients allergic to hymenoptera venom by preventing systemic reactions. Routine diagnostic tests like skin tests and specific IgE don't provide information about clinical protection given by immunotherapy and the sting challenge test is a complex procedure that requires special equipment and resources and that comprises an important risk of anaphylaxis. The basophil activation test (BAT) is a non-invasive, in vitro test that has been used to monitor VIT. The purpose of this study was to evaluate basophil activation in patients in different moments of VIT.

**Method:** A cross-sectional study was performed in a total of 14 patients (4 female, 10 men) with a median age of 42 years (min 8, max 68) and history of anaphylaxis to hymenoptera venom who were receiving VIT. For 3 patients BAT was performed at the time of diagnosis, 5 patients were in the 1st year of VIT, 1 patient in the 2th year, 3 patients in the 3th year, 1 patient in the 4th year and 1 patient in the 5th year of VIT. All patients collected blood samples for specific IgE of the culprit hymenoptera at the same time as for BAT determination.

**Results:** A total of 4 patients had negative BAT despite 3 of them had positive specific IgE (1 in the zero time of VIT, 1 in the 2nd year, 1 in the 3th year and 1 in the 4th year of VIT). One patient with positive BAT, 14.9 kUA/L IgE specific and in the 5th year of VIT had anaphylactic reactions in two administrations of VIT. In these case activation was 39.1% of the basophil population for as low a concentration as 10 ng/mL.

**Conclusion:** In the group of patients treated for 2 or more years BAT was negative in 50% of the patients. It is also interesting to see that the patient who suffered from systemic reactions during the 5th year of VIT showed positive BAT in a lower concentration tested. In relation to IgE specific BAT showed a sensitivity of 77%. BAT results could help to monitor VIT in a safely way, however more longitudinal studies are needed.

## 1241 | Clinical features of patients allergic to vespula and polistes venom in Madrid area

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**Background:** There are few data analyzing the allergic reactions to wasp stings in large cities, where the exposure is much lower than in rural areas. A considerable number of patients have consulted for adverse reaction to Hymenoptera in our hospital, located in the center of Madrid.

**Method:** To analyze epidemiological and clinical features of patients allergic to wasps in an urban area.

We performed an observational descriptive study of patients who consulted for adverse reaction following wasp sting in an allergy service of a tertiary hospital, between April 2008 and November 2017.

**Results:** We recorded 232 patients with adverse sting reactions to diverse Hymenoptera. The mean age was 40 ± 21.3 years (range 3-88), 57.3% were men.

Most of them (82.8%) recognized the insect involved. Of these, 74.5% were wasps, 16.1% bees and 9.4% other hymenopteran insects.

After the allergy workup, wasps were determined as the culprit insect in 82.3% of patients.

Of these, 52.3% consulted for local reactions (73% large local reaction), 33% for anaphylaxis and 14.7% for generalized urticaria.

The skin tests were positive in 76.4% of wasp allergic patients (25% prick, 75% intradermal) (28.6% *Vespula*, 20.2% *Polistes*, 51.2% both). 29.8% had specific IgE exclusively to *Vespula* (mean 6.4 kU/L), 8.4% exclusively to *Polistes* (mean 1.66 kU/L) and 61.8% to both (mean *Vespula* 8.44 kU/L, *Polistes* 7.6 kU/L).

30.4% of patients had hobbies or outdoor professions that conditioned an increased risk of stings, and 33% had comorbidities that could be a risk factor for severe reactions (cardiovascular or respiratory disease, or treatment with beta-blockers or angiotensin-converting enzyme inhibitors). 5 patients were diagnosed with mastocytosis.

Immunotherapy was administered in 69 patients (36.1%) (50.7% *Vespula*, 46.4% *Polistes*, 2.9% both). Of these, 66.7% suffered anaphylaxis, 18.8% generalized urticaria and 14.5% large local reactions. 21 patients presented at least one new field sting (85.7% during immunotherapy period and 14.3% when finished). Only 1 subject had an anaphylactic reaction and 2 subjects a large local reaction.

**Conclusion:** In urban areas such as Madrid, wasps are the Hymenoptera most frequently involved in allergic reactions. Both species (*Polistes* and *Vespula*), are equally responsible with a probable high degree of cross-reactivity between them. The most common clinical

manifestation is local reaction and approximately one third of patients require immunotherapy.

## 1242 | Polistes and Vespula: Evolution of double sensitized patients

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**Background:** Paper wasps, especially *Polistes dominula*, increasingly spread all over Europe as well as in the US constitute a challenge due to double sensitization along with *Vespula*. We ought to determine the evolution of a series of patients double sensitized. after undergoing venom immunotherapy with vespid venom.

**Method:** Four patients with venom immunotherapy to either Polistes or Vespula and Polistes were retrospectively reviewed from 2012 to 2017 using electronic clinical records. Inclusion criteria were: skin test and or specific IgE to these hymenoptera venoms; compatible systemic reaction due to vespids (Grades II-IV following Müeller's classification).

**Results:** See Table.

**Conclusion:** There is a shift or immunomodulation in terms of sIgE to vespids. even in patients double sensitised who were receiving venom of only one of the vespids.

## 1243 | Wasp venom allergy revealed by B-cell proliferation assay

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**Background:** In clinical practice, the diagnosis of hymenoptera venom allergy relies on (a) the evaluation of the clinical symptoms and (b) the analysis of hymenoptera venom-specific IgE. In particular, two different pools of IgE exist: the *bound pool* and *circulating pool*. On the one hand, the amount of specific IgE bound on mast cells is assessed through skin testing, using both skin prick and intradermal tests. On the other hand, the circulating pool of IgE is usually assessed with ImmunoCAP technique. Recently, in grass pollen allergic patients it has been demonstrated the existence of circulating allergen-specific B cells. These cells proliferate upon the cognate allergen encounter. In *Vespula*-allergic patients, we assessed the presence venom-specific IgE (both bound and unbound pool) and the B cell proliferation in response to *Vespula* venom.

**Method:** *Vespula-specific IgE:* bound pool of IgE was assessed by skin prick testing and intradermal testing. Circulating IgE levels were measured by ImmunoCAP technique, in serum samples.

*Lymphocyte collection:* peripheral mononuclear cells (PBMCs) were obtained from the patient's and healthy donors buffy coats by dextran sedimentation followed by centrifugation on Lymphoprep (Nycomed Pharma, Oslo, Norway) and hypotonic lysis of contaminating erythrocytes.

*Proliferation assay:* blood mononuclear cells were stained with carboxyfluorescein diacetate succinimidyl ester (CFSE) and cultured in the presence of wasp venom. After 3-day culture, lymphocyte subsets were analysed by flow cytometry using: anti-CD3-

| Patient | Age | IDR Vespula | IDR Polistes | Date | Total IgE | IgE Vespula | IgE Polistes | IgE Apis | Tryptase | Ves v 1 | Ves v 5 | Pol d 1 | Pol d 5 | Immunotherapy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 38 | Positive 1 μg/mL | Positive 0.1 μg/mL | 10/09/2012 | 845 | 84.9 | 52.1 | 0.37 | 4.4 | No | No | No | 20.6 | Vespula+polistes |
| | | | | 05/01/2017 | 545 | 7.32 | | 0.26 | 3.9 | | | | 7 | |
| 2 | 56 | Positive 0.001 μg/mL | Positive 0.01 μg/mL | 07/02/2013 | 154 | 44.1 | 41.1 | 1.73 | 6 | | | | | Polistes |
| | | | | 23/11/2017 | | 1.05 | 0.34 | <0.1 | 4.7 | | | | 0.59 | |
| 3 | 53 | Positive 0.1 μg/mL | Positive 0.1 μg/mL | 28/09/2012 | 302 | 12.4 | 29.8 | 0.09 | 11.8 | | | | | vespula+polistes |
| | | | | | 187 | | 14.2 | | 10.7 | | 6.62 | | 2.48 | |
| 4 | 60 | Positive 0.01 μg/mL | Positive 0.1 μg/mL | 03/07/2015 | 72 | 11.7 | 4.25 | <0.1 | 6.5 | | | | 3.17 | vespula+polistes |
| | | | | 01/03/2016 | | | | | | 3.88 | 0.44 | 4.06 | | |

Allophycocyanin or anti-CD19-Pacific Blue. Actively proliferating cells were distinguished by excluding cells with high CFSE.

**Results:** Consistently with their clinical status, all the patients had high levels of both bound and circulating *Vespula*-specific IgE. Interestingly, the proliferation of CD $19^+$ cells in the presence of the *Vespula* venom was higher compared to the control. In contrast, $CD3^+$ cells did not show a higher proliferation rate when exposed to the wasp-venom extract. In healthy donor neither $CD19^+$ nor $CD3^+$ cells proliferated in response to *Vespula* venom.

**Conclusion:** we demonstrated that *Vespula*-allergic patients have a population of circulating *Vespula* venom-specific $CD19^+$ cells. These cells can be detected using flow cytometry and their proliferation in response to the cognate allergen can be analyzed using CFSE dye.

## 1244 | Monitoring of allergen-specific antibody responses in birch pollen allergic children undergoing sublingual immunotherapy (SLIT): A real life study

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**Background:** SLIT has been suggested as an alternative route for allergen-specific immunotherapy. Aim of this study was to investigate allergen-specific antibody responses in birch pollen allergic children who had received SLIT for two years using recombinant allergens.

**Method:** Children (n = 28; 5-12 y o) with respiratory symptoms of birch pollen and oral allergic syndromes (OAS) were studied. Ten children received SLIT with Staloral, 10 were treated by SLIT with Microgen, and 8 children received only symptomatic therapy (control group). sIgE and sIgG levels to rBet v 1, rBet v 2, rBet v 4 were measured twice (before therapy started and after two years) using quantitative ImmunoCAP and a panel of more than 170 microarrayed allergens using ImmunoCAP ISAC technology. Clinical efficacy of SLIT was evaluated by recording symptoms upon allergen contact and need of rescue medication.

**Results:** All 28 children were sensitized to the major birch pollen allergen, Bet v 1 and one patient from each of the groups showed to Bet v 2, no patient had sIgE to Bet v 4. After two years of SLIT clinical improvement was observed in the SLIT patients. In the Staloral group there were no respiratory symptoms in 3 patients and a decrease of symptom severity in the other 7 cases as well as a partial or complete tolerance to PR10 allergen-containing food in the 10 patients. Microgen treatment had no influence on OAS symptoms but decreased of pollinosis severity in 8 children. However, there were no statistically significant differences of Bet v 1-specific levels measured before and after treatment in the SLIT and control groups (Mann-Whitney, $P > 0.05$).

**Conclusion:** In this real-life study we found that birch allergic children who had been treated with SLIT showed a reduction of clinical symptoms but we did not find a significant induction of allergen-specific IgG levels in the SLIT-treated group when compared with children who had only symptomatic treatment.

## 1246 | Evaluation of severity of allergic rhinoconjunctivitis symptoms and sublingual immunotherapy (SLIT) efficacy in children

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**Background:** SLIT is effective method of treatment of seasonal rhinoconjunctivitis induced by birch pollen, which allows reducing the symptoms and the development of new sensitizations. Combined clinical and pharmacological assessment is necessary to determine efficiency of SLIT objectively.

**Method:** 47 patients from Moscow 5-17 y.o. with seasonal allergic rhinoconjunctivitis due to birch pollen were given questionnaires for the daily evaluation of clinical symptoms (itchy nose, sneezing, runny nose, blocked nose, itchy/red eyes, watery eyes) during the period of birch pollen. Standardized assessment recommended by EAACI was used with severity scale from 0 to 3, where «0» - no symptoms, «1» - mild, «2» - moderate, «3» - severe. For the evaluation of daily medication score (dMS), children/parents daily indicated used medicines. Herewith, taking antihistamines evaluated as «1», local glucocorticosteroids (in combination or without) as «2», antileukotrienes (in combination or without) as «3» on the basis of stepwise approach. Further, based on received data, average daily symptoms and medication scores were evaluated. For RCS it was (0-3)+(0-3)+(0-3)+(0-3)+(0-3)+(0-3)/6, for pharmacotherapy it was (0-3). Combined symptoms and medication score (CSMS) was also assessed (0-3)+(0-3)= 0-6.

The daily level of birch pollen concentration and weather during 2016 pollen season based on pollen monitoring data was considered. 0 - zero concentration, 1 - low (1-30 units/$m^3$), 2 - average (31-100), 3 - high (100-1000), 4 - very high (more than 1000), 5 - extra (more than 5000). Pollen monitoring data and weather conditions were compared to the intensity of symptoms.

**Results:** In 17 patients who received SLIT with birch pollen allergen average daily symptoms score during the pollen season was 0.45 ± 0.3, average dMS was 2.38 ± 0.75, average CSMS was 2.71 ± 0.88 out of maximum 6. Maximum symptoms severity was from 25 Apr 2016 to 28 Apr 2016, average symptoms score was 0.66, average CSMS was 3.11. During these days birch pollen

concentration in the air was very high (more than 1000 units/$m^3$) and extra (more than 5000), maximum wind speed was 5-6 m/s.

**Conclusion:** Use of standardized questionnaires in combination with evaluation of birch pollen concentration level and weather conditions allows us to evaluate severity of allergic rhinoconjunctivitis and efficacy of SLIT objectively and to administrate SLIT course properly.

MONDAY, 28 MAY 2018
TPS 37
EPIDEMIOLOGIC ASPECTS OF FOOD ALLERGY

## 1247 | Allergy to food additives in children: A retrospective study

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**Background:** Food additives improve food conservation visual aspect or food palatability. Even though they could be responsible for IgE-mediated allergy, allergic reactions to food additives remain rare. The main objective of this study was to describe a pediatric cohort suspected of allergy to food additives, food dye or sodium benzoate. As a secondary objective, families were contacted in order to monitor clinical evolution after the food additives challenge, whatever its result.

**Method:** All the patients who underwent open oral food challenge for sodium benzoate (250 mg), tartrazine, yellow sunset, carmine red, cochineal red, erythrosin, or patent blue V (2.5 mg), between 2013 and 2016 in our department were analyzed retrospectively. A survey was sent to families during year 2017 in order to know if allergic reactions reappeared, and to evaluate feeding behaviors with food additives.

**Results:** Twenty-three patients (median age: 5 years old) were included. Allergological investigations incriminated foods (n = 20; 80%) and/or medicines (n = 7; 30%). Candies were the main suspected foods, found in 11 patients (48%). Forty-six open oral food challenges were performed, only one was positive (urticaria 60 minutes after ingestion of carmine and cochineal red). Subsequently, 98% of the food additives challenges were negative. Fifteen families answered the survey. Despite the negativity of the challenge in all cases, 5 families reported occurrence of supposed allergic reactions to food additives and 6 declared to systematically exclude additives in their child's feeding.

**Conclusion:** Our study confirms the scarcity of food additives allergy. It also suggests that even when the diagnostic of allergy was excluded with a negative oral food challenge, families remain suspicious about industrials feeding products containing food additives. These results should reassure health professionals and parents who incriminate too frequently food dyes and conservators when a manifestation which mimics allergic reactions occurs.

## 1249 | Association between season of birth and prevalence of food allergy under well care for skin: A birth cohort study

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**Background:** Autumn/winter birth has been reported to be a risk factor of food allergy (FA) development. A putative mechanism is that dry/cold weather causes and exacerbates infant atopic dermatitis (AD), which is a major risk factor for food sensitization through inflamed/damaged skin. We investigated prevalence of FA among infants under well skin care in relation with seasons of birth (SoB).

**Method:** We recruited full-term newborn infants without perinatal diseases at an obstetric/pediatric clinic. Participants were followed up for skin status and food allergy symptoms until 12 months of age. SoB were defined as spring (March-May), summer (June-August), autumn (September-November) and winter (December-February). AD was diagnosed based on the United Kingdom Working Party's criteria. Use of moisturizer (Mo) and topical corticosteroids (TCS) was recorded. Primary outcome was FA based on apparent immediate allergic reaction after ingestion of causative food. We classified infants who avoided any food because of sensitization or mother's anxiety as suspected FA.

**Results:** Six hundred and thirty-one infants were screened for 12 month-period and 531 infants were enrolled in this study. Of them, 277 infants were born in spring-summer (S-born) and 254 infants were born in autumn-winter (W-born). FA developed in 24 (4.5%) infants and 31 (5.8%) infants had suspected FA. There was no difference ($P$ = 0.68) in prevalence of FA and suspected FA between S-born and W-born. Multivariate analysis revealed AD at 2 and 7 months of age was a significant risk factor for FA with OR=2.6 (95%: 1.1-6.0) and OR=3.5 (95% CI: 1.4-8.9), respectively. Prevalence of AD at 2 months of age was higher in W-born than S-born but prevalence promptly decreased thereafter and stayed low with early use of Mo and TCS. Prevalence of AD was rather higher at 7 months in S-born than W-born.

**Conclusion:** AD was associated with FA in infants. However, season of birth had no association with prevalence of FA at 12 months of age. Well skin care and early use of TCS to control AD may have cancelled the seasonal effect on FA.

## 1250 | A pilot study of the cross-reactivity between cereal grains among children with IgE-mediated wheat allergy

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**Background:** Although wheat and other cereal grains have a broad range of the in vitro cross-reactivity, the clinical relevance is uncertain. The oral food challenge remains the gold standard to avoid unnecessary avoidance of all cereal grains in patients with IgE-mediated wheat allergy. This prospective study aimed to study the clinical cross-reactivity between cereal grains (barley, oat, and job's tear) among children with IgE-mediated wheat allergy.

**Method:** Patients between the ages of 5 and 15 years with a history of immediate reactions after wheat ingestion were enrolled. Skin prick test (SPT) to wheat, barley, oat, and job's tear and measurement of serum specific IgE (sIgE) to wheat, ω-5 gliadin, barley, and oat were performed. Open food challenge (OFC) to barley, oat, and job's tear were conducted to confirm the status of grain allergy in each patients. Immunoblotting with sIgE to wheat, barley, oat and ELISA-inhibition assay were done to confirm the cross-reactivity.

**Results:** Ten patients were enrolled in this pilot study with the median age of 8 years (range 5-10 years). Nine of them (90%) had a history of wheat anaphylaxis, whereas the other one had only cutaneous symptom (urticaria and angioedema). The median size of mean wheal diameter (MWD) of the SPT and level of the sIgE to wheat was 6 mm (IQR 3.9-10.4 mm) and 86.5 kAU/L (IQR 7.9-228.5 kAU/L). The OFC to each grain was performed only in patients who had MWD of the SPT not more than 5 mm, and did not have history of anaphylaxis. The OFC to barley were performed in 4 patients. All of them had negative result. Among 8 patients whom underwent oat OFC, anaphylaxis developed in one patient. Two patients had history of job's tear anaphylaxis, therefore 8 patients underwent job's tear OFC, and no one developed allergic reaction. Immunoblotting showed a strong signal of sIgE to wheat bound to a 35 kDa allergen which are most likely to be gliadin. SIgE of wheat allergic patients bound to 30-35 kDa protein from barley extract. The ELISA-inhibition assay showed extract of barley, but not oat could inhibit sIgE bind to wheat gliadin.

**Conclusion:** Avoidance of all cereal grains is unnecessary among patients with severe wheat allergy with the negative SPT to these grains.

## 1251 | Prevalence of sIgE to galactose alpha 1,3 galactose (a-Gal) in patients with acute urticaria or anaphylaxis from three different geographical areas of Spain

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**Background:** The aim of this study was to investigate the prevalence of sIgE to α-Gal in subjects with acute urticaria or anaphylaxis from different geographical areas of Spain and to evaluate the relevance of demographic and lifestyle aspects as risks factors for the development of this immune response.

**Method:** Participants were recruited from Allergy Departments at 14 Spanish hospitals. Patients aged 18 years or older presenting with urticaria or anaphylaxis were enrolled into one of two arms; cases (symptoms of unknown origin, after eating meat or innards of mammalian origin, related to gelatin of mammalian origin administration, cetuximab administration, tick bites) and controls (symptoms of known etiology excluding foods of mammalian origin, cetuximab, colloid-based gelatin and tick bites). An interviewer-administered questionnaire recording data of sex, age, place of residence (urban, half-urban and rural), clinical presentation (urticaria/anaphylaxis), blood group, atopy, history of tick bites, suspected trigger agent, practice of outdoors activities, exposure to pets and the presence of cofactors was obtained from each participant. The participant centres were grouped in three areas; Northern, Mediterranean and Center. sIgE to α-Gal and total IgE determinations were performed by using an ImmunoCAP automated platform (ThermoFisher Scientific, Uppsala, Sweden) according to the manufacturer's instructions. IgE levels ≥0.35 kU/L were considered as a positive result.

**Results:** 160 cases and 126 controls were included. The median age was 44 years, (Q1-Q3 33-53). Men and women were almost equally represented (50.35% males). Alcohol consumption associated with the intake of mammalian meat or innards as the trigger factor. The overall prevalence of a positive result of sIgE to α-Gal was

15.7% IC95% (11.5, 20.0); cases _26.3% IC95% (19.4, 33.1) controls _2.4% IC95% (0.0, 5.1)_. Among cases sIgE anti α-Gal positivity rate ranged from 55.8% (rural), to 35.7% (half-urban) and 12.6% (urban). The rates of positivity were 69.5%, (Northern) 1.4% (Center) and 0% (Mediterranean). A positive result of sIgE to α-Gal was more frequently observed among men (24.31%) than women (7.04%) and associated with history of tick bites, practice of outdoor activities, pet's ownership and the antecedent of having eaten mammalian meats or innards previously to the development of symptoms

**Conclusion:** The positivity rate of sIgE to α-Gal has shown strong differences between three geographical areas from Spain

## 1254 | Panallergens the main cause of food allergy?

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**Background:** A special challenge in the 21st century for allergists is allergy to food, which is considered "the second wave" of epidemics of allergic diseases. Panallergens occur in unrelated organisms and perform a similar function in them. In their structure, they have highly conserved amino acid sequence regions and a similar three-dimensional structure, and thus meet the requirements for cross-recognition by IgE.

**Method:** The study group included 50 adult patients, 30 women and 20 men, aged 18-74 with confirmed allergy and who suffered from adverse symptoms after consuming food. The study included patients under the care of the Department and Clinic of Allergology, Clinical Immunology and Internal Disease of Collegium Medicum in Bydgoszcz. Criteria for exclusion from the study group were severe chronic diseases, auto-immunological diseases and cancer. The study also excludes minors and women during pregnancy and breast-feeding. The control group included 20 healthy persons, 12 women and 8 men, aged 18-62 years with a negative personal and family interview towards atopy, no infectious signs and no drugs use.

Blond was taken from all patients to specify the levels of allergen-specific IgE against 112 allergen components of ImmunoCAP ISAC test, the result≥0.30 ISU-E was assumed as positive.

**Results:** In 46 patients (92%) ISAC test has been shown to have specific IgE for panallergen components. Mostly, the presence of IgE for PR-10 proteins has been shown in 41 patients. In 12 patients IgE to LTP; 11 patients IgE to CCD; 6 patients to profilin; 5 patients to tropomyosin; 4 patients to serum albumin, 1 person to TLP. An important aspect is undoubtedly the occurrence of simultaneous sensitization to several panallergens. Analysis of data from the study group showed that isolated sensitization to one panallergen concerned only PR10 proteins (24 patients), tropomyosin (2 patients) and profilin (1 patient). In the remaining 19 patients, the analysis of the ISAC test results showed that two or more panallergens were allergic. In the study group, asIgE for the component responsible for the occurrence of real food allergy was detected in 13 (26%) patients. Mostly, the presence of IgE for Jug r 2 has been shown in 9 patients.

**Conclusion:** In the study group, panallergens were more likely to be responsible for food intolerance than specific food allergens.

## 1256 | Comparison between peanut and tree nut allergy in Korean children

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**Background:** Peanut and tree nut allergies are increasing in prevalence. Peanuts are not the same as tree nuts such as walnuts, cashew, or hazelnuts, but part of the legumes such as soybeans, peas, and lentils. We aimed to investigate the prevalence of peanut and tree nuts allergy and compare clinical characteristics and co-sensitization rate between peanut and tree nuts allergy in children of tertiary hospital.

**Method:** A retrospective analysis of 202 children diagnosed with food allergy in a tertiary medical center, Seoul, Korea. Medical records of 43 children with both clinical history of reactions and sensitization to peanuts or tree nuts were analyzed. Specific IgE to allergens were analyzed using ImmunoCAP (Phadia, Uppsala, Sweden).

**Results:** Of 43 children, 14 children had peanut allergy only, 14 children had tree nut allergy only, and 15 children had both. The mean age was 3.3 ± 1.9 years in peanut allergy, 5.0 ± 3.6 years in tree nut allergy, and 4.2 ± 3.0 years in both. Male to female ratio was significantly higher in tree nut allergy (78.6%) than peanut allergy (42.9%). Among tree nut allergens identified, walnut (75.9%) was most frequent, followed by almond (55.2%), hazelnut (34.5%), pine nut (20.7%), chestnut (13.8%), cashew (6.9%), pistachio (3.4%), and macadamia (3.4%).

Mean serum total IgE level was 888 kUA/L in tree nut allergy and 1440 kUA/L in peanut allergy. Mean serum specific IgE level to peanut, walnut, almond, hazelnut, and pine nut was 30.0, 21.9, 14.2, 22.4, 5.6, and 6.3 kUA/L, respectively.

Children with peanut allergy had higher rate of co-sensitization with soybean and higher soybean-specific IgE levels than children with tree nut allergy. However, there was no difference in co-sensitization rate with tree pollen between peanut and tree nut allergy. Children with peanut allergy showed significantly increased co-sensitization rate with egg white and wheat compared to children with tree nut allergy. A 42.8% of the children with peanut allergy and 28.6% of tree nut allergy showed co-sensitization with aeroallergens. A total of 75% of the children with peanut allergy showed decreased specific IgE levels within 1-5 years.

**Conclusion:** Prevalence of peanut and tree nut allergy is similar. Tree nut allergy develops later than peanut allergy and more common in male. Children with peanut allergy showed higher co-sensitization rate with soybean, egg white and wheat compared to children with tree nut allergy.

## 1257 | Natural history of egg allergy in a large cohort of infants with food allergy shows its high prevalence but also its transient nature in a 36 months of follow-up

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**Background:** The cohort of 80 infants (55 boys,25 girls,3-36 months) with the food allergy has been followed for 36 months. As more than 70% of infants manifested atopic dermatitis (AD), a condition closely linked to egg sensitisation, we focused our attention on egg allergy, following its natural history as well as a development of atopic march.

**Method:** The diagnosis of food allergy was based on a personal history, clinical examination, skin prick tests and/or atopy patch tests with native foods. Laboratory tests were performed within 1 year of age the latest. The specific IgE levels against food allergens were measured using ImmunoCap or Immulite.

Patients with AD were scored according to SCORAD system.

The oral food challenges (OFCs) with cooked/baked egg were done in children at the age of 12 months except for children at risk of anaphylaxis.

**Results:** Within the whole cohort the allergy to cow milk proteins was confirmed in 70 pts (87.5%), to egg in 35 pts (43.7%), to wheat in 8 pts(10%), to lentil in 3 pts (3.75%) to banana in 3 pts (3.75%), to soya in 2 pts (2.5%) and to potatoes in 1 pt (1.25%).

In a cohort of 35 egg allergy patients we found out that: 83% of pts presented the early onset of allergy—up to 3 months of age, 80% of pts presented severe AD (SCORAD >50), 46% of pts showed co-sensitisation to peanuts, 34% of pts had early sensitisation to inhaled allergens, and majority 54% of pts presented with early onset allergic rhinitis and/or asthma.

**Conclusion:** We proved that egg allergy is closely linked with the early onset of allergy symptoms, with severe forms of AD, co-sensitization to peanuts, early sensitisation to inhaled allergens and an early onset of allergic rhinitis and/or asthma.

We also proved that the egg allergy in infancy is transient. The tolerance to baked/cooked egg was achieved in about 75% of pts at the age of 3 years, unlike previously published results claiming the reach of tolerance in 75% of pts at the age of 7 years.

It is not possible to predict the development of egg allergy based on isolated positivity of specific IgE to egg, ovomucoid, ovalbumin at the age of 12 months. Even the high levels of specific IgE to ovomucoid (>50 kU/L) do not predict the persistency of allergy to adulthood. We recommend monitoring the dynamics of laboratory tests and clinical symptoms at the interval of 6 months together with the clinical course and skin prick tests and careful planning of OFC with baked/cooked egg to confirm the tolerance and re-introduce egg into diet.

## 1259 | Food allergy: An increasing disease in the elderly. Aging of the population, aging of illness

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**Background:** The percentage of elderly people is increasing each year, therefore we will meet in medical consultation with about 5%-10% of a new profile of patients with more and different pathologies. Together with other pathologies, allergic diseases also show an increasing incidence in these group of patients.

The purpose of this work is to analyse the food allergic reactions in patients with 60 years old or more.

**Method:** We have carried out a descriptive retrospective study of patients over 60 years of age, who have been attended in our hospital, Fundación Jiménez Díaz, for the first time, from July 1, 2016 to June 30, 2017, consulting on possible food allergy that has happened at the most 2 months before.

In these patients we studied: sex, personal history, type of reaction they presented, time of onset of symptoms and food involved.

**Results:** Out of a total of 1479 patients over 60 years of age (from 60 to 99 years old) who have been attended the consultation for the first time during these period, 70 patients (4.7%) ask about possible allergic food allergies. Of these patients who came for possible allergic pathology, 28 patients (40%) presented positive results.

These are the other item we have studied:

1. Sex of patients: 55% of the patients are women.
2. Food involved: Fish and shellfish: 70%; Fruits: 10%; Nuts: 7%; Cereal: 7%; Vegetables: 3%; Other: 3%
3. Symptoms mainly involved: itching with skin lesion is the common symptom (30%)
4. Time of onset: in a range from seconds to 6 hours after the food intake, with an average of 2.37 hours.

**Conclusion:** 40% of the patients over 60 years old that ask for a possible food allergy, presented positive results for it. This is a important percentage if we consider the age and characteristics of

these patients because of that, it is important to remember that food allergy can also appear in old people.

The food that is mainly involved in our population is fish and seafood. A much higher percentage than in other populations, probably due to the Mediterranean diet of Spain. The symptoms mainly involved are itching and skin lesion, which is the characteristic symptom of a mild allergic reaction.

In our population, there was 3 patients with a anaphylactic shock, a much higher percentage than in other studies.

The experience with this group of patients is still limited. More studies are needed to know better this patient profile.

## 1260 | Screening for cow's milk allergy in pediatric emergency room: A retrospective cohort study of 482 infants under 6 months

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**Background:** Cow's milk allergy (CMA) is the first atopic disease in children. Diagnosis suspicion in the emergency room (ER) is increasingly frequent, however, further assessment by an allergist is often difficult to schedule. Therefore, screening for CMA through a blood test (specific IgE) while the infant is still in the ER has gained momentum in recent years. We set out to analyse (a) symptoms which had led the emergency physician to prescribe specific IgE, (b) the prevalence of confirmed CMA among infants screened in the ER, and (c) the long-term outcome of the screened infants.

**Method:** A retrospective study of medical records and laboratory results was performed. Patients were infants under 6 months, without a previous diagnosis of CMA, attending one of the two Pediatric ER of the University Hospitals of Marseille, France.

Allergy blood tests were specific IgE to cow's milk extract (ImmunoCAP, ThermoFisher, Sweden). In infants with specific IgE to cow's milk extract of 0.12 kUA/L or higher, IgE directed to the main three individual proteins (casein, alpha lactalbumin et beta lactoglobulin) were also measured.

**Results:** 482 infants were included from December 2011 to June 2016. The sex ratio was 1.45. 40% of infants were atopic et 48% were currently or had been breastfed. The most prevalent symptoms were vomiting and reflux. One third of infants were hospitalized after the ER visit.

Following the ER visit, 25% of infants attended a specialized consultation with an allergist. 15% of infants with a follow-up visit were diagnosed with an IgE mediated CMA.

18 infants with CMA developed further food allergies (egg, nuts, cashew…).

**Conclusion:** Symptoms of CMA are very dissimilar and that's why it is difficult to diagnose it. The emergency pediatrician are increasingly confronted to infant with symptoms evoking CMA. Thus they prescribe sIgE and extensively hydrolysed proteins because they know that IgE-positive infants can be IgE-negative during the interval between the ER visit and the follow-up one. After bad results interpretation of blood assay after ER visit, CMA was probably over diagnosed without prick test for IgE positive allergy and no eviction/reintroduction test for non IgE.

The lack of allergist is probably leading to over prescription of blood assay in ER to diagnose CMA and prolonged eviction of milk.

## 1261 | Food allergy in adults—Data from a Portuguese food allergy outpatient clinic

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**Background:** Although more common in children, food allergy (FA) is also common in adults as a prevalent allergy from childhood or new onset.

**Method:** Retrospective data analysis from FA outpatient clinic in an Immunoallergology Department from January 2013 to December 2015. Patients with ≥18 years old (YO) who had their first appointment in that period were included. The FA diagnosis was based in skin tests(ST)[Skin prick (SPT), Prick-prick (PP) and patch tests (PT)], specific IgE (sIgE) and oral food challenge (OFC).

**Results:** A total of 96 patients were included (59% female) aged from 18 to 82YO with an average 33.9 ± 15 years. 77% of patients had history of atopic disease: 60% rhinitis, 30% asthma, 9% prior food allergy, 8% eczema, 6% drug allergy, 5% eosinophilic esophagitis (EE) and 3% chronic urticaria. Mean serum total IgE was 441.9 UI/mL. Sensitization to aeroallergens was present in 63% of patients, the most common were dust mites (22.9%), pollen (15.6%) or both (25%). In 69(72%) patients, first symptoms of FA appeared ≥18 YO, with an average age of 35 ± 15.4 YO. In this group, 4 were diagnosed with EE, 1 with eosinophilic colitis and 2 with eosinophilic gastritis. From the remaining 62 patients, 20 had history of reaction with more than 1 food group (FG). Cutaneous reactions were referred in 60% of patients followed by anaphylaxis (20%) and gastrointestinal symptoms (10%). The FG most commonly implied were: Fresh fruits (N = 26), seafood (N = 19) and tree nuts (N = 6). FA diagnosis was confirmed in 66% of patients, the remaining had negative OFC.

In 27(28%) patients, their symptoms started under 18 YO, with an average age of 11.5 ± 5YO. From this group, 10(44%) were diagnosed EE. From the remaining 17 patients, cutaneous complaints were the most frequent (47%) followed by gastrointestinal (35%) and respiratory symptoms (17%). The most common FG implied were: Fresh fruits(N = 9), seafood(N = 4) and tree nuts(N = 3). Only one anaphylaxis was referred. FA was confirmed in 82%, the remaining had negative OFC.

In patients with history of anaphylaxis 13 of 14 had positive ST and/or sIgE; one had negative SP and sIgE, with OFC positive.

**Conclusion:** Fresh fruits were the most common allergen in both groups and were responsible for more severe reactions. Identifying the responsible allergen or excluding allergy significantly improves the patient quality of life. Specialized consultations are an essential part of their treatment.

## 1262 | Seroprevalence of anti-Anisakis Simplex IgE and possible risk factors associated in a healthy blood donors population from Cantabria (Spain)

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**Background:** *Anisakis simplex* (AS) is a genus of parasitic nematodes. Humans can become an incidental host due to the ingestion of raw or uncooked fish. Cantabria's gastronomy (characterized by fresh and marinated fish consumption) lends itself to contact with live larvae. AS is present in a high percentage of the most abundant species in the Cantabrian Sea. Seropositive anti-AS IgE result without clinical relevance is a frequent finding in our consultations. The objective was to investigate the clinical and risk factors associated with this seroprevalence in Cantabria.

**Method:** Total IgE and anti-AS IgE were determined by means of ImmunoCAP (ThermoFisherÒ) in 401 blood donors, selected at random at the Blood and Tissue Bank. Clinical symptoms related to fish intake, demographics and fish consumption habits, were extracted from an anonymous questionnaire.

**Results:** The 401 blood donors were classified based on their clinical symptoms related to possible AS contact via fish intake: allergic to AS (1%), chronic urticaria (0.5%), unspecific dyspepsia (2.8%) and asymptomatic (95.5%). The prevalence of sensitization (anti-AS IgE >0.35 KUA/L) were 12.7% (IC: 9.6-16.4%; mean 0.69 KUA/L; median 0.03 KUA/L) with a maximum value of 40.70 KUA/L. Raw fish consumption was the only variable associated with statistical significance ($P < 0.05$) to AS sensitization (20.4% vs 9.5%, respectively). Albacore and codfish were the most consumed species associated to seropositive results (15%), followed by hake (10%). Coastal population (13.6% vs 9.3%), non-previously frozen fish consumption (13.7% vs 9.2%) and >3 times per week fish consumption (51.2%) were other seropositive associated factors.

**Conclusion:** The anti-AS IgE seroprevalence found in the general population in Cantabria is similar to previous data reported in other national studies in Spain. Raw fish consumption has been confirmed as the main risk factor to present sensitization to AS. Fish species associated with AS sensitization founded are slightly different to other studies. This could be related to new legal preventive measures for anisakiasis, recently implemented. Further studies including the determination of anti-IgE to AS major allergens should be done to increase the diagnostic accuracy. By reducing the number of false positives due to cross-reactivity with other allergen sources such as dust mites, (high prevalent allergen in Cantabria), we could extract stronger conclusions about the utility of the AS allergy diagnosis tools.

## 1263 | Cow's milk protein allergy: A case series of 130 Indian patients

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**Background:** Scarce data on the presence, clinical features and presenting complaints of cow's milk protein allergy (CMPA) are available from India.

**Method:** A retrospective analysis was undertaken to evaluate the clinical presentations, diagnostic modalities and response to avoidance measures in Indian patients with CMPA. Diagnosis of CMPA were determined by a detailed clinical history and diagnostic tests.

**Results:** Overall 130 patients were found to have CMPA (males - 49.2%; Hb - 11.0 ± 1.9 [mean ± SD). The age at presentation was ≤1 years in 60 (46.2%), 2-5 years in 46 (35.4%), 6-11 years in 18 (13.8%) and ≥12 years in 06 (4.6%) patients. The most common systemic manifestations were respiratory symptoms, skin symptoms followed by gastrointestinal symptoms. Two cases also had angioedema and anaphylaxis. Presence of other food allergies were observed in 13 (10%) of the cases. IgE-mediated CMPA was diagnosed in 85 (65.4%) of the cases and non-IgE mediated CMPA in 45 (34.6%). Patients with IgE-mediated CMPA had more predominantly moderate-severe symptoms (50.8%), while almost all patients with non-IGE-mediated CMPA had mild symptoms (97.8%), $P < 0.0001$. Additionally, failure to thrive was more common in the IgE-mediated group (14 [16.5%]) as compared to the non-IgE-mediated group (1

[2.2%]), $P = 0.0188$. In patients with IgE-mediated CMPA (n = 85), a discrepancy in the results of IgE tests was observed, 43 (50.6%) patients tested positive with the SPT to milk extract, 68 (80%) patients tested positive with the SPT to fresh milk and 54 (63.5%) had a serum milk-sIgE ≥0.35 KAU/L. Presence of eosinophils in the biopsy samples done in cases with non-IgE-mediated CMPA (n = 45) were observed in 30 (66.7%) patients. Challenge tests were found to be positive in 85.9% & 100% of the IgE-mediated CMPA and non-IgE-mediated CMPA patients respectively. All patients improved on elimination of milk in the diet. Extensively hydrolysed formulas (eHF), soya milk and chicken based feeds were used as supplements in our population of patients.

**Conclusion:** This data, probably the largest case series of CMPA from India highlights the importance of this entity in our country. Furthermore, we were able to document the clinical presentations of the patients. Adequate diagnosis is via IgE detection, histopathology, elimination and challenge tests. Challenge tests and elimination tests are the most important confirmatory tests.

## 1264 | Oral allergy syndrome in patients with pollen allergies in Korea: A multicenter cross-sectional study

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**Background:** Oral allergy syndrome (OAS) is an IgE-mediated allergy caused by raw fruits and vegetables in patients with pollen allergy, which is known as the most common food allergy in adults. However, there has been no nation-wide study on oral allergy syndrome in Korea. The aim of this study is to investigate the prevalence and clinical manifestations of OAS in Korea.

**Method:** Twenty two investigators from 19 hospitals and 2 private clinics participated in this study. The patients with allergic rhinoconjunctivitis and/or bronchial asthma with pollen allergy were enrolled to the survey. The questionnaires include demographics, a list of fruits and vegetables, and clinical manifestations of food allergy. Pollen allergies were diagnosed by positive results of one or more pollen allergens including birch, alder, hazel, beech, oak, willow, poplar, bermuda, meadow, orchard, rye, timothy, mugwort, ragweed, *Hop japanese* on allergy skin prick tests (allergen/histamine ratio ≥3+) and/or serum specific IgE levels using Multiple Allergen Simultaneous tests (MAST ≥2+) or immunoCAP (≥0.35 kU/L).

**Results:** A total of 648 pollinosis patients answered the questionnaires. The prevalence of OAS was 41.7% (n = 270). The OAS patients have allergic rhinitis (95.9%), allergic conjunctivitis (55.6%), and asthma (43.3%). The OAS patients was accompanied by cutaneous (43.0%), respiratory (20.0%), cardiovascular (3.7%), or neurologic symptoms (4.8%) in addition to oropharyngeal symptoms. Anaphylaxis was noted in 8.9% of OAS patients. Seventy kinds of fruits and vegetables were suggested as causes of OAS: peach (48.5%), apple (46.7%), kiwi (30.4%), peanut (17.4%), plum (16.3%), chestnut(14.8%), pineapple(13.7%), walnut(14.1%), Korean melon (12.6%), tomato(11.9%), melon(11.5%), apricot(10.7%), etc. in order of frequency. There were also Korean local foods such as taro/taro stem (8.9%), ginseong (8.2%), perilla leaf (4.4%), bellflower root (4.4%), crown daisy (3.0%), Deodeok (3.3%), kudzu root (3.0%), and lotus root (2.6%), which represents Korean eating habits.

**Conclusion:** This is the first nation-wide study for OAS in Korea. The prevalence of OAS in Korea was 41.7%, in which substantial proportion had anaphylaxis. These results will provide useful information for clinicians to apply in clinical practice.

## 1265 | The effects of egg and folic acid intake on food allergy onset by the birth season of children

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**Background:** Reports have demonstrated that food allergy onset in children is affected by the season of their birth. One presumed reason for this is seasonal variations in DNA methylation during the prenatal period. Folic acid is consumed by numerous pregnant women as a supplement for the prevention of spina bifida. However, the effect of folic acid intake during pregnancy on the child remains unclear. Hence, this research aimed to examine the effect of folic acid administration on the child's food allergy onset with the intake of eggs during pregnancy by the birth season of children.

**Method:** We conducted a self-administered, questionnaire-based survey in 2013-15 during the 18-month checkup. Children were considered to have food allergies if they were diagnosed by a physician or if they had been instructed to avoid a causative food after medical examination by interview.

**Results:** We divided the year into three periods. The months of March-June were considered spring, July-October as summer/fall, and November-February as winter. While the season of onset for the 4095 boys occurred in 8.2%, 12.7%, and 15.3% in spring,

summer/fall, and winter, respectively, it was 6.9%, 10.5%, and 12.2%, respectively, for the 3922 girls. Thus, the onset rate was the highest in winter for both genders.

In boys whose mothers did not consume folic acid ($FOL^-$), the food allergy onset rate was significantly higher for boys whose mothers ate no eggs and for boys whose mothers ate 2-5 eggs per week than for those whose mothers ate eggs daily according to the Dunnet multiple comparison test. However, no relationship was observed with egg intake if the mother had consumed folic acid ($FOL^+$).

On the basis of seasons, $FOL^-$ and egg intake by mothers affected only children born in winter, with a significant difference in the Dunnet multiple comparison. Among mothers who did not eat eggs, $FOL^+$ was 15.2% and $FOL^-$ was 28.2%; for mothers who ate 2-5 eggs per week, $FOL^+$ was 16.5% and $FOL^-$ was 12.9%; and for mothers who ate eggs every day, $FOL^+$ was 17.9% and $FOL^-$ was 4.9%. Thus, consumption of folic acid seemingly annulated the effects of eating eggs.

However, for girls, neither folic acid nor eating eggs had any effect on the onset rate.

**Conclusion:** Since this effect varied according to the birth season, consumption of folic acid, a methyl group donor, appeared to affect the allergy onset in children.

## 1266 | Quality of life in food allergy—Perception of caregivers

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**Background:** Food allergy (FA) affects 4%-6% of children worldwide. This is a health problem with a negative impact on the quality of life, and this is a fundamental issue to be addressed in the contact with the patient and their caregivers.

**Method:** Analysis of the impact of FA on quality of life in children and their families. Analysis of demographic data and application of the questionnaire "Food Allergy Quality of Life Questionnaire - Parent Form (FAQLQ-PF)" to the parents of 74 children with food allergy, followed in an external consultation of Immunoallergology, in a consecutive way for 6 months. Children were between 0-12 years old. In the evaluation of the quality of life questions were analyzed, depending on the age of the child. Each question ranged from 0 to 6 (6 = highest impact on quality of life). Statistical analysis was performed using SPSS. The test for the normal distribution of the data was performed using the Shapiro-Wilk test ($P > 0.05$). The groups were divided into age groups. It was studied the existence of a correlation between gender, number of foods involved and type of reaction (anaphylaxis vs without anaphylaxis) with Quality of Life Score (QLS) for each age group.

**Results:** The study included 74 children, 67% of the male gender. The distribution by age group was: 21% with 0-3 years; 35% with 4-6 years and 42% with ≥7 years. Egg allergy (41%) and cow's milk protein allergy (39%) (CMPA) were the most documented, and 43% had multiple allergies. There was a positive, statistically significant and moderate correlation between the number of foods and QLS ($r = 0.577$, $P < 0.001$) in the group [0-3]years; a positive, statistically significant and strong correlation between the presence of anaphylaxis and QLS ($r = 0.77$, $P < 0.001$) in the group [4-6]years, and a positive statistically significant and moderate correlation between the number of foods ($r = 0.509$, $P < 0.01$) and the clinical value ($r = 0.574$; $P < 0.01$) in the QLS in the group aged ≥7 years.

**Conclusion:** From the application of the questionnaire and the analysis of the different variables, it was concluded that in patients with FA, the severity of the manifestations and the number of foods involved are associated with a decrease in QLS. This association suggests that it may be advantageous to apply from the type of questionnaires in the approach of patients with FA.

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## 1267 | Fish allergy without sensitization to parvalbumin, a rare phenotype

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**Introduction:** Fish allergy usually appears in childhood. Parvalbumin, the major fish allergen recognized up to 95% of allergic patients, is usually responsible of cross-reactivity between different fish species.

**Material and methods:** We report a non-atopy 40 years old man outpatient clinic. Since he was 25 years old, immediately after intaking tuna, hake, salmon, sole, monkfish and trout, he only presented lingual and labial pruritus. In 2017, he presented 2 episodes of urticaria and abdominal pain after eating hake with simultaneous NSAIDs treatment. Subsequently he has tolerated NSAID
Skin prick test with fishes commercial extracts and specific IgE were performed. Proteic extracts were performed using boiled salmon, boiled and row tuna and boiled and row hake. Proteins were separated by electrophoresis. SDS-Page was stained, while, on the other hand, proteins were transferred to a membrane and incubated with the patient serum to test IgE reactivity.

**Results:** Skin prick test with commercial extracts of tuna (7 mm), cod (5 mm), rooster (8 mm), hake (6 mm), salmon (4 mm), trout (7 mm) and Anisakis (7 mm) were positive. Fish-specific IgE antibodies were performed with positive results for cod 1.46 kUA/L, tuna 2.63 kUA/L, salmon 1.38 kUA/L, trout 0.95 kUA/L, hake 1.70 kUA/L, rooster 2.08 kUA/L, sole 1.09 kUA/L and Anisakis 6.63 kUA/L. Specific IgE to parvalbumin was <0.35 KU/L. Serum IgE from the patient recognized a pattern of 5 bands from 25 to 70 kDa, in row tuna extract. One of these IgE reactive bands around 40 kDa, was detected in the row hake extract too.

**Conclusions:** We present a special case of fish allergy characterized by:

- Symptoms beginning in adulthood
- Non-steroidal anti-inflammatory drugs may could act as cofactor increasing symptoms from lingual and labial pruritus to a systemic reaction.
- Serum IgE from the patient recognized a special pattern of bands in row tuna and hake extract, including one band around 40 kD that could be responsible for cross-reactivity between different fish species in this case.

## 1268 | Reactions to shrimp in house dust mite sensitized patients: Tropomyosin or not: A case report

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**Introduction:** Shrimp and house dust mite allergies, are common worldwide, and at least 30% of South Africans with allergic rhinitis are sensitized to HDM. Cross-reactions between the muscle protein tropomyosin in dermatophagoides pteronyssinus and crustaceans has been implicated as a cause of clinical reactions to seafood in HDM sensitized individuals. Recent studies have suggested that other proteins might be involved. Here we present a case of a young male with clinically diagnosed allergic rhinitis, sensitization to HDM, and severe reactions to shrimp ingestion, despite negative IgE to shrimp, and to mite tropomyosins.

**Clinical history:** A 23 year old male, from Cape Town, with no significant medical history presented with nasal symptoms and aggravation to dust. He does not have asthma, eczema or any history of food allergy as a child. He resides inland. He had two moderate reactions following shrimp ingestion, involving the skin and gastrointestinal systems. Both reactions were immediate, and responsive to antihistamines.

**Investigations:** IgE testing confirmed a strong sensitization HDM with dermatophagoides pteronyssinus 1 (58.6 kUA/L); dermatophagoides farinae 2 (41.4 kUA/L); blomia tropicalis (9.10 kUA/L). IgE to shrimp, lobster, crab and mixed seafood were all undetectable. Dermatophagoides pteronyssinus 10, to assess for tropomyosins was negative.

**Outcome:** The patient continues to react to both HDM and shrimp, despite undetectable IgE levels to tropomyosin associated components. This is the only testing available in South Africa currently and hence we are unable to look at other proteins.

**Conclusion:** The relationship between tropomyosins in shellfish allergy and mite allergy has been well documented and investigated, but other allergens are now also being implicated in cross-reactions. These include arginine kinase, myosin light chain kinase, and sarcoplasmic calcium-binding protein. Further studies are required on the temporal relationship between allergens in shellfish, and mites, to help diagnose and prognosticate on these reactions.

## 1269 | Allergy to Yerba mate: New allergens detected

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**Background:** Yerba Mate tea (Mate) is an herbal tea beverage extensively consumed in southern Latin American countries and due to globalization in other regions of the world, as the United States and Europe.

**Methods:** A 22 year-old female suffered intense oropharyngeal pruritus and epigastric malaise immediately after every consumption of Yerba Mate. Previously diagnosed of mild atopic dermatitis, allergy to Lipid Transfer Protein (LTP), Oral Allergy Syndrome due to kiwi fruit ingestion, anaphylactic reactions to peanut and pistachio, intermittent asthma due to pollens.

Skin prick tests (SPT) were carried out to the patient using a common battery of pollens, mites, molds, and danders as well as SPT to a common battery of nuts and the culprit foods. Skin prick-by-prick tests with Yerba Mate (infusioned, cooked and crude) were done to the patient and to a group of 5 atopic and non-atopic controls. Specific IgE to peanut, kiwi, LTP and profilin were carried out.

Both the extracts and the molecular weight markers were analyzed using tricine-based SDS-PAGE (acrylamide concentration, 10%-20%) under reducing and non-reducing conditions to yerba mate, peach LTP and marijuana LTP.

**Results:** SPT resulted positive to the following aeroallergens: molds (*Alternaria*, *Aspergillus*), danders (dog and cat) and some pollens: grass (*Datylis*, *Lolium*, *Phleum)*, *Parietaria*, *Artemisia*, *Chenopodium*, *Plantago*, *Salsola*; foods: positive to kiwi fruit, pistachio and peanut and negative to profilin, LTP, latex, hazelnut, almond. Specific IgE to peanut: 90 kU/L; Kiwi fruit: 14.80 kU/L; LTP: 1.19 kU/L, Phl p 12 kU/L: 0.0 kU/L.

Skin prick-by-prick to Yerba mate resulted positive to all the forms in our patient. The patient's serum showed specific recognition of a 10 and 23 KDa band in Yerba Mate. Protein identification showed results highly consistent with the chloroplastic Oxygen-evolving enhancer protein 2 (OEE2). Immunodetection of extracts using peach thaumatin confronted with Yerba Mate extract showed complete inhibition

**Conclusion:** Hereby, we present the first case reported in the literature of a patient with allergy secondary to Yerba Mate tea ingestion. OEE2 has been demonstrated as one of the allergens contained in Yerba Mate. To our knowledge this is the first time LTP, OEE2 and thaumatin have been related to Yerba Mate allergy.

## 1270 | Anaphylactic reaction in patient allergic to shrimp

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**Introduction:** The prevalence of shellfish allergy depends on the climate zone and population. It is assumed that about 0.5%-2.5% of the general population is allergic to shrimps. The best-characterized allergens are tropomyosin, arginine kinase, sarcoplasmic calcium-binding protein and hemocyanin.

**Case Report:** The patient, 28 year old male, was admitted in July 2017 to the Department of Allergology to diagnose the cause of anaphylactic reaction, which occurred 3 months prior to the hospitalization after consumption of king prawns. Immediately after the meal the patient developed pruritus and generalized urticaria as well as swelling of the hands and face. Next the patient developed tachycardia and hypotension. He was administered adrenaline, steroids and antihistamines with good clinical effect.

During the diagnosis, the patient had skin prick tests with extracts of food and inhalant allergens, including standardized shrimp allergen extract - achieving a positive result for *D. pteronyssinus* and *D. farinae*, grass, weeds, cat dander, hazel, birch and alder, but negative for all food allergens tested, including shrimp. The prick by prick tests were performed with fresh royal shrimp (both raw and cooked)—with strongly positive results.

The concentration of IgE specific to shrimp allergen was elevated—5.25 kU/L, while the concentration of IgE of shrimp tropomyosin was not elevated (ImmunoCap). In addition, concentrations of IgE specific for *D. pteronyssinus*—9.86 kU/L, *D. farinae*—7.90 kU/L, grass—19.09 kU/L, cat's dander—2.94 kU/L.

We also established the level of IgE specific to allergen components using the ImmunoCap ISAC method. Allergen-specific IgE was not elevated to any shrimp allergens available in ImmunoCap ISAC: n Pen m1 (tropomyosin), n Pen m2 (arginine kinase) and n Pen m4 (calcium binding sarcoplasmic protein).

**Conclusions:** The patient was diagnosed with a shrimp allergy. The molecular diagnostics used did not explain which allergen component is the patient allergic to. It is possible that the patient is allergic to hemocyanin, which can also cross-react with house dust mite allergens, but confirmation of this diagnosis requires further investigation.

## 1271 | High ara h 2 ige level predicts response to exposure to a small amount of peanut protein

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**Background:** The aim of the study was to evaluate the predictive power of Ara h 2 IgE related to the threshold dose in peanut challenge.

**Method:** 36 children with high suspicion of peanut allergy underwent open peanut challenges (OFC). All participants were sensitized to peanut (Ara h 2 IgE >0.35kU/L).The challenge was performed according to PRACTALL recommendations with peanut protein doses of 5, 25, 50, 200 and 1000 mg (cumulative dose 1280 mg). The severity was assessed using a dose-adjusted severity scoring in the 21 patients with positive OFC. We analyzed the serum Ara h 2 IgE level and its association to the cumulative protein dose (threshold dose), the severity of the response, and the use of adrenaline during OFC. Patients were divided into two groups according to the Ara h 2 IgE level, < or ≥ 10kU/L (Table 1). IBM SPSS-statistic 22 statistics software (SPSS Inc. Chicago, Illinois, USA) was used in the analysis of the results.

**Results:** The groups were identical in terms of the age and sex (Table 1). Ara h 2 IgE correlated (Spearman test) with the cumulative protein dose (threshold dose) $r = -0.439$ ($P = 0.023$) but not with reaction severity $r = 0.091$ ($P = 0.348$), or the use of adrenaline $r = 0.300$ ($P = 0.093$). Patients with Ara h IgE < 10 kU/L had higher threshold doses (644 vs 71 mg) than children whose Ara h 2 IgE was ≥10 kU/L ($P = 0.016$). There were no significant differences in severity of the reaction or in use of adrenaline (Table 1).

**Conclusion:** The level of Ara h 2 IgE is relevant in predicting the threshold dose at peanut exposure. A low reaction threshold dose increases the risk of reaction at an accidental exposure leading potentially to a severe reaction.

**Table 1 Patient characteristics according to Ara h 2 IgE**

| Group | Ara h2 IgE <10 kU/L (n = 13) | Ara h2 IgE≥10 kU/L (n = 8) | Significance |
|---|---|---|---|
| Age (years), Mean, Range | 7.6, 3.39-14.32 | 8.3, 5.58-11.51 | 0.611 x |
| Sex (male) | 7 (54%) | 5 (63%) | 0.528 xx |
| Ara h2 IgE (kU/L) Mean, Range | 1.66, 0.48-9.80 | 90.98, 20-260 | <0.001 xxx |
| Reaction intensity | | | |
| Mild | 5 (39%) | 1 (13%) | 0.346 xx |
| Intermediate/ severe | 8 (62%) | 7 (88%) | 0.346 xx |
| Use of adrenaline | 3 (23%) | 4 (50%) | 0.215 xx |
| Cumulative dose mean (mg), (median) | 644 (480) | 71 (32.5) | 0.016 xxx |
| Range (mg) | 30-1280 | 30-230 | |

x, Independent sample T-test; xx, Fischer exact test xxx Mann-Whitney *U* Test.

## 1272 | Commonest foods associated with IgG antibodies in Saudi Arabia

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**Background:** Hypersensitivity mediated by immunoglobulin G (IgG) to food antigens is a controversial causal association with chronic inflammatory disorders. Currently, different techniques exploring this link is under research focus.

**Objective:** To identify the most common foods associated with an IgG antibodies.

**Method:** Serum samples of patients with chronic illnesses from multiple medical centers in Saudi Arabia were collected over 5 years period. These were analyzed for 268 food items by an ELISA-based ImuPro IgG test by R-Biopharm from Germany.

**Results:** 1644 different patients (55.5% male, 44.5% female) of almost all ages were studied. IgG antibodies positivity were predominant to 14 foods (5%) in more than half of the patients, which include: Oat (82.5%), Barley (79.1%), Rye (76.1%) Cow's milk (75%), Wheat (74.9%), Kamut (74.6%), Spelt (74.6), Gluten (73.8%), Sour cow's milk (65.7%), Rennet cheese cow (62.9%), Ricotta (59.2%), Chicken egg white (57.3%), Cooked milk (56.3%) and Halloumi (52%). Children have a significantly different IgG food profile than adults. Among children below 5 years of age, cow's milk was the predominant food with IgG antibody response (95.74%), followed by oat (92.2%).

**Conclusion:** In this large study in number of patients with IgG food antibodies test, the commonest were typical foods consumed almost daily such as gluten and dairy products. Further research is needed to identify their role in chronic illnesses.

## 1273 | Allergy to European smelt roe: A case report

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**Case report:** Roe of fish or other aquatic species is not commonly reported as a cause of food allergy in Europe, although it is a much more common allergen in Japan, where fish roe is consumed widely. The most of them are about salmon roe (SR) and there were only few cases of white fish roe allergy. Fish roe has 3 major yolk proteins: lipovitelin (Lv), phosvitin, and β′-component (β′-c).Vitellogenin, a precursor of these yolk proteins. Lv and β′-c have high IgE-binding ability. β′-c in particular is a major allergic protein of SR. β′-c was registered as a new allergen "Onc k 5" in the official allergen list of the World Health Organization and International Union of Immunological Societies Allergen Nomenclature Subcommittee in 2012. Additionally, IgE cross-reactivities among fish roes, such as those

from salmon, herring, walleye pollock, Atka mackerel and shishamo smelt have been reported in case studies. Moreover, recent research on molecular analysis has verified the presence of multiple vitellogenins in at least some fish species and there is no data about European smelts.

**Background:** A 52-year-old women presented with oral pruritus, facial, laryngeal angioedema, and urticaria within minutes after eating European smelt (Osmerus eperlanus) caviar. She also experienced oral pruritus and lip angioedema after eating other kinds of fish roe (salmon, bream and herring). She did not report any previous or subsequent symptoms after eating any kind of fish or bird eggs, and she had no past history of allergic disease or atopy. Skin prick tests to common commercial fish (including salmon,tuna,herring and cod), crustaceans, molluscs, egg yolk, egg white were performed, with negative results (Allergy Therapeutics, UK).Prick-by-prick tests carried out with smelt caviar resulted in a wheal of 6 × 9 mm, the rest were negative (boiled egg yolk, raw and boiled egg white, smelt). Serum-specific immunoglobulin E (sIgE) against commercial salmon extract, egg yolk, egg white, ovalbumin, and ovomucoid were negative (ImmunoCAP system). Commercial tests of sIgE against fish roe are unavailable in Lithuania.

**Conclusion:** IgE-mediated allergy to fish roe is possible without concomitant fish allergy. Roe allergy should be explored in patients who test negative to fish but are suspected of having seafood-related allergy. More studies of cross-reactivity between different fish roe and other yolk protein capability of IgE binding are needed, because of heterogeneity of vitellogenin among fish species.

## 1274 | Conclinin: A new allergen involved in allergy to flaxseed

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**Background:** Flaxseed (*Linum usitatissimum*) is an herbaceous plant that belongs to the Linaceae family. It has been used in the textile and food industry and in alternative medicine.

Flaxseed allergy is uncommon and most of the cases reported involved anaphylaxis. Cross reactivity has been described with other seeds.

**Case report:** A 9-year-old atopic girl diagnosed with egg allergy and rhinoconjunctivitis and asthma due to pollens.

When she was eight, she presented two reactions consisting of conjunctival, periorbicular, malar erythema and abdominal pain after eating egg free French toasts cooked with flaxseed. She was treated with oral antihistamines.

The allergic workup included prick-by-prick test with flaxseed which was positive and skin prick tests with mites, molds, cockroach, cat, dog, profilin, LTP and pollens with positive results for olive and grass pollens. The serum total Immunoglobulin (Ig) E was 476 U/L, and specific IgE to flaxseed was 7.23 kUA/L.

The flaxseed extract was resolved with sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and an IgE immunoblotting was performed under nonreducing conditions.

The patient's serum showed specific recognition of a 18-kDa band in the immunoblot.

Proteins were identified using mass spectrometry (MALDI-TOF) that showed results highly consistent with conlinin, a 2S storage protein of flaxseed.

**Conclusion:** We described for the first time a patient with allergy to flaxseed due to conlinin, a 2S storage protein of flaxseed.

## 1275 | Anaphylaxis induced by ingestion of tiger nut milk

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**Background:** Cyperus esculentus is an herbaceous plant that has edible tubers called tiger nuts. In Spain, they are used mainly in the elaboration of the well-known "horchata" or tiger nut milk, which is obtained by macerating tiger nuts with water and sugar.

Tiger nut allergy has rarely been reported, despite of its widespread consumption.

**Case report:** We present the case of a 19-year- old male with a history of oral syndrome allergy with several fruits (peach, melon, banana, kiwi, apple, pear and plum) and seasonal allergic rhinoconjunctivitis due to grass pollen.

He reported oral pruritus, vomiting and cutaneous itching in both arms and hands immediately after drinking tiger nut milk. He became asymptomatic without treatment after 3-4 hours.

The allergic workup included skin prick tests with profilin, LTP, latex and fruits that were positive to melon and watermelon and negative to profilin, LTP, latex and the rest of the fruits. Prick-by-prick tests with melon, banana, kiwi, apple, pear, tiger nut and tiger nut milk were positive.

The serum total immunoglobulin (Ig) E was 68.7 μg/L, and specific IgE was negative to profilin, LTP, bet v1 and all the tested fruits.

The tiger nut extract was resolved with sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and an IgE immunoblotting was performed under non-reducing conditions.

The patient's serum showed recognition of bands ranging from 17 to 22 KDa and from 45 to 70 KDa, highlighting three bands of 32, 36 and 40 KDa in the immunoblot.

**Conclusion:** We present a case of anaphylaxis due to tiger nut allergy without sensitization to profilin, LTP and bet v1.

## 1276 | Prevalence of different specific IgE in Albanian children with suspected food allergies

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**Background:** Specific blood IgE tests for food allergens are mainly used to confirm a suspect food allergy than to diagnose such an allergy. This is due to the low positive predictive value and the high negative predictive value they have. Nevertheless, they are very helpful when they are interpreted in the context of medical history by an experienced allergist. We analyzed the prevalence of sIgE in children with suspected food allergies.

**Method:** We retrospectively analyzed the all the consecutive laboratory tests of sIgE for food allergens during the two-year period (2015-2017). Tests were of children diagnosed or suspected to have food allergies. A quantitative immunoblot assay was used to measure the circulated 30 different sIgE. *T*-test, Wilcoxon Signed Rank test, and chi-square were used to make comparisons.

**Results:** Fifty-six (55.4%) men and 45 (44.6%) females, 3.4 + 3.2 years old with a maximum of 16 years and a minimum of 2 months old were part of 101 children whose tests were analyzed. One-third of the tests (30.7%) reveals more than one sIgE present and 55.4% of the tests resulted negative for the sIgE for the 30 allergens tested (Table).

| Allergenic | Positive % (n) |
|---|---|
| Hazelnut | 23.8 (24) |
| Peanut | 17.8 (18) |
| Wheat flour | 15.8 (16) |
| Carrot | 14.9 (15) |
| Egg yolk | 14.9 (15) |
| Almond | 12.9 (13) |
| Egg white | 12.9 (13) |
| Rye flour | 12.9 (13) |
| Potato | 11.9 (12) |
| Apple | 11.9 (12) |
| Soy beans | 10.9 (11) |
| Walnut | 9.9 (10) |
| Milk | 8.9 (9) |
| Sesame | 8.9 (9) |
| Celery | 8.9 (9) |
| Casein | 6.9 (7) |
| Peach | 5.9 (6) |
| Tomato | 5.0 (5) |
| Codfish | 4.0 (4) |
| Shrimps | 2.0 (2) |

Only 3 (3.0%) children have very high concentrations (>100 IU/mL) of Egg Whites sIgE, and 2 (2.0%) have Egg yolk sIgE. Concentrations of 79.27% of sIgE positive cases were 0.35-3.5 IU/mL.

**Conclusion:** In our study more than half of the children suspected of food allergies resulted negative for sIgE for 30 most common food allergens. Seventy-nine percent of the positive cases had relatively low sIgE. Only a few positive cases have higher sIgE than 100 IU/mL. Our data support the recommendation that sIgE couldn't be decisive in food allergic diagnosis, but they may help if they are interpreted cautiously.

## 1277 | Are angiotensin converting enzyme (ace) inhibitors complicating pollen food allergy syndrome?

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**Background:** Pollen food allergy syndrome (PFAS) is an IgE-mediated allergic reaction confined to the oral cavity following ingestion of foods to which one is previously sensitised to, such as fresh fruits and vegetables and nuts. PFAS is due to homology between the pathogenesis related protein (PR-10) allergens in the foods and the major allergen in pollens resulting in cross-reactivity. It manifests with oro-pharyngeal irritation, pruritus, stinging and swelling. Angiotensin converting enzyme inhibitors (ACEi) can cause episodes of facial and tongue angioedema, in a minority of patients. Concurrent use of ACEi in patients with PFAS, may lead to unusually severe symptoms with exacerbation of tongue and throat swelling after exposure to offending foods.

**Method:** Seven patients with a mean age of 61.4 years and female to male ratio of: 3:4, with a background history of hypertension treated with an ACEi presented with oro-pharyngeal irritation (itch, tingling), face and tongue angioedema and laryngeal constriction, on ingesting fresh fruits (cherries, apples, plums, peaches, apricots, strawberries, grapes), vegetables (parsnips) and/or nuts (peanuts, hazelnuts). Two patients required admission to emergency department and three received adrenaline auto-injector. Six out of seven patients underwent skin prick testing to common aeroallergens and the index foods. In five cases, Immunocap/ISAC testing was undertaken. In one case the diagnosis was based on the history and in one other case it was based on history and skin prick tests.

**Results:** A diagnosis of PFAS was confirmed in all patients through the clinical history, SPT and/or specific IgE serology to the offending food confirming predominant sensitisation PR-10 allergens. Primary food allergy and spontaneous angioedema was excluded in all patients.

**Conclusion:** In the cohort studied, the PFAS symptoms were unusually severe. We therefore postulate that this was secondary to concurrent use of ACEi. The management of these patients

constitutes allergen avoidance and cessation of ACEi use. Angiotensin II receptor blockers are alternative therapies to ACEi. In patients presenting with food allergic reactions, ACEi should be considered as a potential cofactor.

## 1278 | Food anaphylaxis to Campana buffalo mozzarella cheese

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**Background:** Food allergy to ewe's and goat's milk with tolerance to cow's milk is a rare but known entity; on the other hand, buffalo's milk allergy is exceptionally reported. We present a case of associated goat-ewe-buffalo's milk allergy with tolerance to cow's milk.

**Method:** A 6-year old boy with a history of eczema, asthma and food allergy to peanut, ewe's and goat's milk declared two grade 2 anaphylactic reactions after intake of Buffalo Mozzarella cheese, the first time associating general itching, vomiting, laryngeal edema and asthma, and 6 months later generalized urticaria and abdominal pain. He tolerates cow's milk since earliest childhood, but frequently declared accidents related to the hidden presence of ewe's and/or goat's milk in industrial food preparations, due to the fact that declaration of these milks is not mandatory on food labels.

An oral challenge test with Buffalo Mozzarella cheese, proposed 3 months prior to the first reaction on behalf of a suspicion of food allergy with oral syndrome, a doubtful skin prick test to Buffalo Mozzarella cheese and a negative cow's milk prick test, remained negative (cumulative dose of 56 g). However, occurrence of ear or pharyngeal itching lead to very irregular intake of this cheese thereafter.

**Results:** Allergy was confirmed after the last accident by a positive prick test to Buffalo Mozzarella cheese (8/25 mm for a Histamine control of 6/20 mm) while cow's milk prick test remained negative.

**Conclusion:** Only two cases of associated goat-ewe-buffalo's milk allergy with cow's milk tolerance, one case of isolated buffalo's milk allergy and one case of tolerance to this milk associated with cow's milk allergy have so far been reported.

High homologies exist between cow's and other Bovidae's milk proteins (96.1% for buffalo, 91.1% for ewe, 87.6% for goat). Associated goat-ewe-buffalo's milk allergy with cow's milk tolerance may be due to sensitization to a β-casein with high homology between only the first 3 milks. More precisely, the allergen candidate could be γ-casein, which is derived from β-casein by proteolysis, whose abundance increases during cheese production from fresh milk, and which is absent in cow's milk. A lactoglobulin specific to buffalo's milk may also be responsible.

In case of ewe's and goat's milk allergy without cow's milk allergy, sensitization to buffalo's milk should systemically be seeked out.

We recommend inclusion of all mammalian milks in the list of the 14 mandatory allergens for declaration on food products.

## 1279 | Interest of 2D Western blot in the analysis of an allergenic cross-reaction with crickets

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**Background:** Entomophagy is a promising alternative source of protein in food which is becoming more common in European countries. However, the protein composition and the potential molecular allergens present in this new food matrix have still not been studied in detail and described in the literature. The aim of the present study was the analysis of the potential cross-reactivity between the widespread allergens of shrimps and house dust mites (HDM) and those of crickets (*Gryllodes sigillatus*).

**Method:** Twelve patients aged 7-50 y.o. and presenting a shellfish and/or HDM allergy were selected on the basis of their positive specific IgE (sIgE) results on ImmunoCAP250 (Thermo Fisher Scientific) in particular against two tropomyosins, Der p 10 (HDM, from 0.01 to >100 kUA/L) and Pen a 1 (shrimps, from 14.3 to >100 KUA/L). A total *Gryllodes sigillatus* protein extraction was performed and proteins were separated on the basis of their isoelectric point (Ip) and their molecular weight. Furthermore, 1D and 2D Western blot (WB) were carried out to determine the molecular allergen reactivity profile of each patient serum to the extract.

**Results:** The 1D WB confirmed the anti-HDM and anti-shrimp sIgE reactivity to a 37 kDa molecular weight of cricket protein that could be either the tropomyosin or the arginine kinase (AK). The 2D WB confirmed the reactivity against a 37 kDa protein with an Ip of 3-4 that could be the tropomyosin and/or against a 37 kDa protein with an Ip of 6-7 that could be the AK. Furthermore, another spot of interest located around 17.5 kDa with an Ip of 4 could be the troponin C, another protein described as a molecular allergen in HDM and shellfish, presenting high sequence homology with insect proteins.

**Conclusion:** These preliminary results showed a clear IgE cross-reactivity between the cricket tropomyosin and sIgE in the serum of 12 shrimp and/or HDM allergic patients with positive sIgE to Der p 10 and/or Pen a 1. The proteins identified as responsible for this cross-reactivity are tropomyosin, arginine kinase as well as troponin C. These hypotheses will be confirmed by a precise identification by mass spectrometry (LC-MS/MS).

## 1280 | Food challenges in early life: Are they safe?

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**Background:** Food challenges in infants and young children are becoming an increasingly common occurrence in the allergy clinic. This is the result of various factors including (a) recent significant changes in our approach to allergenic food introduction with the aim to prevent the development of food allergy (b) known important advantages in baked milk and egg introduction and (c) importance of differentiating between sensitization and true allergy early in life.

**Method:** We developed a dedicated early life allergy clinic with the aim to encourage food introduction in infants and young children that are able to tolerate this, support introduction of baked milk and egg and differentiate between sensitization and true allergy in young ages. We collected data prospectively on the first 14 patients below the age of 2 years who underwent food challenges with the aim to evaluate safety of this procedure in this age group.

**Results:** Among the first 14 children (median age: 13 months) undergoing food challenges in our clinic, 12/14 (86%) had a negative challenge. Only 2/14 (14%) had a positive challenge and in both cases symptoms were mild and limited to the skin (erythema, hives and eczema exacerbation). Symptoms occurred within 2 hours and treated successfully with a single dose of oral antihistamine. There were no biphasic reactions. Foods challenged included: peanut (5/14), baked milk (3/14), baked egg (1/14), almond (2/14), soy (2/14) and sesame (1/14). In 8/14 the food had never been ingested previously. Median skin test result to the relevant food was 3 mm (range: 0-20 mm).

**Conclusion:** We conclude that food challenges in infants and young children below the age of 2 years are safe; symptoms appear to be limited to the skin when reactions occur. In carefully selected populations, the large majority of food challenges are likely to be negative, with most infants being sensitized rather than allergic to the foods.

## 1281 | Frey syndrome vs food allergy in an infant. A case report

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**Background:** 7 months infant sent to Allergology Department because it presents at 6 months of age, after the taking of fruit porridge (banana, orange, apple), non-pruritic and a few minutes long facial macular lesions. After two hours, the same porridge is given, presenting the symptoms again. Days later, after oral contact with banana, it immediately presented oral micropapular erythema and irritability. It was evaluated the next day at its Health Center where antihistamines are indicated on demand (hydroxyzine)

In a new fruit intake (apple) the same symptoms are reproduced. In none of the episodes there was rejection of food, vomiting, respiratory symptoms or urticaria.

**Method:** Prick tests with fruit battery, LTP and profilin was made. Analytical with blood count, immunoglobulins, triptasa, total IgE and specific IgE to banana, apple and orange. Finally, open oral provocation with fruits was performed.

The diagnostic key was given by the mother of the patient who attended consultations because the infant had erythema in the temporary zone after drinking sea water on the beach. Associated with salivation, the patient presented erythema in the malar area lasting a few seconds many times.

**Results:** The prick tests with fruits, LTP and profilin were negative. Hemogram: 100 eosinophils/μL, total Ig E: 4.9 IU/mL, specific IgE to fruits were negative. Triptase: 5.1 μg/L.

Open oral provocation was performed with banana, apple and orange with good tolerance. Currently the patient performs a normal diet.

**Conclusion:** The Frey syndrome patient is diagnosed in a nursing infant and parents are informed that it is a benign and transient condition.

We present the case of a patient diagnosed with Frey syndrome in a nursing infant. The auriculotemporal syndrome (Frey's syndrome) is characterized by episodes of facial flushing, sweating or both, located in the distribution territory of the auriculotemporal nerve, and which occur as a response to gustatory stimuli that produce hypersalivation. When this syndrome is manifested in childhood and coincides with the introduction of new foods in infants, we can reach the wrong diagnosis of food allergy. That is why we believe it is important to know the existence of the syndrome in order to avoid unnecessary complementary tests as well as avoidable dietary restrictions.

## 1282 | The many faces of nonspecific Lipid Transfer Protein Allergy (nsLTP): A case series of patients seen in an adult tertiary allergy centre in the North West of England with nsLTP allergy

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**Background:** Nonspecific Lipid Transfer Protein (nsLTP) allergy is the most frequent cause of primary food allergy in the Mediterranean area. Sensitisation to nsLTP is uncommon in Central and Northern Europe.

**Method:** Here we describe a variety of cases of nsLTP allergy presenting to a tertiary allergy centre in the North West of England.

**Results:** nsLTPs have been found to be major allergens in various foods and they are likely to produce severe and systemic allergic reactions. This is reflected in the cases we present here. These proteins are highly cross-reactive due to extensive sequence homology and are panallergens. nsLTPs are remarkably heat stable and retains its allergenicity in processed foods. It is assumed that nsLTPs may sensitise both by inhalation and ingestion. An intriguing aspect in nsLTP hypersensitivity is the extreme variability of its clinical expression. Co-factors are often needed for the clinical expression of nsLTP hypersensitivity.

**Conclusion:** Patients regardless of where they are from, presenting with multiple severe/systemic food allergies need to be investigated for nsLTP allergy. These patients require specific dietary advice on foods to avoid and a tailored management plan on how to deal with their allergic reactions.

## 1283 | Isolated goat's and sheep's milk allergy

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**Background:** We present a patient who suffered from multiple episodes of nausea, vomiting, stomach pain and dyspnea shortly after the consumption of sheep's milk cheese and goat's milk cheese. Cow's milk as well as cow's milk products are tolerated.

**Material and Methods:** Skin prick tests with different sorts of milk, cheese and milk proteins were performed, specific IgE antibodies were measured, a basophil activation test with cow's and goat's milk was performed and an oral provocation test (OPT) with cow's milk, cow's milk cheese, raw milk and raw milk cheese was conducted.

**Results:** Skin prick tests were positive for sheep's milk, goat's milk, goat's milk casein, feta, pecorino and parmesan cheese. Elevated specific IgE against goat's milk (12.7 kU/L) and sheep's milk (11.7 kU/L) were detected. Activation of basophil granulocytes after incubation of the patient's blood with cow's milk and goat's milk was measurable but also in the non-incubated control blood. All cow's milk products were tolerated in the OPT.

**Conclusion:** Despite consistent homologies between whey and casein proteins of mammals and high cross-reactivity between cow's, goat's and sheep's milk an isolated goat's and sheep's milk allergy with tolerance of cow's milk is possible. Skin testing and specific IgE help to distinguish from allergy against cow's milk proteins. Diet counseling is possible after OPT.

## 1284 | Salmon roe: An emerging allergen from the East to the West

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**Introduction:** Salmon roe's allergy, without concomitant fish allergy, is rarely described in western countries. There are few studies on its allergenicity.

**Objective:** To report of a case of salmon roe allergy without concomitant fish allergy in a western country.

**Case report:** A 26-year-old male with house dust mite allergic rhinitis and asthma, describes for the 1st time, in 2015, an acute episode of dyspnoea, rhinorrhoea, ocular pruritus, epigastric pain and nausea, a few minutes after the ingestion of a sushi meal with rice, salmon, salmon roe, wasabi, soy and ginger. These complaints motivated observation in the emergency room, where it was still documented uvular oedema. He was prescribed intramuscular adrenaline, intravenous steroids and anti-histamines with complete symptoms resolution. The patient declares not had eaten other foods, taken any drugs including NSAID, been infected or practised exercise. Skin prick tests with food extracts (salmon and other fish, shellfish, soy, rice, egg total, egg white, egg yolk, ovalbumin and ovomucoid) were negative. Skin prick-prick tests were positive for salmon roe (17 × 10 mm) and negative for egg (white and yolk), ginger, salmon, flying fish roe (*tobiko*), sturgeon roe (*caviar*) and black scabbard fish roe. Specific-IgE (sIgE) to salmon roe extract was 0.28 kUA/L (ImmunoCAP-Phadia) and negative against extracts from salmon fish and other fish (<0.1 kUA/L). SDS-PAGE *Immunoblotting* with salmon roes extract showed a 20 kDa-IgE binding band, that may correspond to a lipovitelin. After the allergic reaction the patient have tolerated

salmon fish and other fish roes (*tobiko*, *caviar* and black scabbard fish). No oral provocation test with salmon roes was performed given the severity of the reaction.

**Conclusion:** This report is an example of a severe allergic reaction to salmon roe without concomitant fish allergy, where the clinical history and the in vivo and in vitro tests were important to an accurate diagnosis. The authors believe this is the first report of a salmon roe anaphylaxis in our country and highlight the importance of this allergen in the western countries, given the increase of sushi consumption in these countries.

## 1285 | An "unusual suspect": Allergic reaction with pomegranate in Germany

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**Case report:** The prevalence of food allergy is increasing worldwide and consumer habits are changing. Pomegranate (Punica granatum) was commonly consumed in the Mediterranean area but in the last few years became also popular in the different parts of Europe.

A 5-year-old boy was admitted to our emergency department suffering from allergic reaction within 10 minutes after consumption of pomegranate. He presented with skin pruritus, generalized urticaria and eyelid edema. Symptoms resolved within an hour after oral intake of cetirizine. Prick-to-prick test with pomegranate was positive (wheal diameter 13 × 7 mm). He had a history of anaphylaxis with egg (urticaria and wheezing) at the age of 9 month, meanwhile consumption of egg is well tolerated. An episode of anaphylaxis with unknown origin appeared at the age of 4 years (urticaria, wheezing and abdominal pain). Skin prick tests with aeroallergens revealed birch pollen allergy and he was diagnosed with allergic rhinoconjunctivitis. Dietary elimination of pomegranate was suggested and adrenaline auto-injector was provided.

Only few published cases describe immediate allergic reactions and anaphylaxis after the consumption of pomegranate. Along with the leading causes of food allergy in childhood such as cow's milk, egg and peanuts, rare foods such pomegranate may cause allergic reactions in children. Increase of the awareness by the physicians and the families may help better identification of rare food allergies.

TUESDAY, 29 MAY 2018
TPS 48
THE SPECTRUM OF DERMATOLOGY

## 0867 | Experience with omalizumab in refractory chronic spontaneous urticaria in a third level hospital (Late Breaking Abstract)

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**Background:** Omalizumab is an anti-IgE biological treatment currently approved for chronic urticaria refractory to H1 antihistamines. A retrospective analysis of medical records in the past 3 years of 25 patients (16 female) with refractory chronic spontaneous urticaria (CSU) and treated with omalizumab was performed. Four of them also had history of nonsteroidal anti-inflammatory drug (NSAID) cross-intolerance.

**Method:** We have analyzed omalizumab effectiveness and safety in patients with CSU from our database. Clinical response was categorized as: no response, partial or complete response by using the Urticaria Activity Score 7 (UAS 7). Furthermore, the dosage, administration frequency and any side effects were recorded.

**Results:** Effectiveness: 23 out of 25 patients (92%) achieved complete response. 15 (65.2%) after a single dose of 300 mg (8 patients) or 150 mg (7); 5 patients (21.7%) after two doses of 300 mg (4 patients) or 150 mg (1) and 3 patients (13%) after three doses of 150 mg (2 patients) or 300 mg (1). Finally, 2 patients (8%) did not respond. Furthermore, two patients have not presented any urticarial episodes after omalizumab stopping; one of them had received treatment during one year and the other during 8 months. One NSAID intolerant patient, become NSAID tolerant during the treatment. Controlling dosage and frequency of administration: 7 (30.4%) patients were receiving 300 mg on as needed basis; 1 (4.3%) 150 mg every 8 weeks; 3 (13%) 300 mg every 6 weeks; 11 (47.7%) every 4 weeks (150 mg in 6 patients and 300 mg in 5); 1 (4.3%) 150 mg every 3 weeks. Safety: Two patients (8%) reported adverse events (myalgia) although only one had to discontinue treatment.

**Conclusion:** Omalizumab was effective in 92% of the patients after 1, 2 or 3 doses. On the other hand, 30.4% of them were controlled with 300 mg on as needed basis whereas 47.7% needed treatment with omalizumab, 150 or 300 mg, once every four weeks. Omalizumab is a safe treatment for chronic spontaneous urticaria.

TUESDAY, 29 MAY 2018
TPS 39
GENETICS AND BIOMARKERS IN ASTHMA

## 1287 | Implications of population admixing and ancestry on prevalence of asthma

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**Background:** Differences exist in the prevalence and severity of asthma among different racial and ethnic groups. However, the influence of population admixing on asthma has not been studied. We aimed to determine the effect of population admixing on the occurrence of asthma in Korean population which represents a recently admixed population.

**Method:** Data for this study were drawn from the 11th Korea Youth Risk Behavior Web-based Survey (KYRBWS-XI) by Korea Center for Disease Control and Prevention in 2015. KYRBWS is a population-based survey that represents a nation's middle school and high school population. Of 70 362 students, 68 043 (96.7% response rate) participated in the KYRBWS-XI. Multi-ethnic status was determined by using parental country of birth and prevalence of asthma was determined by questionnaire. Rao-Scott Chi-square test was used for comparison of categorical variables and complex variable general linear model of continuous variables. Risk factors for asthma were investigated with multiple logistic regression methods.

**Results:** Multi-ethnic adolescents accounted for approximately 1.2% of the total sample of adolescents. Prevalence of asthma was significantly higher in multi-ethnic group than non multi-ethnic group. We examined if maternal or paternal foreign born status had a differential effect: in multi-ethnic family with foreign-born father, prevalence of asthma was significantly higher. Parental region of country at birth had a significant influence on the prevalence of asthma. Adjusted logistic regression analysis was used to determine risk factors for occurrence of allergic disease. Residential area, perceived household economic status, parental region of country at birth, and body mass index (BMI) had a significant effect on prevalence of asthma.

**Conclusion:** Population admixing appears to have significant effect on the prevalence of asthma. Further study will be needed to clarify the effect of population admixing on prevalence of allergic disease.

## 1288 | Circulating microRNA signatures in allergic and non-allergic asthmatics with high blood eosinophilia

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**Background:** Nearly 300 million people world-wide are affected with asthma, a heterogeneous disease with a variety of different phenotypes. Asthmatics are currently classified based on their inflammatory cell profiles, such as eosinophils or neutrophils, or by their atopic status. microRNAs (miRs) are ~18-24 nucleotide, non-coding RNAs involved in post-transcriptional gene regulation, usually through the downregulation of targeted messenger RNA (mRNA). Several studies have aimed to explore the possibility of miRs as biomarkers for various diseases. In our study we examined six different miRs, previously shown to be involved in eosinophil development and other immune responses, in serum from non-allergic and allergic asthmatics and healthy control subjects in order to determine their potential ability to be used as biomarkers for varying forms of asthma.

**Method:** Serum from healthy individuals as well as age matched non-allergic asthmatics (NAA) and allergic asthmatics (AA) were utilized. Additionally, the NAAs and AAs subjects had high eosinophila ($\geq 0.4 \times 10^9$cells/L) compared to healthy controls ($\leq 0.1 \times 10^9$cells/L) and eosinophil cationic protein (ECP) in serum was measured. Asthmatic subjects were included irrespective of inhaled corticosteroid usage. RNA was extracted from serum, reverse transcribed and subjected to qPCR analysis. Expression changes in six candidate miRs, miR-126, -145, -146a, -155, -223, and -374, were investigated.

**Results:** Two miRNAs, miR-155 and miR-146a, were significantly upregulated in AAs as compared to NAA or healthy subjects. Additionally, miR-223 was upregulated in NAA, but not AA or healthy subjects. Furthermore, the expression change observed in the AA miRs appeared to correlate with the use of inhaled corticosteroids, but not in the NAA miRs. Finally, miR-223 and miR-374 expression levels were altered based on the number of eosinophils, which correlated to ECP levels, in NAA subjects.

**Conclusion:** Using six miRs found in the literature to be involved in eosinophila or immune responses, we were able to detect expression changes in the serum of healthy and asthmatic individuals. Moreover, were able to distinguish between healthy individuals, AAs, and NAAs on inhaled corticosteroids or with differing eosinophil levels, leading to the possibility that these miRs may be valuable future biomarkers for asthma.

## 1289 | Molecular sensitization profiles in patients with allergy to dust mites and their relationship with the risk of developing asthma: A multicenter study

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**Background:** Some studies report that certain sensitization profiles may increase the risk of a more serious allergic respiratory disease. The aim of this study was to describe the sensitization patterns to major allergens of dust mites in our area and investigate the association of these patterns with a specific clinical picture.

**Method:** Multicenter study performed in 3 hospitals for 4 months. We recruited 133 patients older than 5 years with rhinitis and/or bronchial asthma, with a history of allergy to dust mites and both skin test and specific IgE to *D. pteronyssinus*, *D. farinae* or L. destructor positive.

Der p1 and Der p2 were determined to all of them.

**Results:** We analyzed 133 patients with an average age of 28.25 years, 60.9% women, 9.7% smokers, 69.9% rhinitis and asthma, 17.3% only rhinitis and 12.8% only asthma. 94% of patients presented sensitization to D. pteronyssinus, 83.5% to *D. farinae* and 63.2% to L. destructor. The detected sensitization patterns were: both Der p1/Der p2 positive 73.9%; Der p1 positive 8.4%, Der p2 positive 11.8% and both Der p1/Der p2 negative 5.9%. It was observed that patients with higher specific IgE levels had more severe forms of respiratory disease, with isolated asthma or associated with rhinitis. For D. pteronyssinus, *D. farinae*, Der p1 and Der p2 > 50kU/L there is a greater number of cases of asthma associated with rhinitis, while for L. Destructor >3.5kU/L greater number of cases of asthma. No relationship was observed between a specific sensitization pattern and an increased risk of asthma.

**Conclusion:** 1. Specific IgE values greater than 50 kU/L for *D. pteronyssinus*, *D. farinae*, Der p 1 and Der p 2, were significantly associated with a higher probability of asthma and this association was significant for L. Destructor>3.5 kU/L (class 3).

2. There are four well-defined sensitization patterns in our population that are influenced by geographic location, being the double sensitization to Der p 1 and Der p 2 the most prevalent and allowing the correct characterization of 94% of the cases. None of them increased the risk of asthma.

## 1291 | Eosinophil-derived neurotoxin is a useful biomarker for preschool children with asthma

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**Background:** Reliable biomarkers for diagnosis and management of asthma in young children are needed since pulmonary function test and exhaled NO measurement, good biomarkers for asthma in older children and adults, are difficult to perform in young age. We have developed a sensitive and stable assay system to measure eosinophil-derived neurotoxin (EDN), an eosinophil granule protein, that is released upon activation, and that may serve as a marker for eosinophilic inflammation also in young children.

**Method:** Volunteer children from 0-6 years old were recruited and an ISAAC-based questionnaire was filled out by their caregivers. Venous blood was obtained to measure serum and plasma EDN and eosinophil count. EDN was measured with a research assay developed on the ImmunoCAP® platform.

**Results:** One hundred and fifty-one children were enrolled in the study. Of them, 44 children had a history of wheeze based on ISAAC (ISAAC_ever+), 105 had no history of wheeze ever (ISAAC_ever–) and 2 had unknown history of wheeze. Thirty-six children had a history of wheeze within 12 months (ISAAC_current+), 105 did not (ISAAC_current–) and 10 had unknown history. Twenty-nine children had doctor-diagnosed asthma (D_BA+), 101 did not (D_BA–) and 21 had unknown history. There were no differences in serum and plasma EDN levels between ISAAC_ever+ and ISAAC_ever–, ISAAC_current+ and ISAAC_current-. However, serum and plasma EDN were significantly higher in D_BA+ than in D_BA–, with median (quartile range) at 40.4 μg/L (27.1-59.8) vs 23.6 μg/L (15.2-37.2), $P = 0.0007$, 31.0 μg/L (18.5-51.0) vs 12.2 μg/L (8.0-21.3), $P < 0.0001$, respectively. ROC analysis revealed AUC for serum and plasma EDN to diagnose D_BA, at 0.70 and 0.74, respectively. There was no difference in eosinophil count between the groups defined by any criteria.

**Conclusion:** Blood EDN may be a reliable biomarker for diagnosis of asthma in preschool children.

## 1293 | Budget impact of using feno in the management of asthma patients in Germany

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**Background:** Fractional exhaled nitric oxide (FeNO) is a validated biomarker of Th2 airway inflammation. Compared to other diagnostic

methods, FeNO is easy to measure at the point of care and is an independent and specific measure of airway inflammation. Tailoring asthma interventions based on FeNO leads to improvements in medication use, decreased symptoms and reduced likelihood of future exacerbations. Aim of this study was to evaluate the budget impact of FeNO assisted monitoring of asthma in Germany.

**Method:** A budget impact model with two decision trees was used to examine the financial impact of FeNO on asthma diagnosis and management in Germany. FeNO measurement was compared with standard testing according to guideline recommendations for asthma management. FeNO measurement was compared and/or combined with reversibility testing, bronchial provocation and sputum eosinophil count. These measures were then evaluated with respect to impact on asthma control, including inhaled corticosteroid use, exacerbations and hospitalizations vs symptoms and lung function as in standard care. Resource use and health outcomes were evaluated over a 1-year time frame. Direct costs were calculated from a German payer perspective (base year: 2017). In the base case only costs for FeNO measurement and asthma medication are taken into account. Extensive univariate and multivariate sensitivity analyses explored uncertainty in the model.

**Results:** Despite additional cost for FeNO measurement in asthma diagnosis, the base case demonstrated that routine use of FeNO measurement resulted in cost savings of approx. 2EUR in year 1-25 EUR in year 5 per asthma patient compared to standard diagnostic methods. Incorporating costs for hospitalization, physician visits and standard tests, the savings increased to 4EUR in year 1-31 EUR in year 5. Sensitivity analyses showed the robustness of the model and cost savings in all scenarios at least from the second year onwards.

**Conclusion:** FeNO measurement as an add-on option in asthma management to identify asthma patients with Th2 driven airway inflammation is less costly than the use of standard diagnostic methods. New biologics may have an additional impact on overall asthma treatment costs. Our model demonstrates that incorporating FeNO measurement may help to optimize asthma medication and reduction in physician visits as well hospitalizations due to severe exacerbations.

## 1294 | Peripheral airway inflammation assessed by fractional measurement of the exhaled breath temperature is a leading feature of asthma

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**Background:** Airway inflammation is considered to be a hallmark of asthma. The potential clinical benefits of assessing it non-invasively has led us to develop a method and device for measuring the temperature of the exhaled breath (EBT=exhaled breath temperature) reflecting the thermal state of the airway mucosa. Studies have demonstrated that EBT is increased in asthma, proportionately to the level of control of the disease. In an attempt to further increase the usefulness of this approach, we have further developed a device to allow the assessment of the relative contribution of the central and peripheral airways (Caw and Paw). Now we present the FrEBT data gathered from patients with suboptimal control of their asthma and from healthy subjects.

**Method:** In this cross-sectional study we included 120 volunteers: 71 patients with suboptimally controlled asthma of mild to moderate severity (median age 44, range 18-68 years, 31 men) and 49 non-smoking subjects without respiratory disease (median age 49, range 18-70 years, 17 men). We measured the fractions corresponding to Caw and Paw sampled with a fast reacting inflatable balloon valve system operated by a computer during a single breathing cycle. It allows steering of the expired airflow through channels with sensitive temperature sensors. During an initial deep inhalation, the inspired volume is measured and the sequence of valve openings is adjusted so as to yield volumes of air characteristic of Caw or Paw during expiration. The ratios between [PawEBT-CawEBT] over the total EBT [%] measured during the same manoeuvre (fractional EBT, frEBT) were calculated and compared between asthmatics and controls.

**Results:** There was high statistically significant difference between the frEBT ratios of asthmatics and controls: 16.25 ± 0.51 (mean ± SEM) vs 12.66 ± 0.28, $P < 0.001$. As the magnitude of the ratio depends on the difference between PawEBT and CawEBT, higher values of the frEBT ratio point to bigger contribution of the peripheral lung tissues, presumably indicative of peripheral inflammation. Multiple regression analysis with frEBT ratio as dependent variable identified only asthma diagnosis as significant predictor ($P < 0.001$) and excluded all other anthropometric indices.

**Conclusion:** Peripheral airway inflammation assessed by frEBT measurement appears to be a leading characteristic in asthmatics compared to healthy subjects.

## 1295 | Hypersensitivity to inhalant allergen in patients with severe asthma and fixed airway obstruction

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**Background:** Many of patients with severe asthma have fixed airway obstruction (FAO) defined as postbronchodilator FEV1/FVC<0.7. However, little is known about hypersensitivity to inhalant allergens in severe asthmatics with FAO. The aim of this study was

to assess the hypersensitivity to inhalant allergens in patients with severe asthma who have FAO.

**Method:** We examined 142 outpatients (30% male, aged 18-82 year, mean age 54.7 years) with severe asthma according to ERS/ATS (2014) definition treated with high dose of ICS/LABA± tiotropium, antileukotrienes and omalizumab. Some patients (n = 21) had orally steroid-dependent asthma. They referred to our secondary care center by GPs. Pulmonary function tests were measured by dry spirometer (2120, Vitalograph Ltd., UK). Skin prick tests or serum specific IgE to common inhalant allergens (house dust mite, animal dander, pollen) were used to assess atopic status.

**Results:** Seventy five percent (n = 107) of patients with severe asthma had FAO in 50% of those was diagnosed concomitant COPD. Duration of asthma was 14.6 years in patient with reversible airway obstruction (RAO) and 14.5 years in those with IAO ($P > 0.05$). Early (before age 12 years) onset of asthma was established in 13% of patients with RAO and in 9% of patients with FAO ($P > 0.05$). Prevalence of atopy did not differ between both groups (81% vs 81%, $P > 0.05$) but total IgE level in serum was higher in severe asthmatics with RAO than FAO (924 ME/mL vs 330 ME/mL respectively, $P < 0.01$). Most of atopic patients with severe asthma both with FAO (91%) and ROA (83%, $P > 0.05$) were sensitized to house dust mites (D. pteronyssinus and D. farinae). Hypersensitivity to pollen was diagnosed in 36% patients with FOA and in 17% with RAO ($P > 0.05$), to cat and dog dander in 49% and 25% respectively ($P < 0.05$).

**Conclusion:** The majority (75%) of patients with severe asthma had FAO. Hypersensitivity to house dust mites was most common in severe atopic asthmatics with FOA and ROA where as sensitization to animal danger was associated with presence of FOA.

## 1296 | Loss of smell as a clinical marker of severe asthma and its association with upper airway inflammatory diseases

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**Background:** Asthma is frequently associated with rhinitis and chronic rhinosinusitis (CRS) while severe asthma is more associated with CRS with (CRSwNP) than without (CRSsNP) nasal polyps. Loss of smell (LoS) is associated with CRS, mainly with CRSwNP.
We aimed to assess loss of smell as a clinical marker to discriminate CRS from rhinitis and severe from non-severe asthma.

**Method:** In a cross-sectional multicentric study, asthmatic patients (N = 383) were evaluated by pulmonologists and ENT specialists using GINA, ARIA, and EPOS definitions. LoS was evaluated by severity [VAS scale, 0-100 mm, median (IQR,Inter-Quartil Range)] and by prevalence of anosmia (hyposmia VAS >0-70 mm, anosmia VAS>70 mm).

**Results:** LoS was present in 55.4% of asthmatics (hyposmia 41.5%, anosmia 14.9%). LoS was more severe [22 mm (0-75), $P < 0.001$] and anosmia more frequent (26.4%, $P < 0.001$) in severe persistent asthma than in moderate [10 mm (0-50); 11.4%] mild [0 mm (0-28); 10.7%], or intermittent [0 mm (0-45); 8.6%] asthma. In addition, LoS was more severe [38 mm (2-76) vs 0 mm (0-20), $P < 0.001$] and anosmia more frequent [28.1% vs 3.9%, $P < 0.001$] in CRS than in rhinitis patients. In those asthmatic patients with CRS, LoS was even more severe [50 mm (11-89) vs 20 mm (0-56) $P < 0.001$] and anosmia more frequent (40.6% vs 13.4%, $P < 0.001$) in CRSwNP than in CRSsNP.

**Conclusion:** Loss of smell and specially anosmia may clearly discriminate severe from non-severe asthma and CRS (specially with NP) from rhinitis alone in asthma patients. Thus, LoS may be considered a significant clinical marker of severe asthma and its association with upper airway inflammatory diseases.

## 1297 | Last station in the eosinophilic asthma with chronic rhinosinusitis and/or nasal polyposis march: Eosinophilic asthma with radiological findings associated with blood eosinophilia

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**Background:** Eosinophilic asthma with chronic rhinosinusitis and/or nasal polyposis (EACRS/NP) is a subphenotype of adult-onset eosinophilic asthma. Blood eosinophil levels are shown to be highly elevated in patients with EA-CRS/NP and have potential for tissue infiltration. We aimed to demonstrate the clinical features of the patients who have a blood eosinophil level above 10% and have thorax computed tomography findings due to blood eosinophilia.

**Method:** Patients who were followed up in our clinic between 2012-2017 were retrospectively evaluated. Inclusion criteria were as follows: (a) Eosinophilic severe asthma; (b) Eosinophilia >10%; (c) Chronic sinusitis and/or nasal polyps; (d) Patients with pathologic findings on thorax computed tomography; (e) Regular follow-up for at least 1 year.

**Results:** We identified 36 patients who met the above criteria. We defined this group as "Eosinophilic Asthma with chronic Rhinosinusitis and/or nasal polyposis with Radiological findings related to blood eosinophilia" (EARR). The mean age was 44.9 ± 11 years and 64% was female. Nasal polyps, aspirin exacerbated respiratory disease and atopy was present in 81%, 47% and 25% of the patients,

respectively. The mean blood eosinophil count was 1828.6 cells/mm$^3$ (19%). The majority of EARR patients had upper lobe dominant ground-glass opacities. The mean follow-up period was 3.2 ± 2.5 years. EARR patients did not evolve into eosinophilic granulomatous polyangiitis in the follow-up.

**Conclusion:** This phenotype is the first eosinophilic asthma subphenotype reported in the literature. EARR is the final stage of the allergic march of EA-CRS/NP.

## 1298 | Biomarkers to distinguish asthmatics among those diagnosed as Asthma and COPD Overlap (ACO)

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**Background:** Asthma and COPD Overlap (ACO) is nosological entity of describing patients with concomitant presence of bronchial asthma and Chronic Obstructive Pulmonary Diseases (COPD). Its definition is quite nebulous and vague, possibly leading clinicians to an overdiagnosis of ACO. Therefore, ACO is still a diagnostic challenge as there are no specific biomarkers to differentiate it from asthma or COPD.

**Method:** We aimed to identify features more probably associated with asthma in a unselected group of patients with diagnostic criteria for ACO. We consecutively selected the first 10 consecutive patients with diagnostic criteria for ACO. All patients were evaluated by accurate clinical history interview, assessment of Asthma Control Test (ACT) and COPD Activity Test (CAT), lung function and exhaled nitric oxide ($FE_{NO}$) measurements, sputum cytology, blood eosinophil count, serum total IgE and periostin levels, methacholine and adenosine-mono-phosphate (AMP) bronchial challenges. All these measures were repeated after an oral corticosteroid (OCS) trial of methylprednisolone 32 mg/day for 14 days. We defined 9 parameters that we expected improved after the OCS trial, and therefore considerable as markers of asthma: $FEV_1$, $FEF_{25-75}$, $FEV_1$/FVC, $FE_{NO}$, ACT, sputum and blood eosinophilia, methacholine and AMP challenges. Patients with improvement of at least 4 of these parameters after OCS trials were defined as "responders" to the treatment, and therefore more likely to be asthmatic than COPD or ACO.

**Results:** Five (50%) patients were classified as responders and they were characterized by having basal higher $FE_{NO}$ values (102.8 ± 34.2 vs 13.6 ± 3.5 ppb, $P = 0.032$), greater bronchial reversibility (12.2 ± 2.3 vs 4.4 ± 2.2%$FEV_1$ improvement, $P = 0.04$), and significant reduction in AMP bronchial sensitivity after OCS ($PD_{20}FEV_1$ improvement correlated with the number of significantly improved parameters; $R^2 = 0.825$, $P = 0.004$). Receiving Operating Characteristics (ROC) curves for the response to OCS trial show that $FE_{NO}$ and the degree of bronchial reversibility had Areas Under the Curves (AUC) of 0.96 and 0.84 respectively.

Basal values of serum periostin and total IgE, and blood eosinophils were higher in responders but without reaching the statistical significance.

**Conclusion:** $FE_{NO}$ and the degree of bronchial reversibility (and possibly also the degree of response to an AMP challenge) are reliable biomarkers to distinguish asthmatics among those with suspect ACO.

## 1300 | Altered serum adipokines in obese asthmatic subjects in Eastern India

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**Background:** Obesity is one of the major risk factor for the development of asthma and plays a pivotal role in disease control, severity and considered to be a state of chronic low-grade systemic inflammation, characterized by a dysbalance of pro- and anti-inflammatory proteins derived from fat tissue cells. On the other hand, adipokines which play an important role in systemic inflammation have been also linked to the development of asthma and disease severity. The aim of our study was to address the association between serum leptin or serum adiponectin in obese asthmatic subjects and non-obese asthmatic subjects in eastern India.

**Method:** The preliminary case-control study included 52 obese persons with asthma who were matched for age and sex and 48 non-obese asthma subjects. Non fasting serum levels of adiponectin, and leptin were measured by commercially available immune assay kits, and routine biochemical parameters were analyzed in both the study groups.

**Results:** The results show statistically significant lower levels of serum adiponectin and higher serum leptin levels in obese asthma subjects with respect to non-obese asthma patients ($P < 0.001$). Moreover, an inverse correlation was also observed between serum adiponectin and serum leptin in obese asthma subjects ($P < 0.05$).

**Conclusion:** Our results indicate the association of these hormones might act as a significant predictor in the progression of asthma. Moreover, the role of serum adipokines is promising and might potentially act as a meaningful drug target in the pathogenesis of asthma.

## 1302 | Association between serum leptin and control of asthma in adult Lebanese atopic asthmatics: A real-life study

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**Background:** Overweight/Obesity is known to be a possible factor for poor asthma control. The aim of the study is to determine the serum concentrations of leptin in atopic asthmatic patients and its relationship with body mass index (BMI), asthma severity defined by medical treatment and asthma control defined by the Asthma Control Test (ACT).

**Method:** We randomly selected 33 adult patients previously diagnosed with allergic asthma based on GINA (global initiative for asthma) guidelines, returning for follow-up to an outpatient allergy/immunology clinic during November 2017. Following an informed consent, the patients were asked to fill ACT, their BMI was recorded, and ELISA blood assays for leptin were drawn. Exploratory data analysis, Spearman's correlation (95% CI by bootstrapping), and partial correlations were performed.

**Results:** Female/male ratio was 24/9, mean BMI was 27.2 ± 4.2 Kg/m², and mean ACT was 14.8 ± 4.4. Median serum Leptin level was 63.6 [IQR 18.9-97.5] ng/mL. Leptin distribution unfolded in 2 sub-distributions, essentially driven by gender, with an empirical 50 ng/mL cut-off laying 8 men leftwards and 17 women rightwards to the cut-off. Leptin was correlated significantly with BMI [$r$ = 0.54, 95% CI 0.27-0.72], and was inversely correlated with ACT [$r$ = −0.25, 95% CI −0.58 to 0.12] but missed significance. Partial correlation between leptin and ACT adjusted on BMI and gender yielded a weak non-significant effect size [0.13, 95% CI −0.25 to 0.42].

**Conclusion:** Leptin was significantly associated with overweight/obesity in asthmatic subjects, and showed higher values for women. Leptin inverse correlation with ACT did not reach statistical significance, likely owing to underpowered estimates, in a small sample characterized by an elevated mean BMI and severe allergic asthma.

## 1303 | Investigation of low immunoglobulin level in pre-school recurrent wheezing discovery

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**Background:** Immunoglobulin lowering may be associated with recurrent wheezing symptoms and clinic by increasing the tendency to viral respiratory tract infections. In this study, it was aimed to investigate the frequency of immunoglobulinemia in preschoolers with wheezing.

**Method:** The study was conducted between 01.01.2013 and 01.01.2016 between. University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, The Children Allergy and Immunology Clinic included patients who had been followed up and treated for at least one year with recurrent wheezing attacks within younger than 48 months. The immunoglobulin (G, A, M) values of the patients were retrospectively analyzed. Immunoglobulin levels were determined to be normal and low according to age limits.

**Results:** The study included 585 patients (65.6% male, 34.4% female) under the age of 6 years with a mean age of 26.9 months. The mean follow-up period of the patients is 2.2 years. In 33.7% of these patients, at least one immunoglobulin was found to be low. None of these patients had any signs or symptoms of immunodeficiency. Immunoglobulin A was low in 21% of the patients, immunoglobulin G in 18%, and immunoglobulin M in 7.5% of all patients.

**Conclusion:** Immunoglobulin was found to be low in these patients when there was no immunodeficiency and preschool wheeze was diagnosed. This should be etiologically investigated as to whether if this is a special group in preschoolers with recurrent wheezing and hypogammaglobulinemia combination.

## 1304 | Prognostic factors in severe eosinophilic asthma

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**Background:** Uncontrolled Severe Asthma represents a challenging health problem. Characterized variables that can predict poor control would improve its management.

**Method:** Asthma Severe Unit is formed by allergists, pneumologists, pediatricians and otorhinolaryngologists. Hematologists and immunologists make specific collaborations. We present the partial results of our data collection, which include 75 patients with severe asthma according to ERS/ATS task force, selected by peripheral eosinophils >220 according to Wagener et al. We followed them up to assess control for 1 year. We obtained cellularity in sputum using induced sputum technique. Values of IL of TH2, TH1, TH17 pathway, periostin and ILC were not yet available.

**Results:** Median age was 36 ± 24, FeNO 45 ± 34, exacerbations previous year 1.8 ± 2.4, ACT 17.7 ± 5, FEV1 75% ± 21 and dose of inhaled corticoids (budesonide equivalent) 1235ug ± 618. Most of the patients were sensitized (78%) and 15.9% were polysensitized. The most frequent sensitization was dust mites (81%). 27% had received immunotherapy of whom 35.3% with lack of response. Not sensitized patients were older.

Sputum cell analysis of 54 patients was performed, 37% had sputum eosinophils>3%, mean sputum eosinophil value was 4.1 ± 4.7 and peripherally 518 ± 384. Correlation among sputum and peripheral eosinophilia was 0.097 ($P = 0.485$). The peripherally eosinophil value >220 had a sensitivity of 80% and a specificity of 54% for the detection of sputum eosinophils >3%. No differences were observed in sputum cell count depending on allergic sensitization.

64% had an uncontrolled asthma. Presence of polysensitization, rhinitis or polyposis were not statistically related with the control.

Different patterns were observed in function of cause of poor control:

Patients with obstructive pattern (FEV1 < 80%) were older and received more inhaled treatment. Patients with high rate of exacerbations had more sputum eosinophilia and neutrophilia. Both groups had worse ACT and received more oral steroids.

Patients who received oral steroids were more often sensitized to fungi in some follow-up visits.

Not significant differences were observed in control according to the ACT.

**Conclusion:** Patients with Eosinophilic Uncontrolled Severe Asthma had more sputum neutrophilia, were older, received higher inhaled steroids dose and had adult onset asthma. The only control variable related with sputum eosinophilia was exacerbation. Fungi sensitization was more frequent among patients with oral steroids.

TUESDAY, 29 MAY 2018
TPS 40
TREATMENT OF ASTHMA

## 1305 | The effect of carboxymethyl-glucan as adjunct on step up treatment in asthma control test score & fev1 in adult asthmatic patients: Emanuel study: Randomized, double blind, controlled

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**Background:** Asthma is a common, chronic pulmonary disease affecting 1%-18% of the population worldwide.[1] It is characterized by shortness of breath, wheezing, coughing, chest tightness and a variable expiratory airflow limitation. The presence of airway inflammation is a consistent feature in asthma caused by hyperresponsiveness to a number of host and environmental factors. Immunomodulation to reduce the inflammation process is one of the postulated approaches to treatment. However, there are only a few studies showing the significance of adding an immunomodulator such as CM Glucan as add on treatment to the usual LABA/ICS for partly or uncontrolled adult asthmatic patients. This study determined the effect of CM glucan in preventing asthma among adults.

**Method:** A randomized, double blind, placebo controlled study with 80 patients from the De La Salle University Medical Center with a mean age of 44 with partly or uncontrolled asthma. They were assigned to either cm glucan or placebo group for two months. ACT score and %FEV1 postbronchodilator were assessed at the 1st visit, 4th week follow up, and 8th week follow up visits. An independent and paired t-test were used to determine mean changes in ACT Scores and %FEV1 between the groups.

**Results:** In the two treatment groups, those in the CM glucan group had a greater % FEV1 mean change of −6.95 compared to placebo which had only −14.1, a mean difference of −7.15, and a trend toward significance with a t-test *P* value of 0.061. In terms of changes in ACT score, those in the CM glucan group had a mean change of 10.12 and 9.75 for placebo, a mean difference of 0.37 and was not significant at *t* test *P* value of 0.718.

**Conclusion:** The result of the EMANUEL trial showed a trend of improvement among patients on both groups in terms of ACT score and %FEV1 postbronchodilator. However, it was not statistically significant.

## 1306 | Lung function improvements with tiotropium in patients across all ages: Impact of episodes of asthma worsening during phase 3 trials

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**Background:** Tiotropium add-on therapy has demonstrated efficacy and safety in patients with symptomatic asthma despite ICS ± other controllers. Here, we describe the lung function of patients who experienced episodes of asthma worsening vs those who did not during Phase 3 trials of tiotropium.

**Method:** *Post hoc* analyses involved 6 Phase III, randomized, double-blind, placebo-controlled trials: 4 in patients aged 6-17 years (RubaTinA-/CanoTinA-/VivaTinA-/PensieTinA-asthma) who received tiotropium (5 or 2.5 μg) or placebo, as two puffs once-daily via the Respimat, as add-on to ICS ± other controllers; and 2 in adults (PrimoTinA-asthma replicate trials) who received once-daily tiotropium 5 μg or placebo, as add-on to ICS/LABA ± other controllers. We analyzed change from baseline for peak $FEV_{1(0\text{-}3h)}$ and trough $FEV_1$ at Week 12 in VivaTinA- and PensieTinA-asthma, and Week 24 in PrimoTinA-/RubaTinA-/CanoTinA-asthma, comparing patients with and without episodes of asthma worsening during the trials. Asthma worsening was defined as an episode of progressive increase in day-to-day asthma symptoms (recorded by patients and confirmed by the investigator) or a decrease of patient's best morning PEF ≥30% from mean for ≥2 consecutive days. As a *post hoc* analysis, *P* values are nominal.

**Results:** There were no differences in baseline disease characteristics between those who experienced episodes of asthma worsening and those who did not, within specified age and asthma severity groups. Placebo-adjusted lung function improvements were observed with tiotropium 5 μg in patients who experienced episodes of asthma worsening and those who did not during the trials (Table 1).

| Tiotropium dose | PrimoTinA-asthma (adults; severe asthma) | | | RubaTinA-asthma (12-17 years; moderate asthma) | | | PensieTinA-asthma (12-17 years; severe asthma) | | | CanoTinA-asthma (6-11 years; moderate asthma) | | | VivaTinA-asthma (6-11 years; severe asthma) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N (Tiotropium/placebo) | Overall (422/429) | Asthma worsening (216/278) | No asthma worsening (206/151) | Overall (131/137) | Asthma worsening (29/37) | No asthma worsening (102/100) | Overall (130/132) | Asthma worsening (15/24) | No asthma worsening (115/108) | Overall (134/126) | Asthma worsening (57/66) | No asthma worsening (77/60) | Overall (128/130) | Asthma worsening (34/46) | No asthma worsening (94/84) |
| 5 µg 95% CI, mL P value | 110 (63, 158) <0.0001 | 77 (13, 140) 0.0182 | 137 (64, 209) 0.0002 | 174 (76, 272) 0.0005 | 160 (−59, 380) N/S | 163 (55, 272) 0.0032 | 90 (−19, 198) N/S | 87 (−163, 338) N/S | 67 (−52, 186) N/S | 164 (103, 225) <0.0001 | 135 (47, 223) 0.0029 | 165 (79, 250) 0.0002 | 139 (75, 203) <0.0001 | 169 (41, 297) 0.0099 | 117 (42, 191) 0.0022 |
| N (Tiotropium/Placebo) | N/A | N/A | N/A | 120/137 | 34/37 | 86/100 | 126/132 | 18/24 | 108/108 | 131/126 | 60/66 | 71/60 | 135/130 | 28/46 | 107/84 |
| 2.5 µg 95% CI, mL P value | N/A | N/A | N/A | 134 (34, 234) 0.0085 | −49 (−262, 164) N/S | 176 (63, 289) 0.0023 | 111 (2, 220) 0.0457 | 72 (−164, 307) N/S | 101 (−19, 222) N/S | 170 (108, 231) <0.0001 | 199 (112, 286) <0.0001 | 118 (32, 205) 0.0076 | 35 (−28, 99) N/S | −3 (−141, 135) N/S | 18 (−55, 91) N/S |

CI, confidence interval; $FEV_{1(0\text{-}3h)}$, forced expiratory volume in 1 s within 3 h post-dose; N/A, not applicable; N/S, not significant.

There was some variability in subgroups with low numbers of patients.

**Conclusion:** Once-daily tiotropium add-on had a similar efficacy in adult and pediatric patients with symptomatic asthma, irrespective of whether they experienced episodes of asthma worsening or not during the trials. These data support the broad efficacy of tiotropium and show largely consistent improvements in lung function even in patients who experience episodes of disease worsening.

## 1307 | Cochrane review of the use of antibiotics for acute exacerbations of asthma

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**Background:** Asthma is a chronic respiratory condition affecting over 300 million adults and children worldwide. It is characterised by wheeze, chest tightness, shortness of breath and exacerbations. Acute exacerbations of asthma can be serious, leading to hospitalisation or even death, and may be triggered by various factors. Bacterial infections are responsible for a minority of exacerbations and current guidance states that antibiotics should be reserved for cases with clear evidence of bacterial infection. This Cochrane systematic review aimed to determine the randomised controlled trial evidence for the use of antibiotics vs placebo or usual care in acute exacerbations of asthma.

**Method:** We searched the Cochrane Airways Trials Register, trial registries and reference lists of primary studies. We extracted outcome data and assessed risk of bias in duplicate and used current Cochrane methodology throughout. Our primary outcomes were intensive care unit (ITU) admission, duration of symptoms/exacerbation and adverse events.

**Results:** We included six studies, including a total of 681 adults and children. Trials were of varied methodological quality and we were able to perform only limited meta-analysis. One study reported a single ITU admission but no other studies reported admissions to ITU. Two studies investigating macrolides reported diary card symptom score and showed antibiotics improved symptoms (MD −0.34, 95% CI −0.60 to −0.08). One study including 40 participants reported more symptom-free days in the macrolide group than usual care. One study of a penicillin including 69 participants reported asthma symptoms at hospital discharge; the between group difference was reported as non-significant. Serious adverse events were rare; 10 events were reported across the three trials (n = 502). The pooled effect estimate for all adverse events from three studies was imprecise (OR 0.99, 95% CI 0.69-1.43). No deaths were reported.

**Conclusion:** We found limited evidence that antibiotics given for asthma exacerbations may improve symptoms compared to standard care or placebo. However, findings were inconsistent across the six studies and we have low confidence in the results. Importantly, many participants in the included trials would not have met the current guidance criteria for receiving antibiotics.

## 1308 | Clinical utility of mepolizumab in real-life practice in severe asthma unit of Madrid (Spain)

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**Background:** Mepolizumab is a humanised monoclonal antibody (IgG1, kappa) against interleukin-5 (IL-5). This cytokine join in the growth, differentiation, recruitment, activation and survival of eosinophils. Mepolizumab decreases eosinophils production and survival by blocking the binding of IL-5 to the alpha chain of the IL-5 receptor complex on the eosinophilic cell surface. Therefore mepolizumab is indicated in patients with uncontrolled severe eosinophilic asthma.

**Method:** A retrospective and observational study based on medical record reviews of adults with refractory severe eosinophilic asthma criteria (ATS/ERS criteria of uncontrolled severe asthma and >150 eosinophils/μL) treated with mepolizumab was addressed. Quality of life and asthma control questionnaires (MiniAQLQ and ACT), number of exacerbations, pulmonary function (FEV1), percentage of reduction of systemic corticosteroids and eosinophils counting were recorded at baseline and after week 24 of treatment. We also monitorized the adverse events.

**Results:** 11 patients were enrolled (5 patients were previously receiving omalizumab without clinical response). 5 of 11 patients were on chronic treatment with oral corticosteroids. The main side effects registered were upper airway infections, arthromyalgias, night sweating and headache. We discontinued the treatment in two patients (3rd and 4th doses respectively) due to severe side effects such us upper airway infections and severe arthromyalgias. Finally, clinical and laboratory parameters were analyzed in 9 patients who received at least 24 weeks of treatment. Mean FEV1 increased up 86.67 mL (−630, 1120). ACT and Mini AQLQ results improved in 6 of 9 patients. Mean ACT and MiniAQLQ tests increased up 4.33 points (−8, 14) and 1 point (−1, 2.65) respectively. Clinically significant exacerbations decreased in 8 of 9 patients. The exacerbation rate reduction was 58%. The use of oral corticosteroids was also reduced in 75% of patients with complete withdrawal in two of them. The counting of eosinophils decreased in 100% of patients, with a mean reduction rate up 92.1% (75%, 100%) in the eosinophils count.

**Conclusion:** Mepolizumab can be an effective therapeutic option in uncontrolled severe eosinophilic asthma patients in clinical practice.

## 1309 | Clinical efficacy of anti-IgE therapy in adult patients with atopic severe uncontrolled asthma in real practice

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**Background:** The assessment of clinical efficacy and safety of anti-IgE therapy in patients with atopic severe uncontrolled asthma within 12 months.

**Method:** In 2016 was created a register of patients requiring anti-IgE therapy (38 patients) on the basis of the Regional Clinical Hospital #4 in the Chelyabinsk city. Since November 35 patients received omalizumab - 9 men (26%) and 26 (74%) women aged 18-63 years, average age 44.5 years, the duration of the disease 25.2 years. All patient were examined by allergologist and diagnosed concomitant allergic pathology: allergic rhinitis—in 100%, atopic dermatitis - in 26.5%, food allergy in 44.1%, polynosis in 79.4%. The level of total IgE in the blood from 72 to 787 IU/mL. High sensibilization to household (88.6%), epidermal (62.9%) and pollen (74.3%) allergens was revealed. All patients received basic combined therapy of ICS and LABA in high doses, IV-V stage of therapy. 28 (82.4%) patients additionally took systemic CS, 19 (55.9%) took antileukotriene drugs and 12 (34.3%) took tiotropium.

**Results:** During 12 months of therapy with omalizumab (the drug was administered in accordance with the level of IgE and body weight) were not severe exacerbations requiring hospitalization and administration of systemic CS. The expression of daytime symptoms decreased by 94.8%, nighttime symptoms decreased by 94.5%. The need for using SABA for arresting asthma attacks decreased by 95.8%. The quality of life of patients was significantly improved by the results of the ACT test: 5.6 (95% CI 5-6.8) vs 20.3 (95% CI 17-23.5), $P < 0.001$ and the ACQ-7 questionnaire: 3.7 (95% CI2.5-4.8) vs 1.51 (95% CI 0.57-3.4), $P < 0.001$. In 71.3% of patients did not become symptoms of allergic rhinitis. There was a statistically significant increase in FEV1 −61.1% (95% CI 30.3-96.5) vs 82.8% (95% CI 46.1-115.6), $P < 0.01$. Against the background of treatment adverse events and adverse reactions is not recorded.

**Conclusion:** The use of omalizumab in addition to basic therapy in patients with severe atopic uncontrolled asthma along with significant clinical improvement allows us to achieve the normalization of the functional parameters the function of external respiration.

## 1310 | Omalizumab treatment in atopic severe persistent asthma: A single center long-term real-life experience with thirty eight patients

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**Background:** Omalizumab is a monoclonal antibody that is used as add-on therapy for moderate to severe persistent atopic asthma in patients with persistent symptoms and frequent exacerbations despite step 4 treatment according to GINA guidelines. Real life studies on this treatment option for our country are limited. For this reason, this study aims to assess the clinical efficacy and treatment outcomes of omalizumab in atopic severe persistent asthma.

**Method:** Patients with atopic severe persistent asthma that were treated with omalizumab between 2009-2017 were retrospectively evaluated. We noted and compared baseline and last results of; symptom scores (GINA categorical), controller medications, blood eosinophil counts, forced expiratory volume in one second ($FEV_1$) values and the number of exacerbations that were treated with systemic corticosteroids at least 3 days within last 1 year. Effect of co-existing aspirin exacerbated respiratory disease (AERD) on these parameters was also analyzed. Step-down of other asthma medications were tried in patients with symptom control and without exacerbation history within last 6 months.

**Results:** Thirty-eight patients (mean age 50 years, 30 were female) were included in the study. Four had AERD. After treating with a mean time of 30 ± 22.1 months (min: 6, max: 92 months), 26 (68%) became controlled and 12 partly-controlled (32%), of whom all were uncontrolled before. Mean exacerbation rates within last 1 year were ~78% decreased (8.7 ± 8 vs 1.7 ± 1.5; $P < 0.001$) and $FEV_1$ values were ~14% increased (2075 ± 729 cc vs 2321 ± 800 cc; $P = 0.001$) as compared to baseline levels. Although the reduction in eosinophil count were not significant in all patients (503.8 ± 524.8 vs 370.8 ± 314.5; $P = 0.134$), repeated measures analysis of variance showed a more prominent reduction in eosinophil count in AERD group than non-AERD group independent from the treatment period (F:4.23, $P = 0.049$). Mean inhaled corticosteroid dose (budesonide eq. 1063 ± 397 μg vs 958 ± 439; $P = 0.084$), number of other controller medications and patients with long-term systemic steroid use were decreased after omalizumab therapy. No serious adverse events were recorded during the follow-up period.

**Conclusion:** Our results confirmed that omalizumab significantly improves disease control and is a safe add-on therapy. Also in appropriate patients with controlled disease over time, efforts to step-down other asthma medications will be appropriate.

Table 1 - Patient characteristics and clinical findings at baseline

| | N = 38 |
|---|---|
| Age; years ± SD | 50 ± 10.8 |
| Female gender; n (%) | 30 (79) |
| Median serum total IgE; IU/mL ± SD | 173 (101.8-410) |
| Serum eosinophil count; cells/mL ± SD | 503.8 ± 524.8 |
| Upper respiratory tract involvement; n (%) | |
| None | 5 (13) |
| Chronic rhinitis | 29 (76) |
| AERD | 4 (11) |
| Treatment duration; months ± SD | 30 ± 22.1 |
| Allergen sensitization status; n (%) | |
| Mite | 31 (82) |
| Pollen | 11 (29) |
| Dander | 2 (5) |
| Mold | 15 (40) |
| Single allergen sensitization | 17 (45) |

AERD: aspirin exacerbated respiratory disease; SD: standard deviation.

Table 2 - Comparison of baseline and last symptom scores, exacerbation rates, $FEV_1$ values and eosinophil counts

| | Baseline | Last | Mean change from baseline | P |
|---|---|---|---|---|
| Symptom scores (GINA) | 3.6 ± 0.5 | 0.5 ± 0.7 | −87% | <0.001 |
| Complete-control; n (%) | 0 | 26 (68) | | |
| Partial-control; n (%) | 0 | 12 (32) | | |
| Uncontrolled; n (%) | 38 (100) | 0 | | |
| The number of exacerbations that required SCS for at least 3 days within last 1 year ± SD* | 8.7 ± 8 | 1.7 ± 1.5 | −78% | <0.001 |
| $FEV_1$; % predicted ± SD | 77 ± 18.9 | 86.9 ± 21.2 | 15% | 0.001 |
| $FEV_1$; cc ± SD | 2075 ± 729 | 2321 ± 800 | 14% | 0.001 |
| Serum eosinophil count; cells/mL ± SD | 503.8 ± 524.8 | 370.8 ± 314.5 | −13% | 0.134 |

$FEV_1$: forced expiratory volume in one second; SCS: systemic corticosteroid; SD: standard deviation

*Within last 1 year or from the beginning of omalizumab depending on the duration of treatment.

## 1311 | Population health impact of omalizumab over 15 years of experience in moderate to severe allergic asthma

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**Background:** Asthma affects 334 million persons worldwide. 15 million days are lost due to disability from asthma every year. Omalizumab was first registered in Australia (in 2002 for moderate and 2005 for severe allergic asthma). Until 31st Dec 2016 the estimated exposure worldwide in adult patients was 516 481 patients-years. This analysis estimates the contribution of omalizumab to the reduction in worldwide asthma burden over 15 years.

**Method:** Reduction of asthma burden was estimated in asthma related deaths; exacerbations leading to hospitalization or Emergency Department (ED) visits and improvement in quality adjusted life years (QALYs). Cumulative asthma deaths avoided were calculated by applying exacerbation related mortality on exacerbations leading to: (a) hospitalization (b) hospitalization or ED visit. Annualized exacerbation rates and the QALY gain were based on Brown et al. 2007. Proportions of clinically significant severe exacerbations and of ED visits/hospitalizations by exacerbation type were based on the European registration trial (INNOVATE). Proportion of patients by age was based on a large observational study in 14 countries (eXpeRience) and age specific mortality risks were retrieved from Roberts et al. 2013.

**Results:** Over 15 years omalizumab reduced number of exacerbations leading to: (a) ED visits by 38 580 (2572 per year) and (b) hospitalizations by 74 024 (4935 per year). Overall avoided asthma deaths with type of exacerbation ranged from 527 to 802. At least 37 187 QALYs were gained. Limitations: only deaths avoided in secondary care were included; no inclusion of pediatric population exposed; generalization of mortality risks across different geographies.

**Conclusion:** On average each patient responding to omalizumab gained 1 year and 1 month of full health. Omalizumab reduced asthma deaths by 58% in secondary care. Continuous effort is necessary from all stakeholders to link access to effective treatments to appropriate disease management. Data for asthma mortality risk outside secondary care is warranted.

## 1312 | Effects of intranasal cellulose powder on asthma control in children with mild-to-moderate persistent allergic rhinitis: A single-center, randomized, placebo-controlled trial

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**Background:** Persistent allergic rhinitis (PAR) often co-exists in asthmatic patients. Intranasal cellulose powder (ICP) was reportedly effective in ameliorating PAR. We aimed to investigate whether ICP is equally effective compared with intranasal corticosteroids in improving asthma control as well as nasal symptoms among children with PAR and allergic asthma (AA).

**Method:** Between July 2015 and September 2016, we did a single center, randomized, placebo-controlled trial. Asthmatic children aged 6-14 years with mild-to-moderate PAR were randomly assigned to formoterol/budesonide inhalation (4.5 μg/80 μg, twice daily) plus intranasal budesonide 64 μg twice daily (group A), ICP 250 μg thrice daily (group B), or intranasal placebo 250 μg thrice daily (group C) for 8 weeks. The primary outcome was change in *Asthma Control Test for Children* (C-ACT) score from baseline to week 8 post-treatment. Changes in spirometry, peak expiratory flow (PEF), fractional exhaled nitric oxide (FeNO) and visual analogue scale (VAS) for nasal and ocular symptoms were detected as secondary outcomes.

**Results:** We included 121 patients (38 in group A, 41 in group B, and 42 in group C) in full-analysis set. C-ACT score was markedly higher at week 8 compared with baseline (mean difference: 5.11, 6.05, and 4.85 points in groups A, B, and C, respectively; $P < 0.05$). There were interactions between baseline and treatment in C-ACT scores ($P < 0.05$). Group B demonstrated greater improvement in C-ACT score than group C among children with baseline C-ACT score of 6-18. 95% CIs of group A at baseline overlapped with those of groups B and C. The treatment achieves reduced VAS symptoms in groups A and B but not in group C. Incidence of adverse events was comparable. No serious adverse event was reported.

**Conclusion:** ICP could be recommended for children with PAR and AA who have poorer asthma control.

Table 1 - Baseline characteristics of the full-analysis set

| Parameter | Treatment A | Treatment B | Treatment C | P value |
|---|---|---|---|---|
| No. | 38 | 41 | 42 | |
| Male (No., %) | 32 (84.2%) | 27 (65.9%) | 29 (69.0%) | 0.15 |
| Age (years) | 8.9 ± 2.0 | 8.0 ± 1.6 | 8.4 ± 1.9 | 0.08 |
| Height (cm) | 135.3 ± 13.1 | 127.3 ± 9.8 | 131.3 ± 11.8 | 0.01 |
| Weight (kg) | 31.4 ± 11.0 | 25.9 ± 6.0 | 29.8 ± 8.7 | 0.02 |
| Atopic family history * (No., %) | 23 (60.5%) | 29 (70.7%) | 32 (76.2%) | 0.31 |
| No. of allergen being sensitized | | | | 0.27 |
| Monosensitized | 7 (18.4%) | 6 (14.6%) | 12 (28.6%) | |
| Polysensitized | 31 (81.6%) | 35 (85.4%) | 30 (71.4%) | |
| Duration of allergic rhinitis (years) | 3.3 ± 2.0 | 3.4 ± 1.9 | 3.1 ± 1.5 | 0.73 |
| Duration of asthma (years) | 3.5 ± 2.4 | 3.1 ± 1.9 | 3.6 ± 2.1 | 0.57 |
| Total IgE (kU/L) | 675.7 ± 523.0 | 688.5 ± 555.3 | 762.8 ± 686.8 | 0.24 |
| Blood eosinophil (%)** | 7.4 ± 4.2 | 7.3 ± 4.9 | 8.3 ± 8.7 | 0.82 |
| Blood eosinophil (*$10^9$/L)** | 0.59 ± 0.36 | 0.54 ± 0.29 | 0.74 ± 0.66 | 0.26 |
| VAS for nasal symptoms | | | | |
| Sneezing | 2.3 ± 2.2 | 2.0 ± 2.3 | 2.3 ± 2.4 | 0.84 |
| Nasal discharge | 1.9 ± 2.3 | 2.1 ± 2.3 | 2.6 ± 3.0 | 0.40 |
| Nasal congestion | 1.7 ± 2.3 | 1.9 ± 2.5 | 2.0 ± 2.4 | 0.89 |
| Nasal itching | 2.2 ± 2.4 | 2.2 ± 3.1 | 1.6 ± 2.3 | 0.02 |
| Ocular symptoms | 1.4 ± 2.3 | 1.6 ± 2.4 | 1.6 ± 2.4 | 0.88 |
| Total | 9.5 ± 7.3 | 10.8 ± 9.2 | 10.1 ± 8.0 | 0.79 |
| C-ACT score | 19.6 ± 4.7 | 19.1 ± 3.6 | 18.6 ± 4.8 | 0.57 |
| $FEV_1$ predicted% | 90.4 ± 15.2 | 91.5 ± 12.6 | 91.1 ± 17.9 | 0.95 |
| $FEV_1$/FVC | 81.6 ± 9.1 | 83.8 ± 7.7 | 83.2 ± 8.8 | 0.48 |
| PEF (L/min) | 250.3 ± 63.9 | 228.1 ± 70.4 | 240.0 ± 72.0.7 | 0.36 |
| FeNO (ppb) | 44.5 ± 35.3 | 35.4 ± 27.5 | 38.6 ± 28.3 | 0.41 |

Data are n (%), mean ± SD or n/N (%). C-ACT: Asthma Control Test for children, FEV1: forced expiratory volume in one second; FEV1/FVC: the ratio of forced expiratory volume in one second to forced vital capacity, PEF: peak expiratory flow; FeNO: fractional exhaled nitric oxide, VAS: visual analogue scale

*These included allergic rhinitis, asthma, eczema, atopic dermatitis, food allergy, etc.

**There were 11, 13 and 18 missing data in treatment A, B, and C, respectively.

Table 2 - A list of sensitized aeroallergens in three treatments arms

| Aeroallergen | Total | Treatment A | Treatment B | Treatment C | P value |
|---|---|---|---|---|---|
| No. | 121 | 38 | 41 | 42 | - |
| Dermatophagoides pteronyssinus | 117 (95.1%) | 37 (97.4%) | 40 (97.6%) | 40 (95.2%) | 0.81* |
| Blatella germanica | 59 (48.0%) | 22 (57.9%) | 20 (48.8%) | 17(40.5%) | 0.30* |
| Cat dander | 20 (16.3%) | 8 (21.1%) | 7 (17.1%) | 5 (11.9%) | 0.54* |
| Dog dander | 51 (41.5%) | 16 (42.1%) | 18 (43.9%) | 17 (40.5%) | 0.95* |
| Cladosporium herbarum | 5 (4.1%) | 0 (0%) | 2 (4.9%) | 3 (7.1%) | 0.37# |
| Aspergillus fumigatus | 11 (8.9%) | 2 (5.3%) | 6 (14.6%) | 3 (7.1%) | 0.35# |
| Alternaria alternata | 10 (8.1%) | 6 (15.8%) | 1 (2.4%) | 3 (7.1%) | 0.10# |
| Birch | 12 (9.8%) | 5 (13.2%) | 4 (9.8%) | 3 (7.1%) | 0.64# |
| French Firmiana | 6 (4.9%) | 3 (7.9%) | 2 (4.9%) | 1 (2.4%) | 0.44# |
| Timothy grass | 6 (4.9%) | 1 (2.6%) | 3 (7.3%) | 2 (4.8%) | 0.78# |

All data were expressed as number (%) unless other stated and compared with chi-squared test.

*The *P* value was derived from the comparison among treatment A, B, and C by chi-squared test.

#The *P* value was derived from the comparison among treatment A, B, and C by fisher's exact test.

Table 3 - Adverse events

| | Treatment A | | Treatment B | | Treatment C | | |
|---|---|---|---|---|---|---|---|
| Adverse events | N | Percent (%) | N | Percent (%) | N | Percent (%) | P value |
| Total | 4 | 10.5 | 6 | 14.6 | 8 | 19.1 | 0.59 |
| **Study related** | | | | | | | |
| Nasal discomfort* | 1 | 2.6 | 4 | 9.8 | 5 | 11.9 | 0.34 |
| Epistaxis | 1 | 2.6 | 1 | 2.44 | 3 | 7.1 | 0.62 |
| AS exacerbations | 1 | 2.6 | 1 | 2.4 | 2 | 4.8 | 1.00 |
| AR exacerbations | 1 | 2.6 | 2 | 4.9 | 2 | 4.8 | 1.00 |
| Leading to withdrawal from the study | 0 | 0 | 2 | 4.9 | 2 | 4.8 | 0.55 |

*Nasal discomfort including nasal itching, sneezing and nasal stimulation.

## 1313 | Treatment with the SQ HDM SLIT-tablet improves quality of life in patients with allergic asthma

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**Background:** Asthma is a chronic inflammatory condition of the lower airways that causes coughing, wheezing, chest tightness and breathlessness. It is estimated that over 30 million people in Europe have asthma and 180 000 people die every year due to the disease. Allergic asthma (AA) is a common form of asthma and is triggered by inhalant allergens. House dust mite (HDM) is the most prevalent indoor allergen associated with AA worldwide.

AA in combination with allergic rhinitis (AR) has shown to have a negative impact on individuals' quality of life (QoL), measured by the Short-form health survey (SF-36v2) including 36 questions on health related quality of life.

This study examines the potential treatment effects of SQ® HDM SLIT-tablet on QoL measured by SF-36v2 in people with AA and AR.

**Method:** The analyses are based on data from the MT-04 trial (EudraCT no. 2010-018621-19) and utilize data from the 12 SQ-HDM treatment group (282 subjects) and the placebo group (277 subjects).

Throughout the trial, QoL was measured at each of visit 3-13 via SF-36v2. This yielded psychometrically-based physical and mental health summary measures, as well as a SF-36v2 total score. According to trial design, the use of inhaled corticosteroid (ICS) was reduced by 50% for a three months period (visit 10 and 11) and completely withdrawn for the last three months of the trial (visit 12 and 13).

**Results:** By estimating a simple regression on differences in SF-36v2 total score from baseline measurements (visit 3), a positive and statistically significant treatment effect on the overall QoL of the 12 SQ-HDM treatment compared to the placebo group in visit 9 and 10 was found.

Further analyses show that the QoL improvements are mainly driven by increases in the general mental health score, which are carried through to visit 12. In particular, the mental health and role emotional domains show statistically significant improvements.

**Conclusion:** The results show that the SQ® HDM SLIT-tablet improves QoL measured by SF-36v2 in patients with HDM induced AA and that this effect is driven by improvements in the mental health domains.

## 1315 | Impact of treatment prescription, adherence to treatment and use of inhalers in asthma control—Results of the EFIMERA study

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**Background:** Asthma exacerbation is one of the most frequent consultations in hospitals emergencies, and often it's due to bad asthma control. This study aimed to determine the proportion of patients that display the following factors which decrease therapy efficacy: inadequate or insufficient drug prescription, lack of adherence to pharmacological treatment and mistakes in use of different types of inhalers.

**Method:** Cross-sectional multicenter observational study conducted with patients who use any type of medication with inhaler devices. Patients referred from primary care and seen by a pneumologist or allergist for the first time were evaluated. The following data was collected in a single visit: adequate prescription according to GINA2015 guidelines (GINA); specific and general treatment adherence using Morisky-Green questionnaire (MG) and Inhaler Adherence Test (TAI); disease control with Asthma Control Test (ACT) and assessment of inhaler use technique were measured with the extended TAI.

**Results:** Patients included in this study (n = 1682) had a mean age of 45 ± 17 years, an average disease evolution of 14.9 ± 14.1 years, 64% of which were women. According to GINA recommendations, 35.9% of patients have insufficient or inadequate prescription. When measured by the MG test the 68.5% of patients showed bad adherence, meanwhile measured by the TAI test adherence was 76.8% Measurements of inhaler use technique resulted in 17% of patients having one or more mistakes regardless of whether the device was a MDI or DPI. Several factors showed to be related with bad asthma control: inadequate prescription (OR: 8.05 [5.74-11.27] *vs* GINA and OR: 3.65 [2.87-4.65] *vs* ACT), non-adherence to treatment (OR: 1.58 [1.23-2.03] *vs* GINA and OR: 1.8 [1.42-2.27] *vs* ACT) and inhaler

misuse (OR: 4.76 [3.08-7.34] *vs* GINA and OR: 3.03 [2.18-4.21] *vs* ACT), when performing a univariate Chi-Square analysis. When comparing the asthma control, regardless of the measuring tool (GINA or ACT), it was found that the higher the number of negative conditions, the higher the probability of having a bad controlled asthma, reaching a maximum of 93% with ACT and 100% GINA if all three conditions were met, and 46% with ACT and 54% GINA if none were met

**Conclusion:** In our cohort, one third of patients show insufficient or inadequate prescription, two third bad adherence to treatment, and one sixth inhaler technique mistakes. Overall, in case of patients that had all three conditions at least 90% odds of having bad asthma control were observed.

## 1316 | Asthmatics reported outcomes after switching from cigarette smoking to e-cig

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**Background:** It is well known that the constant and prolonged tobacco smoking affects the natural history of asthma.

Vaping is the act of inhaling and exhaling the vapor produced by an electronic device called e-cigarette (e-cig), whose basic structure includes a power source and an atomizer. two types of vaping are the most popular ("MTL" and "cloud chasing").

**Method:** We have created a web-survey with questions concerning epidemiological data, quality of life and symptoms worsening in asthmatic vapers. The survey has been advertised through various social networks and local press. 2403 people responded, including 437 asthmatics (18%).

The asthmatics were: Males 88%, under 18 3%, 18-25 years 36%, 26-30 years 19%, 31-65 years 42% and over 65 0%. 70% used e-cig-only, 30% smoked and vaped together, 0%. Those who preferred MTL-type of vape were 43% and "cloud chasing" were 57%.

**Results:** To the question: "Has vaping ever worsened asthma symptoms?" 90% answered no, 10% yes.

To the question: "As asthmatic, would you suggest to an asthmatic smoker to start vaping instead of smoking?" 1.3% answered no, 98.7% yes.

To the question: "How much nicotine do your vaping liquids have?" 15% answered 0 mg/mL, 4% 1.5 mg/mL, 62% 3 mg/mL, 11% 6 mg/mL, 6% 9 mg/mL, 1% 12 mg/mL and 0% 18 mg/mL.

To the question: "Do you take medications for your Asthma?" 57% declared to use a drug as needed, 0% used a single drug daily, 16% used more than one drug daily and 27% declared "I don't take any asthma medication".

We related ($\chi 2$ test) the worsening of asthma symptoms with the nicotine content ($P = 0.313$), the type of vaping ($P = 0.305$), the current therapy ($P = 0.123$) and we did not find a statistically significant correlation.

Vaping has undoubtedly shown an advantage in terms of improvement of symptoms compared to cigarette smoking ($P = 0.016$), in particular 82.5% subjects who smoke and vape did not have a worsening of symptoms, while 17.6% of them had a worsening. The vaper-only users who never worsened were 271 (90.6%) and 28 (9.4%) had a worsening.

**Conclusion:** Despite the limits related to the online survey as a data source, e-cigs seem to be a useful tool in the pathway to quit smoking. In fact, 98% of the asthmatics who smoked traditional cigarettes would recommend switching to e-cig and 90% did not worse their asthma symptoms.

## 1317 | Phenotypes of bronchial asthma and personalized therapy

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**Background:** Despite the success of pharmacotherapy, more than half of patients with persistent bronchial asthma (BA) do not achieve disease control. In recent years, the issue of approaches to treatment based on the identification of phenotypes of the disease has been increasingly discussed. This approach becomes the key to optimizing therapy for asthma, allowing the personification of treatment. Anti-IgE-therapy using omalizumab is one of the most researched variants of phenotype-specific treatment.

**Method:** Aim of our study was to investigate of the causes of uncontrolled predominantly atopic asthma, the frequency and effectiveness of the personalized therapy in real clinical practice. 54 patients with uncontrolled severe atopic asthma were examined in outpatient department of the city hospital during 2017. All patients underwent physical examination, pulmonary function testing, and total serum IgE evaluation.

**Results:** 35% of patients had uncontrolled asthma due to inadequate basic therapy of the disease. The change in therapy allowed them to achieve control of the disease. Obstructive sleep apnea syndrome (OSAS) was revealed in 11.1% of patients. These patients underwent CPAP (Continuous Positive Airway Pressure) therapy. 13% of patients had gastroesophageal reflux disease (GERD). 25% of patients had an elevated level of serum IgE level and needed anti-IgE therapy. In 7.4% of cases, the initial serum IgE level was more than 1500 IU/mL which was a contraindication to therapy of omalizumab. 8 patients received omalizumab therapy. This therapy led to relief of symptoms and decreased frequency of asthma exacerbations.

**Conclusion:** Patients with severe uncontrolled atopic bronchial asthma need a differentiated approach to diagnosis, evaluation of concomitant diseases and personalized therapy.

## 1318 | Features of clinical course and strategy of treatment for patients suffering from bronchial asthma in combination with obesity

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**Background:** Obesity considered as one of the risk factors for the development of bronchial asthma (BA) and the reasons for lack of control can probably influence the inflammation of the respiratory tract. However, the nature of these relationships needs to be clarified. The aim of the research was to characterise it clinically, functionally, allergologically and endocrinologically, to highlight the features of the course and to define the tactics of treating patients suffering from bronchial asthma in combination with obesity

**Method:** A statistical analysis of 367 patients treated in inpatient conditions due to exacerbation of asthma of various severity and different body mass index (BMI) was performed. 40 patients with BA who satisfied all inclusion criteria and did not have exclusion criteria were treated in outpatient conditions. Patients were divided into two groups. The main group consisted of 20 patients suffering from asthma and having a BMI of more than 30 kg/m$^2$. A control group consisted of 20 patients suffering from asthma and having a normal BMI.

**Results:** It was found that the prevalence of obesity among the 367 patients with asthma and being treated in inpatient conditions in 2013-2015 was 44.9% of patients, which is comparable to the prevalence of obesity among the population in general.

**Conclusion:** The data of the patients suffering from asthma and obesity treated both in inpatient and outpatient conditions, was analyzed and it is set that obesity does not affect the severity of the clinical course of asthma. It is shown that obesity does not affect the control of symptoms of asthma. Thus, the control of asthma symptoms depends on timeliness of diagnosis, the adequacy and terms of appointment of basic asthma therapy, the presence, severity and adequate treatment of concomitant diseases, psychoemotional background of patients, their compliance and adherence to therapy.

## 1321 | Features of smoking cessation in patients with bronchial asthma

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**Background:** Recent studies have shown that smoking contributes to the development of respiratory diseases and increases the risk of their severity. Our aim was to study the psychological characteristics of patients with asthma, to identify the most informative signs for assessing the early resumption of smoking.

**Method:** 50 asthmatics and 100 control group smokers with similar age were examined. The criterion for smoking cessation was the evaluation of exhaled carbon monoxide. Degree of nicotine dependence (ND, Fagerstrom test), motivation to smoking (Horn), level of anxiety and depression (hospital anxiety and depression scale - HADS), personal adaptive capacity (PAC), including behavioral regulation (BR), communicative features (CF) and moral normativity (Russian version of MMPI) were evaluated.

**Results:** The causes of smoking in asthmatics were not significantly different from the control ($P > 0.05$). Patients most often used smoking as "support for emotional stability". The motivation to smoking cessation was higher in the asthmatics group (58%) than in the control group. The main reason for smoking cessation was a deterioration in health - 60%. The majority of smokers - 85%, performed attempts for smoking cessation. Low level of BR was revealed in 90% asthmatics (27% non-smoking asthma patients and 18.5% of cases in the control group, $P < 0.001$), CF had low values and was lower in asthmatics group in compare to the control group ($P < 0.05$). The PAC values correlated with the level of BR: a low level was determined in 100% in smoking asthmatics, in 50% in non-smokers with asthma and 7.4% in smokers of the control group ($P < 0.01$). PAC correlated with the duration of smoking ($r = 0.53$, $P = 0.039$), with the number of cigarettes smoked per day ($r = 0.48$, $P = 0.046$), and the severity of withdrawal syndrome ($r = 0.58$, $P = 0.027$). Disorders determined by HADS: 25% for anxiety and 8% for depression. Smoking cessation success was lower in the presence of anxiety and depression ($P < 0.05$) of any degree of severity, with a low level of BR.

**Conclusion:** Personal adaptive capacity (PAC) correlated with duration of smoking in asthmatics. Smoking effects on the adaptive resources of patients with asthma. It demonstrated additional argumentation for smoking cessation regardless of the age and the smoking duration. During smoking cessation, it is necessary to take into account anxiety and depression levels and perform cognitive-behavioral therapy (correction of psychological disorders).

## 1322 | Impact of CPAP therapy in asthmatic patients with OSA

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**Background:** Statistic data show high prevalence of Obstructive sleep apnea (OSA) in asthmatic patients. Our aim was to find if CPAP therapy has impact of asthma patients.

**Method:** Our study include 51 patients (age between 18-60 years) with well controlled mild allergic asthma with new diagnosed

Obstructive sleep apnea (OSA). All of the patients were on regular treatment with low dose inhaled corticosteroids for at 12 months and start treatment with continuous positive airway pressure (CPAP).To assess quality of life, we used asthma symptom control tools (Asthma control test) .Patients performed daily peak flow meter and Spirometry (once a week) during period of 4 weeks after start using CPAP.

**Results:** During the study, 47 of the followed patients had no exacerbation of asthma. Four of patients during this period had exacerbation, due to upper airway infection so they were excluded from study.

Results of following showed that there was improvement in quality of life in all 47 patients included in study but there no statistically significant improvement in pulmonary function tests FPT.

**Conclusion:** Conclusion: CPAP treatment of OSA in stabile mild allergic asthma may improve quality of life but not show significant improving of the pulmonary function tests.

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## 1323 | The relationship between preterm birth and childhood allergic rhinitis in Taiwan

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**Background:** At present, the effect of preterm birth on allergic rhinitis in pediatric populations has remained inconclusive. We aimed to investigate the relationship between preterm birth and allergic rhinitis among Taiwanese children.

**Method:** This study included 613 children (aged 6.3 ± 0.3 years; 345 boys, 56.3%) participating in the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS) cohort. Information of demography, epidemiology and physician-diagnosed rhinitis was collected from a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Preterm birth was defined as gestational age less than 37 weeks. Atopy status was determined by Phadiatop Infant. Multiple logistic regression models were used for data analysis. Adjusted confounders included gender, age, number of older siblings, maternal allergic rhinitis, maternal age at delivery and socioeconomic status.

**Results:** The rate of preterm birth among the study subjects was 18.2%. The prevalence of physician-diagnosed rhinitis was 50.6%. There was no significant association between preterm birth and physician-diagnosed rhinitis ($P$ = 0.43). When stratifying by atopy status, we found that preterm birth was associated with physician-diagnosed rhinitis among children without atopy (adjusted OR [AOR] = 0.33, 95% CI = 0.12-0.93, $P$ = 0.04), but not among children with atopy ($P$ = 0.77). When further classifying by gender, greater protective effect of preterm birth on rhinitis was only found in boys without atopy (AOR = 0.12, 95% CI = 0.03-0.56, $P$ = 0.007).

**Conclusion:** The results suggest that preterm birth may have a protective effect against the development of childhood rhinitis in our study population. The protective effect is only observed in boys without atopy. Further investigations will be merited to confirm these findings and to investigate underlying mechanisms.

## 1324 | Maternal folic acid supplementation during pregnancy in relation to childhood rhinitis: A cohort study in Taiwan

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**Background:** Folic acid supplementation (FAS) during pregnancy has been suggested due to its protective effect against neural tube defects. At present the effect of FAS during pregnancy on childhood rhinitis has remained unclear. We aimed to investigate the relationship between FAS during pregnancy and childhood rhinitis.

**Method:** A total of 613 children (age 6.3 ± 0.3 years; 345 boys, 56.3%) participated in the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS) cohort were included in this study. All study subjects were interviewed by board-certified pediatricians; and demographic, epidemiologic and clinical data were collected based on a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Maternal FAS during pregnancy was categorized into three groups (never; <3 months; and >=3 months). Atopy status was determined by Phadiatop Infant. Logistic regression analysis with covariate adjustment was performed. Adjusted covariates included sex, age, number of older siblings, breast feeding duration, maternal smoking during pregnancy, maternal allergy, maternal education level, maternal age and socioeconomic status

**Results:** The prevalence of physician-diagnosed rhinitis was 55.3%. There is a significant association between FAS and physician-diagnosed rhinitis (adjusted odds ratio [AOR] = 2.07; 95% confidence interval [CI] = 1.25-3.43 for FAS ≥3 months) compared to the group of never use. In the stratified analysis by atopy status, maternal FAS during pregnancy was significantly associated with physician-diagnosed rhinitis in the atopic group (AOR = 1.91, 95% CI = 1.07-3.40 for FAS <3 months; and AOR = 2.34, 95% CI = 1.19-4.58 for FAS ≥3 months), but not in the non-atopic group. When further stratified by gender, significant association between maternal FAS during pregnancy and physician-diagnosed rhinitis was only found in boys with atopy (AOR = 3.23, 95% CI = 1.39-7.50 for FAS <3 months; and AOR = 4.02, 95% CI = 1.51-10.72 for FAS ≥3 months).

**Conclusion:** The results demonstrate that maternal folic acid supplementation during pregnancy might increase the risk of childhood rhinitis, especially among boys with atopy. Further investigation will be needed to validate our findings and to understand potential underlying mechanisms.

## 1326 | Causative agents of the respiratory and enteric viral infections and their combined form in children

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**Background:** Viruses cause an estimated 60% of human infections, and most common illnesses are produced by respiratory and enteric viruses. The aim of this study is to evaluate contribution of different enteric and respiratory viruses in etiology of acute respiratory infection (ARI), enteric infection (EI) or both respiratory/enteric infection (REI) in children. We focused on dual infections (viruses detected in one patient in stool and nasal samples simultaneously) and mixed infection (several viruses detected in one patient in particular sample type (feces or nasal swab)).

**Method:** The clinical samples (nasal swabs and feces) from 151 hospitalized children with symptoms of ARI (N = 56), EI (N = 63) and REI (N = 32) were collected during 2015-2017 in Moscow. Swabs were analyzed by multiplex real-time PCR (mrtPCR) targeting influenza viruses type A and B (IVA and IVB), parainfluenza viruses type 1, 2, 3, 4 (PIV1-4), adenoviruses (AdV), respiratory syncytial virus (RSV), rhinoviruses (RV), enteroviruses (EV), coronaviruses (CV) and bocaviruses (BV). The feces were analyzed by mrtPCR targeting AdV, EV, rotavirus A (RVA), noroviruses (NV) and astroviruses (AV). Positive BV and AdV amplicons were sequenced to identify type.

**Results:** Out of the 151 feces and swabs analyzed, 60 (40%) and 36 (24%), respectively, were positive for one or more agents.

Of the 10 (16%) positive feces in ARI group (%): 8 were RVA, 3 -AV, AdV, EV. Of the 36 positive feces (64%) in EI group (%): 30 were RVA; 29 - NV; 7 - AdV and 4 - EV. Of the 14 (44%) positives feces in REI group: 19% were NV, RVA and 13- AdV.

Of the 28 (44%) positive swabs in ARI group (%): 13 were RV,11-BV; 6-CV and RSV, 5-AdV and PIV1, 3 - PIV3, IVA. Of the 3 positives swabs (5%) in EI group: 4% were AdV, 2-PIV3. Of the 5 (16%) positive swabs in REI group: 6% were RV and 3 - CV, PIV3 and AdV. According to sequence data 13 from 16 detected AdV (in all groups of patients) belongs to species F 41 type and 3 samples to species C 1 type (REI group). BV type 1 was identified in 3 strongly positive ($Ct \leq 25$) swab samples in ARI group.

**Conclusion:** Simultaneous testing of respiratory and stool samples together shown that at least 6.6%/7.9% of 151 study subjects had dual/mixed infections, respectively, including 11%/9.5% of 63 respiratory disease patients, 3.6%/7% of 56 gastroenteritis patients and 3.1%/6.2% of 32 patients with combined respiratory/enteric infections. We found no virus combination specific for different groups of patients.

## 1327 | Neonatal respiratory supports and future asthma-like presentation in prematurity with bronchopulmonary dysplasia

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**Background:** Bronchopulmonary dysplasia (BPD) is the most common form of chronic lung disease in prematurity and cause long-term morbidity. Antenatal and postnatal factors can make impact in lung development. Mechanical ventilation and oxygen toxicity may cause alveoli injury and impaired lung function in the future. Asthma and BPD are both obstructive lung disease and share some clinical features in childhood, but not totally the same mechanism. In the population with prematurity and BPD, we want to find the differences of respiratory cares in antenatal and postnatal period between children with and without asthma symptoms in young childhood.

**Method:** 441 children with preterm birth (gestational age (GA) <37 weeks) and BPD were enrolled in Mackay Memorial Hospital from 2004 to 2015. All subjects' medical records were retrospectively collected up to 2-8 years of age. All subjects were divided into asthma group and non-asthma group. Enrolled in asthma group were subjects with physicians' diagnosed asthma and under corticosteroid control (inhaled or oral forms). Age and gender matched subjects without asthma were enrolled in non-asthma group. Analyzed parameters between the two groups were recorded from the first birth hospitalization, including GA, birth body weight (BBW), respiratory distress syndrome (RDS) grade, administered antenatal corticosteroid doses, administered surfactant doses, endotracheal tube inserted days, mechanical ventilator supported days, continuous positive airway pressure (CPAP) supported days, total oxygen supplied days. The oxygen-supplied days were calculated from birth to total discontinuation of oxygen after discharge.

**Results:** 441 children aged of 2-8 years were enrolled. Asthma group had 128 children, and non-asthma group had 313 children. Asthma group has longer endotracheal tube inserted days (30.87 ± 28.42 vs 24.34 ± 25.85; $P = 0.027$), mechanical ventilator supported days (45.19 ± 36.61 vs 37.22 ± 28.87; $P = 0.031$), CPAP supported days (24.94 ± 26.35 vs 19.37 ± 15.91; $P = 0.029$), total oxygen supplied days (156.25 ± 97.46 vs 125.60 ± 69.11; $P = 0.001$) than non-asthma group. There were no significant differences between the two groups in GA, BBW, RDS grade, antenatal corticosteroid doses, surfactant doses.

**Conclusion:** In children with the history of prematurity and BPD, those with asthma-like symptoms in 2-8 years old had longer mechanical ventilation supports and oxygen necessaries in neonatal period than those without asthma-like symptoms.

## 1328 | Prevalence of pneumoallergen-specific IgE in Albanian children with allergic diseases

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**Background:** Patients with respiratory allergy, allergic conjunctivitis, and atopic dermatitis have specific IgE against the allergen that causes the disease. Serum specific IgE tests are widely used to identify the allergen responsible for respiratory allergies in children in Albania. This study is intended to evaluate the frequency of specific IgE in children with respiratory allergies in Albania.

**Method:** Laboratory data of specific IgE tests for a three-year period (2014-2017) of 171 tests of pediatric patients with or suspected respiratory allergies, allergic conjunctivitis and atopic dermatitis were analyzed. Tests were performed with a quantitative immunoblot assay for circulating specific IgE with 30 allergens per test. Comparisons were made using chi-square and t-test and Wilcoxon Signed Rank test.

**Results:** Of all the tests analyzed 54.4% were males and 45.6% females with a mean age 5.7 ± 4.8 years old. Half of the tests (49.2%) reveals positive specific-IgE to more than one allergen and 38.6% (66) have no serum specific-IgE for the tested allergens (Table 1).

Sixteen patients (9.4%) have very high concentrations (>100 IU/mL) of *Derm. Pteronyssinus* specific IgE, 13 (7.6%) of *Derm. Farina*, 7 (4.1%) of *Rey pollen* and 6 (3.5%) of *Oak* and *Timothy grass pollen*.

**Conclusion:** The results reveal the prevalence of specific IgE to children with respiratory allergies, allergic conjunctivitis, and atopic dermatitis. The most common IgE found in this patient category are those specific to *Derm. Farina*, *Derm. Pteronyssinus*, *Alder* and *Birch* pollens. Most higher concentrations of specific IgE resulted from those specific to *Derm. Pteronyssinus* and *Derm. Farina*.

| Allergen | Positive % (n) |
|---|---|
| Derm. farinae | 36.3 (62) |
| Alder | 33.3 (57) |
| Derm. pteronyssinus | 31.8 (54) |
| Birch | 31.3 (53) |
| Timothy grass | 29.8 (51) |
| Dog epithelium | 29.2 (50) |
| Horse epithelium | 29.0 (50) |
| Cat epithelium | 26.3 (45) |
| Oak | 25.6 (44) |
| Hazel | 24.9 (42) |
| Rey | 22.9 (39) |
| Mugwort | 22.5 (39) |
| Acarus siro | 20.8 (36) |
| Plantain | 18.8 (32) |
| Grass mixture | 11.7 (20) |
| Rabbit epithelium | 10.8 (18) |
| Cladosporium herbarum | 9.5 (16) |
| Alternaria alternata | 8.9 (15) |
| Penicillium notatum | 7.7 (13) |
| Ragweed | 7.6 (13) |
| Hamster epithelium | 6.96 (12) |
| Aspergillus fumigatus | 6.15 (11) |
| Latex | 4.00 (7) |

## 1329 | The impact of sex hormones on lung function in 11-year-old children: Body composition as mediator

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**Background:** There is no direct epidemiologic study of relation between sex hormone and lung function, although pulmonary function improvement is achieved in the pubertal stage. Our hypothesis is that sex hormone profile positively affects lung function in adolescent.

**Method:** We prospectively recruited 620 children (10-12 years-old) who participated in the $SAP_{2017}$ cohort, sponsored by the Seongnam City Government (Republic of Korea). This study provided assessments of breasts and genitals development according to 5 Tanner stages by the questionnaire and line drawings. Moreover, we also determined each subject's blood sex hormone profile (estradiol and testosterone), oscillometric lung function, body composition (using multifrequency bioelectrical impedance analysis).

**Results:** Among total of 620 children enrolled in the $SAP_{2017}$ study group, 457 (73.7%) children met the study criteria for completing the oscillometric lung function test, body composition test, blood sampling. Mediation analysis showed that percentage of lean body significantly involve the association between serum testosterone levels and reactance area (AX) adjusted by age, gender, height, prematurity or low birth weight, passive smoking, aeroallergen sensitization, ever wheezing, and 25-OH vitamin D. Moreover total, direct, and indirect effect effects of testosterone on oscillometric lung function through lean body mass were statistically significant (direct, coefficient = −0.055, $P$ <0.001; indirect, coefficient = 4.020, $P$ <0.001). The estimated indirect mediation proportion explanted 24.68% of the association.

**Conclusion:** The levels of different testosterone were associated with the lung function through lean body mass in adolescent, either directly or indirectly.

## 1330 | Monitoring and analysis of serum IgE levels in children with respiratory allergic diseases

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**Background:** The purpose of this study is to investigate the changes of serum IgE levels in children with respiratory allergic diseases during the childhood.

**Method:** Retrospective analysis of children with respiratory allergic diseases who have detected of serum IgE from 2007 to 2016 in the First Affiliated Hospital of Guangzhou Medical University. Minimum detection interval is three months. Maximum detection interval is 4 years. The detection items including total IgE(tIgE), Dermatophagoides pteronyssinu (D.p),egg white and cow's milk sIgE.

**Results:** 55 children were included in the study. Among them, 29 cases were detected tIgE. 30 cases were detected D.p sIgE. 29 cases were detected egg white sIgE. 32 cases were detected cow's milk sIgE. The average ages of the first and second detection of tIgE group were 2.7 ± 2.1 years vs 3.8 ± 2.3 years. The level of tIgE in second detection was higher in 75.9% children than the first detection. The average level of tIgE was higher in second detection than the first [(345.00(88.65 786.00) vs 184.00(65.80, 422.00)kUA/L],but the difference has on statistically significant($Z = -1.547$, $P = 0.122$); The level of D.p sIgE in second detection was higher in 76.7% children than the first detection. The average ages of the first and second detection of D.p sIgE group were 3.3 ± 1.5 vs 5.4 ± 2.1 years. The average level of D.p sIgE was higher in second detection than the first [23.00 (3.99, 78.20) vs 1.27 (0.06, 20.45) kUA/L],the difference has statistically significant ($Z = -2.840$, $P = 0.005$); The average ages of the first and second detection of cow's milk sIgE group were 3.0 ± 1.5 vs 5.0 ± 2.2 years. The level of cow's milk sIgE in second detection was lower in 78.1% children than the first detection. The average level of cow's milk sIgE was lower in second detection than the first [0.33 (0.10, 0.53) vs 0.77 (0.23, 1.56) kUA/L],the difference has statistically significant ($Z = -2.612$, $P = 0.009$); The average ages of the first and second detection of egg white sIgE group were 3.2 ± 1.4 vs 5.2 ± 2.2 years. The level of egg white sIgE in second detection was lower in 65.5% children than the first detection. The average level of egg white sIgE was higher in second detection than the first [0.21 (0.10, 0.94) vs 0.15 (0.09, 1.18) kUA/L], the difference has no statistically significant ($Z = -0.109$, $P = 0.913$).

**Conclusion:** D.p sIgE has a greater level change than tIgE, egg white sIgE and cow's milk sIgE. The children with respiratory allergic diseases should monitor the IgE level closely.

## 1331 | TGF-beta in human milk and allergic outcomes in children: A systematic review

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**Background:** Human milk (HM) cytokines and in particular transforming growth factor-beta (TGF-ß) appear to be essential in developing and maintaining appropriate infant immune responses. However, role of TGF-ß in the prevention of allergic diseases remains controversial. This systematic review aims to provide comprehensive analysis of published studies on the association between HM TGF-ß and allergic outcomes in infancy and early childhood. We considered a wide range of allergic outcomes including eczema, food allergy (FA), asthma, allergic rhinoconjunctivitis (ARC) and allergic sensitization, confirmed by skin prick test and/or sIgE measurement.

**Method:** Extensive search was conducted in MEDLINE, EMBASE and Cochrane Library for any prospective, retrospective and cross-sectional human study published in English. The risk of bias was assessed in duplicate using the Cochrane Risk of Bias tool and the National Institute for Clinical Excellence methodological checklists for intervention (IS) and observational studies (OS).

**Results:** Of 353 hits identified in the databases search 103 relevant papers were screened. Of these, 27 that met the selection criteria were reviewed and 21 studies (9 intervention and 12 observational) were included in the systematic review. Among health outcomes measured, 3 studies assessed the association of HM TGF-ß1 and TGF-ß2 concentrations and risk of asthma and/or wheezing and/or ARC; 11 risk of eczema and/or FA; and 7 studies assessed both groups of outcomes. Results indicate that TGF-ß1 shows either a neutral or protective effect for infant allergic outcomes (IS: neutral effect 86% (6/7), positive 14% (1/7); OS: neutral effect 67% (8/12), positive 33% (4/12)). TGF-ß2 shows more mixed results (IS: neutral effect 25% (1/4), negative 50% (2/4), positive 25% (1/4); OS: neutral effect 60% (3/5), negative 40% (2/5), positive 20% (1/5)), with one study showing differential results for TGF-ß2 in colostrum (negative) and mature milk (neutral). There was a high level of heterogeneity among the studies and some studies carried high risk of bias.

**Conclusion:** HM TGF-ß is involved in the regulation of inflammation and development of allergy in infancy and may potentially regulate immunological responses during postnatal life and childhood.

Further studies are needed in order to elucidate the effect of these cytokines on allergy development and protection.

## 1333 | Daily yogurt consumption in infancy is associated with reduced skin hypersensitivity to histamine

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**Background:** Probiotics consumption during perinatal and postnatal periods reportedly reduces the risk of atopic dermatitis in the offspring, whereas such probiotics consumption did not affect IgE levels or the risks of other allergic diseases; the precise mechanism how probiotics consumption reduces the risk of atopic dermatitis remains unknown. We hypothesized that probiotics consumption may reduce skin hypersensitivity to histamine. To test this hypothesis, we investigated whether perinatal/postnatal consumption of yogurt associates with skin hypersensitivity to histamine or not.

**Method:** This was a cross-sectional study enrolled 256 mother-infant (≥6-months-old) pairs. Physician-diagnosed allergic diseases and food consumption, such as milk, fermented drinks, and yogurt, by mothers during the third trimester of pregnancy and by infants during the first 6 months of life were assessed using self-questionnaires. Skin prick tests (SPTs) to saline and 1 mg/mL histamine were performed using bifurcated needles, and wheal sizes were measured 15 minutes after the puncture.

**Results:** The SPT wheal sizes in infants with eczema/atopic dermatitis (n = 44) were significantly larger than those in infants without eczema/atopic dermatitis (n = 156; 4.6 ± 1.9 mm vs 3.8 ± 1.8 mm, respectively, $P = 0.015$), and thus these infants were excluded from the further analyses. The SPT wheal sizes to histamine in infants with daily yogurt consumption during the first 6 months of life were significantly smaller than those without daily yogurt consumption (n = 10, 2.6 ± 1.3 mm vs n = 193, 4.0 ± 1.8 mm, respectively, $P = 0.010$), However, consumption of the other foods showed no effects on the SPT wheel sizes among infants. Perinatal consumption of yogurt by the mothers revealed no associations with SPT wheal sizes in both mothers and infants. Both in mothers and infants, the wheal sizes of SPTs to saline had no associations with taking any kinds of the foods at any timing.

**Conclusion:** Daily yogurt consumption may reduce skin hypersensitivity to histamine and thereby reduce the risk of atopic dermatitis during infancy. The role of probiotics/yogurt consumption in the regulation of skin hypersensitivity to histamine warrants further study.

## 1334 | Sensitization to profilins in children with pollen-food allergy

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**Background:** Sensitization to plant-derived foods is frequent among patients with pollen allergy. The profile of sensitization depends on various factors such as: nature of the allergen, patient's age and individual immune response, genetic background and environmental exposure.

The aim of this study was to evaluate the prevalence and clinical relevance of sensitization to profilins in atopic patients with food allergy.

**Method:** The study was performed on a group of 43 children age 2-14 years with sensitization to at least one plant-derived food allergen (IgE > 0.7 KU/L). The included patients had never been treated with allergen immunotherapy before the study. The presence of IgE to recombinant (*r*) rBet v 2, rArt v 4 and rAmb a 8 in serum was evaluated using ELISA method as previously described (JBC 2016; 291:15447). In addition serum level of IgG4 to rBet v 2, rArt v 4 and rAmb a 8 was also evaluated.

**Results:** Sensitization to profilins was found in 8 out of 43 (18.6%) patients (P+). Sensitization to all 3 studied profilins was demonstrated in each P+ patient. The remaining 35 children, with pollen-food sensitization, were not sensitized to any of the studied profilins and they served as a comparator group (P−). Analysis of the clinical status revealed that asymptomatic patients in regard to plant-derived food hypersensitivity were found more frequently among P+ (75%) than P− (37.1; $P < 0.01$) patients. Sensitization to profilin was associated with positive IgE to the same food allergens as in the control group. Clinical manifestation of pollen-food sensitization expressed as allergic rhinitis, bronchial asthma and atopic dermatitis was comparable between groups, except of oral allergy syndrome, which was not seen among P+ children. Similarly, history of anaphylaxis to plant-derived foods was registered only among P− (11.4%) patients. Interestingly, all patients with sensitization to profilins had also elevated level of serum IgG4 against rBet v 2, rArt v 4 and rAmb a 8.

**Conclusion:** Lack of association between profilin sensitization and food-related IgE-mediated hypersensitivity in combination with high serum profilin IgG4 concentration may indicate naturally occurring tolerance to those allergens in our patients. Further studies are warranted to characterize the clinical relevance of sensitization to profilins.

## 1335 | Association of preterm birth with childhood eczema: A prospective cohort study in Taiwan

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**Background:** Previous studies assessing the relationship between preterm birth and childhood eczema have not reached a consensus yet. This study aimed to examine whether the risk of developing eczema among children in Taiwan is influenced by preterm birth.

**Method:** This study consisted of 613 children participating in the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS) cohort. The study children (age 6.3 ± 0.3 years; 345 boys, 56.3%) were born in 2010-2011 at the Chang Gung Memorial Hospital, Taiwan. Birth information of the study subjects was obtained from medical records. Demographic, epidemiologic and clinical information were obtained from a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Atopy status was determined by Phadiatop Infant. Logistic regression analysis with covariate adjustment was performed to determine the association between preterm birth and childhood eczema. Adjusted covariates included gender, age, caesarean section, breastfeeding, parental allergic diseases, maternal education level, maternal age at birth, and maternal smoking during pregnancy.

**Results:** No significant difference of physician-diagnosed eczema ($P$ = 0.88) or current eczema ($P$ = 0.82) was observed between children born full-term and preterm. After stratifying by atopy status, we found that children born preterm had a more than three-fold higher risk of having physician-diagnosed eczema (adjusted OR (AOR) = 3.92; 95% CI = 1.25-12.29; $P$ = 0.02) and current eczema (AOR = 3.16; 95% CI = 1.06-9.41, $P$ = 0.04) than their counterpart in the non-atopic group. No statistical significance was observed for the association between preterm birth and eczema in the atopic group. No association between preterm birth and eczema was found when stratifying by gender.

**Conclusion:** Our results reveal that non-atopic children born preterm have a higher risk of developing eczema. The results suggest potential modifiable effect of atopy on the association between preterm birth and eczema. Further studies with a larger sample size are needed to validate the findings in this study.

## 1336 | Factors of importance for transition: Experiences of living with allergy from adolescent and a parenting perspective

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**Background:** There is a need for more knowledge about factors of importance for a successful transition from childhood to adulthood among adolescents with allergic disease and especially those with severe allergy. Therefore the aim of this study was to describe experiences of living with severe allergy from the adolescents and their parent's perspective and thereby identify factors of importance for transition from pediatric to adult care.

**Method:** A qualitative study was performed based on six focus groups interviews, two with adolescents and four with their parents. In total 11 adolescents (age 10-16 years old) and 21 parents participated. The interview guide contained questions about experiences of living with severe allergy. The transcribed data was analysed using systematic text condensation.

**Results:** In total four themes were presented, two themes occurred in both the adolescent and the parent's focus groups, *to be special* and *to be prepared*. For two themes there was a difference between the adolescents and their parents. The theme, *the importance of the parents*, only occurred in data from the adolescents and the theme *the meetings with health care* only occurred in the parent's data.

The adolescents felt that they had low priority in the class and several stated they were teased at school and their parents felt that focus on their child often was in a negative way. The adolescents described that they took responsibility for their diseases while their parents expressed a need to protect. The adolescents stated that one of the parents were always present or had been during the years, the reason being safety and security. Only the parents mentioned experiences from healthcare. Parents who described that they had continuity in healthcare meetings and where met by high competence and with a professional approach were more satisfied with the support from the health care. One factor that was felt to be important was whether the doctor involved the youth in the conversation or not.

**Conclusion:** The teenagers in this study relied on their parents while also taking responsibility for their illness at the same time. Parents, on the other hand, showed a tendency to overprotect their adolescents. For healthcare professionals it is important to involve the adolescents in the care to facilitate the transition.

## 1337 | Antibiotics use in relation to asthma in schoolchildren

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**Background:** Early-life antibiotic exposures have been reported to increase the risk of allergic diseases. The aim of the study was to examine the impact of current antibiotics use on asthma in schoolchildren in The Republic of Macedonia, as a developing country with a high rate of antibiotics use and a low prevalence of asthma.

**Method:** Data from 2310 schoolchildren aged 5-15 years obtained through a parental-completed questionnaire in randomly selected primary schools in Skopje, the capital of Macedonia, in 2015/2016 was used. The frequency of antibiotics intake ≥3 and <3 times yearly *vs* never antibiotics intake for respiratory infections in the last 12 months was correlated to current asthma-like symptoms and ever-diagnosed asthma after adjustment for confounding factors using multiple logistic regression.

**Results:** 50.9% of the children used antibiotics currently and 21.0% out of them used antibiotics ≥3 times yearly. Current wheeze (W) was established in 6.5%, sleep-disturbing W in 3.6%, exercise-induced W in 1.7%, dry night cough apart from a cold in 12.2%, and asthma in 2.3%. Current antibiotics use ≥3 times yearly was positively associated with current W (aOR: 13.37; 6.14-29.11; $P < 0.001$), sleep-disturbing W (aOR: 7.87; 3.34-18.57; $P < 0.001$), exercise-induced W (aOR: 5.44; 1.89-15.61; $P = 0.002$), dry night cough (aOR: 3.80; 2.29-6.29; $P < 0.001$), and diagnosed asthma (aOR: 5.68; 1.96-16.50; $P = 0.001$) while antibiotics use <3 times yearly was positively associated only with current W ($P = 0.003$) and dry night cough ($P = 0.011$).

**Conclusion:** The results suggest an aggravating role of antibiotics use on asthma in school age thus further supporting the recommended restriction of antibiotics exposure.

## 1338 | Evaluation of the learning conditions for students with chronic respiratory diseases

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**Background:** Hygienic evaluation of the learning conditions for students with chronic respiratory diseases.

**Method:** The study included 114 students of which 44 boys (38.6%: 95% CI, 29.6-48.2) and 70 girls (61.4%: 95% CI, 51.8-70.4) they are questioned, during the cold season, to assess morbidity by chronic respiratory diseases. Investigations microclimate parameters and the concentration of $CO_2$ - employing the IAQ Monitor *IAQ Monitor/aq—S 001 Indoor Air Quality Monitor NOW* (SUA).

**Results:** After questioning 31.6% 95% CI, 23.2-40.9 were suffering from respiratory diseases, having symptoms of chronic disease: cough—86.1%, wheezing—41.66%, tightness in the chest—27.7%. The risk factors (passive smoking, open fire house warming and no air conditioning) were commonly met in major cases at ill children rather than healthy ones (68.4% 95% CI, 59.1-76.8). As a result of studies made of the equal to 17.5 ± 0.3, comparative the end of lessons equal 19.2 ± 0.2 ($P \leq 0.05$); Air relative humidity varies during lessons equal with 62.9 ± 1.4 (Norma toilet 30%-60%); CO2 concentration exceeds allowable limits −0.3 ± 0.02 (MAC −0.1%).

**Conclusion:** Respiratory morbidity in high school examined has a tendency to increase. We noticed deviations from the hygienic norms: the indoor temperature and relative humidity was lower and the $CO_2$ level was twice higher than the normal one.

## 1339 | Asthma definitions in population-based birth cohorts: A review

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**Background:** Asthma is one of the most common chronic childhood diseases. Birth cohort studies are used to investigate asthma epidemiology. To date, there is no single "gold-standard" for asthma diagnosis. Our objective was to review how asthma is defined in population-based birth cohort studies.

**Method:** A literature search of the MEDLINE database and of birth cohort repositories, reference searches and author correspondence. After reviewing abstracts and repository information, 110 non-duplicated cohorts were identified and 65 of them were included in the final review. Reasons for exclusion were methodology of asthma diagnosis not stated, no follow up after 4 years of age, outcome of wheezing rather than asthma, non-cohort study design.

**Results:** The majority of cohorts (60 out of 65) used parental completed questionnaires to define asthma. For 48 cohorts, questionnaires were a sole source of information, while 12 cohorts also used other sources: medical records (general practitioner's (GP) records and/or prescription registry information), study physician assessment and/or clinical tests.

Asthma definitions were pooled into broader categories of "Asthma ever", "Current asthma" and "Asthma unspecified".

The "Asthma ever" outcome was reported in 32 cohorts. 28 cohorts defined this as parental reported asthma (with or without specifying that it was doctor-diagnosed), 2 cohorts used GP records as the only source of diagnosis, and 2 used parental report or GP records.

The "Current asthma" outcome was reported in 40 cohorts. There was little consistency with how current asthma was defined or worded, with 23 different definitions used. The most common definition of current asthma, reported 16 times, was "asthma ever AND EITHER asthma symptoms in the last 12 months OR asthma medication in the last 12 months". Other criteria included in asthma definitions were bronchial hyper-responsiveness, reversible airway obstruction, positive exercise test, and asthma symptoms reported at a previous questionnaire. Only one "current asthma" definition was based exclusively on prescription data: "dispensed two asthma medication during the past year".

Nine cohorts reported asthma outcomes without specifying how it was defined, and were categorized as "Asthma unspecified".

**Conclusion:** "Asthma Ever" and "Current asthma" are two main asthma outcomes used to define asthma in child cohort studies. Definitions of asthma vary substantially across cohorts.

## 1340 | Atopic and nonatopic phenotype of asthma in children: Clinical observational study

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**Background:** Evaluation of atopic and nonatopic phenotype in children.

**Method:** Evaluation of atopic and nonatopic phenotype in children. The children were examined serologically for humoral immunity total IgE .Serological tests were effectuate with ELISA tests.

**Results:** The children were divided into two groups: with asthma atopic (31 children - 68.9%: 95% CI, 53.4-81.8) - main group, and asthma nonatopic phenotype (14 children—31.1%: 95% CI, 18.2-46.6)—batch control. Lots of studies have been subjected to a comparative evaluation according serum total IgE, at children in the main group equal 599.4 ± 197.5 ME/mL, compared with the control group children, in that the mean concentration of total IgE was 25.8 ± 12.6 ME/mL, ($P < 0.05$). The range values of total IgE in children with asthma atopic phenotype was appreciated concentration equal to 84.7-2227.8 ME/mL. In the group of children with asthma nonatopic phenotype total IgE concentration present values of 8.8-45.1 ME/mL. Detection of IgE values much higher in the main group confirms the role of serum IgE marcher maintaining atopic status in children with asthma.

**Conclusion:** Atopic asthma phenotype is more common in children, it appreciated the IgE-mediated allergic mechanisms

## 1342 | Atopic diseases and autism spectrum disorders (ASDs)

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**Background:** ASDs is characterized by a wide spectrum of manifestations such as deficit of social interacting and personal skills, impairment of verbal and nonverbal communication and stereotypic movements. The rate of this disorder is one in 45 children in USA and its prevalence differs in many studies but it is globally underestimated. This children disorder is increasing nowadays in developing countries. Recently several studies have reported an increased risk of atopic disease such as asthma, allergic rhinitis and atopic dermatitis in children with ASD.

**Case report:** Thereby we present two case reports of two children with impairment verbal communication as part of ASD and allergic diseases.

The first patient was a 3 year old boy with sneezing, rhinorrhea night cough and eye redness. He had been suffering for almost 2 years from the above mentioned symptoms. He had family history for atopic diseases and was for 7 month breastfed. Specific IgE revealed sensitization to birch, alder, hazel, oak, mugwort pollen and dog epithelia and Dermatophagoides farinae. Specific IgE resulted positive for nuts and rye flour.

The second patient was almost 3 year of age in the tame that he presented in our hospital. He cried and screamed all the time because of severe atopic dermatitis and typical symptoms such as itching all over the body and his impairment of verbal communication. Specific sensitization showed sensibilization to egg white and egg yolk, to nuts, rye and wheat flour. The food specific IgE leaded to positive results to alder, birch, hazel and oak pollen, but also to grasses, ragweed and mugwort. Prick by prick test showed positivity to egg white and egg yolk. Atopy patch test to pollens resulted negative.

**Results:** The first patient symptoms were well controlled after treatment with antileukotrienes. His verbal communication was also improved after a year or more.

The second three year old patient after required a combination of specific treatment with antihistamines, corticosteroids, immunosuppressive drugs and diet recommendation. Afterwards he had a reduced level of itching and anxiety but compared to other children he had a severe eczema.

**Conclusion:** The treatment of these subjects is complex due to their impairment communication skills. However the improvement of allergic symptoms may have impact on ASD behavioral symptoms and vice versa.

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## 1343 | Atopic dermatitis and gluten-related disorders in children hospitalized to the dermatology department

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**Background:** In the dermatology department of our hospital, about 60% of patients are with atopic dermatitis. Among these patients, gluten-related disorders such as asymptomatic celiac disease (CD) and dermatitis herpetiformis, have often become revealed. The aim of our study was to find out how often gluten-associated disorders can be found among paediatric dermatology patients.

**Method:** Patients with atopic dermatitis, as well as dermatitis of unidentified etiology and alopecia, were tested for antibodies to tissue transglutaminase-2 IgA, IgG by immunoferment assay (Orgentec, Germany), when positive, gastroscopy with duodenal biopsies and histological and immunohistochemical study to determine the amount of $CD3^+$ intraepithelial lymphocytes, as well as HLA-typing (PCR) to determine the haplotypes DQ2, DQ8 were done. Nutritional status was assessed using the WHOAnthroPlus program.

**Results:** We had 1576 dermatologic patients in 2015-2017. The diagnosis of CD was confirmed in 16 children aged 3.5-17 years, which was 1.0% of the total number of patients and 1.7% of patients referred to us with a diagnosis of atopic dermatitis. All these children received ineffective treatment for atopic dermatitis for a long time.

Five patients had total alopecia or alopecia areata; in 4 the herpetiform dermatitis (confirmed histologically) was established, the rest had celiac disease combined with atopic dermatitis. Low- or asymptomatic course of celiac disease in our patients should be noted: only 1 girl was malnourished (HAZ −2.42, BAZ −1.16); GI symptoms were rare and mild (inconstant stool in 4, abdominal distension in 3, abdominal pain in 4), mild anemia in 3, enamel defects in 4 patients. A significant increase in total IgE (745-3000 U/L) was found in only 3 patients with atopic dermatitis.

All children with atopic dermatitis and dermatitis herpetiformis had pronounced positive effect of gluten-free diet with significant decrease or disappearance of skin rash and pruritus, improvement of well-being; beginning of hair growth in 2 children with alopecia areata after 3-6 months of diet.

**Conclusion:** Although the detected incidence of CD in our dermatological department is not so high compared to the global figures, we consider it necessary to perform screening (antibodies to tissue transglutaminase) among patients with poorly treatable atopic dermatitis, all types of atypical dermatitis and alopecia, since a gluten-free diet in case of revealed CD is extremely effective in relation to the skin process.

## 1344 | Home remodeling increase the severity of atopic dermatitis

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**Background:** Atopic dermatitis (AD) is the most common chronic dermatosis in children. The aim of this study is to investigate the effect of home remodeling in the severity of AD in children.

**Method:** A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to survey 1591 children of 11 elementary schools from Seongnam, Korea. SCORing Atopic Dermatitis (SCORAD) score were graded by pediatric allergic specialists, blood eosinophil count and skin prick tests (SPTs) were also measured.

**Results:** Parental history of AD (aOR, 3.76; 95% CI, 1.66-8.53) and past history of home remodeling (aOR, 2.09; 95% CI, 1.02-4.30) were independent risk factors for current AD. Children with high upper tertile level of mandelic acid had increased risk for moderate to severe AD (aOR = 3.76; 95% CI = 1.06-13.28, $P$ = 0.04).

**Conclusion:** There was relationship between home remodeling and severity of AD in children in this study.

## 1345 | Educating parents on infant skincare: Survey on actual skincare practices

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**Background:** We sought to investigate education on proper skin care for infants, based on results of a survey on skin care practices in Fukuyama City, Japan.

**Method:** We sent questionnaires to parents with infants undergoing 18-month health check-ups in Fukuyama City between June and November 2017, and collected the responses at the health check-up for evaluation of uncounseled parents (health-check group). Concurrently, we provided skincare education (as an early intervention) to parents of infants with a high risk for atopic dermatitis (AD), and asked these counseled parents (education group) to complete the same questionnaire for comparison purposes. Investigated questionnaire items were (a) washing; (b) moisturizing; (c) skin-care practices; and (d) onset of AD symptoms.

**Results:** The proportion of mothers encountering infant dermal health issues exceeded 80% for both the education and health-check groups; however, among children in the education group, there were significantly fewer AD diagnoses (by a physician) before the age of 18 months compared with the health-check group (5% vs 37%) [[Please confirm.]]. Many parents who had received individual education on skin care in the prenatal and neonatal periods understood proper skin care and could apply these practices appropriately. Conversely, few uncounseled parents understood proper skin care.

**Conclusion:** We suggest that parental acquisition of proper skin care practices in the early neonatal period may prevent AD through practical application. In the future, we plan to present cases effectively utilizing visual and other materials, which we consider to be important for increasing the number of parents educated on infant skincare.

## 1346 | Omalizumab-induced erythema multiforme in a patient with chronic spontaneous urticaria

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**Case report:** Omalizumab is an immunoglobulin E (IgE) specific, recombinant humanized monoclonal antibody that reduces levels of circulating IgE and expression of high-affinity IgE receptors on mast cells. By these effects it decreases proinflammatory mediator release and reduces allergic inflammation. Omalizumab has been approved by the FDA for children aged 12 years and older with chronic spontaneous urticaria who are symptomatic despite treatment with H1 antihistamines. Most common adverse events are immediate reactions such as urticaria or anaphylaxis.

Erythema multiforme (EM) is an acute, immune-mediated, mucocutaneous condition that is most commonly caused by infection and drugs. It is characterized by targetoid lesions, sometimes accompanied by oral, genital or ocular mucosal erosions. There was no pediatric patient that had previously been reported in the literature with development of type 4 reaction after omalizumab treatment. We presented a case who developed EM to omalizumab therapy.

An 16 year-old female patient was admitted to pediatric allergy clinic with complaints of fever and rash. She had been diagnosed with chronic spontaneous urticaria (CSU) 8 years ago and she was planned to treat with omalizumab (75 mg, subcutaneously every 2 week) because of the inadequate response of antihistamines at a medical center. Her complete blood counts, liver, renal, thyroid function tests and serum C3,C4,C1 esterase inhibitor protein levels and functions were within normal limits. The serum IgE level and anti-thyroglobulin antibody was 112 IU/mL and 258 IU/mL (positive), respectively. 15 days after the second administration of omalizumab, she developed itchy target lesions distributed symmetrically on the hands and fever. On the third day of the rash, purpuric, urticarial and target lesions spreaded to the face, trunk and extremities, with palmoplantar involvement and edema on the hands, accompanied by oral mucosa erosions. She was hospitalized with initial diagnosis of EM and treated with topical and systemic steroids (prednisone 40 mg/d), intravenous fluids and antihistamines. There was no ocular mucosal involvement. Skin biopsy was compatible with EM. During follow-up, lesions and fever was resolved within 1 week.

Omalizumab treatment can induce delayed type immunologic reactions. It is important to follow up patients for delayed type reactions as well as immediate type reactions of patients after treatment.

## 1347 | Case reports of eczema herpeticum emerging during atopic dermatitis treatment in infancy

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**Introduction:** Eczema herpeticum is a disseminated viral infection that arises from pre-existing skin disease, mostly atopic dermatitis (AD). Deterioration of skin barrier integrity and imbalance of the immune system play a role in the pathogenesis. Infants who have other atopic diseases with severe AD have a higher risk of developing eczema herpeticum. In here we report five cases of infants who have been diagnosed as Eczema herpeticum in the course of AD treatment.

**Conclusion:** Eczema herpeticum can be severe, potentially life threatening disease that occurs mostly in patients with AD. Diagnosis is based upon the clinical findings. Patients often present with grouping vesiculopustular skin lesions over the eczematous skin.

| Case | Gender | Age/ Onset of AD age (month) | Age of eczema herpeticum diagnosis (month) | Distribution and characteristics of skin lesions | Fever | Atopy | Absolute eosinophil count/ Total IgE (IU/mL) | HSV Tip 1-2 IgM/IgG | Therapy |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 9/2 | 9 | grouping vesiculopustular eruption over the eczematous skin of cheeks, and extremities, with secondary impetiginization | - | Cow' s milk<br>Egg | 4530<br>618 | -/- | Iv Ampicillin/ sulbactam<br>Iv Acyclovir<br>Topical steroid |
| 2 | F | 10/1 | 9 | Crusted grouping vesicles on the eczematous skin of the face extensive eczematous plaques on the neck and trunk | - | Cow' s milk<br>Egg | 900<br>24 | -/- | Topical steroid<br>Topical Acyclovir |
| 3 | F | 15/1.5 | 4 | Multiple grouping vesiculopustular with local ulceration over the cheeks with secondary impetiginization,<br>vesicles on the eczematous skin of hand and forearm eczematous plaques on the trunk | - | Egg | 4700<br><18 | -/- | Iv Ceftriaxone<br>Iv Acyclovir<br>Topical steroid |
| 4 | M | 14/4 | 2 | Multiple grouping blisters on the distal extremities and face impetiginization on the cheeks, extensor aspects of the knees and elbows | + | Cow' s milk<br>Egg<br>wheat<br>Potato | 3200<br>743 | -/- | Iv Acyclovir<br>Iv Ceftriaxone<br>Iv Fluconazole<br>Topical steroid |
| 5 | F | 7/4 | 4 | Grouping vesicles on the face, with secondary impetiginization | - | Egg | 300<br>59 | -/- | Iv Ampicillin/ sulbactam<br>Iv Acyclovir<br>Topical steroid |

Fever, malaise, lymphadenopathy, keratoconjunctivitis, meningitis, encephalitis may be seen in the clinical course. Therapy should be started without delay, with high suspicion (blisters in child with AD). Infants with severe atopic dermatitis with extended skin lesions, atopic dermatitis accompanying food allergy, having a long-lasting topical steroid treatment, high serum IgE levels, and high absolute eosinophil count in the peripheral smear are striking identic sings in our case series. Early recognition of this clinical condition in infants will decrease the mortality and dissemination of the disease.

## 1349 | Chronic urticaria and celiac disease in a child: A case report

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**Introduction:** Celiac disease is an autoimmune disease triggered by exposure to gluten in genetically predisposed individuals and characterized by chronic inflammation of the small intestine. Chronic urticaria is a skin disease, characterized by the appearance of pruritic wheals with or without angioedema, whose underlying mechanism cannot be identified.

**Objective:** To report a sporadic case of an 11-year-old boy with chronic urticaria associated with celiac disease.

**Methods:** An 11-year-old boy(weight 31 kg, 3rd-10th percentiles) was admitted to our clinic with a 6-year history of chronic urticaria. During the first three years, he was under antihistamine treatment(of incremental doses)and occasionally received preparations of cortisone according to the EAACI guidelines. He was asymptomatic for 2 years until treatment was discontinued. Eight months earlier, after a viral infection, a recurrence of urticaria, involving the trunk and extremities without angioedema was noted. Subsequently, he was under antihistamine treatment with cetirizine but had an UAS-7 score of 11. Total laboratory investigations were performed.

**Results:** Laboratory control was negative except for positive antibodies to celiac disease(Anti-transglutaminase >200 U/mL, anti-endomysial, gliadin antibodies).Further control with colonoscopy and biopsies (from duodenum and stomach) were obtained. The histopathological findings along with the clinical findings indicate celiac disease, type 3b Marsch-Oberhuber and grade B1 Corazza-villanacci. In the past, similar cases have been reported. Efforts have been made to associate chronic urticaria with celiac disease, although the mechanism remains unclarified. Evidence suggests that the duration of gluten exposure, among otherwise asymptomatic patients with celiac disease, is related to the development of other autoimmune mechanisms. This can be explained by resolution of urticaria manifestations after the onset of gluten-free diet. In our

case, three months after gluten-free diet, an improvement of urticaria with decreased UAS-7 score of 5 was observed.

**Conclusion:** he specific case of subclinical diagnosis of celiac disease in a child with chronic resistant urticaria further reinforces the suggestion that screening for celiac disease should be included in the diagnostic approach of chronic urticaria.

## 1350 | Allergy to gingival balm in an infant with cow's milk protein allergy

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**Introduction:** Cow's milk protein allergy (CMPA) is the most frequent food allergy in children under three years of age. The avoidance of these proteins is a difficult procedure in view of the widespread use of cow's milk in our diet. Nevertheless, precautions to avoid them should not be restricted to foods.

**Case report:** Seven-month old boy referred to our immunoallergy department for suspected CMPA. He had been exclusively breastfed up to four-months of age. At this age, immediately after his first cow's milk formula intake, he developed an episode of perioral urticaria, with spontaneous resolution in thirty minutes. He featured several subsequent reproducible episodes, with no complaints from other systems. For this reason, a partially hydrolyzed milk was introduced keeping breastfeeding, with good tolerance. Specific IgE assays performed for CMP were negative. At seven-month old immediately after the application of first teeth gingival balm, he started episodes of reproducible perioral urticaria identical to those observed with CMP with spontaneous resolution in less than sixty minutes. Skin prick tests (SPT) performed with commercial extracts (Bial-Aristegui Lab) for cow's milk and its protein fractions and the culprit balm were positives. We also carried out SPT with the balm in five atopic controls that were all negatives. It was found milk proteins in the ingredients list of the balsam under the name of "Lactis proteinum". Based on these results it was recommended absolute avoidance of CMP and extensively hydrolyzed formula as an alternative to breast milk.

**Conclusion:** We report a case of an infant with a diagnosis of CMPA with an allergic reaction to a gingival balm caused by the presence of CMP in its constitution. Furthermore, it is important to reinforce that milk proteins were labeled in an unusual form which might increase the risk of misunderstanding. These findings illustrate the difficulty in implementing total avoidance of common food allergens as well as the need to improve their labeling, particularly in non-food products.

## 1351 | Effect of psychological stress in atopic dermatitis

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**Background:** Children are often affected by atopic dermatitis. It appears in all ages of children. They suffer from itching and skin infections. The level of stress is related with different kind of allergic diseases such as atopic dermatitis and eczema that infants, toddlers and other children can develop.

**Case report description:** A nine year old boy presented to our hospital clinic with severe itching and severe atopic dermatitis complicated with infection. Her grandmother and her uncle took care of him and brought him to the hospital as his father lives in another country and he is working abroad to secure with very difficulties incomes for his family as a construction worker. Her mother works night and day to earn something for the whole family as they have a difficult life in a village. Both of the parents have low level of education. The symptoms had begun three years ago with itching and skin redness in hands and face. During the last 2 years he had also cough during the night and after effort or exercise. He had a positive family history for atopic diseases.

Methods and materials: The pediatric specific IgE revealed sensitization to soya, dog epithelia and cat epithelia. The boy loved of play with dogs and cats and he spent lots of time with them instead of staying with other kids, who refused to stay or teased him on a regular basis because of the skin lesions. This was the major boy's problem. He suffered o lot and everyone could recognize disappointment in his face. Skin prick tests to foods and inhalant allergens resulted negative. The properly performed pulmonary function testing demonstrated no abnormalities.

**Results:** After specific treatment with corticosteroids, antihistamines, emollient creams, disinfectants and antileukotriens he was feeling better, he was smiling again and wished to have the chance to play with his classmates again.

Conclusion: this case report shows an association between level of stress and risk for atopic dermatitis. As previously showed children with low educational level parents and boys with higher stress have increased risk of having severe atopic dermatitis as compared to "no stress" boys. So early treatment and diagnoses are key important factors improving the children`s social life.

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## 1352 | Race and allergy: A new epidemic?

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**Background:** The prevalence of atopy is increasing worldwide, especially in Western countries. Protection by the past rural environment is progressively lost, making immigrants more susceptible to atopic disorders. Sensitization in migrants is directed towards host country allergens, independently of ethnicity.

**Method:** We aimed to: (a) portray the turnout of immigrants in our outpatient clinic; (b) investigate the differences of allergic sensitization between immigrants and native-born patients. We retrospectively reviewed records of patients seen at our Allergy Unit from January 1, 2017 to June 30, 2017. Clinical history, clinical examination and skin prick test results were collected and examined. The immigrant group was then compared with an Italian group of patients seen during this period in terms of age, sex, clinical presentation and type of sensitization.

**Results:** The data cover 69 immigrants (mean age 39.0, range 8-62) and 232 locals (mean age 40.8, range 9-80). A slight difference in male prevalence (30.4% vs 47%, $P = 0.01$), and pet possession (20.2% vs 41.8%, $P = 0.01$) were found between immigrants and locals, respectively. No differences were find in term of age and symptoms at presentation. The pattern of sensitization to the different allergens showed no statistically significant differences between migrants and controls. The rate of monosensitization resulted slightly higher in migrants (27.5%) than controls (21.1%). Pollen-only sensitization was statistically higher among migrants than control (39.1% vs 22.4%, $P < 0.01$). Monosensitization was more frequent among patients who have been living in Italy for less than 4 years (52.6% vs 20%, $P = 0.05$). The opposite phenomena can be seen among polysensitized patients.

**Conclusion:** Migrants are more frequently monosensitized than locals and tends to cluster towards either a pollen or dust mite sensitization. Sensitization to house dust mite tends to appear early (< 4 years of stay). Pollen or mixed sensitization is more frequent the longer the residence time.

## 1353 | AllergenOnline.org: Update of comprehensive allergen and celiac protein searchable databases for risk assessment of novel food proteins

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**Background:** Food safety regulators in most countries require an evaluation of the potential allergenicity and potential for eliciting celiac disease (CD) from proteins introduced in genetically engineered crops and for novel proteins in processed foods. Allergy and CD are triggered by one to a few proteins in a food source, with unique proteins triggering responses in different patients. Avoiding consumption of triggering foods is necessary to protect allergic and CD affected consumers. There are no highly specific tests to predict the potential allergenicity or CD potential of individual proteins. Thus identification of offending proteins and comparison of new proteins is essential to evaluate safety. Allergen and CD databases on www.AllergenOnline.org were updated in January 2018 to provide tools for comparison.

**Method:** Entries in the NCBI Protein database and the WHO/IUIS Allergen Nomenclature database were reviewed to identify potential new allergens. Literature searches were performed using PubMed for references demonstrating IgE binding and allergenic as well as CD activity. Sequences and references were entered into an archival system. Data collection and expert reviews were as published in 2016 for allergens (PMID: 26887584), and as presented in the EAACI Congress in Geneva in 2013. The CD database includes sequences of peptides from prolamin and glutelin proteins of wheat, barley, rye and oats that bind HLA DQ 2 or DQ 8 and stimulate $CD4^+$ T cells from CD patients. A few that are toxic to intestinal epithelial cells are included. Peptides described by the European Food Safety Authority in 2017 for CD are included.

**Results:** AllergenOnline version 18 was updated in January, 2018. It includes 2101 protein sequences from 834 taxonomic protein groups representing allergens or putative allergens (IgE binding proteins) for FASTA comparisons. Version 17 included 2035 proteins from 808 groups. The CD database includes 1013 peptides and 72 representative glutens for exact match and FASTA comparisons. Use

of the database is free and no information is collected on users or sequence queries. Instructions are posted online.

**Conclusion:** Allergen and CD databases have been updated following a described review process. They can be used to identify proteins that might represent risks of food allergy or CD for affected consumers.

## 1354 | Stress affects symptom severity and quality of life in patients with allergic rhinitis

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**Background:** Stress can change the immune response and aggravate various allergic diseases. We already demonstrated in previous allergic rhinitis cohort (ARCO) kids study that stress might be a risk factor for pediatric allergic rhinitis (AR). The aim of this ARCO study is to investigate relationship between stress intensity, symptoms severity and quality of life as well as allergic markers in adult AR patients.

**Method:** A total of 752 patients were enrolled in this study from October 2013 to March 2015 at 8 medical centers and subjects were grouped according to stress intensity and symptom severity. Clinical characteristics, AR symptom severity, visual analogue scale (VAS) score of AR symptoms and the rhinoconjunctivitis quality of life questionnaire (RQLQ) scores as well as the levels of allergic markers were assessed in each group.

**Results:** As stress intensity increased, the proportion of moderate-severe AR patients was significantly increased. AR patients in high stress group was likely to belong to moderate-severe group (OR, 1.60; 95% CI, 1.01-2.50). Global VAS of AR symptom was 7.0 ± 1.9 in high stress group and 6.7 ± 2.0 in low stress group, respectively. The each 7 RQLQ domain score was significantly higher in high stress group than in low stress group. Total RQLQ scores were 75.3 ± 35.5 in high stress group and 57.4 ± 36.0 in low stress group, respectively. However, as the level of stress increased, there were no significant changes in serum levels of allergic markers.

**Conclusion:** Our results suggest that stress may affect AR symptom severity and quality of life in AR patients.

## 1355 | Skincare and synbiotics for the prevention of atopic dermatitis or food allergy in newborn infants: A 2 × 2 factorial randomized non-treatment controlled trial

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**Background:** Atopic dermatitis (AD) is a common disease mostly seen in early childhood. Skin barrier protection in early life by moisturizing has shown to be beneficial in preventing AD. Primary prevention of AD may also protect against the allergic march. Recent studies have also shown benefits of probiotics in preventing AD. Fructooligosaccharides (FOS) promote the growth of probiotic bacteria and thus the effect of probiotic and FOS combinations (synbiotics) may be more than that of probiotics alone. This study evaluated the prevention of AD and sensitization to food allergens using skin care and synbiotics in infants.

**Method:** A 2 × 2 factorial, randomized non-treatment controlled trial was designed and 605 pregnant women were recruited at 24-32 weeks of gestation over a period of 2 years (October 2014 to September 2016) (UMIN ID: UMIN000010838). A family history of atopy was not required for inclusion. Babies born at term were randomized according to gender, mode of delivery and family history of atopic diseases. They received no intervention (n = 121), skincare only (n = 124), synbiotics only (n = 114) or skin care and synbiotics (n = 118). The skin care group was advised to apply an emollient 2-3 times/day especially on cheeks and peri-oral area. The synbiotics group consumed a mixture of FOS (1 g) and *Bifidobacterium bifidum*OL6378 ($7 \times 10^9$)/day. The last group received both. Emollient application was not prohibited in the no-intervention group. Interventions were carried out from birth to 6 months of age. The development of AD was assessed at 1 month, 6 months and 9 months by a pediatrician and at 1 year by a questionnaire. AD was diagnosed using guidelines of the Japanese Society of Dermatology. Sensitization to food allergens was assessed by allergen-specific IgE levels at 9 months of age.

**Results:** Skin care and synbiotics, alone or in combination, did not prevent the development of AD at 1 year of age or the sensitization to food allergens at 9 months of age.

**Conclusion:** Our data suggest that skin barrier protection using emollients may be insufficient to prevent the development of AD as other factors affecting skin barrier integrity and trans-epidermal water loss such as the method of skin washing may have an additional effect. The probiotic bacterial species used may also affect the outcome as Lactobacilli have been shown to be more beneficial.

More studies are required to confirm the effects of skin care and synbiotics on AD.

## 1356 | Geographical differences in occurrence of specific immunoglobulins E to inhalant allergens in various regions of Poland

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**Background:** The number of allergic diseases has grown dynamically, which requires preventive action in relation to individuals from all risk groups. Taking these facts into account, local control of real threats has been conducted and disease maps as well as maps of most frequent sensitizers have been drawn up. One of markers of sensitization prevalence can be sIgE (specific immunoglobulins). The aim of this study was to assess the prevalence of specific IgE in relation to inhalant allergens in a Polish population of children and adults likely to be allergic, and evaluating the obtained data for potential geographical differences.

**Method:** Results of sIgE were collected from different labs in Poland performing the quantitative multiparameter enzyme-linked immunosorbent assays (Polycheck®, Biocheck GmbH, Münster, Germany). Collected results were arranged according to voivodeships. Statistical analysis was done using Statistica 10 (StatSoft Polska).

**Results:** This study collected 237 017 results of sIgE concentration (in kU/L) for 46 inhalation allergens which were analyzed for 16 267 patients with a suspicion of allergy. Data from 13 among Poland's sixteen voivodeships were collected. Voivodeships where the number of assays was less than 100 were excluded in the analysis. Gender proportions were approximately balanced. 42% of total number of patients were children younger than 3 years old.

Among inhalant allergens, 10 with the largest number of positive results were these against *Dermatophagoides farina* (25%), *Dermatophagoides pteronyssinus* (23%), alder (22.5%), dog (22%), hazel (22%), rye (19%), birch (19%), timothy grass (18%), cat (18%) and oak (13%).

A comparison of positive test results for 10 inhalant allergens analysed in 9 voivodeships showed differences between individual regions of Poland (Figure 1). The highest number of positive test results was observed in the Lubuskie and Dolnośląskie voivodeships, whereas the lowest number in the Lubelskie voivodeship. Analysis of results showed significant statistical differences between these voivodeships ($P < 0.0001$).

**Conclusion:** The collected data indicated differences in the occurrence of sIgE to inhalant allergens in various regions of Poland. In the Lubuskie, Dolnośląskie and Śląskie voivodeships the number of the researched with hypersensitivity to airborne allergens was considerably higher than in the Lubelskie voivodeship.

## 1357 | Prevalence of allergic children's population

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**Background:** Goal of our work included study of prevalence of allergic diseases and risk factors in the children's populations of Tbilisi, Kutaisi and Batumi, regarding geographical climatic conditions

**Method:** Study group of 2579 children from 3 to 16 (girls: 58.4%; boys: 41.6%). At the first stage of epidemiological study the large-scale work was performed, through questionnaire of interviews with the parents and further was specified through telephone interviews. Key data of the screening questionnaire were directed towards initial diagnostics of allergic diseases and population stage of the studies possibility of identification of the potential risk factors (included obstetrics anamnesis, data about child's development before one-year age etc.). On the second stage of epidemiological studies part of the patients with allergic diseases (928 children) were subjected to clinical allergy study, with measurements of IgE level in the blood and prick-testing was conducted, study of external respiration function. At the last stage mathematical-statistical data processing was provided by means of software SPSS/V12.5 (Statistical Package for Social Sciences).

**Results:** In the population number of girls exceeded the one of boys ($P < 0.001$), especially within the age group from 4 to 15 years. Questioning, for 12 months, symptoms of allergic rhinitis (rhinorrhea, sneezing, nose itch, nasal obstruction and eyes' itch) were identified in 19.5 ($P < 0.05$); symptoms of bronchial asthma (wheezing (14%), episodes of cough at night (8.3%), intolerance to physical load (2.5%), indoor and outdoor (13.6%), coughing and rales in response to stimulus (7.2%)) in 9.8% of the population; atopic dermatitis (dermatitis, itch, revelation in early age, involvement of large areas in early age, damage of extremities bending and stretching surfaces in adults)—5.7% ($P < 0.01$); food allergy—3.7% ($P < 0.001$) etc. At the second stage of clinical studies, on the basis of prick-testing, average IgE, in our case, was 3-5 times greater than normal level. Results of study of allergens showed sensibilization to domestic dust (D.F. and D.P.) (64, 43%) ($P < 0.05$). In 25.46% of cases there was stated sensibilization conditioned by cat and dog epidermal allergens

**Conclusion:** In development of allergic diseases share of controllable risk factors is quite high and this could provide basis for development of targeted and effective prevention measures in children's population.

## 1358 | Maternal sensitization during pregnancy

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**Background:** Allergic sensitisation in infancy may be preceded by maternal, pregnancy-related and early life factors. The PreventADALL (Preventing Atopic Dermatitis and ALLergy in children) study investigates strategies for allergy prevention and explores factors involved in allergic disease development. The aim of the present study was to explore the frequency of IgE-sensitization, and to determine the rates of mono- and poly-sensitisation for food- and inhalant allergens and allergic diseases in pregnant women.

**Method:** The 2701 pregnant Swedish and Norwegian women aged 18-42 years were enrolled within 22 months from December 2014 in three hospitals at the 18-week ultrasound investigation. From the 18-week investigation, blood samples were analysed for IgE reactivity against inhalant (birch, grass, dog, cat, house dust mite) and food (egg, milk, peanut, wheat) allergens by ImmunoCAP, regarded as positive if ≥0.35 kU/L, and doctor's diagnosis (DD) of asthma (DDA), allergic rhinitis (DDAR) and of food allergy (DDFA) were recorded in electronic questionnaires.

**Results:** Among the 2624 women with available serum, 39.3% were sensitized of whom 12.5% were monosensitised, and 25.3% polysensitised (to two or more allergens). Sensitisation to inhalant allergens dominated (38.9%), with grass being most common (25.5%). Only 4.0% were sensitized to food allergens, most often to peanuts (2.6%), while among the 11.4% who reported DDFA, IgE reactivity to foods were identified in 17.5%. Compared to women with no asthma, women with DDA (14.9%) were in a significantly higher degree poly-sensitised 20.0% vs 51.0%, while the corresponding figures for DDAR (17.6%) and DDFA were 10.8% vs 66.7% and 18.7% vs 55.1% (*P*-values <0.001), respectively.

**Conclusion:** Polysensitisation was significantly more common among women with doctor's diagnosis of allergic disease compared to non-allergic women. The prevalence of allergic sensitization in the mothers in PreventADALL is comparable to similar cohorts. Reported food allergy in 11.4% was associated with s-IgE in only 17.5% of women.

## 1359 | Lack of exercise is a risk factor of atopic dermatitis in Korean adolescents

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**Background:** Regular exercise has been known as beneficial that it reduces the risk of chronic diseases including allergic diseases. However, little has known regarding the relationship between exercise and allergic diseases in Korean adolescents. We analyzed the national data whether exercise is related to the prevalence of allergic diseases in the population of Korean adolescents

**Method:** Data from sixth Korean National Health and Nutrition Examination Survey (2013-2014) that included 1272 adolescents from 12 to 18 years old was analyzed. We defined regular exercise according to physical activity guidelines for Americans. Multivariate regression analysis was performed to find whether lack of exercise could be a risk factor for allergic diseases.

**Results:** The prevalence of asthma, allergic rhinitis (AR) and atopic dermatitis (AD) were 1.3%, 9.3% and 5.2% in Korean adolescents, respectively. After adjusting for factors, lack of exercise was not associated with asthma and AR, but was significantly related to AD in Korean adolescents (adjusted odd ratio 3.254, 1.202-8.810, $P = 0.021$)

**Conclusion:** This study suggested lack of exercise is a risk factor of atopic dermatitis in Korean adolescents. These findings may be helpful for disease management and improving the quality of life in AD of Korean adolescents.

## 1360 | Epidemiological features and risk factors for early development of atopic dermatitis in children

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**Background:** The aim of this work was to perform an epidemiological study on prevalence (ESP) of atopic dermatitis (AD) in children (Ch) of different ages in Primorsk Territory of Russia and define significant risk factors (RF) of disease.

**Method:** The ESP of AD among 3634 Ch of 6-7 (1G) and 13-14 (2G) years old (y.o.) were performed under the program ISAAC (Vladivostok, Russia) along with definition of basic triggers affecting its development. All Ch held general clinical and allergological examinations (AE). We used SCORAD scale to define AD severity level (SL).

**Results:** It was found that over 43% of Ch up to 14 y.o. having the AD within allergic disease (ADs). The most significant symptom was a long-lasting itchy rash lasting for 6 month in 12.42 ± 0.56% of 1G and 9.23 ± 0.49% of 2G. The first morbidity of AD was noticed at the age of up to 2 y.o. among 56.29 ± 1.27%. At the age of Ch 2-4 y.o. and older than 5 y.o. the skin ADs onset was noticed for 31.12 ± 1.11% and 12.58 ± 0.57% accordingly. The AD SL was determined as follows: 52% - moderate (Mo), 12% - severity (S), 36% - mild (Mi). The AE results displayed a high degree of aeroallergens sensibilization. When the focalized form of AD in 100% of cases noted the Mi form, when diffuses—S AD, when extensive form of AD: 2/3 cases—Mo, 10%—S and 3% - Mi. Each 3rd Ch of 1G and each 2nd Ch of 2G having AD clinical symptoms of the disease were combined with asthma symptoms - BA and/or allergic rhinitis—AR. AR was found twice more often in 1G Ch (76.02 ± 0.94%). BA and AR were of the same frequency for 1G Ch - 90.90 ± 0.48% and 2G Ch - 98.48 ± 0.08%.

The most important RF of AD early development are: maternally inherited predisposition - 63%; abnormal texis - 2/3 Ch; irrational nutrition Ch in the first year of life; Ch's statical and/or functional pathology of gastro-intestinal tract; frequent virus infection (herpetic infection - 17%, acute respiratory disease - 44%.

**Conclusion:** Therefore the real picture of AD prevalence rate among Ch 6-14 y.o. was formed, basic RF promoting the AD were determined. Considering new patterns shall contribute to timely medical-preventive activities in order to prevent the AD prevalence among Ch.

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## 1361 | Atopic Dermatitis is related to regular physical activity in Korean male adolescents

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**Background:** Physical activity (PA) is essential for promoting and maintaining health, especially in adolescents and the elderly. However, there is controversy as to whether PA reduces the risk of allergic diseases, especially atopic dermatitis (AD). So we investigated the relationship between PA and AD in Korean adolescents.

**Method:** We used data obtained from the 2016 Korea Youth Risk Behavior Web-based Survey (KYRBWS-VII) of 65 628 adolescents. We defined regular PA according to Guidelines for physical activity for Koreans. Multivariate regression analysis was adjusted by social, physical and behavior variables, using a complex sampling design.

**Results:** The prevalence of AD was 25.1 ± 0.2% in entire adolescents, 21.3 ± 0.2% in males, 29.4 ± 0.3% in females, respectively. After adjusting for factors, regular PA was significantly related to AD in Korean male adolescents (adjusted odd ratio 1.130, 1.003-1.274, $P = 0.045$). But female adolescents didn't relate to regular PA, aerobic PA and strengthening exercise.

**Conclusion:** This study provided evidence that regular PA is related to development of AD in Korean male adolescents. Further research is needed to identify why sufficient PA could be a risk factor of AD in male adolescents.

## 1362 | Vitamin A and vitamin D levels in allergic children

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**Background:** Vitamin A and D levels may affect development of allergic diseases. In this study we aimed to evaluate vitamin A and D levels in allergic diseases.

**Method:** We evaluated vitamin A and D levels of children (n:235) followed up because of asthma (n:118) allergic rhinitis (n:77), atopic dermatitis (n:12), chronic urticaria (n:14), food allergy (n:14) and 15 controls.

**Results:** Average symptom onset ages of 97 girls and 138 boys were 41.8 ± 35 months. Consanguinity was 12.7%, prematurity was 5.7%. Family history of atopy was 51.9%. Passive smoking was 23.5%. Half of the parents had low income. Forty-one percent of the patients had eosinophilia, 54.4% of the patients aeroallergen-spIgE was positive. Average aeroallergen- spIgE and total IgE levels

were 13 ± 10 kuA/L, 344 ± 132 IU/L respectively. Skin prick tests were positive in 43.4% of the patients (61.7% multiple allergens). Grass pollens (53%) and dermatophagoides (45.2%) were the most common allergens.

Average vitamin A and D levels were 469.8 ± 108 μg/L (257-832), 54.8 ± 21.3 (13-187) respectively. Thirty percent of the patients vitamin D levels were mildly low, 8.6 percent was low. In control group 20% was mildly low, Vitamin A levels was low in 6.7% of the patients. None of the children in control group had low vitamin A levels. We didn't find any statistical significant difference for both vitamin levels between patient and control groups. Vitamin A deficiency was mostly found in asthma patients whereas Vitamin D deficiency was mostly in allergic rhinitis and asthma groups. Passive smoking and vitamin D deficiency was significantly related ($P = 0.09$). There wasn't any relation between asthma attacks and vitamin levels.

**Conclusion:** In conclusion vitamin A and D levels weren't found significantly related with allergic diseases but was found lower than control group.

## 1363 | Concepts about primary prevention of asthma vary among specialists and primary care physicians in Mexico

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**Background:** The increase in the prevalence of asthma also rises the need to identify approaches to primary prevention. Exclusive breast-feeding and avoidance of exposure to environmental tobacco smoke can be safely recommended. However, some concepts about primary prevention of asthma vary among different specialists and generalists. Mexican Asthma Guidelines (GUIMA 2017) were published as an effort to unify asthma diagnosis and management.

**Method:** As part of GUIMA dissemination strategy and to detect distinct physicians' current concepts on Asthma, an online survey was sent out to members of participating societies containing some of the clinical questions of GUIMA. Replies concerning prevention of asthma were analysed per specialty against the GUIMA 2017 experts' recommendations/suggestions; differences between specialists (allergists, pulmonologists, ENT, paediatricians and primary physicians) were investigated.

**Results:** Vaccination against bacteria or virus does not increase risk for development of asthma and therefore GUIMA recommends that complete immunisation schedules should be administered promptly. Most clinicians (>90%) from all specialties were aware of this. GUIMA recommends decreasing tobacco smoke exposure to reduce the risk for asthma development. Most clinicians (>85%) from all specialties agreed. As for diet and nutrition, GUIMA recommends against a hypoallergenic diet in pregnant/breastfeeding women as a measure of primary prevention of asthma in the child. Only half of the clinicians agreed on this statement (50-61.2%), indicating many physicians still tend to prescribe restriction diets to pregnant and breastfeeding women. GUIMA recommends against the delayed introduction to allergenic food in children to decrease the risk of developing asthma. However, most clinicians answered in favour of delayed introduction. There were important differences between ENTs, allergists and paediatricians (respectively, 82.4%, 65.4% and 53.6% in favour of delayed introduction).

**Conclusion:** There are several factors that might increase or decrease the risk of asthma development, some of them amendable to manipulation. Their correct identification is quite important. Throughout this work we could detect knowledge-gaps especially in the field of the recently adjusted nutritional recommendations for mothers and young children. GUIMA proposes an updated, national guideline to solve these disparities with high-quality transculturised suggestions and recommendations.

## 1364 | The impact of chronic diseases in drug allergies prevalence

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**Background:** The frequency and the duration of exposure toward allergens are stated to be an important factor of developing allergy. Patients having chronic diseases are one of the population groups that are chronically exposed to drugs. This study aims at evaluate the impact of this factors in developing drug allergies in the medical staff.

**Method:** This was a cross-sectional study that included 639 nurses from the UHC "Mother Theresa" of Tirana. They were asked to fill up a questionnaire where questions about chronic diseases and drug allergies were included. 92.18% were females and the mean age was 43.28 (+10.71) years old. Relative Risks with 95% CI were calculated for different groups.

**Results:** 40.69% (260) nurses reported to have at least a chronic disease. The most common non-atopic disease was HTA followed by the groups of autoimmune and thyroid diseases. Nurses who had one chronic disease have a RR of 1.82 (95% CI = 1.03-3.21, $P < 0.05$) to develop a drug disease higher than those who didn't had any chronic disease, and those who have more than one chronic

disease have a RR of 5.16 (95% CI = 1.51-17.60, $P < 0.05$) to develop a drug disease.

**Conclusion:** The presence of chronic diseases can be a risk factor to develop a drug allergy probably through the increased risk to drug exposure. These patients may be exposed to drugs not only through therapy but also through hospitalizations and other forms of health care.

## 1365 | Implementation of latex allergy clinical care pathways

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**Background:** The key to managing latex allergies in healthcare professionals and patients lies in correct recognition and appropriate action.

7.7 million people are employed in the health care sector. While there are no overall statistics on the prevalence of latex allergy in that work force, studies do indicate that 8%-12% of health care workers regularly exposed are sensitized, compared with 1%-6% of the general population.

Latex allergy is defined as an immune mediated reaction to latex products (e.g. balloons, contact dermatitis for gloves, condoms, surgical catheters); these encompass immediate and delayed hypersensitivity reactions.

**Method:** Based on the experience of the Belgian Dutch Pathway Network, a 7-phase method to develop, implement, evaluate and continuously follow up a care pathway for latex allergy was designed and implemented.

The purpose of the study was to develop and implementation of latex allergy clinical care pathways

to provide all staff at Ghent university Hospital with appropriate knowledge and skills to identify and manage patients who have a known latex allergy or those at risk of developing latex allergy.

**Results:** Care pathways, also known as clinical pathways, are used all over the world to implement and monitor patient-centered care processes in a transparent way. Care pathways are defined as a complex intervention. 7 -phase method consists of: 1) screening phase; 2) project management phase; 3) diagnostic- and objectification phase; 4) development phase; 5) implementation phase; 6) evaluation phase and 7) continuous follow-up phase. This phased approach is based on the Deming cycle, better known as the "plan-do-study-act" (PDSA)-cycle.

**Conclusion:** This method can offer support to multidisciplinary teams (re)designing and implementing safe, efficient, effective, person-centered, timely, equitable, continuous and integrated care processes. However, the method is no guarantee to success. The key to success is the collaboration and critical attitude of the entire multidisciplinary team when implementing pathways.

The objective of the development of care pathways is to optimise patient and health care professionals' safety and to improve health care quality.

## 1366 | Predictive capacity of cord blood IgE for allergic symptoms in adulthood: Prospective study in Slovakia

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**Background:** Cord blood IgE (CB-IgE) were considered to be a useful predictive tool for allergic symptoms especially in early childhood. There is only sparse knowledge about their importance for health in later life. The aim of our work was to determine the importance of CB-IgE for allergic symptoms in young adults. We also studied the possible modifying factors for CB-IgE concentration.

**Method:** Our studied population consisted of young adults with the history of CB-IgE sampling at birth during the period 1989-1993. All the enrolled subjects underwent complete clinical, laboratory and physical examination.

**Results:** We found the most significant correlation between atopy and CB-IgE concentration ($P = 0.05$), atopy and a positive family history of atopy ($P = 0.008$), eosinophilia and atopy ($P = 0.055$). Male gender, Caesarean section and birth during a winter season were the most important factors associated with higher CB-IgE at birth (0.036, 0.05, 0.05 respectively). Unfortunately, we were not able to confirm any predictive value of CB-IgE for allergic manifestations in early adulthood.

**Conclusion:** According to our knowledge, this is the first study analysing the clinical meaning of CB-IgE for adult allergic diseases in Slovakia. We did not find any relationship between CB-IgE and allergies in young adults, but we identified several modifying factors for CB-IgE, which should be taken into account in clinical evaluation of this parameter.

## 1367 | Corticoids and antihistamines in prevention of anaphylaxis: A bibliometric review

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**Background:** Despite the lack of evidence, it is common to prescribe corticosteroids and antihistamines as preventive of anaphylaxis. The objective of this study was to perform a bibliometric analysis on the use of this drugs in the prevention of anaphylaxis.

**Method:** Active search for articles in Scopus database with the terms "anaphylaxis and prevention and steroid or antihistaminic" in title, abstract or key word published until October 2016. The selected articles were read searching for the specific use of steroid and/or anti histamine in the prevention of anaphylaxis.

**Results:** There were 292 articles published until October 2016 in the Scopus database. When searching for the 104 eligible complete articles, only 49 articles were included in the study because of their reference to the use of the drugs in the prevention of anaphylaxis and their digital availability. None of the 49 articles addressed specifically the role of corticosteroids and/or antihistamines in the prevention of anaphylaxis.

**Conclusion:** There is currently no evidence in the literature that the use of corticosteroids and antihistamines is beneficial or is detrimental in the prevention of anaphylaxis.

## 1369 | Cholinergic urticaria features in adult population of Kazakhstan

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**Background:** Cholinergic urticaria (Thermal urticaria; Stress-induced urticaria; Micropapular urticaria) is a type of physical hives and is associated with heating and sweating. True prevalence is unknown. Despite the fact, that population of the Republic of Kazakhstan is a multinational, it has similar socio-economical, cultural and nutritional characteristics.

The aim of the study was to compare the clinical peculiarities of cholinergic urticaria in different population groups.

**Method:** Our clinical study was performed in allergological center "Umit", Astana, Kazakhstan in 2010-2017, and enrolled totally 34 patients with cholinergic urticaria. The special allergological questionnaires were completed. All patients signed written informed consent for publication. Diagnosis was made on the basis of approved GA$^2$LEN consensus panel recommendations (2009). Study population was divided into two groups: 12 (35.3%) Mongolian and 22 (64.7%) Caucasian.

**Results:** In the first group there were 9 (75%) men and 3 (25%) female with mean age of 24.3 ± 2.3 years, whereas in the second group (Caucasian) there were 17 (77.3%) men and 5 (22.7%) female with mean age of 26.5 ± 1.9 years, showing the prevalence of male gender in both study groups and age homogeneity. Onset of the disease in both study groups did not reveal any statistical significance and was 25.8 ± 4.5 and 24.9 ± 4.3 respectively ($P \geq 0.05$). Concurrent atopic manifestations were found in 3 (25%) patients of the first group and in 10 (45.4%) patients of the second one, showing 1.8 times higher sensitization rate in Caucasian population. The incidence rate of spontaneous remission in five years was 4 (33.3%) in the first study group whereas it was 9 (40.9%) in the second one. For the treatment of developed cholinergic urticaria, first and second generation antihistamines were prescribed in all patients along with corticosteroids as appropriate.

**Conclusion:** Clinical manifestations of cholinergic urticaria are characterized by allergic rash, developing after sweating. Young age, male gender, concurrent atopic sensitization and Caucasian ethnicity are risk factors and should be concerned for the early diagnosis and disease prevention.

TUESDAY, 29 MAY 2018
TPS 44
POLLEN AND OTHER AEROALLERGEN EXPOSURE

## 1370 | Cupressus arizonica, platanus acerifolia and plantago lanceolata pollen counts in a new monitoring site in Madrid

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**Background:** Infanta Leonor University Hospital is located at the South-East of Madrid city with an assigned Healthcare population of more than 350.000 habitants. Since the flora and vegetation in our working area differs from others in Madrid city, the aim was to monitor *Cupressus arizonica*, *Platanus acerifolia* and *Plantago lanceolata* airborne pollen concentrations in our region.

**Method:** Airborne pollen amount was recorded at the Infanta Leonor University Hospital pollen station using a Hirst-type volumetric sampler.

The sample collection, preparation and pollen counts were carried out between January 2017 and May 2017, using methods recommended by the Aerobiology Committee of the Spanish Academy of Asthma and Clinical Immunology.

The sampler was located at 12 meters over the ground and had a suction chamber with a flow rate speed of 10 L/minutes. The aspirated airflow blows in front of a clear glycerined tape placed around the rolling drum rotating at 2 mm/h.

Pollen grains were viewed at 400 × magnification with an optical microscope and counted, obtaining a daily mean of pollen concentration per air cubic meter in 24 hours.

**Results:** Resutls shown as daily mean, pollen grains/m³: Table 1.

**Conclusion:** The daily means of pollen concentrations of *Cupressus arizonica*, *Platanus acerifolia* and *Plantago lanceolata* in our area differs from other sites in Madrid city.

Although *Cupressus arizonica* and *Platanus acerifolia* counting were lower, *Plantago lanceolata* counts were higher, representing a relevant pollen in our area.

The clinical relevance of these findings is under evaluation by our group.

Table 1.

| | Cupress/ Taxaceae | | Platanus | | Plantago |
|---|---|---|---|---|---|
| 28 Jan. | 59 | 17 Mar. | 53 | 30 Mar. | 11 |
| 29 Jan. | 97 | 18 Mar. | 29 | 31 Mar. | 6 |
| 30 Jan. | 126 | 19 Mar. | 21 | 01 Apr. | 2 |
| 01 Febr. | 25 | 20 Mar. | 24 | 2 Apr. | 5 |
| 02 Febr. | 16 | 21 Mar. | 7 | 3 Apr. | 8 |
| 04 Febr. | 19 | 23 Mar. | 17 | 4 Apr. | 16 |
| 09 Febr. | 22 | 24 Mar. | 82 | 5 Apr. | 3 |
| 10 Febr. | 42 | 25 Mar. | 119 | 7 Apr. | 24 |
| 18 Febr. | 6 | 26 Mar. | 135 | 8 Apr. | 20 |
| 01 Mar. | 9 | 30 Mar. | 128 | 9 Apr. | 16 |
| 03 Mar. | 29 | 31 Mar. | 51 | 10 Apr. | 23 |
| 4 Mar. | 72 | 01 Apr. | 47 | 11 Apr. | 27 |
| 5 Mar. | 13 | 2 Apr. | 54 | 19 Apr. | 87 |
| 6 Mar. | 395 | 3 Apr. | 39 | 20 Apr. | 12 |
| 7 Mar. | 10 | 4 Apr. | 37 | 21 Apr. | 28 |
| 8 Mar. | 56 | 5 Apr. | 22 | 22 Apr. | 25 |
| 9 Mar. | 97 | 6 Apr. | 0 | 23 Apr. | 43 |
| 10 Mar. | 11 | 01 Apr. | 28 | 24 Apr. | 39 |
| 11 Mar. | 45 | 8 Apr. | 25 | 25 Apr. | 34 |
| 12 Mar. | 66 | 9 Apr. | 34 | 26 Apr. | 22 |
| 13 Mar. | 23 | 10 Apr. | 19 | 27 Apr. | 21 |
| 14 Mar. | 16 | 11 Apr. | 16 | 28 Apr. | 7 |
| 15 Mar. | 9 | 19 Apr. | 18 | 29 Apr. | 5 |
| 16 Mar. | 14 | 20 Apr. | 2 | 30 Apr. | 9 |
| 17 Mar. | 12 | 21 Apr. | 5 | 01-May | 6 |
| 18 Mar. | 9 | 22 Apr. | 6 | 02-May | 18 |
| 19 Mar. | 13 | 23 Apr. | 4 | 03-May | 14 |
| 20 Mar. | 6 | 25 Apr. | 11 | 04-May | 18 |
| 21 Mar. | 5 | 27 Apr. | 8 | 05-May | 16 |
| 24 Mar. | 3 | 28 Apr. | 2 | 06-May | 5 |
| 27 Mar. | 3 | 29 Apr. | 5 | 07-May | 6 |
| 31 Mar. | 5 | 30 Apr. | 2 | 08-May | 22 |
| 02 Apr. | 2 | 01-May | 4 | 09-May | 24 |
| 3 Apr. | 0 | 02-May | 0 | 10-May | 2 |
| 4 Apr. | 1 | 03-May | 0 | 11-May | 4 |
| 5 Apr. | 2 | 04-May | 0 | 12-May | 17 |
| 6 Apr. | 0 | 05-May | 0 | 13-May | 16 |
| 7 Apr. | 1 | 06-May | 1 | 14-May | 25 |

## 1371 | Madrid, 38 years of pollen observation: Poaceae pollen counts in a changing weather

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**Background:** The principal objective is to check and find out if the weather and the climate change affect the pollen counts in Madrid.

**Method:** Grass pollen counts were performed since 1979-2016 using a Burkard 7 days spore trap located in our allergy center in Madrid.

The beginning of the algid period of pollination was considered the first of three consecutive days with more than 10 grains/$m^3$ and the end, the last day of three consecutive days with more than 10 grains/$m^3$.

Madrid, Barajas meteorological station data, was used.

Skin prick tests (PT) to grass pollen was also studied in comparison with a total of PT in 1979 (n = 100 pollinosis patients), 1994 (n = 316 pollinosis patients) and annually from 1999-2016 (n = 40.998), annual media of 2.411 patients with pollinosis.

**Results:** The quinquennial media concentrations since 1979-2016 were 3.745; 5.949; 4.122; 5.119; 5.119; 4.172; 4.006 and 5.024 grains/$m^3$.

The quinquennial media temperatures were 14.2; 13.8; 14.3; 14.9; 14.2; 14.7; 14.9 and 15.8°C. Increase of 1.4°C ($r_s$ = 0.9 $P < 0.05$).

The quinquennial media temperatures between May and July were 14.3;19.9; 21.1; 21.1; 21.1; 21.9; 21.8 and 23.0°C. ($r_s$ = 0.9 $P < 0.05$).

The actual season beginning advanced 6 days calculated since May 1st and the end has shortened in 16 days in regard to the period 79-83. The duration of the season shortened in 11 days.

The annual prevalence of positive prick tests to grass pollen in 1979 was 90% and 87% in 1994. The quinquennial media from 1999 to 2016 was 85, 78, 75 and 73%.

**Conclusion:** Total grass pollen concentration did not suffer any increase or decrease in its counts despite the dramatic increase of the temperature.

An advance at the beginning and the end of the season was seen. These changes significantly correlate with the temperature increase during may and july.

Discrete decrease in the sensitization prevalence.

## 1373 | Alternaria spores as a summer allergen inducing hay fever symptoms in Ukraine

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**Background:** There are high levels of sensitization in Ukraine to *Alternaria* allergens. This needs to be considered when assessing summer outbreaks of hay fever symptoms often associated with grass and weed pollen.

**Method:** Spore and pollen counts were obtained from 2009 to 2017 using volumetric methods employing a Burkard trap placed at a height of 25 meters above the ground on the roof of a Vinnitsa Medical University building. Samples were taken from March 1 until October 31. Slides were analyzed with a mean of three horizontal transects in the years 2009-2012 and by the 12 vertical transects since then. Daily average pollen and spore concentrations were calculated and analyzed.

**Results:** Intense *Alternaria* spores concentrations overlapped with grass, mugwort and ragweed pollen seasons, beginning in May and ending in October. The highest *Alternaria* spore concentrations were seen in the mid of July during a short gap between intense Poaceae and *Artemisia* pollination followed by start of *Ambrosia* season. High levels of *Alternaria* spores, exceeding the symptom threshold for this spore type (100 spores per cubic meter of air) were seen during the ragweed high pollen season. *Alternaria* season lasted at least two weeks longer than that of pollen producing species including *Ambrosia*. Thus, *Alternaria* can be a potential trigger of symptoms in late September and in October when pollen counts are low.

**Conclusion:** *Alternaria* should be considered as the potential agent of seasonal allergy from May to October in Ukraine when grasses and weeds pollinate. Further studies are needed to determine the connection between high *Alternaria* spore concentrations and symptoms of sensitive individuals.

## 1374 | Mugwort season in Ukraine in association with the ragweed pollen season

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**Background:** *Artemisia* pollen is an important allergen, which initiates the weed pollen season in Ukraine. Due to its occurrence overlapping with *Ambrosia* pollen, symptoms that have been induced by mugwort pollen often continue during the ragweed pollen season.

This study analyzes the timing of *Artemisia* season in Central Ukraine and overlap with the *Ambrosia* pollen season.

**Method:** Pollen counts were obtained from 2009 to 2017 using volumetric methods employing a Burkard trap placed at a height of 25 meters above the ground on the roof of a Vinnitsa Medical University building. Samples were taken from March 1 until October 31. Slides were analyzed with a mean of three horizontal transects in the years 2009-2012 and by the 12 vertical transects since then. Daily average pollen concentrations were obtained and analyzed.

**Results:** *Artemisia* season onset varied from July 3 to July 30 with tendency for earlier pollen season start during the years of research. *Artemisia* pollen peak varied within 10 days from August 5-15. The season ended September 10 to October 19. No clear tendency to a later peak or season end was observed. The annual mugwort pollen index decreased up to 3.8 fold in 2015 when droughts were recorded in Ukraine in comparison with the years of most intense pollination (2011-2012).For *Ambrosia* this coefficient was 5.4 showing greater impact of droughts on ragweed pollination. The *Artemisia* season was characterized by two pollination waves in every year, the first being more intense from July 21 to August 25, the second being from September 4 and 22, almost completely coinciding with the second period of intense *Ambrosia* pollination seen in September in Vinnytsia. From August 11 to August 23, mugwort season overlapped with the high ragweed season in Vinnytsia, the *Ambrosia* season starting 17 days later than *Artemisia*. Intensity of the both seasons decreased gradually after September 24 but some mugwort pollen could be seen in the second fortnight of October.

**Conclusion:** Active mugwort pollination is seen in Vinnytsia from mid of July to the end of October with overlap from mid August to the end of the season with ragweed pollination, intense pollen emission from both species noted from August 16-23 and from September 4-22.

## 1377 | Alternative Method for the measure of the biological particles in the air: Rapid-e example

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**Background:** The particles with a biological origin transported by the wind, as pollen grains and mold spores, are present in the air sometimes in very important concentrations according to the seasons. Depending on their allergy potency, these particles can cause symptoms of allergy for sensitive persons: in Europe, 20% of the population suffers from hay fever.

Since several years, the reference method to monitor the biological particles concentrations has been the Hirst method: a volumetric pollen trap, located on the roof of building for background measurements, sucks continuously 10 L of air per minute, particles depositing by impaction on a coated tape. The tape is then analyzed by optical microscopy.

The Hirst method produces accurate but past data. Nowadays, many researches are focused on the development on new devices to get real time information.

**Method:** Rapid-E from Plair SA is a device using red laser beam to determine the size and the shape of sucked particles and an ultraviolet ray to measure the fluorescence of these particles.

The French Network of Aerobiology (RNSA) set up a Rapid-E in March 2017 in Brussieu, along a Hirst trap. The device needed several calibrations to recognize and differentiate pollens and molds.

**Results:** The correlation coefficients got between Rapid-E and Hirst trap are higher than 70% for most of calibrated pollens, this correlation reaching 86% for all pollen taxa:

- Plane 99%
- Pine 99%
- Birch 96%
- Oak 82%
- Plantain 75%
- *Dactylus* 73%
- *Urticaceae* 55%

**Conclusion:** New calibrations are planned for 2018 and a real time information will be set up.

## 1378 | Madrid, 38 years of pollen observation: Platanus pollen counts in a changing weather

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**Background:** The principal objective is to check and find out if the weather and the climate change affect the aerobiological behavior of the *Platanus* pollination and its pollen counts in Madrid.

**Method:** *Platanus* sp pollen counts were performed since 1979-2016 using a Burkard 7 days spore trap located in our allergy center in Madrid.

The beginning of the algid period of pollination was considered the first of three consecutive days with more than 10 grains/$m^3$ and the end, the last day of three consecutive days with more than 10 grains/$m^3$.

Madrid, Barajas meteorological station data, was used.

Skin prick tests (PT) to *Platanus hispanica* pollen was also studied in comparison with a total of PT in 1979 (n = 100 pollinosis patients), 1994 (n = 316 pollinosis patients) and annually from 1999-2016 (n = 40.998), annual media of 2.411 patients with pollinosis.

**Results:** The quinquennial media concentrations since 1979-2016 were 3.866; 4.903; 6.610; 13.454; 9.501; 7.248;11.027 and 19.406 grains/$m^3$.

The quinquennial media temperatures were 14.2; 13.8; 14.3; 14.9; 14.2; 14.7; 14.9 and 15.8°C. Increase of 1.4°C ($r_s$ = 0.9 $P < 0.05$).

The beginning and the end of the actual season advanced 5 days respectively in regard to the period from 1979 to 1983.

The annual prevalence of positive PT to *Platanus* in 1979 was 2% an 52% in 1994. The quinquennial media from 1999 to 2016 was 50, 38, 26 and 29%.

**Conclusion:** *Platanus* pollen counts had a dramatic increase that meaningfully correlates with the dramatic increase of the temperature.

A discreet advance at the beginning and the end of the season was seen. These changes did not influence in a longer duration of the season.

We observed a significant increase in *Platanus* pollen sensitization prevalence whiting Madrid pollinosis patients.

## 1379 | Madrid, 38 years of pollen observation: Cupressaceae pollen counts in a changing weather

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*Clinica Subiza: Centro de Asma y Alergia, Madrid, Spain*

**Background:** The principal objective is to check and find out if the weather and the climate change affect the aerobiological behavior of the Cupressaceae pollination and its pollen counts in Madrid.

**Method:** Cupressaceae pollen counts were performed since 1979-2016 using a Burkard 7 days spore trap located in our allergy center in Madrid.

The beginning of the algid period of pollination was considered the first of three consecutive days with more than 10 grains/$m^3$ and the end, the last day of three consecutive days with more than 10 grains/$m^3$.

Madrid, Barajas meteorological station data, was used.

Skin prick tests (PT) *Cupressus* spp and/or *Juniperus oxycedrus* pollen was also studied in comparison with a total of PT in 1979 (n = 100 pollinosis patients), 1994 (n = 316 pollinosis patients) and annually from 1999-2016 (n = 40.998), annual media of 2.411 patients with pollinosis.

**Results:** The quinquennial media concentrations since 1979-2016 were 1963, 4813, 5455, 6948, 6985, 5976, 6727 and 9298 grains/$m^3$.

The quinquennial media temperatures were 14.2; 13.8; 14.3; 14.9; 14.2; 14.7; 14.9 and 15.8°C. Increase of 1.4°C ($r_s$ = 0.9 $P < 0.05$).

The actual season beginning advanced in 51 days and the end has shortened in 25 days in regard to the period from 1979 to 1983. The duration of the season increased in 26 days.

The annual prevalence of positive PT to *Cupressus* in 1979 was 0% and 20% in 1994. The quinquennial media from 1999 to 2016 was 44, 45, 49 and 47%.

**Conclusion:** Cupressaceae pollen counts had a dramatic increase that meaningfully correlates with the dramatic increase of the temperature.

An important advance at the beginning of the season was seen. This change influence in a longer duration of the season. Dramatic increase in the sensitization prevalence.

## 1380 | Allergy risk in central Spain in relation to the spatial distribution of the olive groves

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**Background:** The olive tree has a considerable agricultural and economic value in central Spain, and the *Olea* pollen grains are a major cause of allergy in the Mediterranean area. The aim of this work is to analyze, from an aerobiological point of view, the general behavior of *Olea* pollen in the atmosphere of central Spain and to relate the allergy risk of the olive pollen according to the abundance of the olive grove surfaces.

**Method:** Sampling was carried out in central Spain at six pollen stations of the Castilla-La Mancha Aerobiology Network, located in the main cities of Castilla-La Mancha region. *Olea* pollen grains were recorded during a period of five years (2009-2013) using Hirst volumetric spore traps, following the protocol established by the International Association of Aerobiology. The Annual Pollen Integral, APIn (summation of the average daily pollen concentrations during the year) and the number of days on which daily pollen concentrations exceeded allergy-risk thresholds proposed for the Spanish Aerobiology Network, were calculated.

**Results:** Results showed that the olive pollen season in central Spain started between the end of April and the second week of May, and ended between the second week of June and the beginning of July. The highest APIn values for the period of five years have been obtained in Ciudad Real and Toledo, although with a high year-to-year variability (7754 ± 2771 and 7171 ± 3056 pollen grains/$m^3$ and year). These two cities, capitals of their provinces, have similar olive cultivation areas that cover almost 270 000 ha, which represents up to 70% of the olive groves in the region. Ciudad Real and Toledo also showed the highest amounts of the maximum daily pollen concentrations (977 ± 284 and 1441 ± 925 pollen grains/$m^3$) and the greatest number of days with high risk allergenic levels (14 ± 5 and 11 ± 4 days). The number of days with moderate allergenic levels (50-200 pollen grains/$m^3$) was close to 10 days in all six pollen stations, including those where olive groves are more reduced.

**Conclusion:** There is a clear relationship between a large surface of the olive groves and the high APIn and the days with high risk of allergy. But, the number of days of moderate allergy risk has been similar at all sampling sites regardless of the surface of olive groves. To study the general behavior of *Olea* pollen in an aerobiological network in central Spain allows to classify different areas in order to optimize the prevention of the pollen allergy.

## 1381 | A 5-years aerobiological study (2013-2017) in Tbilisi, Georgia

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**Background:** Today, more than 300 million of the population is known to suffer from one or other allergic diseases affecting the socio-economic quality of life. Major causative agents implicated are pollen grains, fungal spores, dust mites, insect debris, animal epithelia, etc. Several aerobiological studies have been conducted in different parts of the world to ascertain air concentration and seasonality of pollen grains and fungi. The flowering time of higher plants are events that come periodically in each season, but the time of blooming may differ from year to year, in different geographic locations. Based on differences recorded in several years of observations in airborne pollen, pollen calendars are drawn as an aid to allergy diagnosis and management. The aim of this study was to create 5-years pollen calendar for the capital of Georgia.

**Method:** The airborne pollen monitoring was performed with a Burkard Seven Day Volumetric Spore-trap (Burkard Manufacturing Co Ltd, UK) during 5 years (2013-2017), following the recommendations of European Aerobiology Society. Pollens concentration was calculated and expressed as the number of pollen grains per cubic meter of air ($p/m^3$). Pollen index was defined as the total number of pollen grains during the pollination period. The main pollen season includes 95% of the seasonal total pollen count, starting on the day on which 2.5% of total pollen was recorded and ending on the day on which 97.5% of total pollen was registered.

**Results:** The pollen calendar includes 34 pollen types. Cupressaceae (43.6% of total annual amount), Platanus (10.3%), Morus (6.5%), Ulmus (5.9%), Artemiasia (4.3%) and Populus (3.9%) are the main pollen produced taxa. The annual Pollen Index is 36 895 grains, 82.6% of pollen is recorded during the February-May. The longest pollination period was observed for Asteraceae - season duration was 162 days and Poaceae—season duration was 132 days. The obtained results show that Corylus started the pollen season in Tbilisi at the middle of January. The latest flowering taxa was Cedrus, the exposure of pollen started the late of October.

**Conclusion:** This pollen calendar for Tbilisi is the first that has been created based on 5 years pollen count data. It represents a useful tool for clinical guidance intended for local allergy sufferers, either the local or foreign population and can be used to prevent and manage allergic respiratory diseases.

## 1382 | Detection of birch pollen allergen in household dust correlates with tree seasonality

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**Background:** Symptoms of pollen allergy are associated with the exposure of an affected individual to airborne pollen allergens, such as birch (*Betula verrucosa*) which is regarded as the most allergenic form of tree pollen in the majority of Europe. However, routes other than inhalation should also be considered and may be an important factor in sensitisation. Our primary objective was to determine whether Bet v 1 could be detected in settled house dust samples taken during the birch pollination season, and consequently, at what levels the allergen is present.

**Method:** All dust samples were obtained using DUSTREAM® collectors in homes across Western and Central European countries. From these samples, a final selection was made based on country of origin and the date collected to provide us with a cohort reflective of the flowering season which spans from late March to May. Bet v 1 allergen was measured quantitatively in household dust extracts using multiplex assay technology (MARIA) and a specific Bet v 1 ELISA 2.0 EP kit.

**Results:** Over 60% of house dust samples collected between April and May from Central European countries were found to contain Bet v 1 allergen at levels well above the Limit Of Detection of 0.0039 μg/g for ELISA 2.0 EP kit and 0.001 μg/g on MARIA. Samples were found to have much higher levels of Bet v 1 allergen from mid-to-late April, particularly those that were collected in Germany, Belgium and Hungary. Samples taken from outside of the pollination season were tested and found to be negative for Bet v 1.

**Conclusion:** In conclusion, we found that Bet v 1 allergen can be detected and quantified in house dust samples. These data suggest that household dust is a source of pollen allergen and could therefore be contributing to asthma and allergic rhinitis symptoms in individuals affected by pollen allergy. Household dust may also be considered as a source of Bet v 1 allergen which could contribute to allergic sensitization.

## 1383 | Cupressaceae pollen in the atmosphere of alentejo: Disruption of pollen grain during air transport

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**Background:** *Cupressaceae* family include several species that are widely used as ornamental plants pollinating in late winter—early

spring, depending on the temperature. Despite being considered moderately allergenic, it might be responsible for winter allergic outbreaks. As ornamental trees, they are found scattered throughout the territory but are more abundant in pockets of wild forest, outside Alentejo. Despite being more common in mountain, this pollen type is captured in considerable amounts in Alentejo, Portugal, where its aerobiological features and allergenic impacts are poorly characterized.

The aim of this work is to characterize the aerobiology of *Cupressaceae* pollen, to evaluate the effect the meteorological conditions and the source of this allergenic pollen type in the atmosphere of Evora, Alentejo.

**Method:** Pollen were collected using a Hirst type 7-day pollen trap and pollen was identified following standard methodology. Temperature (°C), relative humidity (RH; %), precipitation (mm) and wind speed and direction were obtained from ICT/CGE platform. Back trajectories (12-hour) of air masses arriving at Évora were calculated using the HYSPLIT model (Hybrid Single-Particle Lagrangian Integrated Trajectory). All trajectories have been computed at 12:00 and 15:00 UTC at different height levels.

**Results:** Elevated daily concentrations of *Cupressaceae* pollen were detected, reaching maximum value of ~1600 grain/$m^3$; One remarkable feature was that a significant amount of the pollen grains, ranging between 18% and 50% on different days, were disrupted, showing a distended intine and released cellular content. Higher levels of disrupted pollen coincided with RH >70%. Temperature, wind speed or direction did not correlate with elevated pollen grain disruption. Hourly counts, performed for days with the highest pollen loads, have shown that pollen peaked around 13 hours, suggesting local origin. Back trajectory analysis suggested that pollen was mostly from local origin, but did not exclude the contribution of long-range transport.

**Conclusion:** To our knowledge, this is the first report of a considerable fraction of disrupted *Cupressaceae* pollen grains reaching the sampler, releasing cell contents, which may significantly increase ambient free allergen and contribute to enhance allergenic activity of this pollen type. A better understanding of this phenomenon may contribute to improve allergy risk management.

## 1384 | Towards personalized pollen exposure measurements using hand held pollen samplers

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**Background:** Allergic rhinitis caused by pollen is one of the most common allergic diseases. The presence of pollen in the air is currently centrally monitored at roof top levels, and not in the direct living environment of sensitized subjects. In the current project we aimed to develop a handheld pollen sampler, called pollensniffer, that can collect pollen in the living environment of the allergic subjects. As a first step this device was validated against the standard Burkard pollen sampler and used to monitor local pollen concentrations at street level in the city of Leiden.

**Method:** Rooftop level pollen were monitored routinely by a Hirst type pollen sampler (Burkard, UK). The pollensniffer (6 × 14 cm) consists of a conical inlet and a ventilator powered by a commercial powerbank. The pollen were collected on a cellulose strip. For the validation of the pollensniffer, the device was mounted on top of the Burkard sampler. All pollen collected on the strip from the Burkard and the pollensniffer were counted microscopically. Street level pollen were monitored once every week (April-June) at three locations in the city of Leiden, during the morning, midday and evening. Statistical analyses were performed using the software package STATA 14.0 (StataCorp, TX).

**Results:** The correlation between the different pollen types collected by the pollensniffer and the Burkard sampler was high (correlation coefficient [CC] >0.8). During the validation experiments the pollensniffer appeared to collect on average 7 times more pollen than the Burkard sampler. Street level (pollensniffer) and roof top level pollen counts (Burkard sampler) showed a very good correlation (CC > 0.85). Local street level measurements in the city of Leiden showed that plane trees in one park produced pollen a week before the plane trees in another park. Grass pollen were observed at street level 4 weeks before the pollen were observed at roof top level.

**Conclusion:** Pollen numbers collected by the pollensniffer and the Burkard correlate well, but the pollensniffer collected on average 7 times more pollen than the Burkard sampler. Street level measurements showed differences in pollen loads between locations. Furthermore, street level grass pollen were detected 4 weeks before they were observed at rooftop level. These findings suggest that the pollensniffer is well suited for the measurement of pollen (and maybe other allergens) in the living environment of sensitized subjects.

## 1385 | Does the allergy risk due to pollen exposure information is useful for the allergy sufferers?

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**Background:** In France the information for the allergy sufferers is not made with pollen counts, which have not a real signification, but with the allergy risk due to pollen exposure.

**Method:** Since more than 20 years, RNSA (Réseau National de Surveillance Aérobiologique), the French aerobiology network, has

measured the pollen exposure in the main cities of France, using nearly 80 pollen traps. This pollen counts permit to obtain exposure index. Since 12 years, a sentinel doctors' network has helped RNSA by filling every week a clinical bulletin informing about the reality of the pollinosis, the type of symptoms and their gravity. A clinical index is then calculated from these bulletins.

**Results:** The exposure index permits to follow the evolution of the pollen exposure for each allergenic pollen, year after year. An increase of 20% has been observed since 20 years. The annual clinical index gives information about the health impact due to pollen along the season (trees, grasses, herbaceous). The curve of the annual index (since 2006) shows a real stabilization of the health impact due to pollen.

**Conclusion:** Despite a regular increase of exposure for allergy sufferers, the felt symptoms remain stable, the preventive information allowing them to stabilize their symptoms.

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## 1386 | Pattern changes in diagnostic tests of allergic diseases; using big data of 48.1 million South Korean health-care records

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**Background:** The incidence of allergic diseases has been increasing worldwide for the past few decades. Although the clinician can diagnose allergic diseases after a careful review of the history and physical examination, specific diagnoses are rarely evident without use of the tests. Some tests should be help to diagnosis, treatment, and prevention on specific parts of the allergic diseases.

**Method:** To investigate the changing pattern of tests (total IgE C2290, total eosinophil count, TEC; B1070, Immuno CAP C2310, MAST C2320006, and allergen skin test E7151)used in diagnosis of allergic diseases (asthma, allergic rhinitis, and atopic eczema), we analyzed the nationwide database (National Health Insurance Corporation) which included the health-care records of 48.1 million individuals between January 1, 2009 and December 31, 2014.

**Results:** There has been a pattern of increasing number of diagnostic tests (total IgE, TEC, Immuno CAP, and MAST) in Korea; total IgE of which 192 778 (2009), 222 542 (2010), 246 144 (2011), 265 832 (2012), 293 826 (2013), and 346 911 (2014); TEC 204 935 (2009), 214 402 (2010), 230 885 (2011), 247 855 (2012), 268 057 (2013), and 284 689 (2014); Immuno CAP 81 023 (2009), 87 015 (2010), 92 403 (2011), 101 049 (2012), 110 103 (2013), and 125 898 (2014); MAST 195 406 (2009), 220 979 (2010), 262 849 (2011), 305 869 (2012), 362 921 (2013), and 432 425 (2014).

However, there was a tendency of decreasing in allergen skin test; 259 521 (2009), 252 755 (2010), 254 710 (2011), 241 516 (2012), 233 873 (2013), and 224 099 (2014); especially in primary health care clinic rather than secondary or tertiary care hospital; primary health care clinic of which 193 077 (2009), 142 381 (2014); secondary care hospital 7961 (2009), 16 858 (2014); tertiary hospital 58 483 (2009), and 64 850 (2014).

**Conclusion:** There has been a increasing pattern in total IgE, TEC, Immuno CAP, and MAST of which number of test, except in allergen skin test. Especially, primary health care clinic has decreasing pattern in number of allergen skin test. So, further study will be needed.

## 1388 | Allergic sensitizations in 5-6 year old rural vs urban children in Germany

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**Background:** The effect of environmental factors on allergic sensitizations is still unclear. Rural areas vs cities have different exposure levels to pollutants and aeroallergens. These differences could give clues on the causes of higher allergic sensitization rates in children exposed to city air.

**Method:** Two studies with children aged 5 years old were initialized to analyse the airborne drives of allergic sensitization: SEAL (Günzburg, 350 children) and Ae2R Kids (Munich, 200 children). Capillary blood was collected and the parents filled in a questionary. Sensitization rates were quantified using the ImmunoCAP® ISAC sIgE array. Pollen data were measured at both locations.

**Results:** In Günzburg more children were sensitized to aeroallergens, however Munich children showed significant higher sensitization to Phl p 1 ($P < 0.05$), despite the lower concentration of pollen. In Günzburg 66% children had no sensitization at all compared to 58% in Munich. 80% of the children in Munich spend at least 1 hour per day outside and 91% of the total have no animals at home. 23% felt symptoms of hay fever in the last 12 months, the majority between March and June, which correlated with the pollen flight.

**Conclusion:** The importance of combining the ISAC sIgE-diagnosis with clinical history is shown in this study. Differences in lifestyle between rural and city affect allergic sensitizations and are crucial to understand the underlying causes.

## 1390 | The value and strategy of allergen screening in Chinese adult patients with chronic respiratory diseases

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**Background:** Chronic respiratory disease (CRD) caused by allergy is increasing year by year, this study will explore the characteristics of sensitization in CRD patients and the value and strategy of allergen screening.

**Method:** Detection of Phadiatop sIgE and tIgE in 252 adult patients with chronic respiratory diseases, including 85 of asthma, 98 of chronic obstructive pulmonary disease (COPD) and 69 of other CRD.

**Results:** The total rate of atopy in CRD patients was 36.1%, and asthma patients was the highest (45.9%). The positive rate of Phadiatop in urban asthma patients (56.0%) was significantly higher than that in rural areas (25.0%, $P < 0.05$) and the Phadiatop positive rate of office staff (62.5%) was significantly higher than that of outdoor workers (37.5%, $P < 0.05$). The total rate of atopy in COPD patients was 32.7%, and in patients with acute exacerbation was 42.9%. Beside, atopy is a risk factor for dyspnea (OR = 1.22, $P < 0.05$), and the FVC levels in COPD patients with atopy were significantly lower than those without (2.06 L vs 2.63 L, $P < 0.05$). Optimal scaling analysis show that, there were a correlation between the tIgE and smoking coefficient (Cronbach's Alpha = 91.1%). In addition, the correlation between the level of tIgE and Phadiatop sIgE was so strong in the patients with mild to moderate asthma ($r_s = 0.709$, $P < 0.001$), but it was weak in severe asthma patients ($r_s = 0.486$, $P < 0.001$), and up to 35.0% of the GOLD III IV patients with low Phadiatop level (≤10 kU/L) had a high level of tIgE (≥1000 kU/L) compared GOLD I II (5.5%).

**Conclusion:** The rate of atopy in patients with CRD is high, and atopy is an important factor affecting the process of CRD. The patients with severe COPD or asthma is likely to has high serum tIgE level but the level of common allergen sIgE is low, so the allergy screening strategy should be adjusted and we should pay attention to those patients, Therefore, it is necessary to screen the sensitization situation of CRD patients at first, and the results can guide the treatment, management and prevention of CRD.

## 1391 | Epidemiological screening of severe asthma-patients with thorough allergy-testing (ESSAy)

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**Background:** Due to a limited amount of epidemiological data [1] it has been thought that many severe allergic asthmatics in Germany remain unidentified and are therefore not adequately treated. A pilot project demonstrated that more than 50% of patients, having been classified as non-atopic based on standard allergy testing procedures, were indeed sensitized (positive allergen-specific IgE) to at least one perennial allergen, if tested with a broad allergen spectrum [2].

**Method:** The purpose of this project was to prospectively collect epidemiological data about the cohort of asthmatic patients using an online survey. Subsequently, the immune response against different inhalant allergens was determined in a subgroup by performing a comprehensive allergen-specific Singleplex IgE-test (ImmunoCAP spec. IgE, Phadia ThermoFisher) [3].

**Results:** 392 out of >65 000 participants in the online-survey were further analysed in out-patient sites (74.2% female, age mean (SD [Min/Max]) 43.0 (15.9 [8/80]), mean (SD) duration of disease 16.5 (13.2) years. Overall, patients had a high burden of symptoms, the most frequent symptom was breathlessness (93.1%), followed by cough (84.2%) and chest tightness (71.4%). For 78.9% patients allergic comorbidities were documented; most common were rhinitis and rhinoconjunctivitis (62.5%), respectively. The maintenance therapy was inhaled corticosteroids (98.6%) with long-acting ß-agonists (96.9%). Less than one fifth received long-acting muscarinic antagonists (19.6%) or oral steroids (16.1%).

Mean total IgE (SD) was 366.4 (692.2) kU/L. 26.5% of the patients had no sensitization towards any of the specific IgEs tested, whereas 24% were positively tested on 5-10 allergens and further 23.5% showed sensitizations towards >10 allergens.

**Conclusion:** Approximately 75% of 392 online recruited (severe) asthmatics had a total IgE level of >30 kU/L and ≥1 sensitization (allergen-specific IgE) towards atopic allergens. This further supports the high prevalence of atopy in asthma.

[1] Lommatzsch M, Virchow JC; Dtsch Arztebl Int 2014; 111: 847-55.

[2] Schreiber J, Garg K; AJRCCM 2016; 193: A1443.

[3] Kleine-Tebbe J, Jakob T; Allergo J Int 2015;24: 185-97.

## 1392 | The prevalence of specific immunoglobulins E to inhalant allergens among Polish children and adults with suspicion of allergy

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**Background:** Epidemiologic data suggests that the prevalence of allergy has increased dramatically in recent decades. Inhalant allergens play an important role in developing allergic diseases. Specific immunoglobulin E (sIgE) level is one of an important risk factors for the development of allergy diseases, for example asthma. The aim of this study was to assess the prevalence of specific IgE in relation to inhalant allergens in a Polish population of children and adults likely to be allergic.

**Method:** Results of sIgE were collected from different labs in Poland performing the quantitative multiparameter enzyme-linked immunosorbent assays (Polycheck®, Biocheck GmbH, Münster, Germany). Collected results were arranged according to voivodeships. Statistical analysis was done using Statistica 10 (StatSoft Polska). In order to make estimates with statistical accuracy 0.01 (1%) and typical confidence level, the analysis covered allergens tested in min. 7203 patients.

**Results:** This study collected 237 017 results of sIgE concentration (in kU/L) for 46 inhalation allergens which were analyzed for 16 267 patients with suspicion of allergy. Gender proportions were approximately balanced. 42% of total number of patients were children younger than 3 years old[EM1].

In the study, the prevalence rates of sensitisation was 49.5%. The largest number of positive results was against inhalant allergens of *Dermatophagoides farina* (25%), *Dermatophagoides pteronyssinus* (23%), alder (n = 22.5%), dog (22%), hazel (22%), rye (19%), birch (19%), timothy grass (18%), cat (18%) and oak (13%), Plantago lanceolata (9%), *Alternaria tenuis* (9%), *Artemisia vulgaris* (7%), horse (7%), *Penicillium notatum*, *Cladosporium herbarum* and *Aspergillus fumigatus* (5% respectively).

**Conclusion:** The frequency of positive results of specific IgE in serum to airborne allergens in children and adults with suspicion of allergy in the overall Polish population, amounted to 49.5%. The most frequently inhaled allergens are *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus* and alder pollen, dog fur and the pollen of hazel, rye and birch, cat fur, timothy grass pollen and oak pollen.

## 1394 | Sensitization to allergens in patients from Bangalore, India

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**Background:** The aim of this study was to identify the common allergens seen in atopic patients from Bangalore, India.

**Method:** This was a retrospective analysis of the patients with a clinical history of allergic disorders undergoing the skin prick test (SPT) from May 2015 to April 2017. SPT was performed with standardized allergens marketed by Merck, Allergopharma, Hollister Stier and nonstandardized allergens (for those where standardized allergens are not available) marketed by a local Indian manufacturer. As a clinical practice, allergens for the SPT were selected as per the presenting history of the patients. A wheal diameter of ≥3 mm was taken as a positive reaction.

**Results:** A total of 297 patients underwent the SPT (age: 0.5-74.3 years; males: 56.2%). The maximum number of patients (147; 49.5%) were in the age group of ≥0.5 to≤12 years old. Of the 297 patients, 235 (79.1%) patients showed positive skin test to ≥1 allergen; with 20 (6.7%) being monosensitized, 35 (11.8%) sensitized to 2 allergens and 180 (60.6%) patients sensitized ≥3 allergens. An age trend towards increase in the number of sensitizations (≥3) was evident from our data, in the age group of >18 years 71.6% were sensitized to ≥3 allergens compared to 49.7% in the ages≥0.5 to≤12 years. The house dust mites—which were tested in 287 patients—were the most common sensitizers in our population (*D. pteronyssinus* [184; 64.1%] and *D. farinae* [180; 62.7%]). The other common sensitizers were the cockroach (42.6%), [HM1] *Lepidoglyphus destructor* (36.4%), mosquito (27.4%), *Prosopus juliflora* (18.5%), shrimp (17.3%), *Plantago lanceolata* (16.4%), *Acarus siro* (16%), and *Chenopodium album* (12.8%). Along with the house dust mites the above allergens were the top 10 sensitizers in our population. Amongst the moulds and animal dander the most common sensitizers were *Alternaria alternata* (11%) and Cat dander (12.3%).

**Conclusion:** This data reemphasizes that most patients presenting to a speciality allergy clinic are polysensitized and that there is an increase in the number of sensitization with an increase in age. Additionally, it strengthens the importance of the house dust mites as a major sensitizer in Indian patients (especially the Pediatric patients). Also, clinicians can use this data to compare the sensitization rates in their clinical practice.

## 1395 | The most common aeroallergens among allergic rhinitis patients in Birjand city, Iran

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**Background:** Allergic disorders are among the most common health problems around the world and their prevalence has been increased during the last decays. Allergic rhinitis and conjunctivitis are the most prevalent forms of allergy and have negative impacts of quality of life as well as productivity of patients. Pollens and indoors allergens are the main triggers of allergic symptoms but the pattern of sensitization is varied in different parts of the world. The aim of this study was to identify the most common aeroallergens in allergic rhinitis patients at Birjand city of Iran.

**Method:** patients who were referred to Birjand Allergy clinic during 2013-2017 because of any allergies, clinically evaluated by specialist and skin prick test with a battery of at least 20 common outdoor and indoor allergenic extracts performed based on standard method.

**Results:** 875 patients (mean age: 26 ± 11.9 years, range 2-64 years, M/F ratio: 0.89) who suffered from allergic rhinitis or allergic rhinoconjunctivitis enrolled in this study. Highest rate of skin sensitivity was for weeds/grasses pollen including Salsola Kali, Amaranthus Retroflexus, Chenopodium Album and Compositae family (74.3%, 62.5%, 50.9% and 39.3% respectively). Among tree's pollen; Ash (49%), Walnut (46.9%) and Mesquite (29.3%) were the most common. Less than 20% of patients showed skin reactivity to indoor allergens and Storage mites, mix of Cockroaches and house dust were the most common (17.6%, 17.3% and 9.8% respectively).

**Conclusion:** The results of current study confirmed the importance of weed/grass and trees pollen as the major source of allergic sensitization in our area. Interestingly the rate of sensitization to indoor allergens was low which can be explained by geo-climatic situation.

## 1397 | Aeroallergen sensitization pattern and clinical profile of 1157 patients from Jammu and Kashmir, India

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**Background:** Currently, no evidence on the sensitization pattern is available from Jammu and Kashmir which is situated in the Indian Himalayas. Due to different flora, data from other parts of India (especially pollen) cannot be extrapolated to Jammu and Kashmir.

**Method:** This retrospective, cross-sectional study aimed to identify patterns of aeroallergen sensitization (especially Himalayan allergens and allergens previously not reported in skin prick test [SPT] literature) in atopic patients and present their clinical profiles. Records—demographic details, disease, severity and seasonality of symptoms and allergen sensitization—were evaluated for patients who underwent the SPT in the period May, 2015 to May, 2017. Standardized extracts by Merck, Allergopharma were used for most of the allergens. A wheal diameter of ≥3 mm was taken as positive.

**Results:** A total of 1157 individuals were included (age: 3.5-75 years; males: 42.2%). Allergic rhinitis was reported in 83.3%, while 29.6% patients had allergic asthma. Symptoms were severe in 25.8%, moderate in 62.4%, mild in 11.2%, perennial in 64.4%, seasonal in 32.9% and perennial with seasonal exacerbations in 2.6%. All patients were found to be polysensitized. Sensitization to house dust mites were 75% for *D. farinae* and 68.7% for *D. pteronyssinus*, respectively. Amongst the other allergen groups greatest sensitization was observed for *Poa pratensis* (31.1%) in grasses, *Plantago lanceolata* (27.1%) in weeds, *Acacia sp*. (33.3%) in trees, *Alternaria alternata* (24%) in moulds, Cat dander (35.6%) and Cockroach (32.9%). The Himalayan tree allergens Birch (30.9%), Alder (13.9%), Hazel (27%), Maple (30.1%), Poplar (27.5%) and Willow (26.4%) were found to be strong sensitizers in our population. Additional allergens which have not been evaluated by the SPT in India showed the sensitizations as, pollens—*Phleum pratense* (25.8%), *Lolium perenne* (20.5%), *Festuca pratensis* (11.6%), *Urtica dioica* (25.3%) and *Robinia pseudoacacia* (25.2%) and storage mites—*Blomia tropicalis* (69.5%), *Tyrophagus putrescentiae* (48.1%), *Lepidoglyphus destructor* (25.4%) and *Acarus siro* (9%).

**Conclusion:** Our data provides the Indian clinicians adequate resources to select their allergen panel for diagnosing allergen sensitization in patients who are from the Indian Himalayan regions such as Jammu and Kashmir. Furthermore, it establishes the role of specific pollen allergens which are present in the local environment but not utilized for the SPT, also demanding further research.

## 1398 | Sensitization patterns to aeroallergens & food allergens in Indian patients

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**Background:** The local sensitization pattern is an important reference for the practicing allergist. A review of literature revealed that there is no pertinent data on the allergen sensitization pattern with standardized allergens from India.

**Method:** A retrospective analysis of patients undergoing the skin prick test (SPT) in the years 2016 & 2017 was undertaken to evaluate the allergen sensitization pattern. Extracts from Merck (Allergopharma) were utilized for the SPT, while a few nonstandardized extracts were procured for some of the locally prevalent allergens.

**Results:** Overall 603 patients underwent the SPT (ages 0.5-65 years) & 598 patients were found to be sensitized to ≥1 allergen.

A combination of indoor & outdoor symptoms was recorded in 46.8% of the patients, while 39.6% patients revealed predominantly indoor symptoms & the rest as outdoor symptoms only. Similarly, most patients reported that their symptoms were perennial with seasonal exacerbations (66.8%). Five (0.8%) patients did not show any sensitizations, 23 (3.8%) patients were monosensitized and rest (95.4%) were polysensitized. The most common aeroallergen sensitizers - >30% sensitizations - were *D. pteronyssinus* (66.4%), *D. farinae* (60%), American cockroach (*Periplaneta americana*, 54.1%), *A. siro* (48.8%), *Mosquito* (42.3%), *L. destructor* (42.1%), *T. putrescentiae* (39.4%) and German cockroach (*Blattella germanica*, 36.8%). Amongst the pollens, sensitization rate of >20% was found for *Poa pratensis* (23.9%), *C. dactylon* (23.1%), *P. pratense* (22.1%), *P. hysterophorus* (23.3%), *C. album* (22.8%) & *A. spinosus* (22.1%). The common fungal sensitizers were *A. fumigatus* (22.9%), *A. alternata* (18.3%) & *C. herbarum* (16.2%). Sensitization to cat & dog dander were found in 9.9% & 10.7% of patients. In foods, sensitization >15% was observed for—shrimps (28.3%), milk (16.1%), Chana dal (15.9%), apple (15.3%), wheat (15.3%), eggs (15.2%) & gluten (15.2%).

**Conclusion:** As found in our study the clinical history of the patients & SPT results (using majority of standardized allergens) were correlated to allergy due to indoor allergens such as mites or insects. High reactivity to shrimps may result from the cross-reactive allergen (tropomyosin) that it shares with mites and cockroach. Pollen allergen sensitization although comparatively less were frequently found in our population which further correlates with the clinical history of patients having perennial symptoms with seasonal exacerbations.

## 1399 | Prevalence of skin sensitivity to temperate and subtropical grasses in patients with seasonal allergic rhinitis in Bahía Blanca, Argentina

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**Background:** There are few studies of cutaneous sensitivity to gramineae in our region. Mostly of them use allergens of foreign species. The study aims to estimate the prevalence of skin sensitivity to widespread grasses in our region.

**Method:** This is a retrospective observational study of 894 patients with seasonal allergic rhinitis. Patients were studied using skin tests with pollens extracts from *Pooideae*, *Chloridoideae* and *Panicoideae* grass species.

**Results:** The prevalence of positive reaction to pollen from *Pooideae* subfamily was 86.8% (IC: 84.4%-88.9%). In turn, prevalence of allergy to *Panicoideae* subfamily pollens was 69.6% (IC: 66.5%-72.5%) and positive reaction to *Chloridoideae* subfamily reach 48.1% (IC: 44.8%-54.1%). Cochran test suggests that prevalence in those three groups is different ($\chi2 = 319.11$, $P < 0.01$). When comparing just the groups of allergens from *Pooideae* and *Panicoideae* differences are also significant ($\chi2 = 71.43$, $P < 0.01$). In particular, 52.5% (IC: 49.2%-55.7%) of patients were allergic to *Paspalum notatum*. Regarding cross-reactivity between subfamilies, we find a no cross-correlation between *Pooideae* and *Panicoideae* ($\chi2 = 2.197$, $P = 0.138$).

**Conclusion:** In Bahia Blanca, patients with seasonal rhinitis are sensitive to *Pooideae*, *Chloridoideae* and *Panicoideae*. *Paspalum notatum*, belonging to *Panicoideae*, has a significant prevalence, high reactivity and low cross-reactivity within the group of species studied. This last species is relevant because it is a native grass from the Northwest region of our country, Paraguay and the South of Brazil.

Prevalence of grass positive skin tests in patients with seasonal rhinitis by species.

| Species | Allergen | Frequency | Percentage | 95% CI |
|---|---|---|---|---|
| Lolium perenne | Lol p | 504 | 56.4 | [53.1-59.6] |
| Festuca arundinacea | Fes a | 534 | 59.7 | [56.5-62.9] |
| Phalaris arundinacea | Pha a | 556 | 62.2 | [59.0-65.3] |
| Cynodon dactylon | Cyn d | 430 | 48.1 | [44.8-51.4] |
| Paspalum notatum | Pas n | 469 | 52.5 | [49.2-55.7] |
| Sorghum halepense | Sor h | 454 | 50.8 | [47.5-54.1] |

## 1400 | House dust mites sensitization in a concrete zone and comparison with previous results

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**Background:** House Dust Mites (HDM) development is basically conditioned by humidity and temperature. Several years ago it was defined a sensitization profile in our province, but we have seen that it could be different. Our aim is to describe the sensitization profile of a population living in a concrete zone and to compare these results with the established profile.

**Method:** Patients living in our zone (politically described as region) more than 10 years and with perennial rhinitis were selected. After performing a medical record focussing in other allergies, we perform prick test (SPT) with a house dust mites battery (*D. pteronyssinus*, *D. farinae*, L. destructor, *B. tropicalis*, Tyrophagus, Euplyphus, Chorto, Tropomiosin, Glycyphagus, A. sito; Leti™ laboratories) and a blood test in order to confirm the in vivo results.

**Results:** 103 patients (46 males and 57 females; mean age 32.48 years) were selected. Asthma was diagnosed in 58 patients, and atopic dermatitis in 7 patients. SPT was positive to L. destructor (66), D. pteronyssinus (55) or D. farinae (52). Mean Total IgE was 152.54 (14.6-1085), and specific IgE was positive to D. pteronyssinus (mean 15.28), D. farinae (mean 10.82) or L. destructor (mean 1.70). Our results were compared with the established profile, showing a higher sensitization to L. destructor and a similar sensitization to Dermatophagoides group and other mites.

**Conclusion:** Dermatophagoides group is the most common HDM sensitization in our population (as was described in the previous results). According to previous results, in our region there is a high sensitization to L. destructor. Other sensitization are very similar between the populations.

## 1401 | Evaluation of diagnostic methods for *Dermatophagoide farinae*, *Dermatophagoide pteronyssinus* and *Blomia tropicalis* in a tropical region: Skin prick test according to diameter and area vs sIgE

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**Background:** Skin prick tests (SPT) for the study of patients allergic to mites are based on the use of allergenic extracts from European countries and their concentrations have not been studied in patients living in tropical regions.

**Objective:** To evaluate different concentrations of allergenic extracts of in vivo test for Dermatophagoide farinae (Der f), Dermatophagoide pteronyssinus (Der p) and Blomia tropicalis (Blo t) compared with in vitro test in patients from a tropical region, to determine the adequate diagnostic concentrations.

**Method:** Four concentrations of allergenic extracts were used for SPT; for Blo t and Der p were used concentrations of 300, 30, 3 and 0.3 μg/mL and for Der f concentrations of 400, 40, 4 and 0.4 μg/mL. The serological evaluation was carried out using ImmunoCAP and the SPT was evaluated using a larger diameter of the wheal according to the international guidelines and the area by prick film. Correlations were analyzed by Spearman coefficient, concordance by Lin coefficient, Bland-Altman graph and Cohen's Kappa coefficient; similarly, diagnostic performance tests were performed.

**Results:** Correlation analyzes were performed between sIgE and SPT and area results. The concentration with the highest correlation by diameter and area for Blo t was 30 μg/mL and for Der f of 400 μg/mL. In the case of Der p the concentration with the highest correlation for the diameter was 30 μg/mL and for the area of 3 μg/mL. When evaluating the reproducibility of the results according to the area and the greater diameter of the SPT, a strong agreement was observed for Blo t in the concentrations of 3 μg/mL and 0.3 μg/mL.

**Conclusion:** The diagnostic performance showed that the lower concentrations of Blo t had better diagnostic sensitivity, while the lower concentrations for Der f and Der p had better diagnostic specificity.

## 1402 | The aspergillus and alternearia skin prick test positivity in Ege university hospital adult allergy clinic

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**Background:** Mold fungi are very diverse and difficult to idenfify. The prevalence of mold susceptibility is estimated to be between 3% and 10%. The aim of our study was to investigate the susceptibility of aspergillus and alternaria detected by skin prick test (SPT) in patients admitted to our allergy clinic.

**Method:** SPT results of patients who admitted to Ege University Hospital adult allergy clinic with chronic rhinosinusitis, between January 1 2017 and July 1 2017, were retrospectively scanned. 1218 patients were included in study. Olive, grass mix, artemisia, plantago, parietaria, D.farinea, D.pteronissinus, cat, aspergillus and alternearia were included in allergen content of SPT. Age, gender, presence of coexisting asthma, serum IgE and absolute eosinophil counts were recorded. Analyzes were done with SPSS Statistics 21.0 package program.

**Results:** The mean age was 34 (±13.3), 788 patients (64.7%) were female and 430 (35.3%) were male. 643 patients (52.8%) had negative SPT. 165 patients (13.5%) had accompanying asthma. 125 patients (10.3%) were mold (aspergillus and/or alternaria) positive on SPT. When patients with negative SPT were excluded, the rate of mold positive patients was found as 21.7%. There was no statistically significant relationship between presence of asthma and mold susceptibility. 92% of mold positive patients (115/125) had polysensitization on SPT.

**Conclusion:** The majority of mold susceptible patients were polysensitized. There are reports that mold sensitivity enhances inflammation from other allergens by activating the innate immune system. However, the accuracy of the tests is affected by the low quality of the allergen extracts and the cross-reactive molecules with weak allergenic activity. The clinical correlation of mold susceptibility with the test results was not included in our study.

In the literature, mold sensitivity is reported as a risk factor for the development of asthma, however, our study there was no correlation with mold susceptibility and asthma.

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ALLERGY DIAGNOSIS AND IMMUNOGENETICS

## 1403 | Atopic patients are not an homogeneous population but present several distinct humoral immune endotypes

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**Background:** Atopics [AP] are allergic patients with elevated IgE and/or a familial trait.

**Method:** Serum IgE, IgA, IgM, IgG and IgG sub-classes (evaluated by nephelometry) of 4700 new patients investigated for allergic symptoms between 2003 and 2013 were compared. Adults (18-90+): 3385 (68% F, 32% M), children (0-17): 1315 (44% F, 56% M).

**Results:** AP (IgE > 100 KU/L) were identified in 32.2% (61% F, 39% M) of the investigated adults [APad] and in 61% (38% F, 62% M) of the children [APch]. IgA abnormalities were observed in 28% of APad (IgA 25%, IgA 3.1%) and in 44.9% of APch (IgA 13.5%, IgA 31.5%). Increased total IgG was found 18% of APad but in only 6.7% of APch; decreased total IgG in 14.6% of the APch and only 1.6% of APad. An abnormal ratio of IgG1/IgG2 associated clinically with inflammatory symptoms was observed in 71.7% of APad (IgG1/IgG2$^3$ 2.5: 27%; IgG1/IgG2 $\leq$ 1.5: 44.9%) and in 83.1% of APch but with an inversed pattern: IgG1/IgG2$^3$ 2.5: 76.4%; IgG1/IgG2 $\leq$ 1.5: 6.7%. In APad these dysbalances were related more to a relative excess of IgG1 than to a real lack of IgG2, observed in only 2.4% of adults. Abnormally increased amounts of IgG2 were found in 7.9% of APad but were not seen in APch. Low values of IgG2 were however observed in 25.8% of APch. IgG4 abnormalities were observed equally both in APad (41.7%) and in APch (41.6%). Low or absence of IgG4 was found 11.0% of APad and close to 17% of APch. High amounts of IgG4 were measured in respectively 30.7% and 24.7% of APad and APch.

**Conclusion:** Those differences in endotype account most probably for the sometime poor response observed with classic drug treatment and/or immunotherapy. Taking into account those differences may allow different drug and immune strategies for a personalised treatment.

## 1404 | Necessity and opportunities for early diagnosis of allergies in children

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**Background:** Conducting screening studies of phased diagnostics of AD using standardized questionnaires and methods is the most important prerequisite for early detection of the disease and verification of the diagnosis. Statistical data, as a rule, are based on indicators obtained by referring patients to medical institutions, which does not correspond to the true prevalence of the disease (irreversible, hypodiagnosis, substitution of diagnosis, negative attitude of parents, etc.).

**Method:** The purpose of the study: early detection of children with signs of AD and children at risk of their development on the basis of the definition of markers. 265 children aged 7-8 years old, residents of Tashkent (Uzbekistan) were examined at the same time. Diagnostics included two stages of the survey: at the first stage, questionnaire screening was conducted using the international questionnaire ISAAC, at the II stage - immunolaboratory examination. With a positive test, 68 children (27%) were identified by the questionnaire. The questionnaire screened three groups of children. Group I included children (21) with a previously diagnosed allergic disease (food allergy, atopic dermatitis, allergic rhinitis, bronchial asthma). The second group included children with a primary allergic disease (47), the third group included healthy children (20) who had no abnormalities in the ISAAC questionnaire, but with a positive family history of atopy.

**Results:** An increase in the level of total IgE, a decrease in T-lymphocyte (CD3), T-helper (CD4), and an increase in IL-4, IL-5, was revealed in both the first and second groups compared to the group of healthy children. At the same time, a significantly increased content of Th2-marker cytokines IL-4, IL-5 was also noted in the group of healthy children. And when carrying out an allergic-specific examination (RIDA qLine® Allergy, Germany), the presence of sensitization by various allergens at the level of subclinical values was established.

**Conclusion:** The revealed changes in immunological indices with the corresponding anamnestic data give grounds for the development of programs for primary prevention of allergy in persons who are predisposed to the development of this disease.

## 1405 | Allergenic cross-reactivity between Anisakis simplex and house dust mites, German cockroach and shrimps

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**Background:** The nematode *Anisakis simplex* is a common parasite of fish and other seafood. It can induce IgE-mediated allergic responses after consumption of infected fishery products. *A. simplex* proteins are homologous to allergens in other nematodes, insects,

and shellfish indicating cross-reactivity. The present paper analyzes the allergenic relationship between *A. simplex* and house dust mite species, German cockroach and shrimps.

**Method:** Serum samples collected from 22 patients allergic to dust mites were analyzed for specific IgE to *A. simplex*, *Dermatophagoides (pteronyssinus*, *farinae*), cockroach, shrimps and some of their components (Pen a1, Der p2, Der p10, Der p1) by CAP FEIA. Total concentration of IgE was measured by EIA.

**Results:** The serum concentration of IgE to *A. simplex* was 0.86 (0.11-2.29) IU/mL. 70% of these results were positive, and 60% of them were in class 2. Significant positive correlations between IgE to *A. simplex* and IgE to *D. farine* (0.61) and cockroach (0.82) were observed. The relationship between IgE to *A. simplex* and IgE to shrimp was insignificant. IgE to A. *simplex* was significantly positively correlated with tropomyosins from shrimp (0.89) and *Dermatophagoides* (0.89). There was no correlation between IgE specific to *A. simplex* and IgE to *D. pteronyssinus*, and with IgE specific to house dust mite components (Der p1 and Der p2). In all patients with IgE specific to both tropomyosins in class 0, sIgE to *A. simplex* was also negative. In the case of one patient with an *A. simplex* IgE result in class 2, no IgE to tropomyosins from house dust mites or shrimp was found. A statistically significant positive correlation between IgE to *D. farinae* and IgE to house dust mite tropomyosin (0.46) and IgE to shrimp tropomyosin (0.46) was found. High total IgE concentration was observed in the serum of all patients (100.18—above 2000.0 IU/mL).

**Conclusion:** The results show allergenic cross-reactivity between allergens (probably tropomyosin) in *A. simplex* and *D. farinae*, shrimps and cockroach. Tropomyosin is a protein with a conservative structure that occurs both in the muscles of invertebrate and vertebrate organisms. In patients allergic to *D. farinae* or shrimps, antibodies against cockroach and *A. simplex* are also observed. It may be the result of infection with this nematode or of cross-reactivity between these organisms. The clinical significance of this cross-reactivity remains to be evaluated.

## 1406 | Analysis on correlation between serum IgE to carbohydrate cross-reactive determinants and plant-related allergens sIgE

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**Background:** To detect the serum IgE to carbohydrate cross-reactive determinants(CCD) and plant-related allergens sIgE, and analyse their correlation evaluating the characteristic of cross reaction, occurring in both CCD and plant-related allergens, for providing some reference value to the diagnosis of plant-related allergens sensitization.

**Method:** We collected 94 patients having a history of plant-related allergen sensitization to detect 21 allergens, including CCD, peanut (f13), soybean (f14), ragweed (w1), mugwort (w6), trees-mixed (poplar/willow/elm, ts4), humulus(u80), mites-mixed:(house dust mites/flour mites, ds1), house dust (h1), cockroach (i6), dog epithelium (e2), cat hair (e1), moulds-mixed (penicillium/aspergillus/cladosporium/alternaria, ms1), egg white (f1), milk (f2) and crab (f23), shrimp (f24), fished-mixed 1(cod/lobster/scallops,)(fs33), beef(f27), lamb (f88), fished-mixed 2(salmon/bass/carp, fs34) in the western blot, and to analyse the correlation CCD and plant-related allergens.

**Results:** Among the 94 patients, the majority of allergens-positive was t20, accounting for 60.6%, followed by f14 (59.6%), f13 (58.5%), ds1(57.4%) and CCD (56.4%). The prevalence of plant-related allergens (t20, w1, f14, f13, w6 and u80) in CCD-positive patients were significantly higher than those in CCD-negative patients (all $P < 0.01$). The prevalence of CCD in plant-related positive patients was significantly higher than that in plant-related negatived patients (all $P < 0.01$), and the CCD class-positive focused on class 3-4 in plant-related positive patients. 23% of the patients showed co-sensitization to all planted-related allergens,and the prevalence of CCD increased with increasing co-sensitization cases. The correlation between t20 and w1 was the strongest($r = 0.77$), followed by f13 and f14 ($r = 0.56$,), w6 and t20 ($r = 0.55$) there was different correlation among CCD and all plant-related allergens ($r = 0.39$-$0.84$, all $P < 0.01$), among which, the correlation of CCD with w1($r = 0.84$) was the strongest; followed by correlation of CCD with t20 ($r = 0.72$).

**Conclusion:** Our study showed that the prevalence of plant-related allergens increased in CCD-positive patients and vice versa, Meanwhile, There was correlation, in varying degreased, among all plant-related allergens and CCD.

## 1407 | Allergic rhinitis after avocado pollen inhalation: Case report and studies performed

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**Case report:** Background: In the South of Spain, avocado trees flourish between January and March (active flowering). Each avocado flower presents female and male structures. Nectar and pollen attract bees. Our aim is to describe a patient with a severe rhinitis after avocado pollen inhalation and the studies we performed.

**Patient and Methods:** A 25 year-old patient came to our Allergy Department referring during the last 5-7 years a severe rhinitis from February to June, without asthma symptoms, with a big relationship with the flowering of a avocado trees estate in front of her house. After the medical report, we performed skin prick test (SPT) with the most frequent aeroallergens in our zone, prick-by-prick with avocado pollen, specific IgE against the most typical pollens in our city and a

Western Blot to demonstrate the possible avocado pollen influence in the symptoms referred by our patient.

**Results:** Our patient presented positive SPT to Olea pollen and positive prick-prick to avocado flower (5 healthy controls presented a negative result), being negative to the other aeroallergens tested (House Dust Mites, Pollens, Moulds, Cat and Dog dander, profilin, polcalcine and LTP). Specific IgE (KU/L) to Olea europaea pollen was 27.4; Platanus acerifolia 0.42; Cupressus sempervirens 0.12 and Lolium perenne 0.64, being negative in other studied aeroallergens. Western Blot showed a 26-27 KDa band, that could be a TLP, because the molecular weight was very similar to kiwi TLP. Apple TLP was negative in Western Blot, and cross inhibition demonstrated that no cross reactivity was found between the culprit protein and kiwi LTP in our patient (cosensitization).

**Conclusions:** We present a patient with an avocado pollen sensitization, being demonstrated with in vivo and in vitro studies. We have to perform more studies to confirm the function or to characterize the culprit protein.

## 1408 | Evaluation of clinical relevance of intradermal test Results in 48 atopic dogs

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**Background:** Canine atopic dermatitis (AD) is an inflammatory and pruritic skin disease and in most cases associated with IgE antibodies against environmental allergens. To date, the only causative therapeutic option is allergen immunotherapy (AIT). Offending allergens for AIT can be identified by intradermal testing (IDT) or serum allergen-specific IgE testing (SAT). The aim of the study was to evaluate positive IDT results considering the atopic dogs' clinical history.

**Method:** An IDT was performed on 48 atopic dogs and their owners completed a questionnaire about the seasonal course of their pruritus.

**Results:** The most common positive IDT reactions were observed to mite allergens (33.3%-62.5 %). Prevalence of positive reactions to individual weeds, grasses and tree pollen ranged between 8.3% and 25%. Moulds and epithelial allergens produced positive reactions in only 0%-6.3 %. A correlation between positive IDT reactions and course of pruritus could neither be found for perennial nor for seasonal allergens.

**Conclusion:** The measurement of IgE -mediated intradermal mast cell degranulation may not be an optimal method for identification of clinically relevant allergens in canine atopic dermatitis and needs to be interpreted in light of the patient's history.

## 1409 | Evaluation of patients with high serum total IgE levels

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**Background:** Serum total IgE levels are detected at normal levels in approximately one-fourth of allergic patients while it may also be elevated in other than allergic pathologies. High total IgE level may indicate presence of an atopic condition in the patient, but it does not give information about the condition of the patient and which allergen is sensitive.

**Method:** The results of patients with IgE levels in pediatric clinics between January 2013 and December 2016 in Health Sciences University Ankara Child Health and Diseases Hematology & Oncology Training and Research Hospital were reviewed. Patients with serum IgE level >1500 mg/L were included in our study and the file records and laboratory values were retrospectively analyzed.

**Results:** 246 (72.8% male) patients with a mean age of 8.16 ± 4.48 years were included in our study. When the diagnoses of patients were examined, it was found that there were 152 (62%) allergic diseases, 8 (3.2%) immunodeficiency, 7 (2.8%) parasitic disease, 3 (1.2%) hypereosinophilic syndrome, 1 (0.04%) leukemia, 1 (0.04%) Langerhans Cell Histiocytosis. No reason was found to explain IgE elevation in 74 (30%) patients.

**Conclusion:** It should be considered that Serum IgE levels can be elevated in allergic diseases as well as it may rise in many cases other than allergic diseases. The reason of high IgE levels may not always be find in spite of the recommended screening tests. Further studies are needed for long-term prognosis of these patients.

## 1410 | Food antigen-specific IgE in dogs with suspected food reaction

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**Background:** Knowledge of cross-reactions in food-sensitive dogs will influence the choice of elimination diets and the long-term management of those patients.

**Method:** Results of IgE tests from 788 dogs submitted to three laboratories were evaluated statistically. After the tested allergens were grouped by their phylogenetic relationship, Odds ratios as well as a sensitivity analyses of the Odds ratios were performed to

evaluate if concurrent positive IgE results to two allergens occurred more often than expected.

**Results:** Within related allergen pairs 16 of 32 (50%) pairs can be considered as associated. For the unrelated allergen pairs only 24 of 121 (19.83%) analyzed pairs were considered associated. Strong correlations were shown in the group of ruminant allergens, especially beef and lamb, and grain allergens. High rates of concurrent reactions were also detected in the poultry group, especially between chicken and duck, as well as between pork and ruminant allergens, and soy and grain allergens.

**Conclusion:** As our results showed not only correlations within related but also between non-related allergens, the possible relevance of carbohydrate moieties as well as panallergens for canine hypersensitivities warrants further study. Further investigations are necessary to distinguish co-sensitization from cross-reactions and determine the clinical relevance of food-specific IgE reactivity.

## 1411 | Improving immunological diagnosis: towards point of care detection of schistosoma infections using new poc tests, recombinant proteins and monoclonal antibodies technologies fsymptoms of rhinoconjunctivitis in August

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**Background:** Control constraints of Schistosomiasis include the lack of diagnostic methods with high sensitivity.

**Method:** We develop a prospective study in southeast Brazil to standardize new sensitive and rapid diagnostic methods for *Schistosoma mansoni* infection. We have investigated 6 endemic areas (>400 individuals with chronic infection) and 84 travelers infected in a freshwater pool (with acute infection). Sera, urine, feces and saliva samples were used for the standardization/validation of innovative methods, including acute, chronic and post-treatment patients. Comparisons were performed with eggs in feces by 24 Kato-Katz slides and 2 analyses of Saline Gradient and clinical symptoms. New methods included ELISA-MEAr, ELISA-MEArb, ELISA-CCAr, Immunomagnetic Separation Technique (IMS)-MEAr, IMS-CCAr, FluoIMS-CCAr. IMS and FluoIMS techniques are based on the use of magnetic microspheres and monoclonal antibodies for peroxidase or fluorochrome reaction, allowing qualitative and quantitative analyses.

**Results:** With our new point-of-care methods using a selected recombinant protein e other markers, we were able to detect the disease early as 10 days post-infection and more than 95% of positive cases from chronic and low endemicity areas (which are characterized by hard to detect patients with extremely low parasite load, <10 eggs per gram of feces) were obtained. Plus, chromatography POC-CCA® test was improved by our group with a urine concentration step that turned its sensibility from 6% to 56%.

**Conclusion:** Monoclonal antibody and recombinant protein technologies allowed superior detection methods when comparing it to the conventional ones. In conclusion, data showed 100% of sensitivity of chronic patients and 98% of acute patients.

## 1412 | Only ambrosia?

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**Background:** Allergic rhinitis is a disease that affects about a quarter of the population, a disease with an important negative impact on daily activities, both on learning and working ability, as well as spending leisure time or sleeping. In the Western part of Romania, the most popular and blamed allergen is Ambrosia, in the late summer months. It is a plant of the Compositae/Asteraceae family, along with goldenrod, sunflower, dandelion, cocklebur, chamomile, wormwood, daisy, etc.

Allergen identification is important for applying prophylactic measures, but especially for determining the allergen to be desensitized.

Considering the possible cross-reactivity within the Compositae plant family, as well as the possibility of co-sensitization, as well as the number of patients sensitized to these pollens, which is steadily increasing, I considered is necessary a broad screening for a more precise identification of the allergen and increase chances for a successful desensitization.

**Method:** The observational study includes 37 patients who presented on October for testing with standardized allergen extracts, as recommended.

*Criteria for inclusion*: Patients with specific symptoms of rhinoconjunctivitis in August and September, with or without asthma symptoms, who returned for allergic prick test after the end of treatment.

*Criteria for exclusion*: Patients who disagreed with cutaneous testing, who did not discontinue antihistamine treatment or who had been treated for other diseases with drugs that influence skin testing.

**Results:** Of the 37 patients, 25 (65.7%) presented type I hypersensitivity evaluated by positive prick test to at least one tested allergen, one patient had severe dermographism and tests could not be interpreted. From the 25 patients who tested positive, 22(88% of the positives and 59.4% of total) were positive to weeds pollen and 19 (76% of the positives and 51.3% of total) presented hypersensitivity to more than one type of weed pollen.

**Conclusion:** The presence of co-sensitization and cross-reactivity between weeds pollen requires extensive testing of the pollen of these weeds, but also

investigation of specific IgE to the components of these pollens (eg Amb a1, Art v1, Art v6) in order to make a correct decision on allergen-specific immunotherapy.

## 1413 | Positive house dust mite skin test in a non-atopic patient with scabies

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**Case report:** A 21-yr old nonatopic man was referred for allergy evaluation with a history of an intensely pruritic eruption on his trunk and bilateral upper and lower extremities for the past 7 months. Initially, he presented to the emergency department with rectal bleeding. During the same visit, he was diagnosed as having folliculitis. He was started on oral steroids for his newly diagnosed ulcerative colitis, and subsequently the skin eruption became more widespread with more intense pruritus. A skin biopsy showed spongiotic dermatitis with possible allergic contact dermatitis. He was treated with numerous high-potency topical steroids, which made his condition unbearable. During his allergy evaluation, a skin test reaction for house dust mite (Dermatophagoides pteronyssinus and Dermatophagoides farinae) was positive. The negative control containing 0.9% saline showed no reaction. The panel of antigens also included trees, grasses, weeds, and molds, which produced negative reactions. Owing to the positive skin test reaction to the house dust mite, he was referred to a dermatology clinic to rule out scabies. The differential diagnosis included scabies, folliculitis, impetigo, arthropod bites, tinea, eczema, and contact dermatitis. A skin biopsy showed a subcorneal mite in the spongiotic epidermis. A brisk lymphocytic infiltrate with numerous eosinophils was present in the dermis. The characteristic skin biopsy findings were diagnostic of scabies. He was started on oral ivermectin and permethrin 5% cream, which resulted in complete resolution of his symptoms and the eruption within a few days. The scabies mite (Sarcoptes scabiei) and the house dust mite are related phylogenetically. Circulating immunoglobulin E antibodies against scabies mite antigens show cross-reactivity with house dust mite antigens and result in positive skin test reactions in most patients with scabies. The positive skin test reaction to the dust mite antigen and the fact that it was the only positive skin reaction among the panel of antigens being tested were helpful in the diagnosis of scabies in this otherwise non-atopic patient. It is very important that allergists be aware of the antigenic cross-reactivity between house dust and scabies mites and its implications. The case report reminds the allergist of this possibility.

## 1414 | Prolonged liposome design for RNA delivery

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**Background:** In recent years, cationic liposomes are thought to be the most effective and non-toxical nucleic acids` transport system, so most of gene therapy drugs are developed on their base. However, lipoplexes are quickly captured by reticuloendothelial system cells after the injection and taken out of a blood stream. There are many modification methods of liposomal surface for liposomes with prolonged pharmacokinetic properties production. Addition of hydrophilic polymers (PEG) is seemed to be the most promising approach, that is able not only to create steric barrier on the particle`s surface and prevent the interaction with blood plasma lipoproteins, but also inhibits the protein adsorption, opsonisation and subsequent degradation in human body. The aim of this study is the evaluation of liposomal surface modification by hydrophilic polymers influence on nucleic acids` lipoplexes conjugation and on their physico-chemical and biological properties.

**Method:** Liposomes preparation (including PEG-modified liposomes), size determination by photon-correlation spectroscopy, examination of transfection efficacy by luciferase assay.

**Results:** The liposomes based on lipodipeptides (OrnGlu(C16H33)2) were obtained. Also the modified liposomes were produced by addition of 5% of PEG (by mass) during thin lipid layer preparation step. The size distribution was analysed by photon-correlation spectroscopy. It was shown that PEG addition does not increase the particle diameter very much (135 nm in case of unmodified liposomes and 148 nm in case of PEG-liposomes). For transfection efficacy analysis the different liposome/RNA ratio was examined. In spite of increasing in transfection efficacy for unmodified liposomes from low to high liposome/RNA ratio the other correlation was observed for PEG-liposomes. It was found that the most effective ratio is 8/1 for modified liposomes in opposite to 16/1 for pure liposomes.

**Conclusion:** It can be noted that addition of PEG can change the lipoplex formation but the cationic liposomes still remain an effective RNA delivery system. And PEG modification will be able to impart prolonged properties for the vehicle in bloodstream.

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## 1416 | Rabbit allergy: A retrospective analysis

Frelih N

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**Background:** Laboratory animal workers who work with rabbits can develop allergic rhinitis, conjunctivitis or asthma. Rabbit allergy is becoming increasingly important because rabbits are becoming more popular as a domestic pet. Consequentially we have started to notice allergies to rabbits among rabbit owners.

Rabbit's allergens have been found in dander, epithelium cells, urine, saliva, serum or fur. The three most important families of allergens in mammals are lipocalins, secret globulins and serum albumins. Rabbit allergens mostly belong the family of lipocalins.

Ory c4 may cause a cross reaction with Fel d4 (cat), Can f6 (dog), Equ c1 (horse), Mus m1 (mouse) and Rat n1 (rat).

**Method:** In a retrospective analysis between February 2015 and February 2017 eight patients that were treated at our institution were diagnosed with rabbit allergy.

**Results:** All eight patients with the diagnosis of rabbit allergy presented with signs of upper respiratory involvement.

Two patients had itching teary eyes, watery nasal discharge and sneezing while feeding farm rabbits. One of those also presented with dyspnea.

Four patients developed problems whenever in contact with domestic rabbits. One patient developed allergic rhinoconjunctivitis whenever she was home—her parents own a rabbit, but while away in her college room she had no problems. Another patient had dyspnea whenever visiting his girlfriend's house. She owned a rabbit. Two patients developed asthma-like symptoms, one also presented with angioedema. The other two had developed allergic rhinoconjunctivitis.

Two patients have problems in contact with cats, one of them also with cows, however skin prick tests were also positive to rabbit.

Three out of eight patients developed allergic asthma with a positive methacholine test. Six patients had a positive house dust mite prick test.

All patients were diagnosed with a positive prick tests to rabbit allergens. All were treated with a nasal steroid and antihistaminesic. They were also advised to avoid contact with the animal.

**Conclusion:** Domestic rabbit-induced asthma and/or allergic rhinoconjunctivitis is possible, however it is still rare in our environment.

It is very important to always ask the patient about their pets in general, not just focusing on cats or dogs. Only with a thorough examination and history we can find the true cause of the patient's allergy where pets play an important role.

## 1418 | Stability of the extracts from the pollens of allergenic importance in Korea

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**Background:** Accurate diagnosis and effective immunotherapy of pollinosis are greatly dependent on the potency and stability of the extract. However, information on the standardization and stability of pollen extracts are limited. This study aimed to examine the factors such as temperature, storage buffer composition for stability of allergen extracts from the pollens of allergenic importance in Korea.

**Method:** We prepared four pollen allergen extracts from *Quercus acutissima*, *Humulus japonicus*, *Ambrosia artemisifolia*, and *Artemisia vulgaris* which are most important causes of seasonal rhinitis in Korea. Changes of protein and major allergen concentration were measured over one year by Bradford assay, two-site ELSIA, and SDS-PAGE after reconstitution of the lyophilized allergen extracts in various buffer (normal saline, 0.3% phenol saline, and 10 or 50% glycerol with saline) and stored at room temperature (RT, 18-26°C) or refrigerated (4°C).

**Results:** More than 90% of the initial protein concentration in all four extracts examined was detected over one year when 50% glycerol was added and refrigerated, whereas 57.9%-94.5% remained in the extracts at RT. The addition of 50% glycerol to the storage buffer was found to prevent protein degradation at RT. All four extracts were found to be stable when reconstituted in 50% glycerol. Amb a 1, a major allergen of ragweed, was almost completely degraded in 9 weeks at RT when reconstituted in a buffer without 50% glycerol. However, 55.6%-92.8% of Amb a 1 content was detected after one year of incubation at 4°C in all buffer conditions except 0.3% phenol.

**Conclusion:** Addition of 50% glycerol as well as refrigeration was found to be the important to increase the shelf-life of allergen extracts from pollens of allergenic importance.

## 1419 | Standardization of pollen extract from sawtooth oak, the most important cause of spring pollinosis in Korea

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**Background:** Oaks are the most common trees in Korea, and sawtooth oak, *Quercus acutissima*, was shown to be a major sensitizing source of pollinosis in spring. However, none of the standardized oak pollen extracts commercially available.

**Method:** For the standardization, bioequivalent allergy unit (BAU) was determined by quantitative intradermal skin test using sawtooth oak pollen extracts. IgE reactivity was compared with oak mix (red, virginia live, and white oak) pollen extract (1:20 w/v, 20 000 PNU/mL), which is widely used for the diagnosis and immunotherapy even though none of these oaks are native to Korea.

**Results:** Strong IgE reactions to 17 kDa allergens, putative PR-10 family proteins, were observed by IgE immunoblotting in both sawtooth and white oak pollen extracts. Sums of erythema of 50 mm by intradermal skin test were calculated to be 13.05th dilutions. Therefore, the allergy potency of sawtooth oak pollen extract was 35 391.8 BAU/mL. Consequently, it could be calculated that 1:20 w/v (20 000 PNU/mL) is equivalent to 28 508.1 BAU/mL (i.e. 0.701 BAU/PNU).

**Conclusion:** Allergy potency of sawtooth oak pollen extract was determined by a standardized method. Standardized sawtooth oak pollen extract will facilitate the development of improved diagnostic and immunotherapeutic reagents.

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HEREDITARY ANGIOEDEMA: BASIC MECHANISM AND TREATMENT MODALITIES

## 1420 | Novel SERPING1 mutations in bulgarian patients revealed by a targeted next generation sequencing platform

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**Background:** Hereditary angioedema (HAE) is a rare autosomal dominant disease characterized by swelling of the face, lips, tongue, larynx, genitalia, or extremities, with abdominal pain caused by intra-abdominal edema. HAE is caused by mutations affecting the C1 inhibitor gene (SERPING1), resulting in low levels of C1 inhibitor (Type I HAE) or normal levels of ineffective C1 inhibitor (Type II HAE).

**Method:** Genotyping was performed by means of a targeted next generation sequencing platform of the SERPING1 in 30 C1-INH-HAE type 1 patients, belonging to 13 HAE families. The newly developed and validated custom NGS platform targets the entire 11q12-q13.1 loci, including the promoter, coding, intron-exon boundary as well as intronic regions of the SERPING1 gene. Complement fractions and clinical symptoms were analyzed in relation to revealed gene mutations. Consent was obtained from all of the patients.

**Results:** This is the first genetic study of the Bulgarian HAE patients. Genetic defects were identified in 10 HAE families are: 3 nonsense, 2 splice-site defects, 2 frameshift mutations, 1 indel non frameshift, 1 missense, and 1 large deletion of exon 4. Novel mutations, not previously reported in human gene mutation databases were discovered, and were predicted to be deleterious due to the expected effect on DNA transcript and protein.

**Conclusion:** We identified 10 mutations of the SERPING1 gene in 13 HAE Type I families form the Bulgarian population (comprising 50% of the diagnosed HAE families in the country), revealing novel mutations, causative for C1-INH deficiency. A recently developed and validated targeted NGS platform was used for SERPING1 genotyping, presenting excellent potential for the future of HAE genetic diagnostics.

## 1421 | Improved health-related quality of life in pediatric patients with hereditary angioedema (HAE): a phase 3 study of C1 inhibitor for attack prevention

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**Background:** Patients with HAE have recurrent episodes of subcutaneous and submucosal tissue edema that negatively affects their quality of life (QoL). C1 inhibitor (C1-INH; Shire, Lexington, MA, USA) is currently approved to treat and prevent pre-procedure angioedema attacks in patients ≥2 years old (EU), and to routinely prevent attacks in patients aged ≥6 (EU) and ≥12 years (US). The QoL of children aged 6-11 years who received C1-INH for the routine prevention of angioedema attacks was assessed.

**Method:** Children in a multicenter single-blind study (NCT02052141) were required to have an average of ≥1.0 angioedema attacks/month that were moderate, severe, or required acute treatment during a 12-week baseline observation period (BOP). Patients received 500 U or 1000 U intravenous (IV) C1-INH, every 3-4 days for 12 weeks in a crossover design. Patients completed the youth version of the EuroQol 5-dimensional (EQ-5D-Y) descriptive system and Visual Analogue Scale (VAS) questionnaire at screening, weeks 5 and 9 of the BOP, and weeks 1, 5, and 9 of both consecutive 12-week treatment periods. Descriptive statistics were used to summarize the EQ-5D-Y descriptive system responses and VAS scores by treatment and visit.

**Results:** Twelve patients with HAE type I and a median (range) age of 10.0 (7-11) years were enrolled, 7 (58.3%) of whom were female. During BOP, treatment with 500U C1 INH, and 1000U C1-INH, ≤33.3%, ≤22.2%, and none of the patients, respectively, reported having problems with mobility, self-care, doing usual activities, pain or discomfort, and feeling worried, sad or unhappy. The mean [SD] EQ-5D VAS scores increased from 78.3 (13.8) at baseline (average of all pre-dose visits during the BOP) to 92.9 (17.7) at week 9 of treatment with 500U C1-INH and 98.5 (1.6) with 1000U C1-INH, indicating better overall health. The mean (SD) change in the VAS score from baseline to week 9 of treatment with 500U and 1000U C1-INH was 10.4 (19.0) and 21.6 (13.4), respectively, suggesting an overall improvement in QoL, particularly with the higher dose.

**Conclusion:** These data in 12 children aged 6-11 years indicate that treatment with both 500U and 1000U IV C1-INH (but particularly with 1000U C1-INH) for the routine prevention of HAE attacks improved patients' overall health status or QoL as measured by the EQ-5D-Y.

## 1422 | A booklet for the management of pediatric hereditary angioedema due to C1-INH deficiency addressed to parents: an experience of patient engagement

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**Background:** Angioedema due to C1-INH deficiency (C1-INH-HAE) imposes a considerable burden on patients and their families, both during and between angioedema episodes. Clinical manifestations exhibit high intra- and inter-individual variability and angioedema attacks occur with unpredictable frequency and severity. The reasons for the high variability and unpredictability of C1-INH-HAE manifestations are still poorly understood. Physical trauma, stress, anxiety, and low mood are among the trigger factors most frequently reported by patients. Initial results from a qualitative research in pediatric HAE show that, in the attempt to "avoid HAE triggers", parents may impose heavy limitations in children's everyday life and even implicitly suggest them to deny unpleasant emotional states and distress. This may paradoxically worsen children's competence to manage the disease and have a negative impact on health outcomes.

A multidisciplinary team composed by psychologists and medical doctors developed a tool based on the lay experts' voice that could help parents of children with C1-INH-HAE to foster an effective management of their children's disease and reduce its psychological burden.

**Method:** Information included in the booklet are based on qualitative data collected by semi-structured interviews on the disease experience administered to parents of children with C1-INH-HAE in four Italian HAE referral centers. This project is part of a broader mixed-method research on the relation between emotional processing and HAE in pediatrics which showed impaired emotion regulation and high levels of perceived stress among children with C1-INH-HAE.

**Results:** the Italian booklet addressed to parents contains suggestion for the management of their children disease in daily life. The main areas discussed are: prompt symptoms recognition and self-management of the disease, fostering children's autonomy, dialogical exchanges tailored on children's need for knowledge on the disease.

**Conclusion:** patients and their caregivers are the stakeholders and the direct experts of their disease. More efforts are needed to involve them in research-design and acquisition of knowledge especially in rare diseases. Clinician too can rely on the booklet to promote a wider space for parents' comprehension, elaboration and management of the disease.

## 1423 | Evaluation of a 5-weight-band dosing strategy for icatibant in pediatric patients with hereditary angioedema with C1-inhibitor deficiency type I/II

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**Background:** Hereditary angioedema (HAE) with C1-inhibitor deficiency type I/II often manifests in childhood or adolescence. However, evidence-based treatment guidance for paediatric patients (particularly those aged 2-5 years) is scarce, and safe dosing for these patients is critical. Weight-based dosing of icatibant (0.4 mg/kg) for acute treatment of HAE attacks in children and adolescents was well tolerated and effective in a phase 3 study, but resulted in lower exposure (area under the curve [$AUC_{0-6}$]) than the recommended adult 30 mg (3 mL) dose. Additionally, calculating weight-based dosage during a HAE attack can be burdensome, particularly in time-sensitive situations. A 5-weight-band (5WB) dosing strategy was evaluated for its ability to achieve comparable icatibant exposure to weight-based dosing in paediatric patients.

**Method:** Modeling and simulation of the relationship between age and weight with exposure and peak concentration of icatibant in paediatric patients was conducted using 6000 virtual patients based on Centers for Disease Control growth charts for age groups 2-5 years, 6-11 years, and 12-17 years. Monte Carlo simulations were performed for the weight-based approach (0.4 mg/kg) and the 5 WB dosing strategy shown in the Table.

**Results:** Overall, the model-derived median exposure and peak concentration across all weight ranges in paediatric patients is predicted to be higher with 5 WB vs weight-based dosing (Table). The effect was most pronounced in patients aged 2-5 years, where the 5WB dosing achieved approximately 30% higher values than weight-based dosing for median $AUC_{0-6}$ (1251 ng hour/mL vs 853 ng hour/mL, respectively) and $C_{max}$ values (777 ng/mL vs 529 ng/mL, respectively). The 5WB levels are closer to those in adults receiving 30 mg icatibant (median $AUC_{0-6}$ 2975 ng hour/mL; median $C_{max}$ 1254 ng/mL) but never exceed them.

Table - Median $AUC_{0-6}$ and $C_{max}$ values with 5WB and WB dosing regimens

| | 5-Weight-band dosing | | Weight-based dosing | |
|---|---|---|---|---|
| Weight Group and Dose | $AUC_{0-6}$ | $C_{max}$ | $AUC_{0-6}$ | $C_{max}$ |
| 12-25 kg: 1.0 mL (10 mg) | 1211 | 747 | 869 | 534 |
| 26-40 kg: 1.5 mL (15 mg) | 1370 | 775 | 1176 | 672 |
| 41-50 kg: 2.0 mL (20 mg) | 1617 | 867 | 1474 | 795 |
| 51-65 kg: 2.5 mL (25 mg) | 1783 | 924 | 1617 | 839 |
| >65 kg: 3.0 mL (30 mg) | 1836 | 907 | 1776 | 868 |

**Conclusion:** Pharmacokinetic modeling of a 5WB regimen for icatibant suggests exposures closer to those in adults, with acceptable safety margins. The 5WB approach provides a safe and effective dosing strategy during HAE attacks in children and adolescents.

## 1424 | Short-term prophylaxis with recombinant human C1 inhibitor in 9 patients with hereditary angioedema: A case series

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**Background:** Recombinant human C1-inhibitor (rhC1-INH) is registered for intravenous treatment (IV) of hereditary angioedema (HAE) attacks. Short-term prophylactic treatment (STP) with C1-INH is recommended in patients who will undergo invasive, surgical or dental procedures, and/or stressful events, much likely to provoke a HAE attack. STP with rhC1-INH is currently not licensed, and usually not investigated in clinical trials, due to the rarity of the disease. Therefore, it is important to publish these cases as a basis for informed decision making in an otherwise complex disease.

**Method:** SPT with rhC1-INH was initiated to cover 11 interventions in 9 HAE Type 1 patients: 5 men, mean age 51 years (17 - 73 years); mean weight 80.7 kg (60 - 98 kg). Patients were planned for invasive medical procedures: 6 dental procedures, 2 colonoscopies, 1 quadrantectomy with axillar lymph node dissection for invasive breast carcinoma (during common anesthesia), 1 cervical conization (with local anesthesia), and 1 mountaineering adventure holiday. All of the patients were evaluated to have a fragile course of the disease with frequent and/or severe HAE attacks. After ethical implications were discussed, a decision for STP with either 1 or 2 vials of 2100 U rhC1-INH, in the day of the procedure was initiated. Patients were followed closely and post-procedural periods analyzed.

**Results:** All patients experienced a safe peri- and post-procedural period with no breakthrough HAE attacks. STP with rhC1-INH was introduced 60-360 minutes (mean 148 minutes) before deemed interventions. No adverse events from the drug and/or medical procedures were observed. The patient with breast surgery developed prodromal signs of an abdominal attack on day 3 after the surgical intervention, which was successfully prevented with a dose of rhC1-INH. The average dose of rhC1-INH used for STP was 46.85 U/kg. Referring to the summary of product characteristics (SPC), 4 patients followed the prescription regimen for up to 4200 U (for weight above 84 kg), 3 patients used a higher dose (up to 64.61 U/kg), 2 patients used a lower dose (up to 28.75 U/kg): overall, 7 patients used 2 vials and 2 patients—1 vial of rhC1-INH.

**Conclusion:** Short-term prophylactic treatment with rhC1-INH could be a safe and viable option for HAE patients. Based on the case series, the prophylactic treatment should occur within 6 hours of the procedure or event. The dose indicated in the SPC for treatment of acute HAE attacks seems suitable also for STP.

## 1425 | Reduction of attack severity with fixed-dose subcutaneous (SC) C1 inhibitor liquid in hereditary angioedema patients: Results from the phase 3 SAHARA study

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**Background:** Ready-to-use SC SHP616 liquid (2000 IU in 4 mL) was shown to be superior to placebo in reducing HAE attacks in a Phase 3 SAHARA study in adult and adolescent patients with HAE with C1 inhibitor deficiency. A secondary study objective was to assess HAE attack severity in patients who received SHP616 as long-term prophylactic treatment (LTP).

**Method:** Patients in the randomized, double-blind study (NCT02584959) were aged ≥12 years with ≥2 monthly attacks pre-screening or pre-LTP. In a partial crossover design, 80% of subjects were randomly assigned to placebo or SHP616 2000 IU every 3-4 days for 14 weeks and crossed over from active to placebo or vice versa for another 14 weeks. The remaining patients were randomized to receive SHP616 2000 IU every 3-4 days for 28 weeks. Icatibant was used for breakthrough attacks. Patients in crossover sequences with ≥1 post-baseline observation were analyzed for efficacy. Attacks were rated as mild, moderate, or severe. Cumulative attack severity was the sum of the maximum symptom severity score recorded for each HAE attack and cumulative daily severity was the sum of the maximum severity scores recorded for each day of symptoms across all body locations.

**Results:** Of 81 patients screened, 75 were enrolled; 60 were randomized to the crossover sequence and 15 to the 28-week SHP616 arm. The mean (SD) age of patients was 41.3 (14.6) years and the mean (SD) weight was 84.0 (26.5) kg. During 12 months before screening, 90.7% received HAE therapy and 50.7% had a history of LTP with C1-INH or androgens. Of 57 placebo-administered patients, 8.8% were attack-free and 5.3%, 22.8%, and 63.2% had HAE attacks of mild, moderate, and severe maximum severity, respectively. Of 56 SHP616-treated patients, 37.5% were attack-free and 8.9%, 26.8%, and 26.8% had attacks of mild, moderate, and severe maximum severity, respectively. Relative to placebo, there were statistically significant reductions in cumulative HAE attack severity and cumulative daily severity (normalized per month) with SHP616, with a median reduction of 83.3% (least squared mean difference [LSMD] of -4.9; $P < 0.0001$) and 85.1% (LSMD of -12.4; $P < 0.0001$), respectively.

**Conclusion:** LTP with a fixed dose (2000 IU in 4 mL) of ready-to-use SHP616 led to fewer severe attacks, a higher proportion of attack-free patients, and a clinically meaningful and statistically significant reduction in cumulative attack severity and daily severity in HAE patients relative to placebo.

## 1426 | Management of German hereditary angioedema patients: comparison to other regions in the icatibant outcome survey

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**Background:** The Icatibant Outcome Survey (IOS; NCT01034969) is a Shire-sponsored, international, observational study monitoring safety and effectiveness of icatibant, a bradykinin B2 receptor antagonist approved for the acute treatment of adults with hereditary angioedema with C1 inhibitor deficiency (HAE-C1-INH). We report IOS data comparing demographic and icatibant-treatment outcomes in HAE-C1-INH patients from Germany to HAE-C1-INH patients from other IOS countries.

**Method:** A descriptive, retrospective, comparative analysis of data from of a total of 685 IOS patients with HAE-C1-INH from seven centers in Germany (n = 93) vs centers from Austria, Brazil, Czech Republic, Denmark, France, Greece, Israel, Italy, Spain, Sweden and the United Kingdom (n = 592, July 2009—January 2017). Icatibant treatment outcomes were retrieved from patients with complete attack outcome data for time to treatment, time to resolution and attack duration (160 attacks in 93 German patients and 1442 attacks in 592 patients from other IOS countries).

**Results:** German patients reported significantly fewer severe or very severe attacks (38.7% vs 57.5%, respectively) ($P < 0.0001$). The proportion of attacks treated with a single icatibant injection was significantly higher in German patients (97.1% vs 91.6%, $P = 0.0003$). The median time to treatment (0.0 hour vs 1.5 hours), time to resolution (3.0 hours vs 7.0 hours), and attack duration (4.3 hours vs 10.5 hours) in German patients vs other IOS countries, were all significantly shorter (all $P < 0.0001$). Overall, German patients did not use rescue medication at a higher rate ($P = 0.138$), however they did report significantly more use of C1 INH as rescue medication (129/576 attacks, 22.4%) than patients from other IOS countries (325/4303 attacks; 7.6%, $P < 0.001$). No meaningful differences were identified between patients from Germany and other countries, respectively, with regard to sex (62.4% vs 57.9% females), median age at enrollment (42.8 years vs 39.0 years), median age at symptom onset (11.0 years vs 12.0 years) and median age at diagnosis (21.9 years vs 20.8 years).

**Conclusion:** German IOS patients share similar demographic characteristics to patients from other IOS countries yet treat their attacks with icatibant significantly earlier and have markedly fewer severe or very severe attacks. Factors including regional access to and availability of icatibant may drive these outcomes and warrant further investigation.

## 1427 | Early vs late administration of icatibant in patients with hereditary angioedema

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**Background:** The relationship of the timing of icatibant self-treatment to demographic and treated attack characteristics for patients with hereditary angioedema due to C1-inhibitor deficiency are poorly understood.

**Method:** The Icatibant Outcome Survey (IOS, NCT01034969) is an ongoing, international, prospective, observational study designed to monitor the safety and effectiveness of icatibant treatment in the real-world setting. IOS data from patients in 11 countries were used to evaluate early vs late icatibant self-treatment (patients with median time-to-first injection <1 hour vs ≥1 hour from attack onset, respectively).

**Results:** Of 301 patients analyzed, 119 (39.5%) had median time-to-first injection <1 hour (median [Q1, Q3] for 829 icatibant-treated attacks, 0.3 hour [0.0, 0.6]) with no difference observed between early and late treating groups when comparing males and females. Early self-treatment varied across countries, ranging from 79.1% (Germany) to 11.1% (France). Early treaters vs late treaters treated attacks localized to skin, abdomen and larynx at a similar rate ($P = 0.814$, $P = 0.506$, and $P = 0.862$ respectively). No statistically significant difference between early vs later treater groups was observed based on pooled-attack severity (very mild/mild/moderate vs severe/very severe; $P = 0.135$). Comparing early vs late treatment, respectively, a significant reduction ($P < 0.001$) in median (Q1,Q3) time to resolution [4.2 hours (1.0, 10.0) vs 9.0 hours (3.5, 24.3)] and median (Q1,Q3) attack duration [5.0 hours (1.5, 11.0) vs 14.7 hours (6.5, 33.0)] was observed (269 patients; 1693 attacks with complete information on time to treatment, time to resolution and duration of attack).

**Conclusion:** Early treaters had significantly shorter time to resolution and attack duration compared to late treaters, indicating the importance of early use of icatibant during attack development. Differences in local practice patterns, icatibant availability, and tendency of early treaters to treat any symptoms without delay may drive prevalence of early use across countries.

## 1428 | Pharmacokinetics and pharmacodynamics of lanadelumab in patients with HAE in the phase 3 HELP study

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**Background:** Lanadelumab is a monoclonal antibody plasma kallikrein inhibitor with a half-life of approximately 14 days, which was shown to be efficacious in preventing attacks in hereditary angioedema (HAE) in the phase 3 HELP Study (NCT02586805). The pharmacokinetics and pharmacodynamics of lanadelumab in the HELP Study were evaluated.

**Method:** Patients with type I/II HAE received placebo or lanadelumab (150 mg q4 wks, 300 mg q4 wks, or 300 mg q2 wks) over a 26-week treatment period. Blood samples for measurement of lanadelumab and cleaved high molecular weight kininogen (cHMWK), a pharmacodynamic marker of plasma kallikrein activity, were collected at 0, 8, 14, 20, and 26 weeks. Lanadelumab concentrations were measured by ELISA. Levels of cHMWK were measured by western blot.

**Results:** Samples from 124 patients were analysed. Lanadelumab concentrations in plasma increased with higher doses and dosing frequencies. Steady state was reached around week 10 (range week 8 to week 14 as evaluated by predose concentrations). At baseline, mean (SD) cHMWK levels were 49.9% (28.8), 47.7% (27.1), 53.7% (24.5) and 48.4% (30.0) for patients in the placebo and lanadelumab 150 mg q4 wks, 300 mg q4 wks and 300 mg q2 wks treatment arms, respectively. By Week 14, mean (SD) cHMWK levels decreased to 24.0% (13.3), 28.7% (17.2), and 22.4% (11.5) following treatment with lanadelumab 150 mg q4 wks, 300 mg q4 wks, and 300 mg q2 wks, respectively, and remained reduced throughout the treatment period. Conversely, cHMWK levels remained elevated at 52.3% (28.1) at Week 14 in patients who received placebo. Patients in the placebo group had the highest attack rates over the 26-week treatment period (mean 2.46 attacks/month), whereas the rates were markedly lower in patients treated with lanadelumab 150 mg q4 wks (0.48 attacks/month), 300 mg q4 wks (0.60 attacks/month) and 300 mg q2 wks (0.31 attacks/month).

**Conclusion:** Plasma lanadelumab concentrations increased in a dose- and frequency-dependent manner. Exposure to lanadelumab was associated with decreased cHMWK levels (indicating inhibition of plasma kallikrein activity) and lower HAE attack rates, corroborating the efficacy findings and utility of cHMWK as a bioactivity marker in the HELP Study.

## 1429 | Efficacy of lanadelumab in patients with HAE is independent of body mass index: Findings from the HELP study

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**Background:** Treatment with lanadelumab, a fully human monoclonal antibody targeting active plasma kallikrein, provided rapid and sustained protection against hereditary angioedema (HAE) attacks

| | | Lanadelumab | | |
|---|---|---|---|---|
| **Efficacy Outcome** | **Placebo, N = 36** | **150 mg q4 wks, N = 27** | **300 mg q4 wks, N = 26** | **300 mg q2 wks, N = 25** |
| Normal BMI | n = 12 | n = 11 | n = 6 | n = 6 |
| LS mean monthly attack rate[a] | 1.77 | 0.33, $P < 0.001$ | 0.25, $P = 0.005$ | 0.11, $P = 0.010$ |
| % change vs placebo (95% CI) | | −81.0% (−92.5%, −51.8%) | −86.1% (−96.5%, −45.4%) | −93.8% (−99.3%, −48.2%) |
| Overweight BMI | n = 13 | n = 8 | n = 12 | n = 10 |
| LS mean monthly attack rate[a] | 2.29 | 0.55, $P = 0.001$ | 0.68, $P < 0.001$ | 0.36, $P < 0.001$ |
| % change vs placebo (95% CI) | | −75.9% (−89.8%, −43.2%) | −70.3% (−84.3%, −43.7%) | −84.4% (−93.5%, −62.4%) |
| Obese BMI | n = 11 | n = 8 | n = 8 | n = 9 |
| LS mean monthly attack rate[a] | 2.35 | 0.69, $P = 0.001$ | 0.62, $P < 0.001$ | 0.23, $P < 0.001$ |
| % change vs placebo (95% CI) | | −70.5% (−86.0%, −37.5%) | −73.5% (−86.9%, −46.4%) | −90.1% (−96.7%, −69.8%) |

[a]Attack rates are presented as attacks/4 weeks and are adjusted for baseline attack severity. Results are from a Poisson regression model. *P*-values are not adjusted for multiplicity.

over 26 weeks of treatment in the phase 3 HELP Study (NCT02586805). A subgroup analysis was conducted to evaluate the potential impact of patient body mass index (BMI) on lanadelumab efficacy and safety.

**Method:** Patients with type I/II HAE received subcutaneous injections of placebo or one of 3 regimens of lanadelumab (150 mg q4 wks, 300 mg q4 wks or 300 mg q2 wks). In this analysis, patients ≥18 years of age were categorized by BMI: normal (18.5 to <25 kg/m$^2$), overweight (25 to <30), or obese (>30). The baseline-adjusted number of attacks/4 weeks for each lanadelumab treatment group over the 26-week treatment period was compared to placebo.

**Results:** A total of 114 patients (normal [n = 35], overweight [n = 43], obese [n = 36] BMI) were included in the analysis population. The mean BMI at baseline was 27.5, 26.9, 28.1, and 31.0 kg/m$^2$ for patients in the placebo, lanadelumab 150 mg q4 wks, 300 mg q4 wks and 300 mg q2 wks groups, respectively. Treatment in all lanadelumab regimens resulted in a significant reduction in attack rate vs placebo in the normal, overweight, and obese BMI groups (Table).

**Conclusion:** All lanadelumab treatment regimens significantly and consistently reduced the HAE attack rate compared to placebo regardless of patient BMI.

## 1430 | Pharmacokinetic (PK) and Pharmacodynamic (PD) effects of BCX7353 in patients with hereditary angioedema with C1-inhibitor deficiency (C1-INH-HAE): Results from APeX-1 study

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**Background:** C1-INH-HAE is a rare, potentially life-threatening disease characterized by episodes of subcutaneous and/or submucosal swelling. APeX-1 was a Phase 2, double-blind, placebo-controlled study to evaluate the prevention of attacks with BCX7353, a once daily oral kallikrein inhibitor, in patients with C1-INH-HAE.

**Method:** Patients with C1-INH-HAE with a history of at least 2 HAE attacks per month were randomized to receive four different doses of BCX7353 (350 mg, 250 mg, 125 mg, 62.5 mg) or placebo for 28 days. Blood samples for BCX7353 concentrations and kallikrein inhibition were obtained from patients before dosing and for 24 hours post-dose on Day 14. PK analyses and PK-PD modeling were done in Phoenix WinNonlin v 8.0 and SAS v 9.3.

**Results:** The PK population included 16, 14, 14, and 7 subjects in the 350 mg, 250 mg, 125 mg, and 62.5 mg groups respectively. After daily dosing achieved steady state, $C_{max}$ was reached at a median of 3-4 hours after dosing. There was a greater than dose proportional increase in exposure ($AUC_{tau}$ and $C_{max}$) over the 62.5-mg to 350-mg dose range, with an approximate 14-fold increase in exposure with a 5.6-fold increase in dose. At doses ≥125 mg, which showed statistically significant and clinically meaningful reductions in HAE attack rates, geometric mean plasma trough concentrations ($C_{tau}$) were maintained at or above the minimum target concentration (4-fold $EC_{50}$) estimated to be required for adequate plasma kallikrein inhibition. Percentages of study subjects at steady-state with BCX7353 plasma concentrations>4-fold $EC_{50}$ were 0%, 57%, 100% and 100% in the 62.5, 125, 250, and 350 mg dose groups, respectively. A 125-mg dose provided a mean $C_{tau}$ of slightly above 4.0-fold $EC_{50}$, with a corresponding reduction in HAE attack rate of 69% ($P < 0.001$) compared with placebo. Consistent with the exposure data, a dose dependent inhibition of kallikrein was observed with BCX7353 treatment over the dose range. The drug effect on kallikrein inhibition was highly correlated with exposure ($r = 0.867$).

**Conclusion:** In patients with C1-INH-HAE, BCX7353 treatment at doses ≥125 mg resulted in clinically meaningful reductions in the mean weekly HAE attack rate. Concentrations of BCX7353 at doses ≥125 mg were maintained at or above a $C_{tau}$ of 4-fold the kallikrein inhibition $EC_{50}$ in most patients, and kallikrein inhibition was highly correlated with BCX7353 plasma concentrations.

## 1431 | BCX7353 improves health-related quality of life in hereditary angioedema with C1-inhibitor deficiency (C1-INH-HAE): Findings from the APeX-1 study

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**Background:** C1-INH-HAE is a rare, life-threatening disease characterized by recurrent episodes of subcutaneous and/or submucosal swelling that lead to considerable morbidity and a poor quality of life (QoL). APeX-1 was a Phase 2, double-blind, placebo-controlled study to evaluate the prevention of attacks with BCX7353, a once daily oral kallikrein inhibitor, in patients with C1-INH-HAE.

**Method:** Patients with C1-INH-HAE with at least 2 HAE attacks per month were randomized to four different BCX7353 doses (350 mg, 250 mg, 125 mg, 62.5 mg) or placebo. Subject-reported QoL assessments were conducted at the start and end of treatment using the disease specific angioedema quality of life (AE-QoL) questionnaire that measures 4 domains (function, fatigue, nutrition, fear/shame) and has minimal clinically important difference (MCID) of 6 points. The changes from baseline in total and domain scores was compared between the treatment and placebo groups. Modified angioedema activity score (AAS) values across 4 domains (daily activities, appearance, physical discomfort, overall severity) were calculated for each attack and a total score was derived for each subject by summing scores from each attack. Total scores were compared to placebo using an ANCOVA model with adjustment for qualifying attack rate. Reduction of attacks was statistically significant for all 3 top doses and there was a dose related increase in adverse events.

**Results:** In the 125 mg dose group, QoL assessed by AE-QoL was significantly improved after 4 weeks of treatment compared to placebo for AE-QoL total score (-26.0, $P < 0.001$) as well as across all 4 domains (function: -28.2, $P = 0.002$; fatigue: -12.7, $P = 0.05$; fears/shame: -36.5, $P < 0.001$; nutrition: -23.4, $P = 0.012$). All other treatment groups showed a trend towards improvement. QoL improved the most in the125 mg group, and 92% of subjects in the 125 mg group showed AE-QoL reduction of more than 6 points. Disease activity as assessed by the AAS was significantly reduced in the 350 mg, 250 mg and 125 mg dose groups as compared to placebo, whereas there was no significant reduction in the 62.5 mg dose group.

**Conclusion:** Treatment with 125 mg BCX7353 daily results in significant QoL improvement. 350 mg and 250 mg of BCX7353 also significantly reduced QoL impairment, albeit less so than 125 mg. This may be because mild to moderate study drug-related gastrointestinal AEs occurred in patients treated with 250 mg or 350 mg, which may have affected their QoL.

## 1432 | Analysis of gastrointestinal (GI) symptoms in patients with hereditary angioedema with C1- inhibitor deficiency (C1-INH-HAE) treated with BCX7353: Results from APeX-1 Study

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**Background:** Hereditary angioedema (HAE) is characterized by unpredictable attacks of debilitating swelling. Intra-abdominal attacks are common, severely painful, and often mistaken for other diseases such as appendicitis or small bowel obstruction. APeX-1 was a Phase 2, double-blind, placebo-controlled study to evaluate the prevention of HAE attacks with BCX7353, a once daily oral kallikrein inhibitor.

**Method:** Patients with C1-INH-HAE with at least 2 HAE attacks per month were randomized to four different doses of BCX7353 (350 mg, 250 mg, 125 mg, 62.5 mg) or placebo. Adverse events (AE) were collected throughout the study. Subjects completed diaries for daily recording of details of angioedema attacks, including location, severity, triggers, duration, and acute medications administered.

**Results:** Analysis of the AE profile identified a dose-related incidence of gastrointestinal (GI) events, that was highest in the 350 mg (44%) and 250 mg (50%) arms, and was markedly lower in the 125 mg (29%) and 62.5 mg (14%) arms, which were comparable to placebo (18%). A post-hoc analysis demonstrated that events representing abdominal pain, diarrhea and nausea/vomiting were primarily responsible for the increased incidence of GI AEs at higher doses. No diarrhea, nausea or vomiting were reported in the 125 or 62.5 mg arms. More than 2 GI events were reported by 39%, 14%, 7%, 0% and 5% subjects, respectively, in the 350 mg, 250 mg, 125 mg, 62.5 mg, and placebo arms. GI events were generally mild to moderate in severity; one patient in the BCX7353 350 mg arm experienced severe abdominal pain that led to discontinuation of study drug. GI AEs in the 125 mg and 62.5 mg arms were all mild. Abdominal-only events recorded by subjects as symptoms of angioedema attacks were more prevalent at the 350 mg and 250 mg arms than for the other dose groups.

**Conclusion:** The frequency of abdominal-only HAE attacks at higher doses, the length of these attacks despite treatment and the dose relationship of GI AEs suggest that the efficacy at BCX7353 at 250 mg and 350 mg was likely masked by GI AEs that may have been misattributed as early symptoms of abdominal HAE attacks. While all doses were generally well-tolerated, reported GI AEs were more common in the 250 mg and 350 mg BCX7353 arms. Doses lower than 250 mg are recommended for further study.

## 1433 | Safety, effectiveness, and impact on quality of life of self-administration with plasma-derived nanofiltered c1 inhibitor in patients with hereditary angioedema

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**Background:** Hereditary angioedema with C1 inhibitor deficiency is a disabling, potentially fatal condition characterized by recurrent episodes of swelling. Self-treatment is recommended, in order to reduce admissions to the Emergency Room and the time between the onset of the attack and the treatment, resulting in a better treatment outcome and an improved quality of life (QoL). The purpose of this study is to assess the safety, tolerability, and effect on QoL of self-administration of pnf C1-INH.

**Method:** An observational, monocenter, prospective study was designed, which enrolled 20 consecutive patients referring to a center for angioedema in the period March 2014-July 2015 who attended a self-infusion training course. The primary endpoint was to monitor the safety and feasibility of pnf C1-INH self-infusion. The secondary endpoint was to evaluate the effect of self-infusion on the QoL, by means of the HAE-QoL questionnaire. Patients' medical history data were collected upon the first visit and questionnaires were filled after each attack treated with pnf C1-INH (diary and *Treatment Satisfaction Questionnaire for Medication*) and upon the first visit and the follow-ups (HAE-QoL).

**Results:** Fifteen patients completed the study. A total of 189 attacks were recorded (annual median rate of 4 attacks/patient). Patients waited a median of 2 hours (IQR: 1-4) before self-administration, and the resolution of the attack occurred after a median of 6 hours (IQR: 4-11). Most attacks were abdominal (39%) and peripheral (22%). 92% of the attacks were treated through self-/caregiver-administration. In most attacks no side effects were reported. The number of attacks with side effects decreased over time, from 37% to 13%. Global satisfaction grew over time during the study period, reaching statistical significance over the first 6 months. The median total HAE-QoL score at baseline was 86 (IQR: 76-103) and improved in a non-significant manner throughout the study period. 8% of the attacks treated with pnf C1-INH required ER admission/healthcare professional help in the study period, compared with 100% in the three years before enrollment ($P < 0.0001$).

**Conclusion:** Self-administration of pnf C1-INH is safe, and increases patients' confidence in the treatment, showing also a trend towards an improvement in QoL. It reduces the need for ER admission/healthcare professionals help for the acute attacks, as well as the related costs.

## 1434 | Individually tailored prophylaxis with C1-INH concentrate in four pediatric patients with Hereditary Angioedema (HAE): Real life data

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**Background:** Hereditary angioedema due to C1-inhibitor deficiency (HAE-C1-INH) is a rare autosomal dominant inherited disease. The recurrent symptoms are subcutaneous edema and colic-like abdominal pain. Laryngeal edema is rare, but life-threatening if untreated and negatively affects quality of life (QoL). C1-INH is currently approved for prophylaxis to routinely prevent attacks in patients aged ≥6 (EU) and ≥12 years (US). Real life data in four pediatric patients with HAE who received C1-INH concentrate for the routine prevention of angioedema attacks was documented and followed up.

**Method:** After giving informed consent the following data was collected and analyzed from patient's diaries and records 1 year before

onset of and after introduction of prophylactic treatment: age at first manifestation and diagnosis, age at first treatment, frequency and location of attacks, prophylactic respectively on-demand therapy regimen.

**Results:** Four patients (3 male/1 female) aged 11.8-17 years with HAE-C1-INH type I were enrolled. Attacks affected mainly abdomen and extremities but also face. A history of laryngeal attacks was reported in two patients. Attack frequency before onset of prophylaxis ranged from 3 to 11 attacks/month. Prophylactic treatment consisted of 1000 U C1-INH, every 3-4 days i.v.. Due to frequent breakthrough attacks in 2 patients the prophylactic regimen had to be intensified to every 2 days regimen. Individually tailored prophylaxis with C1-INH resulted in zero break-through attacks during 7-24 months, including laryngeal attacks.

**Conclusion:** Although our data refers to only four pediatric patients, this real life data strongly indicates that prophylaxis regimes should be tailored according to the individual patient's needs in order to achieve favorable results.

## 1435 | Long-term prophylaxis with recombinant human c1 inhibitor in patients with hereditary angioedema: Extended experience with intramuscular administration

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**Background:** Recombinant C1-inhibitor (rhC1-INH) is registered for intravenous treatment (IV) of hereditary angioedema (HAE) attacks. Intravenous prophylactic treatment (PT) with C1-INH is an opportunity in patients with frequent and/or severe episodes. Bioavailability of intra-muscular (IM) C1INH should also be higher compared to a sub-subcutaneous route of administration. As off today intramuscular (IM) administration is not investigated in clinical trials, but is known for its ease of self-administration.

**Method:** Off-label IM PT with rhC1-INH in 2 HAE Type 1 patients (S1: 59-y-female, 85 kg; S2: 73-y-male, 90 kg) suffering 6-12 HAE attacks/month with difficult IV access, causing unnecessary treatment delays. After all ethical implications were discussed, a regular IM PT with 4200 U (2 vials, each reconstituted in 10 mL WFI) twice/weekly was initiated. Patient diaries were analyzed, which included documentation for pain by the visual analogue scale (VAS). C1-INH antigen and C4 plasma levels were recorded before and during LTP.

**Results:** Both patients showed good efficacy of the 386 IM PT administrations (Treatment period: S1: 41 weeks, S2: 56 weeks). Two breakthrough attack occurred. Six prodromal symptoms were registered and rhC1-INH was administered IM, coping an attack onset. VAS (pain) for IM rhC1-INH (1.32, 0.57, respectively) was comparable to a comparable IM (1.3, 0.5), and less than IV (2.5, 2.0) injections. Mild bruises and transitory edema at the injection sites were observed (S1: 7/164; S2: 0/222 administrations). No serious adverse events were reported. Plasma C1-INH antigen and C4 values did not show changes before and during LTP.

**Conclusion:** Prophylactic intramuscular administration of rhC1-INH could be an alternative to the intravenous administration. Intramuscular application of 10 mL solution of 2100 U of the drug seems to be safe and well tolerated. VAS (pain) for IM rhC1-INH is comparable to similar IM injections.

## 1436 | Hereditary angioedema: A Chinese perspective

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**Background:** Hereditary angioedema (HAE) is a rare, autosomal dominant disease, which is characterized by unpredictable and recurrent attacks of painful swellings. The research of HAE in China began in the 1980s. Later studies identified clinical characteristics of Chinese patients different from the western population. The Objectives of this study are as follows: (a) to summarize the past research progress of HAE in Chinese population; (b) to evaluate the economic burden and health-related quality of life (HRQoL) in China for the first time.

**Method:** Forty-two articles concerning HAE (both in English and in Chinese language) since 1980 were systematically reviewed to describe the characteristics of Chinese patients. A web-based survey focusing on economic burden and HRQoL (using SF-36) was performed recently.

**Results:** Type 1 HAE (98.73%) accounts for the majority of Chinese HAE patients while no type 3 HAE patient has been diagnosed in China to date. Compared with other populations, the onset age (21.25 years) of Chinese HAE patients is later, and the percentage of abdominal attacks (34.18%) is lower. The first mutation spectrum of *SERPING1* has been established and a total of 56 mutations have been reported among Chinese patients. Currently, there is no approved drug for acute attacks in Chinese market, and the choices for long-term prophylaxis are limited to Danazol and Tranexamic acid. Danazol has demonstrated good efficacy and was tolerated in most of Chinese patients although it has some side effects, especially at the beginning of the treatment with higher doses. Edematous attacks could be effectively prevented with a dosage at or under 200 mg/d in 80% patients. Our recent study (unpublished) reported a 152.1(0-553) months' diagnostic delay, resulting in inappropriate use of medical resource and negative influence on productivity, education and social activities. We evaluated HRQoL in 93 HAE patients, reporting significant reduction in all basic health scales but physical functioning.

**Conclusion:** Chinese HAE patients show different clinical characteristics from the western population, indicating an important role of

genetic and environmental factors in the pathogenesis of HAE. HAE causes a heavy economic burden to patients and impairs HRQoL. Currently, medications available to Chinese patients are long-term prophylaxis. Studies on molecular mechanisms and therapeutic interventions including traditional medicine are deserved in the future.

## 1437 | The economic and humanistic burden of hereditary angioedema in China

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**Background:** Hereditary angioedema (HAE), which is characterized by unpredictable and recurrent attacks of painful swellings, is a rare but debilitating disease with wide-ranging impacts. This study was designed to assess the economic and humanistic burden associated with HAE in China.

**Method:** This is a cross-sectional study, in which two web-based surveys were conducted in 94 and 89 patients respectively, to assess the economic and humanistic burden before and after confirmed diagnosis. Collected information includes individual's health care resource use, direct and indirect costs, and impacts on work, school and social activities.

**Results:** Seventy-five and eighty-four HAE patients responded to two surveys with complete information, respectively. Patients spent a mean of 152.1(0-553) months, visit 5.5(1-20) hospitals and 11.4(1-100) doctors before confirming diagnosis. Before HAE diagnosis was established, patients on average paid 5.2 (0-30) visits to outpatient clinics, 2.6 (0-20) visits to emergency rooms and 1.1(0-8) visits to in-patient departments each year. Patients reported a direct cost of 13232.0 CNY (1679.6 EUR) and indirect cost (transportation, productivity loss) of 10968.2 CNY (1392.2 EUR) per year before diagnosis. Workers lost a mean of 27.4(0-200) days annually while students lost 11.7(0-60) days per year. Swellings impeded social activities in 96 percent HAE patients, which resulted an annual loss of 21.4(0-200) social-active days. After diagnosis and treatment, patients reported significantly less working day loss (14.3 days/year, $P < 0.001$), direct costs (1132.1 CNY/year, $P = 0.032$) as well as indirect costs (3224.4 CNY/year, $P = 0.003$). Visits to out-patient clinics (2.8 times/year, $P = 0.001$), emergency rooms (1.3 times/year, $P < 0.001$), in-patient departments (0.5 times/year, $P = 0.007$) are also significantly decreased. Patients also suffered from less social-active day loss after diagnosis and treatment (17.7 days/year, $P < 0.001$).

**Conclusion:** Our study was the first to describe the economic and humanistic burden of HAE in China. The diagnosis of HAE is considerably delayed in China, resulting in inappropriate use of medical resource and negative influence on productivity, education and social activities. More attention should be paid on relieving the economic and humanistic burden of HAE in China.

## 1438 | Treatment of severe Hereditary Angioedema (HAE) during pregnancy and lactation period

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**Background:** We report a 26 years-old lady with positive family history for Hereditary Angioedema (HAE) over 4 generations. Symptoms started during puberty and were of mild nature and appeared at the beginning of the menses each time and sometimes also at the time point of the ovulation. She was prophylactically treated only with cyklokapron (tranexamic acid) since she was 9 years old and took the medication very irregularly due to lack of efficacy. One year before presentation at our clinic, she married and moved to Vienna.

**Method:** We started a treatment with the bradykinin-2 receptor-antagonist icatibant SC at the beginning of the menses and if needed a second time at the time of ovulation. She responded well until she got pregnant. During pregnancy, she developed weekly attacks with increasing severity. Therefore, a weekly treatment with human-plasma-derived, pasteurized, nanofiltered C1-inhibitor (INH)-concentrate, 1000 Units IV once a week was started and had to be increased to twice per week after one month of therapy due to increasing number and severity of attacks.

**Results:** With this treatment attack frequency and severity attenuated. In January 2016 she had a normal delivery at term and gave birth to an otherwise healthy son. Treatment had to be continued during 1 year of lactation period and also thereafter due to persistent attack severity.

**Conclusion:** There are only limited data for the use of human-plasma-derived, pasteurized, nanofiltered C1-INH concentrate during pregnancy and lactation period. This case confirms the safety and efficacy of the named drug during these periods.

## 1439 | The French side of the global angioedema registry

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**Background:** Angioedema is a recurrent localized swelling of cutaneous and mucosal tissues. Potentially life-threatening, creates temporary disability which deteriorates quality of life. Mostly associated with wheals, it is common symptom of allergic reactions and chronic urticaria. Rare diseases exist, where it is the primary pathologic

event. Seven inherited or acquired forms of angioedema without wheals are yet classified. The best characterized stem from hereditary or acquired C1 inhibitor deficiency (C1-INH-HAE and C1-INH-AAE).

Last year, the French angioedema network (CREAK) joined the registry of angioedema without wheals (Cloud-R HAE). Here we present the contribution of the Grenoble Alpes University Hospital (CHUGA) to this disease registry.

**Method:** The study population is composed of patients with a proved diagnosis of C1-INH-HAE/AAE.

The following items are collected: patients' personal-demographic data, clinical/laboratory/genetic characteristics, major comorbidities, treatments (prophylaxis/acute attacks). Data from existing registries at CHUGA are merged into Cloud-R HAE and missing data obtained at follow-up visits. As from Cloud-R HAE structure, patients can directly provide information on angioedema attacks and their treatment through a dedicated electronic app, web connection or paper support, which is then transferred into the registry at CHUGA.

The Study Protocol has received approval from the Ethical Committee.

**Results:** 132 C1-INH-HAE and 8 C1-INH-AAE patients, who signed informed consent, are present into the registry and 110 of them provide prospective data on angioedema attacks. Within C1-INH-HAE, age range is 2-88 years, type II represents 6%. Average yearly attack rate is 9.5. Median age of patients with C1-INH-AAE is 69. 50% have an associated lymphoproliferative disease. Due to the frequency of symptoms 15% of them are on long-term prophylaxis with tranexamic acid, 16% with danazol and 17% with C1-INH concentrate or C1 Inh recombinant. Most of women achieve a significant improvement thanks to progestin treatment.

**Conclusion:** Angioedema registry gives the possibility to gather information to define natural history of angioedema and to evaluate treatment efficacy in real life. The possibility that data from single countries merge into a global structure facilitates improvement and dissemination of the knowledge on this rare disease and its treatment.

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## 1440 | The relevance of CMV reactivation in immunocompromised patients suffering from chronic inflammatory skin diseases

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**Background:** Reactivation of latent CMV infection is a serious complication in immunocompromised patients. This might be in particular true for patients with chronic skin diseases fulfilling two major prerequisites of CMV reactivation in the human organism, namely ongoing inflammation and therapy-induced immunosuppression. The aim of this project was to elucidate the role of a potential reactivation of CMV infection in chronic skin diseases which require long-term immunosuppressive treatment.

**Method:** In a retrospective study, we included a total number of 48 patients, suffering from a chronic skin disease, whose lesions did not improve or even worsened under immunosuppressive treatment (18 chronic ulcers/pyoderma gangrenosum, 21 bullous autoimmune diseases, 9 skin lymphomas). FFPE tissue was examined for the presence of CMV DNA by PCR. Next, within the framework of a small prospective study (n = 29) we analyzed the seroprevalence of CMV as well as the presence of CMV DNA in lesional skin in patients that had been diagnosed with a chronic skin disease and in whom long-term immunosuppressive therapy had been initiated.

**Results:** In the retrospective study CMV DNA could only be detected in 1/18 chronic ulcers/pyoderma gangrenosum (5.6%), but not in bullous autoimmune diseases and skin lymphomas. 21/29 patients (72.4%) of the prospective study group were seropositive for anti-CMV-IgG, as compared to 55/87 patients (63.2%) in an age- and sex-matched control group. Anti-CMV-IgM could be detected in 5/29 patients (17.2%), thereof one patient (A) was diagnosed with pyoderma gangrenosum, one (B) with pemphigus vulgaris and one (C) with ulcers. In addition, CMV DNA was detected in lesional skin biopsies of patient A and C. Despite being treated with high-dose steroids, and specific therapy regimens in addition (infliximab in A and rituximab in B), lesions worsened. In all three patients, treatment with ganciclovir was initiated leading to profound improvement of skin lesions and/or health status. Besides, CMV DNA could be detected in lesional skin of one patient who did not show anti-CMV-IgM. Taken together, we found CMV DNA in 3/19 lesional skin biopsies (15.8%).

**Conclusion:** Our study showed that the seroprevalence of CMV is elevated in patients suffering from chronic inflammatory skin diseases under immunosuppressive treatment. The presented cases highlight that awareness of the phenomenon of CMV reactivation and prompt antiviral treatment might speed up improvement of health status.

## 1441 | Patients with Epidermolysis Bullosa (EB) due to mutations in collagen type 7 show markedly higher IgE sensitizations to allergens than EB patients with mutations in keratins

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**Background:** Epidermolysis bullosa (EB) is a heterogeneous group of a rare hereditary skin diseases characterized by blistering and erosions in response to minor mechanical impact. EB simple form is caused by mutations in the genes KRT5 and KRT14. EB dystrophic type - by mutations in the gene COL7A1 coding for type 7 collagen, which is responsible for the stability of the structure of connective tissue fibers of the skin and other organs. Itching is a dramatic symptom of BE lesions. Aim: To study the profile and frequency of IgE sensitization in children suffering from different forms of EB.

**Method:** We studied 67 children with EB, 18 patients with simple EB, 49 patients - with dystrophic EB. We used a panel of more than 170 micro-arrayed allergens and ImmunoCAP (food allergens extracts+mixture of house dust mite) to assess IgE sensitization

**Results:** There was a statistically significant more frequent IgE sensitization in children with dystrophic EB. Among them 28.6% showed IgE reactivity to ≥1 allergen, 40.8% had a positive history indicative of IgE sensitization, 24.5% - had both IgE and clinical results. Among patients with simple EB, 16.7% showed IgE reactivity to ≥1 allergen, 27.8% - a positive clinical history, 11.1% - were double-positive (sIgE+history). According to the chip data the sensitization to ragweed, mugwort, birch, Alternaria, latex, peanuts, walnut, cow's milk, egg white, apple, peach, kiwi, house dust mite, dog, cat, and venom were most frequently encountered in children with dystrophic EB. Patients with a simple EB were sensitized only to house dust mite, cow's milk and egg white allergens. ImmunoCAP technology showed that IgE-reactivities to allergen extracts of soy, meat, fish, cereals, fruits were detected significantly more often in children with dystrophic EB, whereas patients with the simple EB had antibodies only to banana extracts

**Conclusion:** Patients with EB due to mutations in collagen type 7 show markedly higher IgE sensitizations to allergens than EB patients

with mutations in keratin genes which may be due to a defect in barrier function.

## 1442 | Mapping of disease severity in patients with scleroderma

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**Background:** Systemic sclerosis (SS) is a severe autoimmune disease with a high mortality rate. Characterized by increased synthesis of collagen and damage to small blood vessels, first symptoms are thickening of the skin and poor blood flow to the fingers. Objective disease scoring is crucial for optimal disease monitoring and appropriate treatment. Most frequently the Rodnan skin score (RSS) is used as a primary or secondary outcome measure in clinical trials and daily routine. However, it is based on subjective assessment of the skin thickness and therefore does not represent an objective measurement tool.

**Method:** In this study, we aimed at testing the diagnostic potential of skin function measurements in SS. Sixteen patients with conformed diagnosis SS were enrolled in the study. Skin fibrosis was assessed by conventional RSS and involvement of inner organs and serum inflammation parameters were determined. Four objective criteria, namely transepidermal water loss (TEWL), corneometry, pH and elasticity, were assessed at nine predefined sites of the body. Results were compared to patients with atopic dermatitis (n = 19) and acne vulgaris (n = 22).

**Results:** Although SS patients varied in disease severity and levels of systemic inflammation, skin function measurements of SS patients represented the most homogeneous group at all sites of the body in contrast to atopic dermatitis patients and acne patients. As expected skin elasticity was exclusively lowered in SS. Interestingly, we detected a decreased TEWL at the fingers and hands of patients with SS, indicating a link between impaired microcirculation and skin barrier, while skin humidity and skin pH of SS patients were not altered compared to controls.

**Conclusion:** Our results demonstrate that skin function at the extremities are partially altered in SS patients. However, further studies of additional diagnostic tools are needed for mapping the disease progression more comprehensively and customizing treatment strategies accordingly.

## 1443 | Serum squamous cell carcinoma antigen-2 (SCCA2) is a reliable biomarker for detecting the clinical severity of atopic dermatitis in children

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**Background:** Squamous cell carcinoma antigen (SCCA) molecules are downstream molecules of Th2 cytokine and are elevated in various inflammatory skin diseases including atopic dermatitis (AD). SCCA is classified into two subtypes, SCCA1 and SCCA2. Serum SCCA2 is reportedly more predominant than SCCA1 in adult AD patients. The aim of this study was to verify the usefulness of SCCA2 as a biomarker for evaluating pediatric AD.

**Method:** A multicenter prospective observational study was conducted to investigate the clinical significance of serum SCCA2 in children as a biomarker for AD. Patients with AD younger than 16 years old and age-matched healthy children without any allergic disease were enrolled in this study. The severity of AD was evaluated using the objective SCORAD (O-SCORAD). The serum levels of SCCA2, TARC and total IgE were also measured.

**Results:** In total, 176 patients with AD and 159 non-allergic healthy children were recruited. The serum levels of SCCA2 had the strongest significant correlation with O-SCORAD, compared with TARC and IgE ($r$ = 0.622, 0491 and 0.407, respectively). After standard treatment with topical steroids and emollients resulting in an improvement of symptoms, the serum levels of SCCA2 and TARC decreased significantly. The area under the curve (AUC) for the ROC curve was higher for SCCA2 (0.929) than for TARC (0.871) or IgE (0.820). The difference in AUCs between a single cut-off value and age-dependent cut-off values was not significant for SCCA2, compared with that for TARC (0.042 and 0.064, respectively).

**Conclusion:** SCCA2 is a more reliable biomarker than TARC for the diagnosis of AD and for determining the clinical severity of AD in children.

## 1444 | Mathematical concepts and their challenges in predicting severity of atopic eczema patients

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**Background:** Atopic eczema (AE) is a widespread inflammatory skin disease. A hallmark of AE are alterations in the immune system, which can be detected in the serum of patients as quantitative measurements of serum proteins. Some serum proteins are secreted by nucleated cells and have a local effect within the tissue. If production of these serum proteins gets excessive due to a strong inflammation, cytokines get into the plasma and can be detected in the serum of patients. The relationship between the concentration of serum proteins in patients with AE and the severity of their disease is extensively discussed in the scientific community.

**Method:** We use measurements of 32 serum proteins from patients with AE and healthy controls to model the severity of AE using different statistical tools.

**Results:** Before modeling, we checked for significant differences between patients and controls. These were detected for the levels of CCL17, CCL22, CXCL10, IgE and LDH. Next, we assessed whether single serum proteins already explain disease severity by calculating correlations. Twelve of the proteins, namely GCSF, IL-5, IL-13, IL-22, CCL22, IL-1Ra, CXCL8, IFNg, CCL3, IL-1ß, CCL17, and IL-6, significantly correlate with severity ($r^2$ range: 0.3-0.45). Finally, we built a model for the severity of AE based on all measured serum proteins. Ten of the proteins are included in the best-fit model (adjusted $r^2$=0.47). The overall correlation between original and predicted severity scores is high ($r^2$=0.759) nevertheless the cross validation prediction error is substantial with 19%.

**Conclusion:** Applied in daily practice, a prediction error of 19% translates to a possible miscalculation of 19 SCORAD points in both directions and therefore the model is of no practical use. Aside from using model-based quality measures like cross validation prediction errors to infer the usefulness of predictive models, testing them in independent cohorts could validate these models. Collaborations among scientists working on similar approaches would lead to an increase in statistical power and ideally to more robust models. Only robust and validated models are going to have the chance to take the step forward from being a result of computational modeling to being applied in the clinical practice of assessing disease severity in patients.

## 1445 | Necroptosis as special type of cell death in inflammatory skin diseases

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**Background:** Epithelial structure and homeostasis of the skin depend on the balance between cell survival and cell death. In inflammatory skin diseases (ISD) cell death mechanisms are often dysregulated. This study shows an important role of receptor-interacting protein kinase-3 (RIP3)-regulated necroptosis—one type of regulated necrosis - in keratinocytes besides apoptosis.

**Method:** We did immunohistochemistry of inflammatory skin diseases, characterisation of lesional T cells of inflammatory skin biopsies, necroptosis induction in human keratinocytes, shRNA knockdown of RIP3 and three-dimensional skin equivalent studies.

**Results:** We detected a significantly enhanced epidermal expression of RIP3 in lichen planus (LP) and lupus erythematosus (LE) in comparison to healthy and psoriasis skin biopsies. Additionally, the analysis of T cells from lesional LE and LP skin biopsies revealed a dominant type I immune response with high frequencies of IFN-γ and TNF-α positive cells. These findings indicated a role of IFN-γ and TNF-α in the induction of RIP3 and initiation of necroptosis. In vitro we showed that either IFN-γ or TNF-α but not IFN-α induced the production of RIP3 in keratinocytes and lead to cell swelling and vacuolization of keratinocytes in three-dimensional skin equivalents. Interestingly, shRNA knockdown of RIP3 prevented necroptosis of keratinocytes.

**Conclusion:** Thus, necroptosis and RIP3 in particular represent potential targets for treatment of ISD like LE and LP.

## 1446 | Corticosteroid-embedded dissolving microneedles for dermatological treatment

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**Background:** Intra-lesional corticosteroid injections are frequently performed in dermatological practice for conditions such as pathological scars, alopecia area and prurigo nodularis. The procedure is, however, painful and precludes treatment in children and some adults. In certain conditions, such as keloids, lesions are already inherently hypersensitive.

**Method:** We designed triamcinolone-embedded hyaluronic acid microneedles which induce minimal or no pain during administration.

Preclinical studies in cell cultures, mice, guinea pigs and rabbits, comprising sterility, cytotoxicity, systemic toxicity, skin irritation, delay contact sensitization and phototoxicity tests, demonstrated safety of this therapeutic agent.

We next conducted a single-blinded, intra-individually controlled, 2-phased clinical trial on patients with keloids. The aim was to determine the effects of 1-month therapy on keloid volume and symptoms of pain and itch. Two similar keloids on each subject were selected - one was treated with once-daily, self-administered application of triamcinolone-loaded (0.015 mg/patch) microneedles for 4 weeks, while the other served as control with no intervention. Outcome measures were (a) keloid volume using a 3-dimensional high-resolution (0.1 mm) scanner and (b) pain and itch scores on 0-10 numerical rating scales. Evaluations were performed at baseline, 4 and 8 weeks. In Phase 2 of the trial, the whole process was repeated using microneedles loaded with a higher dose of triamcinolone (0.1 mg/patch).

**Results:** Twenty-seven subjects underwent Phase 1 of the trial while 17 continued to Phase 2. The mean keloid volumes significantly reduced in the intervention group after 4 weeks of treatment (7.7% in phase 1 and 12.9% in phase 2), which were significantly greater than in controls. At 8 weeks (after stopping treatment for 4 weeks), the mean volume in the intervention group increased to near baseline. The reduction in keloid volumes significantly correlated with the dosage of triamcinolone loaded. For pain and itch, the intervention group demonstrated lower scores at 4 or 8 weeks compared to baseline. There were no side effects registered.

**Conclusion:** Treatment with triamcinolone-embedded dissolving microneedles resulted in significant reduction in the keloid volumes and is associated with reductions in pain and itch. The safety and efficacy demonstrated in keloid treatment portends extension of this therapy to other dermatological diseases.

## 1447 | Efficacy of dapsone for treatment of erythema annulare centrifugum in 15-year-old girl with familial cholinergic and cold urticaria

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**Background:** The deep form of erythema annulare centrifugum (EAC) is an uncommon skin disorder that is characterized by non-scaly, non-pruritic, with indurated borders, superficial and deep intense perivascular lymphocytic infiltrate. EAC in many cases is idiopathic. Cold (CoU) and cholinergic urticaria (ChU) are subtypes of inducible urticaria triggered by exposure to cold or heat/sweating, respectively. Here, we present for the first time a rare case of deep EAC in an adolescent with familial ChU and CoU.

**Case report:** A 15-year-old girl was admitted to our department with a single round-shaped lesion in the popliteal fossa which spread to extremities, trunk and face and persisted for several weeks and then faded slowly to residual hyperpigmented patches. Courses of antihistamines, antibiotics, cyclosporine A, fluconazole, hydroxychloroquine, prednisolone and topical steroids were ineffective. Also patient has had history of itchy urticarial rash and angioedema since 5-year-old, suffered from the flares triggered by physical exertion, stress, cold air and water, spicy food, which resolved within 3-4 hours. The patient's father and 7-year-old brother also had chronic urticaria induced by the same stimuli. The physical examination revealed multiple pink-to-red non-scaly, non-pruritic papules coalescing into annular, arcuate, polycyclic plaques (4-5 cm) with central clearing, centrifugal spread, indurated margines (4-6 mm) on her body. Based on skin biopsy and clinical findings we made the diagnosis of EAC. She was diagnosed with familial ChU and CoU by positive ice-cube, tredmill tests, familial history. A two week course of dapsone (100 mg/day) led to decrease in the number of lesions and reduction in erythema intensity. However, the effect disappeared upon withdrawal. Two years later she noted spontaneous resolution of EAC. A few self-healing plaques appear at irregular time intervals, but aren't troublesome for the patient. The symptoms of ChU, CoU have grown worse since the last hospitalization and are poorly controlled by antihistamines.

**Conclusion:** This is the first case of combination of idiopathic deep EAC in a patient with two types of familial inducible urticaria. These skin disorders are rather concomitant than pathogenetically related. The symptoms of EAC in our patient regressed spontaneously and during the treatment with dapsone, but inducible urticaria took a more protracted course interfering with the patient daily activities and performance.

## 1448 | The role of humoral immunity in the pathogenesis of psoriasis

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**Background:** Imbalances of T cell subsets are hallmarks of disease-specific inflammation in psoriasis. However, the relevance of B cells for psoriasis remains poorly investigated.

**Method:** In this study, we characterized humoral immunity in untreated psoriasis patients and compared them to healthy controls and psoriasis patients under disease-controlling systemic treatment.

**Results:** We found significantly increased levels of IgA in the serum of treatment-naïve psoriasis patients correlating with disease score. However, IgA was only observed in dermal vessels of skin sections. We next performed in-depth analysis of peripheral B cell subsets using flow cytometry. Among all investigated subsets, we only found a moderate positive correlation of $CD138^{+}$ plasma cells with IgA levels and disease score in untreated psoriasis patients. However, in the group of treated psoriasis patients, neither did IgA levels drop nor did plasma cells correlate with IgA levels and disease score, rather hinting at an epiphenomenal finding. Confirming our hypothesis that psoriasis can develop in the absence of proper humoral immunity, we present a patient who suffered concomitantly from both psoriasis and a hereditary common variable immune defect (CVID).

**Conclusion:** Here, we provide new insights in the immunology of psoriasis, demonstrating the clear dominance of T cells over shifts in B cell subsets.

## 1449 | Allergic diseases in senior patients

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**Background:** Life expectancy and the number of elderly people are progressively increasing around the world. Recent years have shown a steady growth of allergic disease incidence in the elderly population worldwide.

**Method:** We have analyzed allergic manifestations in the elderly patients as compared to all patients referred to Unit of Allergy and Clinical Immunology at University Clinic of Dermatology from December 2016 - December 2017. Patients underwent in vivo patch, prick, prick by prick, scratch and intradermal testing, as well as peroral provocation tests.

**Results:** Our findings showed that 882 (21% of all) were senior patients (aged >65 years). 47.95% of them had allergic reaction to drugs, mostly antibiotics (19.62%), 10.87% to insulin and 8.98% to Lisinoprils. Cutaneous manifestations were present in 66.89% of all, however only 35.22% were referred to allergy testing and only in 12.2% the allergen was identified. Food allergy was present in 8%.

**Conclusion:** Allergic diseases show an increasing incidence in geriatric age. This is partly due to the growing emphasis on a more accurate and careful diagnosis of the aging population. We must also take into consideration the influence of other factors, besides comorbidities and therapeutic regimens in elderly that might affects the immune response, such as environmental pollution as well as food contamination and changing dietary habits of elderly such as easy access to exotic food.

One of the challenges in the decades to come is recognizing and fulfilling the need for accurate and timely diagnostics of allergic manifestations in elderly patients, as important part of achieving the best possible quality of life for this growing age group.

## 1450 | Gene polymorphisms and serum levels of cytokines (IL4 and IL10) in the immunopathogenesis of psoriatic disease in Russians in Siberia

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**Background:** The cytokine gene polymorphisms associated with the cytokines level in serum plays one of the most important role in multifactorial diseases including psoriasis (PS) and psoriatic arthritis (PsA). IL4 and IL10 are anti-inflammatory cytokines, regulators of the immune response.

**Aim:** To study the frequency of single nucleotide polymorphisms (SNP) of cytokine genes *IL4 (rs 2243250)*, *IL10 (rs1800872*) and their association with levels of IL-4 and IL-10 in blood serum in patients with psoriasis and psoriatic arthritis.

**Method:** We formed 3 cohorts: 1—PS (n = 49), 2—PsA (n = 48), 3—control group healthy blood donors (n = 35). All individuals were Russians from Krasnoyarsk Territory (Siberia). DNA extraction was performed from blood by standard salting-out method. Genotyping of SNPs of *IL4* and *IL10* genes was performed by PCR and restriction fragment length analysis. Cytokine levels were measured by ELISA. Genotype frequencies were tested for deviation from Hardy-Weinberg equilibrium (HWE) by Fisher's exact test also, we used non-parametric test in «Statistica 6.0».

**Results:** The frequency of genotype *C/C (rs 2243250)* gene polymorphism and *(rs 1800872)* gene polymorphism was predominant between studied groups ($P > 0.05$). The concentration of IL-4 in serum was not associated with the genotypes of the *(rs 2243250) IL4* gene polymorphism in PS and PsA in comparison with the control group ($P > 0.05$). Data revealed that the rare A-allele *(rs 1800872) IL10* is statistically significant associated with lower concentration of IL-10 in serum in PS patients ($P = 0.04$), as opposed to C-allele *(rs 1800872) IL10* associated with lower concentration of IL-10 in blood serum in PsA ($P = 0.02$).

**Conclusion:** We identified differences in association of lower IL-10 concentration with rare A-allele (*rs 1800872*) genotype in PS and C-allele (*rs 1800872*) IL10 in PsA. So, potential marker of development PS may be the presence of rare A-allele (rs *1800872*) genotype, whereas C-allele *IL10*—the marker of the psoriatic arthritis. However, it is only the tendency to association as marker of PS and PsA development and type of psoriatic disease progression.

## 1451 | Psoriasis manifestations and vitamin D deficiency

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**Background:** Psoriasis is a chronic immune-mediated multi organ disease occurring in the skin and often the joints with inflammation induced byT cells via cytokines TNF-α, IL-6 and IL-17. The relationship between vitamin D serum deficiency and different forms of psoriasis was assessed.

**Method:** Sixty-eight patients with various forms of psoriasis and 30 healthy subjects (healthy control group) were assessed after informed consent was obtained. All subjects were asked to complete a questionnaire including age, gender, duration of psoriasis, concomitant diseases and medications. In the group of patients psoriasis was with only skin involvement with skin plus joints involvement ranging from moderate to severe. Psoriaticplaques were evaluated by a specialized medical team using the Psoriasis Area and Severity Index (PASI). All patients were seen by a dermatologist and clinical immunologist, who collected data considering the demographic, health status and any other relevant details. Blood samples included serum levels of 25-hydroxycholecalciferol and TNF-α using an ELISA kit (Germany).

**Results:** The median (p25-p75) 25(OH)D levels were: 24.4 (16.4-28.2) ng/mL in skin only psoriasis, 21.9 (13.1-27.0) in moderate psoriasis and 16.2 (12.0-25.4) ng/mL in psoriatic arthritis. 25(OH)D insufficiency was seen in 40.9% skin psoriasis and 25(OH)D deficiency with 6-fold increased levels of circulating TNF-α in the serum in 60.4% of psoriatic arthritis patients with active pain, pruritus, dystrophic nails and conjunctivitis or blepharitis($P < 0.001$). A statistically significant positive association between progression of psoriatic arthritis activity and 25(OH)D deficiency was established(adjusted (adj.) OR = 1.47; 95% CI = 1.08-1.86); $P = 0.011$. This positive association did not reach statistical significance for moderate joint pain (psoriatic arthritis) without any visible skin findings (adj. OR 1.21; 95% CI = 0.95-1.70).

**Conclusion:** Patients with active psoriatic arthritis show an increased risk of having 25(OH)D deficiency compared to patients with skin psoriasis and controls. The serum vitamin D levels were significantly reduced and increased TNF-α levels in patients with psoriatic arthritis, being inversely linked to disease activity ($P < 0.001$). Vitamin D levels could be an important therapeutic consideration in psoriasis.

## 1453 | Spirodela polyrhiza and its chemical constituents exert anti-allergic effects via ORAI1 channel inhibition

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**Background:** Current therapeutic management of allergic diseases aims to reduce relapse and inflammation, and to alleviate symptoms such as itching. Combinations of immunosuppressive agents such as corticosteroids and anti-histamines are usually employed to inhibit the activation of lymphocytes and mast cells. However, these agents can induce severe adverse effects and may not show sufficient efficacy. Therefore, new strategies are needed to develop novel effective therapies for allergic disease. From this perspective, intracellular calcium signaling through the ORAI1 ion channel, which plays an important role in both T cell activation and mast cell degranulation, provides a very promising target for future drug development.

*Spirodela polyrhiza* (L.) Schleid (SP) has anti-inflammatory and anti-allergic effects, but its effects on calcium signaling have not been reported. Our research aims to identify topical botanically derived chemicals for use in chronic inflammatory allergic diseases such as atopic dermatitis.

**Method:** 30% ethanolic extract of SP ($SP_{EtOH}$) and its five major chemical constituents are prepared. To elucidate whether human ORAI1 modulated by $SP_{EtOH}$ and its chemical constituents, conventional whole-cell patch clamp performed in hORAI1-overexpressing HEK293T cell. We also assessed whether $SP_{EtOH}$ and its constituents could inhibit mast cell degranulation and T cell activation.

**Results:** In Jurkat T lymphocytes, we found that 3 mg/mL $SP_{EtOH}$ inhibited ORAI1 current ($I_{ORAI1}$) by 81.0 ± 11.1%, while one of its constituents (Compound V ($Com_v$); 100 μM) inhibited $I_{ORIA1}$ by 48.9 ± 8.71%. Investigation of human primary T cell proliferation induced by co-stimulation with antibodies to cluster of differentiation 3 and 28, and of RBL-2H3 mast cell degranulation following IgE-antigen complex stimulation, revealed that 100 μM $Com_v$ inhibited both T cell proliferation (by 34.8 ± 6.08%) and mast cell degranulation (by 36.7 ± 0.07%); these effects were concentration-dependent, and no cytotoxicity was observed.

**Conclusion:** Considering that most regional plants have not been investigated chemically or pharmaceutically, they remain as untapped potential sources of topical agents for drugs and other application. Our findings suggest that $Com_v$, which derived from $SP_{EtOH}$, represents a promising candidate compound for the development of therapeutic agents for the prevention and treatment of allergic diseases.

## 1454 | Clinical characteristics of an Italian cohort of patients with orofacial granulomatosis: The birth of a national registry

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**Background:** Orofacial granulomatosis (OFG) is an uncommon chronic granulomatous condition with a multifactorial etiology and pathogenesis. Genetic, immunologic, allergic and infectious mechanisms have been implicated. OFG is clinically characterized by recurrent and/or persistent orofacial swelling and oral ulceration. OFG encompasses a spectrum of known granulomatous disease, including localized lip swelling in Miescher cheilitis, as well as more extensive inflammation leading to facial nerve palsy and lingua plicata, a triad known as Melkersson-Rosenthal syndrome. Histopathologic features of OFG include non caseating granulomas, dilated lymphatics and perivascular lymphocytic infiltrate, that are indistinguishable from the features of Crohn disease (CD); importantly, initial presentation of OFG in childhood may be predictive of development of CD.

**Method:** The Italian National Registry for OFG was established in an attempt to better characterize this rare disease and raise awareness among patients and clinicians. Demographical, clinical, laboratory and instrumental data of OFG patients from 5 Italian centers were examined.

**Results:** The cohort consists of 14 caucasian patients. Eight of them (57%) are women. The mean age (and range) at the clinical presentation of disease was 33 years (4-51 years). The mean age at diagnosis for men was 23 years and 48 years for women. All patients have a positive history of recurrent and/or persistent lip swelling, 3 of them (21%) report oral ulceration, 5 cases (36%) have history of previous or current facial palsy and 4 patients (28%) present tongue fissuring. Concurrent CD has been diagnosed in one patient. Biopsy reports were available for 10 patients (71%); in 6 cases (60%) non-caseating granulomas were seen. Various therapeutic approaches have been described: intralesional corticosteroids had a good response in 6 patients, infliximab was partially effective in 3 cases; oral corticosteroids and/or methotrexate seem to cause a partial symptoms improvement.

**Conclusion:** This is the first attempt, in our knowledge, to (a) centralize all data of patients with OFG in a National Registry with the aim of carrying out epidemiological data and (b) develop Italian guidelines including a diagnostic-therapeutic flow chart, shared by the participating centers. The registry will guide the clinicians in the identification and management of the OFG patients, reducing the diagnostic delay and hopefully improving quality of life.

## 1456 | Risky henna tattoo

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**Introduction:** Henna tattoos are very popular among teenagers. This fashion has increased the allergic reactions to paraphenylenediamine (PPD), being one of the most frequent cause of sensitization between children and adolescents.

**Case report:** A 10-year-old girl without personal history of atopy, got a temporary tattoo with henna. After three days, she developed a local exudative, erythematous eruption with painful blisters lesions that followed the contours of the tattoo. She had neither fever nor other lesions. She was treated with topic methylprednisolone-gentamicin showing an important improvement 10 days after. As a liquenoid scar remained in tattoo area, Trofolastin® (*Centella asiatica*, α-tocopherol, hydrolysed collagen, elastin) patch was prescribed to be placed on the scar. Forty-eight hours later, the patch was removed and was newly observed an exudative, erythematous and painful wound that required oral treatment with amoxicillin-clavulanic. After three days, the girl developed on a maculopapular, generalized and itching rash. She was treated with dexchlorpheniramine and methylprednisolone with a complete resolution in 4 days and she was referred to our allergy unit to be studied because of a suspicion of drug allergy to amoxicillin-clavulanic acid.

An allergy workup was performed after obtaining an informed consent.

**Methods:** Oral controlled challenges with amoxicillin-clavulanic acid was performed.

Epicutaneous patch test with the standard set of the Spanish Group for Research in Contact Dermatitis (True test®) were placed on the back of the patient.

Trofolastin® patch was placed in upper back.

**Results:** Oral controlled challenge with the amoxicillin-clavulanic acid (500/125 mg) was well tolerated.

The true test® was very positive to PPD, showing at 48 hours-reading, an ulcerative, maculo-vesicular and erythematous area with blisters. After five days, erythematous plaques located in both legs appeared, especially in thighs, tibial plateau and ankles. Oral corticosteroids and antihistamines were prescribed with complete resolutions in eight days.

**Conclusions:** Epicutaneous tests are considered effective and safe for diagnosis of contact dermatitis, as systemic reactions are extremely infrequent. However, we report a case of an allergic contact dermatitis caused by PPD in a girl with a systemic reaction after performing the patch test.

## 1457 | Allergic contact dermatitis on face: Do we search for the cosmetic products your husband use?

Gül Ü

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**Case report:** It may be sometimes difficult to find the causing allergen in allergic contact dermatitis. Face is a region on which various materials contact. In this manuscript a woman case is presented who shows patch test positivity to her husband's shaving product.

A 35 years old woman applied because of allergic contact dermatitis on her face. It is learnt that lesions have been continuing for a long time, occasionally getting well with corticosteroid creams; but continuing again. Patch test was performed with European standard series and cosmetic products she was using. Negative result was observed. Following, patch test was performed for the products her husband was using. 2 positive results were obtained for the shaving cream of her husband was using. In detailed anamnesis, it is learnt that the lesions developed approximately 1 month after her husband started to use this cream. It is advised not to use this product to her husband. The disease did not repeat again.

It should not be forgotten that cases with allergic contact dermatitis could get in touch with allergenic materials via individuals in close contact.

## 1458 | Tnf-alpha blocker prevent development of allergic contact dermatitis and patch test result

Gül Ü

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**Case report:** TNF-alpha plays role in etiopathogenesis of allergic contact dermatitis (ACD). In mice which lack TNF-alpha, the response of late type hypersensitivity is spoiled. In addition, TNF-alpha blocker are also used in some cases with ACD. In this poster the results of European standard patch test is given in which ACD is observed and TNF-alpha blocker are used without dermatological indication.

3 cases who use TNF-alpha blocker applied because of ACD: There was lesion in one case on face, in other case on face and hand, and in the last case only on hand. European standard patch test was performed to patients who were continuing to use TNF-alpha blocker.

In one case no positive response was observed, while in two cases positive response to more than one allergen were obtained.

In conclusion, TNF-alpha blockages cannot suppress the response of delayed type hypersensitivity.

## 1459 | Case of allergy to nickel on the background of its intake in food

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**Case report:** Nickel is one of the most commonly used metals; it is used for the manufacture of jewelry, plates and dishes, and medical products.

A patient N, 32 years old, female, complains of pruritic rash on the body skin with the itch intensity up to 8-9 points and the number of lesions more than 50.

Allergic background: for quite some time now the patient noted occasional eruptions on her skin after a contact with jewelry made of non-precious metals. Previously patch skin tests with nickel showed a positive reaction.

The patient sought emergency medical care with complaints of a number of itchy lesions erupted on her whole body during the last 24 hours.

On admittance: state of moderate severity, the patient was emotionally labile, focused on her body sensations, tearful. On the skin of face, upper and lower extremities and torso a punctuate purpura with lesions up to 0.5 cm diameter, prone to confluent. A physical status was within normal limits.

In order to control the itching, as well as to sedate the patient, antihistamines of the first generation were administrated parenterally; but the eruptions kept to progress and to intensify; lesions were spread throughout the whole body, merged in gigantic areas. System glucocorticosteroids therapy was administrated, with 120 mg of prednisolone, but then new lesions kept appearing in a large number, including after-meal rash. Water, tea, bakery products, thin yoghurts did not impact the skin condition, whereas the intake of pasta, cereals, and similar products provoked intensifying of eruptions. The patient observation revealed a sharp increase in the rash after such manipulations as intravenous injections or blood sampling from the vein, the process spreading from the injection site to the entire arm.

A detailed anamnesis of the disease: on the eve of the start of hives, the patient purchased a coffee machine (with metal nickel-plated parts) and started to use it.

diagnosis: A systemic contact dermatitis. An allergy to nickel.

The injection treatment was discontinued and a therapy with per oral GCS and antihistamines of the second generation was administrated. A recommendation was given to cook and to eat food using ceramic or wooden utensils. Three days later marked positive dynamics of the skin process has been noted.

the episode of systemic contact dermatitis has developed due to exposure to nickel from ingestion in food, as well as during the parenteral treatment.

TUESDAY, 29 MAY 2018
TPS 49
ANAPHYLAXIS

## 1460 | Pre surgical anaphylaxis

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**Background:** Anaphylaxis reactions during anesthesia can have a mortality of 3%-6%.

2/3 of the anaphylaxis in the operating room are due to the use of neuromuscular blockers. Rocuronium is frequently involved because is oftenly used.

We present a case of a 41 years old man with an anaphylaxis shock due to the administration of Rocuronium.

**Method:** 41 years old man with no personal history of interest that is going to undergo vertebral surgery. Minutes after anesthetic induction with Fentanyl, Propofol and Rocuronium he started with lowering of oxygen saturation. Orotracheal intubation is performed and, with the suspicion of anaphylaxis shock, adrenaline, antihistamines and corticoids were administered. After 20 minutes without improvement, 500 mg of Sugammadex was administered, given the possibility that the condition was secondary to the use of Rocuronium.

Tryptasa level was 63.

**Results:** Skin test to Fentanyl, Propofol, látex and Rocuronium were done 6 weeks after and only Rocuronium test was positive.

**Conclusion:** In summary, the occurrence of anaphylactic shock after neuromuscular blockers is widely described in medical literature.

There are conflicting data about the use of Sugammadex as coadjutant treatment in case of anaphylaxis due to the use of Rocuronium.

We believe is a good option when conventional treatment is not useful.

Sugammadex was introduced in medical practice with the objective of antagonizing the clinical action of Rocuronium by encapsulation of that muscle relaxant.

## 1461 | Perioperative anaphylaxis: The least obvious culprit

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**Introduction:** Perioperative anaphylaxis can occur in response to different medications. In most cases, the responsible drugs include neuromuscular blocking agents, antibiotics or latex. Histamine H2 receptor antagonists are common prescribed drugs and are known to be well tolerated. Anaphylactic reactions to ranitidine have been reported on rare occasions.

**Case report:** A 31-year-old woman with past history of allergic rhinitis and hypertension was admitted to the obstetrics service in labor of first child in April 2016. Epidural anesthesia with ropivacain and sufentanil was administered. As there was no labor progression, eighteen hours later she was admitted to undergo cesarean section and epidural anesthesia was re-administered. Metoclopramide, ampicilin and ranitidine were given intravenously. During ranitidine perfusion, the patient presented general cutaneous erythema and pruritus, tongue, lips and eyelids angioedema and dyspnea. Perfusion was suspended and hydrocortisone and supplementary oxygen administered. She denied any type of previous adverse reaction to drugs and any symptoms with use of latex-containing material. Allergic evaluation revealed negative latex skin prick test (SPT) and negative penicillin, amoxicillin and ampicillin specific IgE assay. Skin prick and intradermal tests with sufentanil, PPL, MDM, amoxicillin and ampicilin were negative. Oral amoxicilin and metoclopramide provocation challenge were negative. SPT and subcutaneous provocation challenge with ropivacain were negative. SPT with ranitidine was negative but skin intradermal test proved to be positive. The patient was taught to avoid histamine H2 receptor antagonists and use as a safe alternative proton pump inhibitors.

**Conclusion:** Anaphylaxis during anesthesia is an unpredictable, severe, and rare reaction. The identification of responsible drugs is a complex task. We report a case in which a commonly used and generally safe drug caused a severe reaction, which demonstrated that even the least obvious culprit should not be disregarded.

## 1462 | Chlorhexidine: A life-threatening hidden allergen

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**Introduction:** Chlorhexidine (CHX) is a commonly used antiseptic and disinfectant in the health-care setting. Anaphylactic reactions to CHX are a rare but potentially life-threatening complication.

Epidemiologic data suggest that the number of cases of CHX allergy appears to be increasing.

**Case report:** 75 year-old male with past history of hypertension under beta-blocker treatment and bladder cancer submitted to tumor transurethral resection in 2014. Surveillance post-surgical cystoscopies under local anesthesia were performed every 6 months. On the 2nd one he developed generalized cutaneous pruritus with no other symptoms and spontaneous resolution in 1 hours. This has been associated to cefoxitin and the patient was charged to avoid 2nd generation cephalosporin. In November 2016, whilst in recovery room 20 minutes after 4th cystoscopy, he developed oropharyngeal tightening, dyspnea, hypotension and loss of consciousness with succeeding cardiorespiratory arrest in asystolia. Cardiac resuscitation was initiated immediately with recovery to sinus rhythm after 2 minutes. Orotracheal intubation was performed and invasive ventilation was initiated with recovery of consciousness. Simultaneously he developed generalized acute urticaria. He was extubated on the same day and transferred to an intensive care unit for clinical stabilization. On follow-up procedures iodopovidone was used as local disinfectant and local anesthesia was performed with lidocaine+chlorhexidine lubricant gel. Prophylactic antibiotic therapy was not performed in all. The allergologic investigation revealed negative specific Ig E for latex and β-lactams, negative skin prick test (SPT) to iodopovidone and latex and negative skin prick and intradermal test to lidocaine, PPL, MDM, amoxicilin, penicillin, cefoxitin, cefazolin and cefuroxime. Subcutaneous provocation challenge to lidocaine was negative and is waiting for provocation test to cefoxitin. SPT to CHX was strongly positive. The patient was instructed to avoid products containing CHX and subsequent cystoscopy was uneventful.

**Conclusion:** Although anaphylactic reactions to CHX have been reported, CHX may be overlooked as a causative agent in the onset of an allergic reaction in medical and/or surgical invasive procedures. CHX frequently is a hidden allergen, increasing the risk of a possibly fatal outcome upon re-exposure in the future.

## 1463 | Chlorhexidine: An underestimated allergen in frequent use

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**Background:** Chlorhexidine is a synthetic chemical with excellent antiseptic and disinfectant quality frequently used in everyday products and medical devices. The prevalence of allergic reactions towards chlorhexidine is rare, though there is increasing evidence for its allergenic potential. In this case we report about a patient with serious perioperative anaphylaxis. Next to multiple potential allergens that he was exposed to, a chlorhexidine containing lubrication gel has been used for urinary catheterisation. Within minutes post-exposure, the patient developed generalized urticaria, bronchospasm, tachycardia and hypotension.

**Material and Methods:** We performed skin prick tests and intradermal tests with all substances documented in the anaesthesia chart, further we analysed specific immunoglobulin E (sIgE) antibodies and performed oral provocation challenges for exclusion.

**Results:** In the skin tests all substances except for chlorhexidine (SPT: 7 mm wheal diameter/31 mm erythema) were negative. A sensitization for chlorhexidine was further corroborated by chlorhexidine- specific IgE antibody (4.08 kU/L) in the patient's serum. In addition, the challenges for the drugs without sensitization (cefuroxime, lidocaine) were tolerated. Considering all potentially relevant allergens that the patient was exposed to and the proof of specific sensitization, we diagnosed an immediate-type allergy towards chlorhexidine.

**Conclusion:** With the ubiquitous use of chlorhexidine an increase in hypersensitivity reactions including immediate-type allergic reactions is observed. Anaphylactic reactions are rare, but potentially life-threatening, the diagnosis is crucial. As a warning declaration in medical devices is missing, the diagnosis of chlorhexidine allergy might be easily under-recognized or misdiagnosed. Unfortunately, until now validated provocation tests are not existent, but the evaluation of combined skin tests and sIgE is sensitive and specific.

## 1464 | An approach to incidence of death due to anaphylaxis in Spain (1998-2011)

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**Background:** Reports about death due to anaphylaxis are still scarce because of its rarity and limited information to few countries. Also, data source analysis is usually not included. We report incidence of death due to anaphylaxis in Spain using two databases.

**Method:** We used a Hospital series of anaphylaxis deaths from the Spanish Hospital System and a series from the National Institute of Toxicology and Forensic Sciences (INTCF) predominantly formed by extra-hospital deaths. Deaths from the Spanish Hospital System were extracted using codes from ICD-9-CM, related to anaphylaxis among all deaths occured in the 1998-2011 period. For extracting deaths due to anaphylaxis at the INTCF in the same period, two allergist researchers identified these deaths among cases with suspicion of anaphylaxis cause. A regression logistic was run to discriminate the probability of anaphylaxis death belonging to each

database. Incidence rates were calculated for the different groups (age, sex) using the Spanish population as the denominator. Temporal trends were calculated from the Hospital database using Poisson regression models with the number of cases of anaphylaxis detected each year as the dependent variable, and age and sex as covariates.

**Results:** There were four positive predictors of fatal anaphylaxis after the logistic model (usual allergen, positive specific IgE, suggestive symptoms and previous reaction to the same allergen). A ROC analysis showed an AUC of 0.94% (CI 0.95%, 0.89-0.98). After this model and allergist assessment, 37 cases of anaphylaxis deaths (out of 122 total deaths from INTCF) were selected and added to the Hospital series. In the Spanish Hospital System, 115 cases of fatal anaphylaxis were detected. The three most frequent causes were: drugs (46.55%), unknown causes (39.66%) and foods (30.56%);while for the INTCF were: drugs (47.22%), insect bites (30.56%) and foods (11.11%). The incidence of anaphylaxis deaths in Spain using both databases was 0.25 (CI 95%, 0.24-0.26) deaths per million person-years. Risk of death from anaphylaxis increased 1.25-1.30-fold for each 5-year period of age, while risk for food anaphylaxis remained stable. Fatal anaphylaxis was more frequent in males than females both for the total group and for the drug anaphylaxis group.

**Conclusion:** Estimated fatal anaphylaxis percentage in Spain was in the lowest range limit of incidence published up to date. No increase of anaphylaxis deaths was observed in Spain during the studied period.

## 1466 | Growing problem, a case report: Life-threatening anaphylaxis to gonadotropin releasing hormone agonists in central precocious puberty

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**Case report:** We were informed that a girl was admitted to the pediatric endocrinology department due to early breast development. She had been diagnosed as central precocious puberty (PP). Later, triptorelin acetate (TA) therapy had been started monthly.

Within 20 minutes after first SC injection of TA at home, she had developed shortness of breath, decreased air entry, and coughing for ten minutes and lastly she had developed vomiting for 15 minutes. Her symptoms were accompanied by a pruritic blanchable maculopapular rash on her ears, cheeks, lips, and eyelids approximately for two hours. Although they had applied emergency department of the local hospital.

Based on the diagnosis of anaphylaxis she was immediately treated with adrenalin. She was subsequently hospitalized for possible recurrence and discharged next day without any further events.

Treatment with another preparation, Leuprolide Aseptate(LA-LUCRIN), as an alternative treatment was started with premedication against anaphylaxis risk only at first time and the patient did not develop any reactions. The patient is still on this treatment with no complications.

Anaphylaxis is diagnosed in the presence of a detectable allergen accompanied by symptoms of two systems. Our patient had symptoms of the three systems as described above, that is, dyspnea with coughing, hives, nausea, and vomiting.

Main treatment of anaphylaxis is the epinephrine use. Early usage maximizes the likelihood of survival.

Diagnostic tests with culprit drug were not performed in our hospital if the patient had the anaphylactic drug reaction and grouped as "physician diagnosed anaphylaxis".

There has been only one report regarding anaphylaxis to TA treatment in CPP in Turkey. In the literature, anaphylactic reactions against TA have been reported only in few pediatric cases.

GnRH analogues are important to ensure the physiological growth in precocious puberty. Because anaphylaxis can be lethal, and GnRH analogues are similar structure; the present case suggests that one should bear in mind the possibility of anaphylaxis in all patients who receive gonadotropin-releasing hormone and anologs and monitor such patients carefully as needed. Furthermore, we must provide sufficient information of adverse reactions, including anaphylaxis, to patients. Hence, managements against anaphylactic shocks should be recognized and treatment should be given immediately.

## 1467 | An anaphylactic shock induced by the rocuronium anesthesia: A case report

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**Background:** The anesthetic act is a unique pharmacological situation, where the patient is exposed to a multitude of substances.Among them, neuromuscular blocking agents are the leading cause of preanesthetic anaphylaxis, with a frequency of between 50%-70%.Followed by latex in second place and antibiotics in third place. Among the neuromuscular relaxants, most reactions are due to suxamethonium or succinyl-choline in 60.6%, followed by atracurium, rocuronium and verocuronium.The one that produces the least reactions is cisatracurium.

**Method:** A 61-year-old woman presented a type III anaphylaxis of the Brown classification during the anesthetic induction in a surgery scheduled for laparoscopic cholecystectomy. For which adrenaline, dexchlorpheniramine, hydrocortisone, ranitidine and sugammadex was administered and was transferred with orotracheal intubation to the anesthetic resuscitation room. Due to good evolution of the patient, she was extubated within three hours. The drugs involved in the reaction were: rocuronium, amoxicillin-clavulanic, fentanyl, propofol, midazolam, lidocaine and atropine. There was a high suspicion by the anesthesiology and resuscitation service that the

reaction could have been due to the neuromuscular relaxant used, in this case rocuronium, since the reaction was reversed with sugammadex. The patient had undergone surgeries under general anesthesia previously without incidents. A specific allergy study was performed with laboratory tests with tryptase, skin tests with drugs and basophil activation test for rocuronium, sugammadex-rocuronium mixture and cisatracurium.

**Results:**

- Serial measurement of serum tryptase: 12.9 U/L, 10.9 U/L y 3.42 U/L
- Skin test:
  - Rocuronium prick test: positive
  - Rocuronium intradermal reaction: positive
  - Sugammadex prick test: negative
  - Sugammadex-rocuronium mixture prick test: negative
  - Sugammadex-rocuronium mixture intradermal reaction: negative
  - Cisatracurium prick test: negative
- Basophil Activation Test: 31.3% positivity for rocuronium. There is no activation of basophils for sugammadex-rocuronium mixture and cisatracurium.

**Conclusion:** The patient is diagnosed with rocuronium allergy.

Sugammadex not only acts as an antidote to reverse the neuromuscular block against rocuronium, but also has antiallergic properties by inhibiting mast cells.

As an alternative for future interventions, the patient can use cisatracurium, as the skin tests and the basophil activation test are negative.

## 1468 | A Case of late onset anaphylaxis caused by tetracycline hydrochloride

Unal D

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**Case report:** Tetracycline hydrochloride may *rarely* cause hypersensitivity reactions.

(HRs). Immediate type reactions are at the level of case presentations and anaphylaxis is reported.

We report a patient with late onset anaphylaxis caused by tetracycline.

A 47- year-old woman referred to our Allergy Outpatient Clinic because of urticaria due to an antibiotic that she does not remember the name of. The patient reported that many years before she had presented urticaria on her arms and legs one hour after taking the drug.

To confirm drug allergy invivo and invitro testing have to performed. For many drugs there was no validated skin test. For all that invitro tests are often less sensitive and more expensive. Therefore single blind placebo controlled drug provocation tests (SBPCDPT) is the *gold* standard in the diagnosis of *drug* hypersensitivity reactions.

We did not know which group of antibiotics were allergy to the patient. Because the patient had history of asthma and atypical pneumonia we were performed the allergy tests with clarithromycin and she had tolerated.

It was necessary to use tetracycline because of patient had vaginal infection. Skin tests have not yet

been validated for *tetracyclines*.

For skin prick tests of tetracycline that is only available as tablet, not in a soluble form.

Therefore, the tablet was smashed and diluted with 0.9% NaCl. It was also tested.

10 healthy controls to exclude irritation. Because of skin prick tests with *tetracycline* negative.

SBPCDPT *was planned. SBPCDPT* was performed by progressively increasing four divided doses at 30 minute intervals.

Two hours after last dose the patient experienced dyspnea, palpitations, and hypotension.

As the reaction was considered to be anaphylaxis, she was given 0.5 mg of intramuscular epinephrine, intravenous 45 mg of pheniramine, and 40 mg of methylprednisolone. The reaction resolved within 3 hours.

Blood tryptase level was 14.9 ug/L taken at the 2nd hour of the reaction approximately 2 months after the anaphylaxis, serum tryptase level was 1.59 ug/L the serum tryptase level and the patient's clinic confirmed anaphylaxis due to tetracycline.

We had proved late onset anaphylaxis due to tetracycline with the patient's clinic and serum tryptase level. Anaphylaxis due to tetracycline is limited to case reports and small series but to our knowledge, there is no previous report of late onset tetracycline anaphylaxis.

## 1469 | Case series of IgE mediated anaphylactic shock due to polysorbate

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**Background:** Polysorbate 80 (polyoxyethylene-sorbitan-20-monooleate) is used as additive in tablets, solubilizing agent in creams, lotions, ointments and in injectable drug preparations. Its implication in type IV hypersensitivity reactions is well known; nevertheless only few cases of IgE mediated reactions have been published. We report 3 cases of IgE-mediated anaphylactic shock.

**Case 1:** An 18-year-old male, with no previous diseases, suffered an anaphylactic shock after the intramuscular administration of a commercial preparation containing dexamethasone 2 mg/mL, lidocaine 30 mg/mL, thiamine hydrochloride 25 mg/mL and cyanocobalamin 125 μg/mL. Skin tests (prick-prick) were positive to the preparation and to polysorbate 80 and 20, and negative to the

individual components, which were tolerated in controlled challenge tests.

**Case 2:** An 86-year-old male patient with hypertension, hypothyroidism and episodes of sustained monomorphic ventricular tachycardia (SMVT), developed an anaphylactic shock after the administration of injectable amiodarone due to SMVT. Serum tryptase levels reached 34.8 μg/L during the reaction (baseline 6.59 μg/L). Skin tests were positive to injectable amiodarone (prick 50 mg/mL, Intradermal 0.5 mg/mL) and polysorbate 80 and 20 (prick-prick). Skin prick-prick to amiodarone and dronedarone tablets were negative. The patient tolerated oral amiodarone.

**Case 3:** A 39-year-old male, with no previous diseases, presented an episode of supraventricular paroxysmal tachycardia that required the administration of intravenous amiodarone. Within minutes, the patient presented an anaphylactic shock with respiratory arrest that required cardiopulmonary resuscitation. Serum tryptase levels reached 522 μg/L during the reaction (baseline 5 μg/L). Skin tests (prick 50 mg/mL, Intradermal 0.05 mg/mL) were positive to injectable amiodarone and polysorbate-80 and 20 (prick-prick). Skin prick-prick to the amiodarone tablets was negative. The patient tolerated oral amiodarone.

**Results:** These 3 cases demonstrate a severe IgE mediated reaction to polysorbate. Moreover, these are the first 2 cases reporting allergic reactions due to polysorbate contained in injectable amiodarone.

**Conclusion:** Although IgE mediated reactions to excipients, are rare, they should be ruled out as causative agents when the allergological study to the active compound is negative given that they are contained in a wide range of drugs.

## 1470 | Ig e mediated anaphylactic shock due to meropenem

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**Background:** Carbapenems (imipenem, meropenem and ertapenem) are broad-spectrum β-lactam antibiotics, typically used as second-line treatment for severe polymicrobial and resistant bacterial infections in hospitals. Also, it is an alternative treatment for those patients with penicillin or cephalosporin hypersensitivity, as cross-reactivity is very low (<1%). Type I hypersensitivity reactions have been described for imipenem, but until now only delayed non-IgE-mediated hypersensitivity reactions have been described for ertapenem and meropenem.

**Case:** A 47-year-old male, with antecedents of Marfan syndrome with aortic mechanic valve, hypertension, hypothyroidism, type A aortic dissection with D3 sensitive-motor spinal cord injury, auricular flutter and urinal tract colonization of multiresistant bacteria, was hospitalized in September 2016 due to fever of a suspected abdominal focus, initiating parenteral treatment with piperacillin-tazobactam. Afterwards, he presented urinal sepsis, subsequently changing the antibiotic therapy to meropenem according to antibiogram. Within minutes after starting the first dose of meropenem, the patient experimented generalized pruritus, wheezing, dyspnea, erythroderma and hypotension. Intramuscular adrenaline, antihistamine, corticosteroids, and even vasoactive support with noradrenaline infusion was necessary to revert the symptoms. Serum tryptase during the reaction reached a peak of 62 μg/L, being the baseline value of 4.75 μg/L. Skin prick test (10 mg/mL) was positive to Meropenem. Skin tests were negative for imipenem (prick 50 mg/mL, intradermal 3 mg/mL), ertapenem (prick 100 mg/mL, intradermal 10 mg/mL), amoxicillin (prick 200 mg/mL, intradermal 20 mg/mL), penicillin G (10.000 UM/mL) and cefuroxime (prick 200 mg/mL, intradermal 20 mg/mL). A controlled parenteral challenge was performed with ertapenem (conditioned by the antibiogram results) assessing correct tolerance. The patient was diagnosed as selective IgE-mediated hypersensitivity to meropenem, and strict avoidance was recommended.

**Discussion:** We present the first reported case of IgE-mediated anaphylactic shock to meropenem. Absence of cross-reactivity with ertapenem was confirmed.

## 1471 | Anaphylaxis during supraventricular tachycardia therapy

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**Background:** Amiodarone has been effective in the treatment of ventricular and supraventricular arrhythmias, and atrial fibrillation. Multiple side effects related to amiodarone (approximately 75% of the patients after 5 years of treatment) have been reported, involving gastrointestinal and neurological system, skin, liver and thyroid gland. Anaphylactic reactions during intravenous administration are unfrequent and only few cases are described in the literature.

**Method:** A 66 year-old hypothyroid female patient treated with levothyroxine and without previously known allergies suffered acute chest pain and fatigue.

Electrocardiogram performed at the emergency department showed supraventricular tachycardia.

Patient was monitored and treated with sublingual nitroglycerin and intravenous amiodarone perfusion.

Immediately, the patient presented cutaneous erythema, upper lip edema, desaturation (88%), swallowing difficulty, respiratory distress, hypotension and cyanosis. After intubation, he was treated with adrenaline and intravenous antihistamines and corticosteroids and transferred to the intensive care unit, where he was treated with

flecainide, recovering sinus rhythm. Serum tryptase was measured 6 hours after the onset of the episode.

**Results:** Serum tryptase level reached 5.4 μg/L, anaphylaxis, while baseline tryptase was 2.3μg/L. Total serum IgE was normal (15.30 kU/L).

The patient was submitted for allergy evaluation, but refused any direct test with amiodarone. Basophil activation test (BAT) performed with amiodarone was positive ($C_1$ 16.67%, $SI_1$: 5.63 $C_2$: 57.14% $IE_2$: 19.30). Baseline SI was 2.96%.

Skin tests with latex, muscle relaxants and anesthetics used during intubation showed negative results.

Chest x-ray and ventricular ejection fraction were normal.

At present, the patient is treated with oral flecainide and maintains sinus rhythm.

**Conclusion:** We report an anaphylactic reaction during the first intravenous administration of amiodarone in a female patient being treated for supraventricular tachycardia.

BAT was positive, suggesting a direct effect on basophil activation, as the patient was not previously exposed to the drug.

## 1472 | Anaphylaxis during labor: Don't forget to think of an amniotic fluid embolism

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**Background:** Oxytocin is a neuropeptide synthesized in the hypothalamus, ovary or testis. Reports of anaphylaxis to synthetically synthesized oxytocin administration, commonly used in obstetrics, are rare.

**Case report:** A 32-year old primigravida (40 weeks of gestational age) was admitted with signs of pre-eclampsia and labor was induced. Benzylpenicillin and ropivacaine (epidural anesthesia) was administered >3 hours before the event. Eighteen minutes after starting an infusion with oxytocin (15 mL/h) and a vaginal toucher, the patient developed a decreased level of consciousness, generalized edema/erythema and thoracic pain, followed within 3 minutes by fetal bradycardia and maternal collapse. After resuscitation, an urgent sectio was performed, and a baby girl was born. Patient was extubated the same day. Serum tryptase, 1 hours after the event, was 11.2 μg/L (basal tryptase level 3.4 μg/L). Allergy workup demonstrated negative specific IgE and skin tests for latex and chlorhexidine, negative skin and provocation testing for ropivacain. However, skin testing was hampered by dermographism: intradermal (IDR) testing of benzylpenicillin (10 000 IU/mL, 1/1000-1/1) and oxytocin (10 IE/mL, 1/10 000-1/100) showed extensive erythema. IDR testing of oxytocin in healthy volunteers showed pallor around the injection site (n = 3). Intravenous provocation with benzylpenicillin was uneventful. A basophil activation test with oxytocin (patient and control) was negative. An additional bone marrow evaluation showed no evidence for mastocytosis. Although clinical criteria for anaphylaxis were fulfilled, a diagnosis of an amniotic fluid embolism (AFE) was concluded. No drugs were prohibited. Patient gave consent for publication.

**Conclusions:** AFE is one of the most devastating conditions in obstetrics, occurring typically during labor and delivery or immediately postpartum. The pathogenesis remains incompletely understood, however, it has been suggested that AFE involves an anaphylactic reaction to fetal tissue exposure associated with breaches of the maternal-fetal physiological barrier, supported by transiently increased serum tryptase levels. The diagnosis is primarily clinical, and generally one of exclusion. No specific antemortem diagnostic tests are available to confirm AFE. Postmortem identification of fetal squames in the maternal pulmonary circulation gives final diagnosis. Differential diagnosis includes drug-induced anaphylaxis or mastocytosis, which were ruled out in our case.

## 1473 | Immediate allergy to macrogol

Extremera Ortega AM[1]; García Rodríguez R[1]; Moreno Lozano L[1]; Gómez Torrijos E[1]; Alfaya Arias T[1]; Urra Ardanaz JM[2]; Borja Segade J[1]

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**Background:** Macrogol or polyethylene glycol (PEG) is a polyether compound. It is widely used as excipient in pharmaceutical and cosmetic preparations because of their stabilizing properties (NSAIDs, antihistamines, evacuant solution…). Different types of PEG exist according to their molecular weight, ranging from 300 g/mol to 10 000 000 g/mol. Several cases of delayed hypersensitivity reactions induced by PEG have been described, but immediate hypersensitivity reactions are rare. Cross reactivity with polysorbate 80 -a macrogol derivative- has been reported.

**Method:**

**First case:** A 9 years old child presented a generalized urticaria twenty minutes after receiving an evacuant solution containing PEG 4000. He had previously tolerated two doses. The reaction resolved spontaneously.

**Second case:** A 29 years old male began with pruritus, generalized rash, chest tightness and dyspnea without cough or wheezing fifteen minutes after an antacid intake (calcium carbonate, sodium bicarbonate, alginate, parahydroxybenzoate, PEG 20000, acesulfame-K). The patient was treated with adrenaline and hydrocortisone.

We performed skin prick test (SPT) with involved drugs and components separately, SPT with polysorbate 80, PEG 4000 and PEG 20000 in atopic and five non atopic controls. Furthermore we performed cytometric basophil activation test (BAT) with PEG 4000 and PEG 20000 in both cases.

**Results:** *Patient 1*: SPT positive (5 × 6 mm) with PEG 4000 (pure). SPT negative with polysorbate 80 and PEG 20000 (100 mg/mL). BAT positive with PEG 4000 (>20% basophil were marked with CD63) and negative with PEG 20000. *Patient 2*: SPT positive (7 × 5 mm) with the antacid involved and PEG 20000 (100 mg/mL) (8 × 13 mm). SPT negative with the rest of antacid components and PEG 4000. BAT negative with PEG 20000 and PEG 4000. SPT with PEG 4000 and PEG 20000 were negative in 5 controls.

**Conclusion:** We report two patients who presented an immediate hypersensitivity to PEG. SPT and BAT suggest an IgE-mediated hypersensitivity mechanism involved. SPT has proven to be very useful as diagnostic tool. This case-report highlights the importance of providing complete information for each excipient in a preparation in order to avoid reactions by hidden allergens in PEG allergic patients.

## 1474 | Allergy to optiray: A case report

Porr CI[1]; Porr PJP[2]

[1]*County Clinical Hospital, Dept. Allergology, Sibiu, Romania;* [2]*Polisano Clinics, Sibiu, Romania*

**Background:** We present the case of a 63-year-old patient who is familiar with complicated type 2 diabetes, arterial hypertension, stage IV inferior limb arteriopathy with right thigh amputation.

**Method:** The patient presented after Hymenoptera stings dyspnoea, generalized erythema with pruritus, edema of the face that required emergency therapy in 3 episodes.

**Results:** An angio-CT was performed at the inferior limbs with Optiray and 5 minutes after the end of the investigation, the patient presented an anaphylactic shock requiring admission to the ICU for 4 days.

**Conclusion:** The patient's progression was slowly favorable.

## 1475 | Allergy to cefizimine: A case report

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**Background:** We present the case of a 23-year-old woman who comes to Urgency Dept. for generalized erythematous rash, with maculas and papules on the trunk and limbs, swelling of the knees, hands and ankles, intense generalized pruritus, nausea and vomiting. These symptoms suddenly started on day 3 of cefizimine administration for a straight othitis. The patient was hospitalized urgently and showed hypopotasemia, hyperglycemia and an inflammatory syndrome. Appropriate therapy with favorable evolution was administered.

One month after admission, skin tests and lymphoblastic transformation test were performed that identified the cause.

**Method:** The patient was hospitalized urgently and showed hypopotasemia, hyperglycemia and an inflammatory syndrome.

**Results:** Appropriate therapy with favorable evolution was administered.

**Conclusion:** One month after admission, skin tests and lymphoblastic transformation test were performed that identified the cause.

TUESDAY, 29 MAY 2018
TPS 50
MANAGEMENT OF DRUG HYPERSENSITIVITY

## 1476 | Treatment of severe cutaneous adverse reactions (SCARs) in Latin America

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**Background:** Severe cutaneous delayed drug reactions (toxic epidermal necrolysis -TEN-, Stevens-Johnson syndrome -SJS-, acute generalized exanthematous pustulosis -AGEP- and drug reaction with eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome -DRESS/DiHS-) among others, are a rare but potentially fatal complications of drug treatment. The main therapeutic measures include the withdrawal of the culprit drug and the support management. Although there is no approved pharmacological treatment for this type of reactions, the little evidence suggests that the use of systemic anti-inflammatory drugs could improve the prognosis in these patients.

**Method:** An online questionnaire was designed to report new and old cases (since 2013). It was a modified and adapted version of ENDA questionnaire for drug allergy interesting group. Three centers from Colombia, one from Argentina, one from Brazil and one from Paraguay were included. An Excel database was created, in which sociodemographic data, type of reaction, culprit drug (s), treatment, complications, mortality and sequelae cases and their treatment were recorded and analyzed.

**Results:** Thirty seven cases were reported. 24 (65%) were women. The median age was 47 years. 19 (51%) had DRESS/DiHS, 6 (16%) TEN, 3 (8%) SJS, 3 (8%) AGEP, 3 (8%) other not classified SCARs, and 1 (2.7%) overlapping TEN/SJS. In 100% of the patients the suspect drug was withdrawn. Thirty one patients (83%) received systemic anti-inflammatory treatment. Twenty six patients (70%) received intravenous (IV) corticosteroids alone, 3 (8%) IV corticosteroids plus IVIG, 1 (2.7%) IV corticosteroids plus IVIG, infliximab and colchicine, and 1 (2.7%) IV corticosteroids plus infliximab and cyclosporin. There were complications in 17 cases (49%), and death occurred in the patient with overlapping TEN/SJS who had received corticosteroids plus immunoglobulin.

**Conclusion:** In this preliminary study of SCARs in Latin America, DRESS/DiHS was the most frequently clinical entity. Most of patients received systemic anti-inflammatory treatment, being IV corticosteroids the commonest pharmacologic therapy. Complications were frequent, but mortality was low.

## 1477 | Anaphylactic reactions to iodinated contrast media: usefulness of skin and challenge testing

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**Background:** Iodinated contrast media (ICM) are increasingly used for diagnostic and therapeutic purposes. Immediate hypersensitivity reactions (IHR) are usually mild, although severe anaphylactic reactions can occur. The underlying mechanism of this type of reactions is yet unknown, having proposed a nonspecific release of mast cell mediators. However, there are evidences suggesting a specific Ig-E mediated mechanism.

In this study, our aim was to evaluate severe IHR to ICM.

**Method:** We retrospectively analysed patient who consulted to our Allergy Unit between July 2011 and July 2016 reporting symptoms within 1 hour after ICM administration. From a total of 109 patients, we selected eight that had suffered an anaphylactic reaction. A written informed consent had been obtained for diagnostic procedures. Skin tests(ST) with iohexol, ioversol, iodixanol and iobitridol were performed, firstly as skin prick test (SPT) and, if negative, as intradermal test (IDT). Finally, a controlled drug exposition test (CET) with an alternative ICM according to ST result and patient history was performed.

**Results:** SPT were negative in all patients. Three patients have a positive IDT: one patient had a positive IDT only to the ICM involved in the reaction, another patient had a positive IDT to three ICMs and the last one had positive IDTs to all ICMs tested. No CET was performed to these patients. These patients were recommended to avoid all ICM.

Five patients had negative STs: on two of them CET was not performed due to previous life-threatening reactions; of the other three patients CETs with an alternative ICM were performed, with good tolerance.

These patients were recommended to avoid all ICM.

**Conclusion:** We present eight cases of anaphylactic reaction after ICM administration, showing positive ST only in three patients despite some of them had suffered from life-threatening reactions. This is in agreement with an IgE mediated mechanism. On the other hand, CETs with alternative ICMs can be useful in some patients that could need a radiological examination with ICMs.

## 1478 | A case of immediate type hypersensitivity with pemetrexed

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**Introduction:** Immediate type hypersensitivity reactions to pemetrexed have been reported as very rare case reports. As limited availability of alternative therapies in chemotherapeutic allergy, desensitization plays an important role in ensuring reuse of the culprit drug. We report a case of pemetrexed anaphylaxis and successful desensitization.

**Case:** 43 years old female patient with lung adenocarcinoma had been treated with cisplatin-pemetrexed as second-line therapy. During the 5th cycle within 5 minutes after the end of pemetrexed infusion she had chest pain, shortness of breath, cough, swallowing difficulty, erythema on face and body, nausea and vomiting. She was diagnosed as anaphylaxis and adrenaline was administered besides antihistamine and methylprednisolone. Symptoms and findings of the patient were improved within 15 minutes.

Oncologists decelerated no suitable alternative therapy for the patient. Although skin tests (prick test with 1/1 concentration, intradermal test with 1/10 000-1/10 concentration) were negative with pemetrexed, taking into account the severity of the reaction, pemetrexed desensitization was applied with the consent of the patient. No reaction was observed during the procedure

**Result:** Desensitization is a successful and safe method of reusing the culprit drug. Successful desensitization of pemetrexed with immediate type hypersensitivity reaction is described.

## 1479 | Eosinophil cationic protein as a marker of DRESS management duration

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**Case report:** Drug associated rash with eosinophilia and systemic symptoms syndrome (DRESS) is a severe idiosyncratic reaction with a long latency period. DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) does not well understand condition. There are many variations of bellowed symptoms: fever, rash, inflammation of internal organs, lymphadenopathy and characteristic hematological abnormalities such as eosinophilia, thrombocytopenia and atypical lymphocytosis. Standardized criteria for the diagnosis have been developed. Unfortunately, the management of DRESS is poorly helpful. For followed patient we decided to use eosinophil cationic protein (ECP) to determine the duration of therapy.

The 28 years old man was admitted emergency department with fever, rash (maculo-papular) and pain in joints. It was the 9th day of taking of amoxicillin. The hematological abnormalities were revealed —eosinophilia, increased erythrocytes sedimentation rate. The level of serum ECP was 183 μg/L. The liver functional tests were increased too. Hepatomegaly and cervical lymphadenopathy were observed. The patient was treated as a DRESS syndrome (infusion therapy, systemic steroids) and discharged after 2 weeks with improvement. All hematologic parameters were in normal limits. Lymphadenopathies were resolved. The level of ECP was retaken – 84 μg/L. Patient was prescribed oral steroids till normalization of limits of ECP. It lasted 2 weeks after discharging.

The serum level of ECP can play key role in the management of DRESS syndrome and in the making of diagnostic processes.

## 1480 | Successful desensitization to polyethylene glycol, a widely used component of colonic cleansing agent

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**Background:** Polyethylene glycols (PEGs) are immunologically stable and widely used as colon cleaning agents for colonoscopy. Until now, allergic or anaphylactic reactions to PEG have been rarely reported. Although patient with hypersensitivity to PEG should avoid PEG-containing drugs or products, patient who needs colonoscopy has few alternative bowel cleansing methods. No successful desensitization to PEG has been reported to date. We report a case of successful desensitization and subsequent safe colonoscopic examination in patient with allergic reaction to PEG.

**Method:** A 50-year-old woman developed generalized urticaria, pruritus, throat swelling, and shortness of breath immediately after taking a bowel preparation solution for colonoscopy. She had the first symptoms 3 years ago, and has had 2 more experiences so far. The symptoms appeared within 20-30 minutes of taking cleansing solution, and the endoscopy was no longer possible. Seven years ago, she underwent endoscopy with no specific symptom. When the last symptom occurred a year ago, she was treated at emergency room because of severe dyspnea and dizziness. The patient came to our clinic for the proper diagnosis of allergy reaction and possible colonoscopic evaluation.

**Results:** Based on detailed review of the medical records of other hospitals where the reaction had occurred, the symptom causing cleansers contained PEG. Skin prick test to PEG were negative, but basophil histamine release (HR) test showed significant histamine release by PEG. Desensitization therapy for PEG was performed for colonoscopy, and the patient underwent colonoscopy successfully without specific symptoms. The HR test after desensitization showed that the basophil histamine release was significantly reduced by desensitization.

**Conclusion:** We present a case with a hypersensitivity reaction to PEG with positive HR test. We used a successful and rapid protocol for desensitization to PEG. It reduces basophil histamine releasibility effectively and allows successful colonoscopic examination in patient with allergy to PEG. To our knowledge, this is the first report of a PEG desensitization protocol, which is safe and highly convenient.

## 1481 | Successful desensitization to vedolizumab in one patient with ulcerative colitis

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**Introduction:** Vedolizumab is a humanised IgG1 monoclonal antibody that binds to the human α4β7 integrin and is produced in Chinese hamster ovary (CHO) cells. Vedolizumab is authorized in the European Union for the treatment of adult patients with moderately to severely active ulcerative colitis or Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha antagonist.

Infusion-related reactions and hypersensitivity reactions have been reported with vedolizumab, with the majority being mild to moderate in severity.

**Objectives:** To describe a successful desensitization to vedolizumab in one patient diagnosed with ulcerative colitis, refractory to infliximab and intolerant to azathioprine and sulfasalazine.

**Methods:** Our patient was a 38 year old woman receiving treatment with intravenous vedolizumab (300 mg/cycle). Cycles 1 and 2 were well tolerated, but in cycles 3, 4 and 6 she experienced hypotension and dyspnea, in spite of premedication with oral dexamethasone and metoclopramide. During cycle 6, she also showed facial angioedema, systemic urticarial reaction and oropharyngeal pruritus treated with methylprednisolone and ebastine.

**Results:** The results of prick (vedolizumab concentration 60 mg/mL) and intradermal skin tests (1:10 and 1:100) with vedolizumab were negative in our patient and in ten healthy controls. Total IgE level was 26.4 UI/mL and specific IgE against *Dermatophagoides* were positive, being negative for hamster epithelium and latex.

Since vedolizumab was the only therapeutic alternative, the patient was planned to undergo vedolizumab desensitization according to an 8-step protocol. *Patient informed consent was obtained previously.* Premedication consisting of ebastine, acetylsalicylic acid, montelukast and methylprednisolone one hour before desensitization was administered. Desensitization protocol was performed with a total duration of 4 hours and 35 minutes and a total dose of 293 745 mg. Dose steps were 0.015, 0.03, 0.3, 0.6, 1.2, 9, 18 and 264.6 mg.

Conclusions: Our 8-step protocol desensitization to vedolizumab resulted safe and effective in our patient and it has allowed the continuation of treatment with vedolizumab for her ulcerative colitis. Our experience may be helpful for similar clinical cases. A careful risk/benefit ratio should be considered and an accurate informed consent is mandatory.

## 1482 | Hypersensitivity reactions to systemic glucocorticoids and desensitization

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**Background:** Systemic glucocorticoids (SGCS) are prescribed for their immunosuppressive, antiproliferative, antiinflammatory and antiallergic effects. They are also administered to prevent late phase anaphylactic reactions. However, SGCS have been associated with immediate hypersensitivity reactions. Our multiple sclerosis (MS) patient with SGCS allergy needs these drugs to manage the acute attacks. Administration of SGCS by a desensitisation has enabled this problem to be solved.

**Objectives:** 41 old MS women with the history of adverse drug reactions to methylprednisolone natrium succinas intravenously and methylprednisolone orally. Within half an hour after SGCS administration, the patient experienced hoarseness, shortness of breath and fever in 2 hours.

**Methods:** We performed skin tests (prick and i.d.) with SGCS, i.d. test was positive. The basophil activation test and specific IgE testing were negative. Skin tests and serum specific IgE examination excluded cow milk allergy, since some compositions may contain traces of this protein.

Montelukast, anti H1 and H2 blockers were used for the pretreatment of desensitization. All procedures (skin and blood tests, desensitization) were carried out with the informed consent of the patient.

**Results and Conclusion:** The successful desensitizations with methylprednisolone hemisuccinate (MPS) in twelve steps for the administration of 1 g were performed according to the published protocol Angel-Pereira D, Berges-Gimeno MP, Madrigal-Burgaleta R et al on February 1 and on April 4, 2017 to manage the sclerosis multiplex attacks.

**Conflict of interest:** None.

## 1483 | Successful desensitization of fever by cisplatin

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**Introduction:** Cisplatin is the first-generation platinum drug and was the first to be approved by FDA in 1978. The most frequent symptoms are cutaneous, respiratory and cardiovascular symptoms. We present an exceptional, non-immediate case of fever after cisplatin and etoposide infusion with positive skin test.

**Case report:** A 63-year-old man, recently diagnostic of lung cancer stadium IV, in first line of treatment with cisplatin and etoposide, started 2 hours after finishing the 2nd infusion: facial erythema that becomes generalized after 4-5 hours from infusion. Twelve hours later, developed warmth sensation, shivering and fever (39°C) that persisted despite the use of several oral antipyretics treatment. Infectious disease was discarded, so he was referred to our department in order to assess further administration of cisplatin and etoposide.

**Methodology:** Skin testing was performed 30 days after the last reaction to minimize false-negative results, as follows (a) cisplatin prick test (1 mg/mL) and intradermal tests (0.1 mg/mL); (b) etoposide prick test (20 mg/mL) and intradermal tests (2 mg/mL); with histamine as the positive control and NaCl-diluent as the negative control.

**Results:** The results of skin test were negative for immediate reading. But two hours later, intradermal test for cisplatin turned into red and itchy and 12 hours later, still associated a wheal.

The patient was classified as high-risk (lung diseases, forced expiratory volume in 1 second <1 L) and underwent programmed inpatient desensitization according to the standardized Birmingham Women's Hospital protocol.

Desensitization was performed in the medical intensive care unit. The patient received only standard oncology premedication. He tolerated the final dose of cisplatin with no breakthrough reactions followed by etoposide standard infusion.

Two additional desensitization procedures were performed, with no breakthrough reactions. Therapy ended when the disease worsened.

**Conclusion:** The importance of this case, lies in the fact that fever has not been described as a clinical hypersensitivity reaction for cisplatin but for oxaliplatin. Although a non-immediate reaction at the 2nd infusion of cisplatin could scarcely suggest a hypersensitivity reaction, the positive skin test and successful desensitization with this drug, could suggest it.

## 1484 | Successful desensitization with propylthiouracil: A case report

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**Introduction:** Propylthiouracil is commonly used as the first treatment option in patients with hyperthyroidism. Although it is generally a well-tolerated drug, it may lead to some side effects including liver damage, leucopenia and skin rash. Among skin rash findings, urticaria is considerably common. Nevertheless, in cases that developed urticaria, a rapid desensitization protocol specific to propylthiouracil has not been encountered. We represented a case in which we applied successful oral desensitization via a scheme in accordance with general desensitization principles in a case that developed propylthiouracil-induced urticaria.

**Case report:** Propylthiouracil at a dose of 50 mg/day was initiated for a 36 year-old female patient with diagnosis of hyperthyroidism in internal diseases clinic. The patient developed widespread itching and swelling in the body 5-6 hours after she took the first dose of the drug. She had experienced a similar reaction with use of propylthiouracil in 2012. The patient who was breastfeeding a baby and did not have any treatment option other than propylthiouracil was referred to us with pre-diagnosis of drug allergy. The patient was thought to have propylthiouracil-induced hypersensitivity reaction and desensitization was planned. We prepared a desensitization scheme in accordance with general desensitization principles (Table 1). In accordance with this prepared scheme, we successfully applied the desensitization protocol with propylthiouracil for the patient.

**Discussion:** We have not encountered with any case regarding application of desensitization in propylthiouracil-induced allergic

| Time solution amount drug dose | | | |
|---|---|---|---|
| **Day 1** | **9:00** | **Solution C** | **(0.05 mg/mL) 1 cc 0.05 mg** |
| | 9:30 | Solution C | 2 cc 0.1 mg |
| | 10:00 | Solution C | 4 cc 0.2 mg |
| | 10:30 | Solution B | (0.5 mg/mL) 1 cc 0.5 mg |
| | 11:00 | Solution B | 2 cc 1 mg |
| | 11:30 | Solution B | 4 cc 2 mg |
| | 12:00 | Solution A | (5 mg/mL) 1 cc 5 mg |
| | 12:30 | Solution A | 2 cc 10 mg |
| | 13:30 | Drug itself | (50 mg) ½ tablet 25 mg (43.5 mg in total) |
| **Day 2** | **9:00** | **Drug itself** | **(50 mg) 1 tablet 50 mg** |
| | | Solution A = 50 mg Propylthiouracil+10 cc of serum physiologic | |
| | | Solution B = 1 cc of Solution A + 9 cc of serum physiologic | |
| | | Solution C = 1 cc of Solution B + 9 cc of serum physiologic | |

reactions. We performed a successful desensitization with the desensitization protocol we organized. This protocol may serve as a model in case of propylthiouracil hypersensitivity.

## 1485 | Desensitization protocol vs oral challenge in a patient with temozolamide anaphylactic reaction: What do you think?

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**Case report:** Temozolamide (TMZ) is an oral imidazotetrazine derivative and cytotoxic alkylating agent. The efficacy of TMZ in the treatment of newly diagnosed and relapse primary malignant brain tumors are now well established (I). Allergy to TMZ had been describe and successful treated with desensitization protocols (II-III). Drug desensitization (DS) is a revolutionary approach for the safe reintroduction of immunogenic drugs. (IV) DS is achieved by incrementally escalating the sub-optimal doses of the culprit drug until the required dose is reached. Produce temporary tolerance which protects to other adverse reaction. (IV) Desensitization is a revolutionary approach for the safe reintroduction of immunogenic drugs, a recent and powerful tool that we can use today as an outstanding procedure in precision medicine. 60-year-old man, non atopy background, diagnosed with Glioblastoma multiforme, had been treated with surgery and chemotherapy in schema STUPP. Oral TMZ was administered in cycles of 75 mg by 5 days each 28 day. One week after cycle 1 presented generalized pruritus controlled with antihistamines. During the cycle 2 TMZ was increase 150 mg/day/5 days/each 28 days. The pruritus continued, even being more intense. During cycle 3 presented nauseas, vomiting, shaking chills, and facial urticaria. Antihistamines and corticosteroids were administered and the symptoms despaired in few hours. Skin prick test TMZ was performed at 1/1 Dil: Negative. TMZ anaphylaxis was diagnosed. Acetylsalicylic acid 300 mg and montelukast 10 mg were administered as a premedication 2 consecutive before the procedure. Oral desensitization protocol was performed (Table:1) 1 day 6 steps, 2 day 3 steps, 3 day 2 steps, 4 and 5 days 1 step. Cycles 4 and 5 presented facial erythema and pruritus EVA 5/10, two hours after the procedure was completed and resolved to dexchlorpheniramine, at the cycle 6 TMZ was stopped by progression of disease.

**Conclusion::** We presented case of successful ultrarapid desensitization of Temozolamide in a patient with Glioblastoma Multiforme, achieving temporal tolerance of the drug with minimal and slight reaction after having given an anaphylaxis to TMZ, despite the STUPP protocol had a favorable impact on overall, but not on progression-free, survival rate.

| • | • | 1. | Administered dose | Accumulated dose | • |
|---|---|---|---|---|---|
| 1. | 1. | • | 1. | 1. | |
| 1. | 1. | • | 1. | 1. | |
| 1. | 1. | • | 1. | 1. | |
| 1. | 1. | • | 1. | 1. | |
| 1. | 1. | • | 1. | 1. | Facial urticaria+ dexchlorpheniramine |
| 1. | 1. | • | 1. | 1. | |
| 1. | 1. | • | 70 mg | 70 mg | |
| 1. | 1. | • | 70 mg | 140 mg | |
| 1. | 1. | • | 1. | 280 mg | |
| 1. | 1. | • | 140 mg | 140 mg | |
| 1. | 1. | • | 140 mg | 280 mg | |
| 1. | 1. | • | 288 mg | 280 mg | |

## 1486 | Successful etoposide desensitization in a preschool age pediatric patient

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**Case report:** Etoposide is derivative of podophyllin and acts by inhibiting mitosis. It is a chemotherapeutic agent which has been used in the treatment of a numerous malignant conditions. Intravenous etoposide is generally well tolerated. It is reported to induce hypersensitivity reactions (HSRs) in 6% of the patients; however, its incidence of anaphylaxis is 0.7% .

We report a 2.5-year-old male patient diagnosed with retinoblastoma in our pediatric oncology clinic and had a hypersensitivity reaction with etoposide. He received his first etoposide infusion without premedication. Twenty-one days after the first dose of the drug, the second etoposide dose was started again without premedication. The patient experienced generalized urticaria, angioedema on the eyelids and lips, cyanosis on the lips and shortness of breath after 10 minutes of etoposide infusion. He was found to be hypotensive (blood pressure=60/30 mm Hg) and desaturated to 80% on pulse oximetry. The infusion was interrupted immediately and 0.01 mg/kg intramuscular adrenaline, 1 mg/kg hydroxyzine and 1 mg/kg prednisolone treatment were given to the patient. Then, the patient was referred to our allergy clinic to be evaluated. The skin tests were performed to demonstrate the hypersensitivity of the patient. Skin prick test (20 mg/mL) and intradermal test (2 mg/mL) results with drug were negative. Etoposide is considered to be a critical

component of an effective treatment of retinoblastoma. Thus, in this case continued use of etoposide was warranted. We decided to apply desensitization. The etoposide phosphate preparation without polysorbate 80 could not be used because it was not available.
To the best of our knowledge, this is the first case in the literature to describe a successful desensitization protocol with etoposide in the preschool age group.

## 1487 | Successful desensitization of albendazole induced anaphylaxis

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**Background:** Albendazole is the only medication used for the treatment of hydatid cysts in combination with surgery or alone. The most common reported side effects are headache, hepatotoxicity, alopecia, abdominal pain and nausea. In rare cases, pancytopenia and Stevens-Johnson Syndrome were reported. Here we present the first late anaphylaxis due to albendazole in an adult patient with hepatic hydatid cysts who was successfully desensitized.

**Case:** A 44 year-old man using albendazole because of hepatic hydatid cysts has been referred to us because of a systemic hypersensitivity reaction. On the 10th day of treatment of 800 mg daily albendazole, generalized urticaria developed after 3 hours of oral intake and therefore was stopped. One week later it was started again in the same dosage. Few hours later, shortness of breath, urticaria and abdominal pain occurred. Since there is no effective alternative medication, desensitization was planned. Cetirizine 10 mg 2 × 1 premedication was given regularly starting from the first day before desensitization. He was successfully desensitized in a 17 day protocol was able to take the target dose of 800 mg albendazole as shown in Table 1-2.

**Conclusion:** This case is the first report of anaphylaxis due to albendazole and the first successful desensitization of a systemic hypersensitivity due to albendazole.

| Minute | 0′ | 2 mg |
|---|---|---|
| Minute | 60′ | 5 mg |
| Minute | 120′ | 10 mg |
| Minute | 180′ | 20 mg |
| Minute | 240′ | 50 mg |
| Minute | 300′ | 100 mg |
| Minute | 360′ | 150 mg |

| Day 2 | 200 + 100 mg | 300 mg | Thursday |
|---|---|---|---|
| Day 3 | 200 + 100 mg | 300 mg | Friday |
| Day 4 | 200 + 100 mg | 300 mg | Saturday |
| Day 5 | 200 + 100 mg | 300 mg | Sunday |
| Day 6 | 200 + 100 mg | 300 mg | Monday |
| Day 7 | 2 × 200 mg | 400 mg | Tuesday |
| Day 8 | 2 × 200 mg | 400 mg | Wednesday |
| Day 9 | 2 × 200 mg | 400 mg | Thursday |
| Day 10 | 2 × 200 mg | 400 mg | Friday |
| Day 11 | 2 × 200 mg | 400 mg | Saturday |
| Day 12 | 2 × 200 mg | 400 mg | Sunday |
| Day 13 | 400 + 200 mg | 600 mg | Monday |
| Day 14 | 400 + 200 mg | 600 mg | Tuesday |
| Day 15 | 400 + 200 mg | 600 mg | Wednesday |
| Day 16 | 400 + 200 mg | 600 mg | Thursday |
| Day 17 | 2 × 400 mg | 800 mg | Friday |

## 1488 | Adalimumab desensitization after anaphylaxis in a patient with behçet disease

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**Background:** Behçet disease (BD) is a primary vessel vasculitis, characterized by recurrent oral ulcerations, uveitis and skin abnormalities. Treatment is symptomatic using steroids and immunomodulatory agents. Adalimumab is a potentially effective treatment for BD in patients who are refractory to conventional therapies. Injection site reactions are the most common adverse effects associated with adalimumab, but anaphylaxis is rare.

**Methods:** We report a case of a 19-year-old woman, with BD, several aneurysms and personal history of atopic disease (rhinitis and seafood allergy), that was referred to our unit after one episode of anaphylaxis (facial angioedema, generalized urticarial lesions and dyspnea) 1 hour after infusion of adalimumab. She has been treated with adalimumab since 2016, after she had developed tuberculosis with infliximab treatment. Her allergic reaction occurred in August 2017. We evaluated the patient 8 weeks after the initial reaction using the European Network for Drug Allergy (ENDA) questionnaire and skin tests with immediate readings (15 minutes). Skin prick test (SPT) to adalimumab was performed at full-strength concentration (50 mg/mL) with histamine as positive control and normal saline as negative control. Intradermal skin test (IDT) was performed with 1:1000 concentration. Given the initial therapeutic success with adalimumab and the failed response to standard treatments, we suggested restart adalimumab therapy using a desensitization protocol.

The patient gave informed consent before testing and desensitization.

**Results:** SPT was negative, but IDT reaction was positive at 1:1000 dilution (wheal of 8 × 8 mm). Ten days later, the patient underwent successful desensitization which was completed in 2 hours. Premedication consisted of montelukast 10 mg, ranitidine 150 mg and hydroxyzine 25 mg 1 hour before administration of adalimumab. Desensitization protocol started with an initial subcutaneous dose of 0.005 mg, which was gradually increased to a cumulative dose of 40.055 mg, with 15-minute intervals between 9 doses. During the procedure, she only experienced hypertension controlled with captopril. She is currently receiving a full-strength, single dose of 40 mg adalimumab every 2 weeks, with no premedication and good tolerance.

**Conclusion:** Desensitization for adalimumab induced anaphylaxis should be considered in patients with BD when alternative treatments are considered inferior and/or more toxic.

## 1489 | Desensitisation or treating through the reaction? Clinical case

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**Case report:** In clinical practice there is a need for desensitization in drug hypersensitivity. In several patients the allergic clinical picture is mild; therefore a possible alternative in the case of drug hypersensitivity is treating through, helping the tolerance induction to the drug. Clinical case: 87 year woman. The patient has a left femur fracture in 2011, complicated by an osteomielitic inflammation which caused one cutaneous fistula. Afterwards, the surgeon choose not to perform a radical clearing, maintaining the intramedullary prothesis.Colture of the deep tissue: positive for *E. Coli* and Proteus, sensitive to cephalosporins, quinolones.The first antibiotic therapy with cefepime was suspended for skin rash. It was then established indication to a chronic treatment with quinolones after desensitization, for the presence of allergy to levofloxacin (urticaria). The patient initiated treatment with ciprofloxacin with a slow challenge procedure, with a starting dose of 50 mg which was however hindered by the onset of diffuse prurigo and urticaria. The clinical choice in this mild clinical situation, with a mandatory necessity of therapy, was to treat the symptoms with antihistamine and steroid drugs. The therapy with ciprofloxacin started from 50 milligrams and ended with 750 milligrams. The antihistamine drug was then continued for years in the domicile. The last admission was motivated by: fracture of the atlas. Ciprofloxacin was suspended at the entrance in the hospital. Uncontrolled symptoms of prurigo came back after reassumption of full dose ciprofloxacin. This event suggested a new loss of immunological or metabolical tolerance. The patient was then subjected to a new slow challenge with the drug, from 50 mg to 500 mg in 4 weeks with an antihistamine drug coverage. This case is an induction of immunological or metabolic tolerance given by the two associated mechanisms of drug suppressive therapy and drug increase in scalar doses, even in the presence of symptoms. The tolerance mechanism type is still not clear, nor the possible underlying immunological mechanism. However, the loss of immunological or metabolic tolerance is clearly demonstrated. There are many clinical situations in which this clinical urgency occur: the purpose of the appropriate and non-substitutable therapy in a particular disease is only to arrive at the therapeutic result. Both the pharmacological attempts and the desensitization procedures must work together for this result.

## 1490 | Successful rapid desensitization modified protocol to intravenous etoposide

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**Background:** Etoposide is a cytotoxic drug that has been mainly used in the treatment of neoplasms such as small cell lung carcinoma, multiple myeloma, non-Hodgkin's lymphomas, neuroblastoma and sarcomas. Adverse effects include bone marrow suppression, gastrointestinal symptoms, peripheral neuropathy and alopecia. In the literature, hypersensitivity reactions (HRs) to etoposide vary from 2% to 6%.

**Method:** We present a desensitization protocol to intravenous etoposide used in a 35-year-old male for non-Hodgkin's lymphoma who was referred to the Department of Allergy at Sotiria General Hospital of Athens. Within 5 minutes after receiving the first dose of the drug, the patient complained for flushing, retrosternal pain, difficulty in breathing and weakness. The infusion was ceased immediately and the patient received proper treatment with gradual recovery of the symptoms. The next day, skin prick test (SPT) and intradermal test (ID) were performed with etoposide at dilution 1:10 (2 mg/mL). Both of the tests, SPT and ID, were negative. Histamine and NaCl 0.9% were also used as positive and negative controls, respectively. A desensitization protocol of three-day cycle with intravenous etoposide was conducted. Premedication for 3 days was administered including methylprednisolone, cetirizine, ranitidine, paracetamol and montelukast.

**Results:** The desensitization protocol of the first day consisted of 11 steps of rapid pulses administered at increasing infusion rates every 15 minutes, and 1 step of drip infusion at a final rate of 60 mL/hour (372 mg/232.5 mL) until completion of the infusion. The following 2 days, the patient received a modified rapid protocol consisting of the administration of the calculated dose of 400 mg in only one step of infusion rate of 60 mL/hour completing in only 4 hours

and 15 minutes. The same protocol was applied in another three-day cycle with no adverse reactions.

**Conclusions:** HSRs to etoposide are rarely described in the literature. We propose a three-day modified rapid desensitization protocol to intravenous etoposide that could be particularly useful compared to other time-consuming desensitization protocols.

| Solution (mg/mL) | Rate (mL/h) | Volume(mL)/Dose(mg) |
|---|---|---|
| 1 (0.016 mg/mL) | 2 | 0.5 mL/0.008 mg |
| 1 | 5 | 1.25 mL/0.02 mg |
| 1 | 10 | 2.50 mL/0.04 mg |
| 1 | 20 | 5.0 mL/0.08 mg |
| 2 (0.16 mg/mL) | 5 | 1.25 mL/0.2 mg |
| 2 | 10 | 2.50 mL/0.4 mg |
| 2 | 20 | 5.0 mL/0.8 mg |
| 2 | 40 | 10.00 mL/1.6 mg |
| 3 (1.6 mg/mL) | 10 | 2.50 mL/4 mg |
| 3 | 20 | 5.0 mL/8 mg |
| 3 | 40 | 10.00 mL/16 mg |
| 3 | 60 | 232.5 mL/372 mg |
| 2nd and 3rd day 3 (1.6 mg/mL) | 60 | 250.00 mL/400 mg |

## 1491 | Management of a cutaneous reaction to imatinib

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**Case report:** Imatinib, a tyrosine kinase inhibitor, sometimes causes cutaneous reactions that can be of various severity. We present a case of a patient who was started on imatinib 400 mg daily and after 3 months developed diffuse mildly pruritic rash with some desquamation of palms of the hands. The dose of imatinib was reduced to 300 mg daily and therapy with prednisone 30 mg was started. After resolution of rash, the dose of prednisone was tapered to 10 mg daily, but the rash reappeared, although milder in intensity. The dose of prednisone was increased and levocetirizine added and rash resolved. Prednisone was slowly discontinued and rash did not appear. In the case of reactions to imatinib the dose of drug can be reduced and short course of oral corticosteroid given. Milder reactions can be treated with antihistamine or topical corticosteroid. Therefore, when adverse skin reaction to imatinib occurs, induction of tolerance to this important drug should be attempted.

## 1492 | Rituximab desensitization

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**Case report:** A 5-year-old girl with autoimmune encephalitis was unresponsive to methylprednisolone and IVIG therapy. For this reason rituximab and cyclophosphamide therapy was planned. During rituximab infusion she developed urticaria and bronchospasm. Adrenalin, antihistamine and corticosteroid were performed for anaphylaxis. She was consulted to our department for drug allergy.

Rituximab was necessary for this patient's therapy so we decided to apply systematic desensitization for rituximab without performing skin prick tests because the reaction was anaphylaxis. Total dose was calculated 230 mg, for the patient with a 14.5 kg weight according to 375 mg/m² daily dose of rituximab. A(1/1000 dilution), B(1/100 dilution) and C(1/10) dilution) solutions including 3 dilutions were prepared. Desensitization was applied with a 1/10 000 beginning dose as 13 steps by increasing doses every 20 minutes at the beginning and every 30 minutes afterwards and lasted 7 hours. There wasn't any reactions during desensitization. According to treatment protocol rituximab had to be performed per week for 4 weeks. The second dose was also applied with desensitization because the half life of the drug can be as low as 60 hours. After the second dose half life increased to 5-70 days so 3. and 4. doses were performed at the clinic with monitorization without any reaction.

In conclusion, we present a rare case with rituximab allergy and a new protocol of rituximab desensitization.

## 1493 | Aseptic meningitis following intravenous immunoglobulin infusion and subsequent tolerance of an alternative product

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**Background:** A 56 year old man with SJS induced progressive cicatrising conjunctival inflammation had failed efforts to control it with several immunomodulatory medications. Intravenous immunoglobulin (4 weekly at 2 g/kg) was suggested.

**Method:** Following the first infusion of Flebogamma 10% he developed aseptic meningitis requiring hospital admission.

**Results:** His medical history was revisited and subsequently the patient agreed to receive Intragam 10 at a slower rate. There was

no adverse outcome from this. The administration rate has since been aligned with the standard rate.

**Conclusion:** Current literature is limited on how to approach this problem and changing the IVIG product or rate is not thought to be helpful. However, this case demonstrates that exceptions to this advice do exist.

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MECHANISMS AND MANAGEMENT OF RHINITIS AND CRS

## 1494 | Roles of aquaporin in nasal polyps

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**Background:** (a) To find out the distribution of AQPl in nasal polyps, and to make sure the relationship between the aquaporin and nasal polyps. (b) To analysis the difference of the infiltration of eosinophils and the expression of the aquaporin in nasal polyps after glucocorticoids controlling, to study the mechanism of glucocorticoids on nasal polyps.

**Method:** In forty samples of nasal polyps, twenty samples were given BUD intranasal spraying before the operation for nasal polyps, twenty samples were given no drug. Seven samples of normal turbinate mucosa. To count the eosinophils with HE dyeing, and to examine the expression of AQPl with the immunohistochemical method and to analyze with statistical method.

**Results:** (a) Comparing the infiltration of eosinophils of normal turbinate mucosa group with nasal polyps without glucocorticoids group, normal turbinate mucosa group is lower, analysed by statistical method and there is observably difference. (b) Comparing the infiltration of eosinophils of nasal polyps with glucocorticoids group and nasal polyps without glucocorticoids group, nasal polyps with glucocorticoids group is lower, analysed by statistical method and there is observably difference. (c) AQPl expressed on the cell of epithelia, vascular endothelia and glandular epithelia. (d) The expression of AOPl positive cells in the glandular epithelium and blood vessel endothelium was statistically significantly less in the nasal polyps with glucocorticoids group compared with the nasal polyps without glucoconicoids group.

**Conclusion:** (a) The observably infiltration of eosinophils on nasal polyps contribute to their mechanism. The expression of eosinophils was reduced after using the BUD intranasal spraying. It may be the one of the mechanism of glucocorticoids on nasal polyps. (b) AQPl positive cells all express in the mucosa of epithelial, glandular epithelium and blood vessel endothelium of normal mucosa inferior turbinate, it may contribute to the function of inferior turbinate. (c) The expression of AQPl positive cells in glandular epithelium and blood vessel endothelium Was more in nasal polyps, it may be a vital factor for the formation of nasal polyps. (d) The expression of AQPl positive cells in glandular epithelium and blood vessel endothelium was reduced in nasal polyps after using the BUD intranasal spraying. It may be the other mechanism of glucocorticoids on nasal polyps.

## 1496 | Exosomes from sinonasal epithelial cell interrupt epithelia cellular proliferation and ciliogenesis

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**Background:** Exosomes as a kind of nanovesicles involved in many significant biological functions. However, its role and the mechanism in the progress of chronic rhinosinusitis are remained unknown and worth exploring. We clarified different proteins from exosomes secreted by sinonasal epithelial cell, as well as intended to explore the function of exosomes in modulating cellular proliferation and ciliogenesis in chronic rhinosinusitis progression and its molecular mechanism.

**Method:** The exosomes were collected from in vitro primary human sinonasal epithelia cell, which derived from three different groups (normal control, chronic rhinosinusitis and chronic rhinosinusitis with asthma). Generation of exosomes in epithelia was confirmed by nanosight, TEM and western blot. The proteins of exosomes were identified by proteomics analysis. The cellular proliferation and ciliogenesis were analyzed by CCK8 and QPCR.The ciliary beat frequency was detected by SAVA system.

**Results:** We found that epithelial cellular exosomes from chronic rhinosinusitis and chronic rhinosinusitis with asthma could reduce the multiplication rate of normal epithelial cell at a certain concentration ($\geq$10 μg/mL).We found that exosomes from chronic rhinosinusitis with or without asthma could interrupt the cellular ciliogenesis and ciliary beat frequency. Using mass spectrometric analysis we demonstrated that the epithelial exosomes contained different proteins in different disease states.

**Conclusion:** Our findings first identified that exosomes could be secreted by nasal epithelial cells. We also demonstrated exosomes from chronic rhinosinusitis with or without asthma could be a pathogenic factor in the remodeling of sinonasal mucosa. It could be considered as a significant biomarker for detecting the progress of chronic rhinosinusitis and a alternative therapy target.

## 1497 | Th17 response against mucosal infection in persistent upper airways is partially impaired in viruses and bacteria coinfection condition

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**Background:** Viral infections, particularly human rhinovirus (HRV) infections, are frequent triggers of airway diseases. *Staphylococcus aureus* (*S. aureus*) also play an important role in the pathogenesis of severe chronic airway inflammation. Th17 related cytokines are key cytokines in the host immune response against mucosal infection. However, the post infectious immune response, especially response after viral and bacterial co-infections, are still poorly understood.

**Method:** 7 Inferior turbinate (IT) and 9 chronic rhinosinusitis with nasal polyp (CRSwNP) samples were separately inoculated with HRV16 alone or together with *S. aureus*. The morphology of infectious explants was checked by immunofluorescence staining. Th17 cell related cytokines IL-6, IL-17, IL-21, and IL-22 were measured in supernatants of model by Luminex. Th17 response related pathways were evaluated by western blot.

**Results:** HRV and *S. aureus* co-infection caused major tissue damage, which HRV and *S. aureus* invaded into the epithelium through the intercellular spaces and occasionally reached the basement membrane, in comparison with HRV infection alone conditions in both CRSwNP tissue and controls. Obviously, more *S. aureus* colonization were observed in CRSwNP tissue than controls. HRV infection induced IL-6 and IL-17 release in CRSwNP tissue, and IL-17 in IT tissue. Cytokines IL-6 and IL-17 were down-regulated, when nasal tissues were infected with both HRV and *S. aureus*. However, IL-21 and IL-22 were up-regulated in CRSwNP mucosal tissue after HRV and *S. aureus* co-infection in comparison with HRV alone and control. In contrast to HRV alone and control, HRV and *S. aureus* co-infection resulted in a decreased expressions of STAT3 and pSTAT3 in CRSwNP tissue.

**Conclusion:** Th17 immune response is partially impaired in HRV and *S. aureus* co-infection in CRSwNP tissue, with a decreased STAT3 and pSTAT3 expressions in JAK-STAT pathway, which might be associated with major tissue damage in coinfection condition.

## 1498 | The effects of allergen (DP/DF) on mucociliary transport of allergic rhinitis patient

In S

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**Background:** Mucociliary transport (MCT) is a major respiratory tract host defense mechanism and chronic exposure to allergen can deteriorate the these defense mechanism. The aim of this study was to investigate the effects common allergen (DP/DF) on human nasal mucociliary transport in allergic rhinitis patients, and to determine the pathophysiology of ciliary beat frequency (CBF) during allergen-induced change

**Method:** Allergic nasal mucosa cells of allergic rhinitis patients were exposed to common allergen (DP/DF), and CBF was analyzed using an optical flow technique with the peak detection method

**Results:** The allergen(DP/DF) exposed group showed a decreased CBF when compared to the control group. In the cytotoxicity assay, difference in survival rates was not found between the two groups. In the allergen(DF/DF)-exposed group, protein kinase C (PKC) activity was increased during a PKC activity assay. The broad PKC inhibitor, Calphostin C abolished the allergen(DP/DF)-induced decrease of CBF. The allergen-induced decrease of CBF was abolished by GF 109203X, a novel PKC (nPKC) isoform inhibitor, whereas the decrease was not attenuated by G€o-6976, a specific inhibitor of conventional PKC (cPKC) isoform.

**Conclusion:** Allergen may inhibit CBF via an nPKC-dependent mechanism. Therefore, we have confirmed that chronic exposure to allergen could decrease CBF by increasing PKC activity.

## 1499 | Metabolic active of lymphocytes for rhinosinusitis polyposa patients

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**Background:** The important role of the metabolic processes in the cells of the immune system are emphasized to ensure the body's homeostasis. Bioluminescence testing can be used to measure metabolic status. The aim of the research is study is to evaluate the immune status and activity of NAD(P)-dependent dehydrogenases in rhinosinusitis polyposa. The subjects of the research were blood lymphocytes, extracted from blood in 54 patients with rhinosinusitis polyposa in the ages from 25-45 years. Disease severity was evaluated with the severity of clinical symptoms, and based on peripheral blood hematological changes.

**Method:** The control group consisted of 71 healthy people of the same age range. We determined the activity of NAD(P)-dependent dehydrogenases in peripheral blood lymphocytes by bioluminescent technique. We characterized the activities of glucoso-6-phosphate dehydrogenase (G6PDH); glycerol-3- phosphate dehydrogenase (G3PDH); NAD(H)-dependent reaction of lactate dehydrogenase (LDH and NADHLDH); NAD(H)-dependent reaction of malate dehydrogenase (MDH and NADHMDH); malic enzyme (NADPMDH); NAD(P)-dependent glutamate dehydrogenase (NADGDH and

NADPGDH); NAD(P)H-dependent reaction of glutamate dehydrogenase (NADPHGDH and NADHGDH), NAD(P)-dependent reaction of isocytrate dehydrogenase (NADICDH and NADPICDH) and glutathione reductase (GR).

**Results:** While determining common and specific peculiarities of metabolism under ARS, we marked the increase of the activity in such enzymes as G6PDH, NADP-dependent reaction of MDH, NAD-dependent reactions of MDH and LDG and NADH-dependent reaction of MDH and decrease in the level of such enzymes as G3DH, NADP-dependent reaction of GDH and NADPH-dependent reaction of GDH as compared to control.

**Conclusion:** We should mention an important role of metabolic processes in immune system cells in homeostasis in an organism. Speed and intensity of immune reactions depend on the initial state of lymphocyte metabolism.

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## 1500 | The effect of ambient titanium dioxide microparticle exposure to the rhinitis mouse model on the expression of inflammatory cytokines in the nose

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**Background:** To investigate the immune response following exposure to airborne titanium dioxide (TiO2) microparticles in the mouse models of rhinitis.

**Method:** OVA-Alum allergic rhinitis mouse model (AR model) and poly(I:C) induced IL-17 dominant mouse model (neutrophil dominant model) were used. Both mouse models were exposed to TiO2 particles for 2 hours twice daily for 7 days, while the controls (n = 5) were not. Sirius red staining for eosinophil infiltration, immunohistochemistry for neutrophil and IL-17A, serum immunoglobulin (Ig) G and E were assayed by using enzyme-linked immunosorbent assay. In addition, the expression of interleukin (IL)-4, IL-17, and interferon (IFN)-γ in the nasal mucosa and cervical lymph nodes was measured by immunohistochemistry, and real-time reverse transcription-polymerase chain reaction (RT-PCR), IL-17 monoclonal antibody (Secukinumab) was administered in vivo to evaluate IL-17A dependency.

**Results:** TiO2 exposure did not influence eosinophil infiltration in both AR and neutrophil dominant model. However, TiO2 exposure increased neutrophil infiltration in both models and neutrophil infiltration was correlated with IL-17 expression in the nasal mucosa. Serum IgG and IgE levels were changed significantly in the TiO2-exposed group. Th2 cytokines (IL-4, IL-5) and Th1 cytokine, IFN-γ were not changed significantly in both models after TiO2 exposure, however, Il-17 were increased in TiO2 exposure group. And these increased type 17 pathway and neutrophil infiltration were reversed after IL-17 monoclonal antibody administration.

**Conclusion:** Exposure to airborne TiO2 induced neutrophil infiltration in the nasal mucosa. The Type 17 response seems to play a dominant role in the nasal immune response following airborne TiO2 exposure.

## 1501 | Toll-like receptor 9 ligands increase type i interferon induced b-cell activating factor expression in chronic rhinosinusitis with nasal polyposis

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**Background:** B-cell activating factor (BAFF) has been proposed to play a crucial role in the pathogenesis of chronic rhinosinusitis with nasal polyp (CRSwNP). However, the mechasim of the effects of BAFF in CRSwNP is still unclear. The aim of this study is to evaluate the role of toll-like receptor (TLR) 9-mediated BAFF activation on the pathogenesis of nasal polyposis.

**Method:** NP tissue and uncinate tissue (UT) were obtained from 17 patients with CRSwNP, 10 patients with CRS without NP, and 18 normal control subjects. The expression of TLR9, high mobility group box-1 protein (HMGB1), type I interferon (IFN), BAFF, and anti-double stranded DNA (dsDNA) antibody were examined in the nasal tissues and the CpG Oligodeoxynucleotide treated dispersed NP cells (DNPCs) by immunohistochemistry, immunofluorescence staining, real-time quantitative polymerase chain reaction, and enzyme-linked immunosorbent assay. Flow cytometric assay was used to explore the cellular origins of the Type I IFN and BAFF in nasal polyp tissue.

**Results:** The protein level of TLR9, HMGB1, type I IFN, BAFF, and anti-dsDNA antibody were significantly elevated in NP tissue compared to the UTs. Exposure to TLR9 agonist increased the production of type I IFN in vitro, which further increased BAFF production in vitro. The main cellular source of the BAFF in the NPs were plasmacytoid dendritic cells, while the main cellular source of the type I IFN in the NPs were B-cells, monocytes, and eosinophils.

**Conclusion:** TLR9 signaling pathway plays a critical role in the pathogenesis of CRSwNP via increasing type I IFN induced BAFF production and may serve as a novel promising therapeutic target in patients with CRSwNP.

## 1502 | Expression PAF receptor in cells and tissues from healthy and inflamed upper airway mucosa (rinopaf-1 study)

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**Background:** The PAF/PAF-r system has been involved in anaphylaxis, asthma, urticaria and recently in allergic rhinitis. However, no studies have investigated the expression of PAF-r in sinonasal tissue and cells from patients with chronic rhinosinusitis with nasal polyps (CRSwNP) compared to sinonasal tissue and cells from healthy (non-inflammatory tissue) controls.

**Method:** Upper airway tissues were obtained from nasal mucosa (NM, n = 6) of control subjects and from nasal polyps (NP, n = 6) of CRSwNP patients during endoscopic sinonasal surgery. Tissue specimens were directly frozen or used to perform submerged cultures of epithelial cells, fibroblasts, and air-liquid interface (ALI) cultures of epithelial cells. Normodense eosinophils were obtained from peripheral blood of CRSwNP patients (n = 3) with >3% eosinophilia. PAF-r mRNA expression was analysed by real-time PCR using TaqMan Gene Expression Assays. Target gene expression was normalized to Glyceraldehyde-3-phosphate dehydrogenase (GAPDH). PAF-r protein expression was assessed by immunohistochemistry using the EnVision+ System-HRP. Data are presented as mean ± SEM.

**Results:** *First*: PAF-r mRNA expression was very low in fibroblasts from NM and NP (data not shown). PAF-r mRNA expression was detected in whole sinonasal tissue, submerged and ALI epithelial cell cultures from both controls NM and NP. PAF-r mRNA was also detected in peripheral blood eosinophils. Although no differences were found between NM and NP tissues and cultures, PAF-r mRNA expression was significantly higher ($P < 0.001$) in eosinophils than in upper airway tissues and cells.

*Second*: Protein PAF-r was found expressed in whole tissue (predominantly in the epithelium and submucosal glands), submerged and ALI epithelial cell cultures from both NM and NP. Peripheral blood eosinophils also showed PAF-r protein expression.

**Conclusion:** Both PAF-r mRNA and protein expression was found in sinonasal NM and NP tissues (epithelium and submucosal glands) and in peripheral blood eosinophils. These findings suggest the PAF/PAF-r system could play a pathophysiological role in CRSwNP through the modulation of structural and inflammatory cell functions.

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## 1504 | The characteristics of the cellular immune status of the patients with chronic rhinosinusitis with nasal polyps, asthma, atopy or NSAIDs-intolerance

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**Background:** Nowadays chronic rhinosinusitis with nasal polyps (CRSwNP) is not well controlled pathology. It is difficult to predict the pathology process development and success of standard conservative or surgical treatment. The most substantial difficulties in determining tactics of patients' management in CRSwNP are associated with asthma, atopy or intolerance to nonsteroidal antiinflammatory drugs (NSAIDs).

Objective: To determine the diagnostic significance of indicators of systemic cellular immunity for pathology process development forecasting in CRSwNP patients.

**Method:** CD3, CD4, CD8, CD16, CD19, CD25, CD27, CD45, CD45R0, CD45RA, CD56 and CD127 subpopulations of lymphocytes were examined in peripheral blood of 60 patients (age 46.7 ± 16.06) with bilateral CRSwNP in remission using a flow cytometry method. The data of the 356 apparently healthy individuals were used in the capacity of parameters of the control group (CRSwNP vs control group)

**Results:** The study revealed rise in absolute (90.14 ± 0.06 vs 0.009-0.078) and relative (8.76 ± 1.65 vs 2-6) quantity of regulatory T cells ($CD4^+$ CD25 bright CD127 low to neg), rise in absolute (0.47 ± 0.21 vs 0.123-0.369) and relative 19.70 ± 6.44 vs 8-17) count of Natural Killer (NK) ($CD3^-$ $CD16^+$ $CD56^+$ ) cells, rise in absolute (0.26 ± 0.13 vs 0.007-0.165) and relative (16.05 ± 4.55 vs 0.5-6) quantity of activated T-lymphocytes ($CD3^+$ $CD25^+$), absolute count (0.07 ± 0.04 vs 0.012-0.04) of memory B-cells ($CD19^+$ $CD5^-$ $CD27^+$), relative quantity of NKT cells ($CD16^+$ $CD56^+$ $CD3^+$) (9.28 ± 6.15 vs 0.5-6) and activated NK cells ($CD3^-$ $CD8^+$) ($CD8^+$ $CD3^-$) (10.94 ± 5.12 vs 1-3). Doing the comparative analysis of immunological characteristics between the subgroups (CRSwNP+Asthma; CRSwNP+intolerance to NSAIDs; CRSwNP+atopy) with the patients with CRSwNP who didn't have such pathology we only have stated proved significant elevation of an absolute number of NKT-lymphocytes (0.22 ± 0.04) and decrease of T-lymphocytes activation index: activated T-helpers and memory T cells ($CD4^+$ $CD45R0^+$) (24.4 ± 1.72) among the patients with CRSwNP with a simultaneous intolerance to NSAIDs. Comparing immunological characteristics of the group of patients with concomitant bronchial asthma with the others, which have CRSwNP, and the patients with atopy and without it the statistical differences (except the elevation of a number of eosinophils) were not detected

**Conclusion:** Our results demonstrate no reason to study of the cellular immune response in routine medical procedure either with diagnostic or therapeutic purpose.

## 1505 | Phagocytic activity of monocytes in patients with rhinosinusitis polypous

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**Background:** The aim of this work is the evaluation of phagocytic activity of monocytes in the presence of the methicillin-resistant *Staphylococcus aureus* strains and sensitive strains in patients with rhinosinusitis polypous (PRS).

**Method:** The objects of the investigation were monocytes, which were isolated from patients with PRS (n = 38, age of patients was from 25 to 45 years old), and *S.aureus* strains tolerant to the oxacillin (MRSA) as suspension of the concentration of oxacillin $10^6$ CFU/mL. As control samples were used the *S. aureus* strains tolerant to the methicillin (MSSA). Phagocytic activity monocytes was determined using MRSA and MSSA labelled FITC. Analysis of coloured cells had been done by fluorescence-based flow cytometry device FC-500 (Beckman Coulter, USA) with monoclonal antibodies to the following construction: FITC/CD14-PE/CD45-PC7/CD16-PC5. Measurement of the intensity of respiratory burst of monocytes was carried out through determination of the activity of lucigenin - and luminol-dependent spontaneous and induced chemiluminescence. Statistical analysis was performed by the software package Statistica 6.1 (StatSoft Inc., 2007).

**Results:** Determination of the functional activity of monocytes in patients with PRS included the assessment of oxygen-dependent phagocytosis system by measuring the chemiluminescent activity of the cells and oxygen-independent phagocytosis. In the study of luminol—and lucigenin-dependent activity of monocytes in response to induction of MRSA, there was registered the decrease of intensity of chemiluminescence of the reaction by 3-fold and increasing activity of monocytes by 1.5-fold related to the spontaneous activity of the cells. Under the study oxygen-independent phagocytosis of monocytes in response to exposure to MRSA relative to MSSA, there was detected a decrease in phagocytic numbers of total monocytes by 2 fold. Evaluation of the activity of the subpopulation composition of monocytes in the presence of MRSA strains showed a decrease in the phagocytic index of the subpopulations $CD14^{low}$ $CD16^{+}$- monocytes and the phagocytic number of $CD14^{+}$ $CD16^{+}$ cells in 2 fold and the phagocytic number of subpopulations $CD14^{+}$ $CD16^{-}$ monocytes in 2 fold relative to MSSA strains.

**Conclusion:** There is a decrease in phagocytic activity of monocytes relative to MSSA, in patients with PRS in response to exposure to MRSA. It can be assumed that the induction of MRSA functional activity of monocytes is suppressed.

## 1506 | Role of toll like receptor9 signal pathway on tissue remodeling in nasal polyp derived fibroblast

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**Background:** Nasal polyposis is characterized by persistent inflammation and remodeling in sinonasal mucosa. Toll-like receptor 9 (TLR9) is a DNA receptor of innate immune system which plays a pivotal role in fibrosis and inflammatory response. However, the expression, mechanism of action, and pathogenic role of TLR9 signaling in chronic rhinosinusitis with nasal polyps (CRSwNP) remain uncharacterized. The aim of this study is to explore the expression, activity and potential pathogenic role of TLR9 signaling in the tissue remodeling in Nasal polyp derived fibroblast (NPDF).

**Method:** Expression of TLR9 were evaluated in NPDFs. NPDF were stimulated with different TLR9 agonist (CpG A and B) and assayed for the fibrotic response. Fibrotic and inflammatory responses elicited by type A CpG oligonucleotide were examined in NPDF by a combination of real-time quantitative polymerase chain reaction, Western blot analysis, enzyme-linked immunosorbent assay and immunofluorescence staining.

**Results:** The mRNA expression level of TLR9 increased in NPDF compared to negative control. Type A CpG induced the protein level expression of α-SMA, fibronectin, and MMPs. Type A CpG also promoted the release of pro-inflammatory cytokines and type I interferon. By using specific inhibitors, we found that type A CpG induced expressions of α-SMA, fibronectin, MMPs and secretion of inflammatory cytokines were regulated by various signaling pathways.

**Conclusion:** Our date indicated that type A CpG triggers immune response via TLR 9 and activates various signaling pathway, which is involved in remodeling of nasal polyps. Disrupting this process with inhibitor targeting TLR9 or its downstream signaling pathways might represented a novel approach to CRSwNP therapy.

## 1507 | Digoxin inhibits nasal inflammation in an animal model of allergic rhinitis

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**Background:** Allergic rhinitis (AR) is an increasingly more common nasal inflammatory disease in which an antigen such as pollen or dust mites triggers symptoms such as itching, sneezing, and rhinorrhea, which can lead to nasal obstruction. AR is mediated by T-helper type 2 cells together with mast cells, eosinophils, and several inflammatory cytokines and chemokines. For example, recent

research indicates that hypoxia-inducible factor 1α (HIF-1α) is involved in the mechanism of AR development. The anti-heart failure drug digoxin has a specific inhibitory effect on HIF-1α, and thus, the aim of the present research was to explore the anti-hypertensive effect and mechanism of digoxin in AR.

**Method:** An animal model of ovalbumin-induced AR was established in guinea pigs. The experimental group was treated with digoxin through the tail vein. For the comparison of symptoms between the experimental and control groups, the incidence of sneezing was recorded, and the eosinophilic interleukin IL-4 and IL-5 levels in nasal secretions were measured by enzyme-linked immunosorbent assays. Western blotting and reverse transcription polymerase chain reaction analyses were conducted to evaluated HIF-1α expression in guinea pig nasal mucosa.

**Results:** The AR symptoms of guinea pigs in the experimental group were significantly improved after administration of digoxin. Specifically, the experimental group exhibited a significantly lower numbers of sneezing times(average 36.0 ± 1.10 vs 7.4 ± 0.78, $P < 0.05$) and lower IL-4 and IL-5 secretion levels ($P < 0.01$) compared with the control group. Moreover, guinea pigs of the experimental group showed less severe nasal mucosa edema, lower HIF-1α production, and reduced eosinophil infiltration in nasal mucosa compared with the control group.

**Conclusion:** The anti-heart failure drug digoxin may ameliorate the symptoms of AR by inhibiting HIF-1α production.

## 1508 | Evaluation of lower airway symptoms in patients with local allergic rhinitis

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**Background:** Similarly to what has been described in allergic rhinitis, there is an important association of local allergic rhinitis (LAR) with lower airway symptoms suggestive of asthma, being self-reported in 24.4% of LAR patients after five years of follow-up, and increasing to 30.7% after 10 years. However, clinical suspicion alone it is not enough for asthma diagnosis and could overstate its real prevalence. The aim was to evaluate the real prevalence of asthma in LAR patients based on validated objective methods.

**Method:** Seventy-five patients (29 with LAR, 20 with non-allergic rhinitis (NAR), 18 with allergic rhinitis (AR)), and 8 healthy controls (HC) were included. All patients had perennial history of rhinitis and bronchial symptoms suggestive of mild-moderate asthma for at least two years. Non-specific airways hyperresponsiveness (methacholine challenge test, using tidal breath method following ATS guidelines) was performed in all subjects.

**Results:** Subjects were mostly young females, non-smokers. Median μg/day of inhaled corticosteroids (budesonide/equivalent dose) was similar in all groups. Median FEV1% in AR group (75.5%) was significantly lower compared to LAR (90%, $P = 0.002$), NAR (85%, $P = 0.007$) and HC (88%, $P = 0.005$). In the LAR group, 15/29 (51.7%) had a positive methacholine, 12/20 (60%) in the NAR, 15/18 (83.3%) in AR group and 0/8 (0%) in HC. Patients with LAR had a significant lower percentage of confirmed asthma than AR ($P = 0.031$) and similar to NAR ($P = 0.771$). No differences were detected between AR vs NAR ($P = 0.155$).

**Conclusion:** Presence of objectively demonstrated asthma was lower in LAR compared to AR, and with better lung function.

## 1509 | Impact of air pollution on rhinitis in South Korea

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**Background:** As a result of rapid industrialization and urbanization, air pollution has increased in Korea. Air pollution can raise the incidence of several respiratory diseases and aggravate them. Rhinitis is a common disease which can be aggravated by specific and/or non-specific inhalant stimuli. This study aims to find the relationship between hospital visit for rhinitis and ambient air pollution.

**Method:** As a retrospective cohort study, this study included patients who visited otorhinolaryngology clinic in a university hospital from January 2014 to December 2015. It excluded patients without available address which is a matching parameter to daily average level of air pollutants, SO2, CO, O3, NO2, PM10, and PM2.5, in South Korea. The influence was evaluated by a time-dependent Cox proportional hazard model. Event of the Cox model is a diagnosis of rhinitis on the day of visiting and follow-up period is time until visiting clinics. The influence of level of air pollutants was adjusted by gender, age, and daily temperature and humidity.

**Results:** In total 68 404 enrolled patients, there was no difference in gender (51.1% male and 48.9% female) and mean age was 34.2 ± 24.4 years old. Among the total patients, 6024 patients were diagnosed of rhinitis (50.8% male and 49.2% female) with mean age 30.9 ± 21.7 years old. CO and NO2 had a strong correlation ($r = 0.618$). PM10 and PM2.5 had a very strong correlation ($r = 0.853$). Most of air pollutant had been controlled under national standard except NO2, PM10, and PM2.5. Increase of SO2, O3, NO2, and PM10 showed statistically significant increase of hospital visit for rhinitis (10.2% as SO2 increase by 0.001 ppm, 16.5% as O3 by 0.01 ppm, 23.4% as NO2 by 0.01 ppm, and 1.7% as PM10 by 10 $\mu g/m^3$).

**Conclusion:** Ambient air pollution influenced the hospital visit of patients with rhinitis, even, the level of pollutants, below the national standard. SO2, O3, NO2, and PM10 could increase an incidence of rhinitis and/or induce an aggravation of rhinitis symptoms. Health care provider might expect upraising patients with rhinitis in the clinic with increase of air pollutants, even under the standard levels.

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## 1510 | Assessment of CD3CD56 and CD16$^+$ Granzyme B+ cells in patients with oral mucosal lichen planus

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**Background:** Oral lichen planus (OLP) is considered a multifactorial disease that develops under the influence of exogenous and endogenous factors, in combination with defects in the immune system, which can determine the nature of the course of the disease pathology. This study assessed CD3$^+$ CD56$^+$ cells and CD16$^+$ Granzyme B+ cells (CD16$^+$ GrB cells) in patients with erosive and non-erosive oral lichen planus in the acute and the chronic disease periods.

**Method:** 97 patients aged 18-60 years were studied including 35 with erosive oral lichen planus, 32 with non-erosive oral lichen planus and 30 healthy control subjects of similar age. The cell profile was assessed by direct immunofluorescence with flow cytometry analysis performed on FACScan with monoclonal antibodies (Becton Dickinson).

**Results:** During relapse of erosive oral lichen planus mononuclear cells obtained from peripheral blood of patients showed increased number of NK-cells CD3$^+$ CD56$^+$ in acute (15.5 ± 4.5%) and chronic (14.9 ± 6.3%) disease periods, and CD16$^+$ GrB cells in acute (18.1 ± 1.5%) and chronic (14.5 ± 2.5%) disease periods, $P < 0.05$. In patients with the non-erosive forms of OLP there were CD3$^+$ CD56$^+$ and CD16$^+$ GrB cells in acute (8.9 ± 2.5%) and (7.3 ± 1.3%) and chronic disease (9.5 ± 2.2%) and (8.2 ± 3.1%), $P < 0.05$. The number of CD3$^+$CD56$^+$ and CD16$^+$ GrB cells in the controls were (9.8 ± 2.1%) and (6.2 ± 5.4%), $P < 0.05$.

**Conclusion:** Acute relapse of erosive oral lichen planus, unlike non-erosive forms, is characterized by increases in the number of CD3$^+$ CD56$^+$ and CD16$^+$ GrB cells. Chronic disease in patients with erosive oral lichen planus showed a steady increase in the number of CD3$^+$ CD56$^+$ killer cells and CD16GrB lymphocytes.

## 1511 | Development of systemic lupus erythematosus after surgical tibial reconstruction with an allograft from a bone bank

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**Background:** Bone allograft implantation in patients who undergo surgical reconstruction after sports—related bone injuries is widely used and it has been considered a safe procedure unless postprocedural infections occur in extremely rare cases.

**Method:** A case-report of a 41-year old, previously healthy female, who was diagnosed with systemic lupus erythematosus (SLE) six months after surgical reconstruction with an allograft from a bone bank, due to traumatic tibial plateau fracture.

**Results:** On admission, she was complaining of subfebrile temperature, joint pain, appetite and weight loss. Clinical examination revealed cervical lymphadenopathy and a painless mucosal ulceration located on the hard palate. Elevated sedimentation rate (82/1 hours) and a normocytic normochromic anemia with haemoglobin level of 98 g/L were detected. Serum protein electrophoresis revealed an elevated gamma globuline fraction (27.1% of total protein). Infective trigger were not identified. Further serum investigation showed C3 and C4 complement components consumption, positive antinuclear antibodies (ANA) of homogeneous pattern at serum titre of 1:640, positivity to multiple autoantibodies such as anti double strain DNA (dsDNA), anti histone, anti nucleosome, anti cardiolipin IgM, anti Ro, Anti La, anti neutrophile cytoplasmatic antibody directed to lactoferrin (Lf), direct Coombs blood test. The patient fulfilled the SLICC classification criteria for SLE: oral ulceration, complement consumption, positive ANA along with multiple autoantibody positivity mentioned above. The treatment consisting of prednisone and hydroxychloroquine sulphate has been suggested.

**Conclusion:** By presenting this case, we wish to point out the possible connection between bone allograft placement and the subsequent induction of an autoimmune disease such as SLE.

## 1512 | Vasculitis and scleroderma

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**Background:** We investigated some clinical and immunological parameters in 7 patients with Scleroderma and vasculitis.

**Method:** We followed the 7 patients with Scleroderma and vasculitis, including 6 women and 1 men, caucasian type, aged 33-62 years, with disease duration of 2-4 years. The study is multicenter and open. Were examined following indicators: biopsy, capillaroscopy, Doppler sonography, anti SCL-70, CRP, ANA, ACA and other.

**Results:** All patients completed the study. Skin tissue biopsy, obtained from all patients, showed typical fibrinous necrosis with polymorphonuclear infiltration and collagen accumulation. All patients have performed capillaroscopy and Doppler sonography and are established complete arterial obstruction, in 2 patients with peripheral gangrene, and in 4 patients incomplete and accompanied by tingling of the fingers. Trophic ulcers the toe tips, such as "rat bite", were observed in 6 patients (85%). Typical hyper- and hypopigmentation were observed in six patients mainly on the fingers and the cheekbones. Fibrosis of the skin of the fingers often leads to flexion contractions, which we observed in 6 patients. We were watching two-sided swelling of the fingers, but it was very pronounced in 5 patients (71%). 86% of our patients have impaired motility of the esophagus. Accelerated ESR and C-reactive protein were found in 5 patients as follows—2 intensively accelerated and 3 moderate. In our patients with positive ANA, we observed 4 patients —at low titer 1:40 at 2 and titration 1:80 in 2 patients. The spectrum of ANA found by us in Raynaud's syndrome patients is closer to scleroderma than to lupus. We underline the importance of ANA (57%) and anti-CC antibodies (27%) for the early diagnosis of Raynaud's syndrome and scleroderma, which is also seen in our patients. Anti-SCL-70 antibodies were observed in 3 patients coinciding with other publications describing about 40% of the patients. Low levels of complement were observed in 2 patients. Low hemoglobin levels were observed in 1 patient, with no iron deficiency.

**Conclusion:** 1. We observed a typical fibrinoid necrosis and polymorphonuclear infiltration, and collagen accumulation in the walls of small and medium-sized blood vessels.

2. Positive ANA and ACA are observed in almost all patients, but in a different titer.

## 1513 | The role of $CD4^+$ lymphocytes in pathogenesis of immune inflammation in ulcerative colitis

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**Background:** Ulcerative colitis (UC) is a clinical type of inflammatory bowel diseases (IBD), which are considered as chronic disorders of the gastrointestinal tract characterized by intestinal inflammation and epithelial injury. The etiology and pathogenesis of UC remains unclear.

UC has long been considered to be associated with a non-conventional Th2 response. Recently the role of Th17 as well as cytokines they release in the pathogenesis of autoimmune inflammation in UC have been noticed. Besides nowadays results from numerous studies indicate a role for innate lymphoid cells (ILC) in the pathogenesis of chronic intestinal inflammation in IBD.

The aim of our study is to analyze the serum levels of following cytokines: IL 4, 17A, IFNγ in UC patients both in the acute stage of disease and remission.

**Method:** Forty eight UC patients in the acute stage and twenty patients in remission were included into the study. Serum cytokine levels were analyzed using multiplex immunoassay (Bio-Rad, Hercules, USA). Statistical analysis was performed using STATISTICA 6.0 Software Package. The control group consisted of 11 healthy volunteers.

**Results:** Statistically significant increase of IL4 level (3.23 pg/mL [2.18; 5.02]; 3.42 pg/mL [2.8; 4.18] respectively) was determined in patients with UC both in acute stage and remission compared to controls (1.87 pg/mL [1.4; 3.2], ($P$ = 0.002; 0.009 respectively). Statistically significant increase of IL17A level (15 pg/mL [12.11; 23.38]); 14.68 pg/mL [11.29; 17.19] respectively) was also observed in patients both in acute stage and remission compared to controls (7.36 pg/mL [5.18; 8.06], $P$ = 0.00007, $P$ = 0.00029 respectively). Besides statistically significant increase of IFNγ both in acute stage (176.15 pg/mL [65.15; 359.84]) and remission (42.6 pg/mL [29.4; 64.45]) compared to controls (16.5 pg/mL [12.3; 23.2], $P$ = 0.00107; 0.0118 respectively) was revealed.

**Conclusion:** Increased levels of IL4 released by Th2 and IL17A released by Th17 might be a sign of involvement of these adaptive subtypes of T-helpers into the chronic inflammation in UC. Besides increased level of IFNγ released by ILC type1 might suggest their overactivity. Thus, Th2, Th17 adaptive subtypes as well as innate lymphoid cells may contribute to chronic immune inflammation in the pathogenesis of ulcerative colitis.

## 1514 | Anti-DFS70 antibodies-a new diagnostic biomarker in autoimmune diseases

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**Background:** The presence of antinuclear antibodies (ANA) is commonly associated with a broad spectrum of connective tissue diseases. Low titres might be detected rarely also in healthy individuals, especially in higher age. An indirect immunofluorescence (IIF) detection of ANA antibodies on Hep- 2 cells is the most frequently used laboratory method in this respect. The method is quite reliable regarding sensitivity, however the specificity of this test is lower. We would appreciate a biomarker for clinical discrimination of ANA-associated autoimmune rheumatic diseases (AARD) from other IIF ANA positive individuals. The autoantigen called DFS70 (dense fine speckled 70) was identified for the first time in patients with interstitial cystitis and chronic fatigue syndrome, antibodies are mostly of IgG isotype and were often detected in healthy subjects and patients with different inflammatory diseases.

**Method:** We evaluated blood samples from a cohort of 157 patients (108 females, 49 males, aged 7-88 years) and control group-thrombocyte donors -15 subjects (8 females, 7 males, aged 26-53 years) for the presence of ANA antibodies (IIF, Hep-2 cells) and for anti-DSF70 antibodies (immunochemiluminiscence CLIA method). Other autoantibodies were tested in relation to basic diagnosis.

**Results:** A cohort of patients was divided into 6 groups according to main diagnosis: immunodeficiency, connective tissue diseases, bronchial asthma and allergic rhinitis, recurrent infectious diseases, gastrointestinal diseases, endocrinopathy and others and the last group was generated from healthy subjects. The presence of anti DFS70 antibodies was highest in the group of recurrent infections, mostly in females. In these subjects homogenous pattern of ANA antibodies by IIF was also detected quite often, probably induced by non-specific activation of immune system. On the other hand, in a group of connective tissue diseases, we have not found any anti DFS70 positive patient.

**Conclusion:** The clinical impact of anti-DFS70 antibodies is not yet finally confirmed, but their low frequency in connective tissue diseases and presence in 5%-10% of healthy subject suggests their potential role as a new biomarker to be used as a negative predictive factor in non AARD. Confirmation of presence or absence of anti-DFS70 antibodies seems to be helpful to exclude potential diagnostic errors in IIF ANA positive patients.

## 1516 | DNA methylation at the interface between environment and multiple sclerosis risk

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**Background:** Multiple sclerosis is a debilitating autoimmune and degenerative condition of the central nervous system, that predominantly affects young adults. Both genetic and environmental factors are associated with increased risk for this disease. We propose that the effect of environmental factors, particularly latitude of childhood, is mediated through epigenetic mechanisms. Specifically, we propose that unfavourable gene methylation predisposes individuals to multiple sclerosis, that this is set in childhood and adolescence, and transmitted from haematopoietic stem cells to progeny.

**Method:** $CD34^+$, $CD14^+$ and $CD56^+$ cell subsets were isolated from peripheral blood of healthy controls. Libraries enriched for CpG islands and promoter regions were generated using modified reduced representation bisulfite sequencing and subjected to next generation sequencing. Site specific methylation profiling of genome wide CpG islands, including MS susceptibility genes was conducted using Methpipe software.

**Results:** Genomic coverage was consistent with other published methylomes using modified reduced representation bisulfite sequencing. The methylation signature of peripheral blood derived subsets showed greater differences in methylation compared to buccal cells than with each other. Individuals displayed differences in $CD34^+$ methylomes, and these were recapitulated in the progeny $CD56^+$ and $CD14^+$ cells for those individuals. Methylation of specific genes regions (e.g. PRF1), were consistent with the known biological function of these genes and their potential contribution to MS risk.

**Conclusion:** The vast majority of CpG islands interrogated show recapitulation of their methylation signature from $CD34^+$ to progeny. However, individual differences and cell subset differences identified, likely reflect the known biological function of these genes in progeny cells. Our preliminary results are consistent with the hypothesis that the epigenetic signature (that predisposes to MS risk) is set in childhood and adolescence. The physiological basis underlying the setting of this epigenetic signature is still to be elucidated, but may involve UV light and/or vitamin D, and may provide novel therapeutic targets, especially at a personalised level, for treatment of MS.

## 1518 | Salivary top-down proteomics in patients affected by auto-inflammatory periodic fever syndromes

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**Background:** Auto-inflammatory diseases are rare disorders characterized by recurrent episodes of fever/inflammation affecting serosal surfaces, joints, eyes and skin without autoantibody production or an underlying infection. Innate immunity is implicated in their pathogenesis and the underlying genetic defect has been identified in a fraction of the syndromes. During last years, the increased knowledge about auto-inflammatory diseases and the difficulty in their characterization aroused great interest to better understand these pathologies.

**Method:** The acidic soluble fraction of salivary proteome of patients and controls (HC) were analyzed by RP-HPLC-ESI-MS. 60 known salivary proteins (salivary acidic proline-rich phosphoproteins (aPRPs), histatins (Hst), salivary cystatins S, SN and SA, statherin, P-B peptide, α-defensins 1-4, cystatins B, C, thymosin β-4, S100A7, S100A8, S100A9, and S100A12 proteins) and several derivatives (acetylated, glutathionylated, phosphorylated, and oxidized forms) were searched in the chromatographic profiles by XIC (eXtracted Ion Current) procedure. 21 adult patients (mean age ± SD: 34.4 ± 10.1; 15 F, 6M) were enrolled and compared with 27 sex/age matched healthy controls (mean age ± SD: 33.4 ± 9.6; 18 F, 9M). Patients are classified on the base of clinical manifestations as follows: 6 patients with FMF (mean age ± SD: 33 ± 7.9; 5 F, 1M), and 15 with Unclassified fever syndrome (Uc) (mean age ± SD: 34.9 ± 11.1; 10 F, 5M).

**Results:** FMF patients showed low levels of α-Defensins 2, 3 and 4, this last was absent, with respect HC, and high levels of the glutathionylated proteoforms of cystatin B, and S100A9, and of antileukoproteinase (SLPI). Similar results were obtained on saliva of unclassified patients, which showed also levels of cystatin C higher than controls.

Interestingly, proteins and peptides typically secreted by salivary glands (cystatin C, histatins, statherin, aPRPs) were found more abundant in Uc patients than in controls, and in some cases also than FMF patients (see Table). An evaluation of relative abundance of phosphorylation of phosphorylated proteins/peptides highlighted a significant hypophosphorylation of Hst-1, PRP-1 and PRP-3 in Uc patients with respect to controls, probably due to a less active Fam20C kinase responsible for their phosphorylation

**Conclusion:** We show by a top-down proteomics approach a wide salivary modification, highlighting dysregulation in neutrophil-derived proteins and significant differences between FMM and Uc patients.

## 1520 | Association of memory T-cells subsets with osteoarthritis inflammatory activity

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**Background:** Osteoarthritis (OA) is a chronic progressive disease characterized by degradation of joint cartilage, synovial inflammation and joint dysfunction. The degree of OA activity may be associated with synovial fluid (SF) and blood T-cell subsets, indicative of inflammation.

**Method:** Blood and synovial fluid samples from 19 patients with the OA of knee (M17.0) were assessed for SF and blood T-cell subsets by flow cytometry: $CD4^+$ $CD45RB^+$ $CD45RA^+$ $CD62L^-$ inflammation-related cells (IRC), Naïve T-cells ($CCR7^+$ $CD45RA^+$), TCM ($CCR7^+$ $CD45RA^-$), TEM ($CCR7^-$ $CD45RA^-$), and TEMRA ($CCR7^-$ $CD45RA^+$).

**Results:** The correlation between the activity of the disease and the percent of SF $CD4^+$ TEM cells ($R = 0.65$, $P = 0.002$), blood $CD4^+$ TEM ($R = 0.61$, $P = 0.006$) and TEMRA ($R = 0.70$, $P = 0.001$) cells and IRC ($R = 0.57$, $P = 0.010$) was shown. Blood TEMRA cells absolute and relative contents were decreased compared with healthy donors (OA patients—8.0 [1.8-37.3], donors—29.9 [21.0-37.0], $P = 0.000001$). The TEM subset comprised the majority of $CD4^+$ (68.3 [58.6-73.0]) and $CD8^+$ (76.9 [64.8-82.0]) T-cells in the SF of OA patients. There was a positive correlation between the blood TEM/TEMRA and SF TEMRA counts ($R > 0.65$, $P < 0.003$) and negative correlation between SF TCM and blood TEMRA count ($R < 0.58$, $P < 0.001$).

**Conclusion:** The associations between the activity of OA and TEM/TEMRA counts in blood and SF as well as blood IRC subsets were established. TEM cells seem to migrate into the affected joints and contribute to immune inflammation. Assessment of these T cell subsets may assist in determination of OA activity.

## 1521 | Membrane markers of subpopulations of B lymphocytes in seropositive variant of development the visceral form of rheumatoid arthritis

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**Background:** Currently, depending on the presence of membrane CD5-antigen b-lymphocytes are divided into two subpopulations of cells: $CD5^+$ (B1-cells) and $CD5^-$ (B2-cells). B1 lymphocytes are potentially autoreactive cells, the main function of B2 cells is the synthesis of highly specific antibodies to endogenous and exogenous antigens and the formation of b cell memory. The results of the study subpopulations B1и B2-lymphocytes in humans and its pathogenetic significance in RA are few and contradictory

**Method:** We examined 30 patients with seropositive variant of the visceral form of RA in the acute stage. The average age of the subjects 53 ± 5 year.

The control group consisted of 10 healthy donors aged 40-50 years. Immunological methods of investigation included determination of membrane antigens b cells: $CD3^-$ $CD19^+$ $CD45^+$, $CD19^+$ $CD5^+$ $CD45^+$, $CD19^+$ $CD23^+$ CD45, $CD19^+$ $CD25^+$ $CD45^+$, $CD19^+$ $CD40^+$ $CD45^+$, $CD19^+$ $CD86^+$ $CD45^+$, $CD3^+$ $CD4^+$ $CD40L^+$ $CD45^+$, $CD19^+$ $CD45RA^+$ $CD27^+$ $CD45^+$, by flow cytometry.

**Results:** In the study subpopulation composition of lymphocytes in seropositive variant form of RA visceral a statistically significant increase in relative amount as B1-cells with immunophenotype $CD19^+$ $CD5^+$ $CD45^+$ (0.6 ± 0.01% 0.12 ± 0.03%) and B2 lymphocytes with the phenotype $CD19^+$ $CD5^-$ $CD3^-$ $CD45^+$ (16.4 ± 1.2% and 7.9 ± 0.5%). In the analysis of the processes of maturation and differentiation of B2 cells detected statistically reliable increase of the relative number of Mature $CD19^+$ $CD3^-$ $CD45^+$ naïve B2 cells $CD19^+$ $CD45RA^+$ CD27 number of Mature $CD19^+$ $CD3^-$ $CD45^+$ naïve B2 cells $CD19^+$ $CD45RA^+$ $CD27^-$ $CD45^+$ (11.8 ± 0.9% and 5.7 ± 0.5%) compared to the control group. In the study of surface markers B2 lymphocytes revealed an increase of expression of costimulatory $CD19^+$ $CD40^+$ (19 ± 1.3% and 7.0 ± 0.42%) molecules and increasing the relative amount of CD40L 0.9 ± 0.2% (0.3 ± 0.05%) ligand on $CD3^+$ $CD4^+$ $CD45^+$ subpopulation of T-lymphocytes.

Analysis of surface antigenic receptor B2 cells in the visceral form of RA showed an increased expression of early markers of $CD19^+$ $CD23^+$ $CD45^+$ (2.9 ± 0.08% and 0.91 ± 0.1%), $CD19^+$ $CD25^+$ $CD45^+$ (1.6 ± 0.4% 0.05 ± 0.01%) activation in comparison with the control group.

**Conclusion:** Thus, when seropositive variant form of RA visceral revealed the increase of the relative number as B1 cells and B2 cells. While B2 cells were characterized by increased expression of early activation markers, costimulatory molecules and a corresponding ligand, which determines the severity of the pathological process in a visceral form, seropositive RA

## 1522 | Clinical and immunological features of reactive arthritis on the background of the epstein-barr virus

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**Background:** The problem of the reactive arthritis (ReA) is connected with its prevalence, complexity of diagnostics, involvement in the pathological process of many organs and systems, insufficiently effective treatment.

**Objective:** To study the clinical and immunological features of the course and diagnostics of the ReA on the background of the Epstein-Barr virus.

**Method:** 32 patients with clinical evidence of arthritis have been examined. Patients have been examined under laboratory, immunological, serological and molecular genetic studies to identify the EBV-infections.

**Results:** All the patients were suffering from the arthritic syndrome. Besides, 8(25%) of patients were diagnosed with prolonged subfebrile condition, 15(46.9%) with the chronic fatigue syndrome, 8 (21.8%) with the respiratory syndrome. According to the findings of the research conducted, 7 (21.8%) of patients were presented with positive rheumofactor, 10 (31.2%) with increase in ERS, 9 (28.4%)—with increased level of AS(L)O and 12 (37.5%) with increase in CRP concentration. High titers of specific antibodies of class IgM, IgG to the capsid and nucleic antigens EBV and EBV-DNA were found in saliva, mucus scrap and blood of the patients. The immunogram test showed the presence of immunodeficiencies of combined lymphocytic phagocytic type in 24 (75%) of the examined, 10 (31.25%) of whom were observed with lymphocytosis. Wherein, with 12 (37.5%) of patients increase of the number of natural killers was detected while with 17 (53.1%) $CD8^+$-lymphocytes changes were detected. With 15 examined (46, 8%) increased level of T-helpers was observed, that can be interpreted as preconditions for the formation of autoaggression.

**Conclusion:** ReA of EBV genesis is the most frequently characterized by increase in ERS, acute-phase proteins. All patients having ReA were diagnosed with immunodeficiency of infectious genesis of the lymphocytic phagocytic type.

**Keywords:** reactive arthritis, EBV.

## 1525 | Association of stiff person syndrome with anti GAD antibodies with immune dysregulation and symptoms of mast cell activation syndrome

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**Background:** Stiff-person syndrome (SPS) associated with anti-GAD 65 antibodies leads to severe muscle rigidity with chronic muscle spasms due to the autoantibody against glutamic acid decarboxylase. Other autoimmune disease may occur with this condition.

**Methods:** A 60 year old female with anti GAD-65 antibodies presented for evaluation of weakness and metabolic instability including wide blood pressure fluctuation.

Results: In this case SPS was associated with Sjogren's Syndrome, Ehlers Danlos Syndrome and adult onset Hypogammaglobulinemia, with low IgG and low IgA noted in the last 3 years requiring IVIG treatment for Common Variable Immune Deficiency. She developed episodes of both hypotension and hypertension suggesting possible dysautonomia. Complicating her health she also has Congenital Adrenal Hyperplasia salt wasting type with 21 hydroxylase deficiency. Generalized allergic responses to multiple opiates suggested mast cell instability such as mast cell activation syndrome (MCAS).

**Conclusion:** Stiff Person Syndrome with Anti GAD-65 antibodies may have not only autoimmune associations but also immunoregulatory abnormalities such as Common Variable Immune Deficiency. The presence here of Ehler Danlos Syndrome and Dysautonomia, conditions associated with Mast Cell Activation Syndrome, suggests an overlap between SPS constellation of conditions and those conditions associates with MCAS.

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RARE IMMUNE DEFICIENCIES AND THEIR CASE REPORTS

## 1526 | Atypical localization of cyst hydatid in selective IG a Deficiency

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**Introduction:** Cyst hydatid is an infection induced by the tapeworm *Echinococcus granulosus*. Selective immunoglobulin A deficiency (sIgAD) is presented with the isolated deficiency of serum IgA and occasionally Ig-G2. *To the best of our knowledge, there are no reports which presented the co-occurence of sIgAD and E. granulosus so far. We are presenting a patient diagnosed as* sIgAD who presented with an unusual localization of *cyst hydatid.*

**Case:** A 44 year-old male patient who works as a dental technician with a history of lung silicosis and recurrent sinusitis applied to an orthopedics clinic for left hip pain and difficulty in walking. He has a history of keeping a dog during childhood. Hip MRI revealed a 5 × 3 cm sized mass on left iliac wing extended to gluteus muscle and subcutaneous tissue. Incisional biopsy was reported as chronic granulomatous osteomyelitis. The lesion was considered as tuberculous abscess. Despite anti-tuberculous (four-drug regimen) treatment for one year, the lesion showed no regression. Excisional biopsy was carried out by the same orthopedics clinic. Chronic inflammatory reaction and fibrosis was considered to be due to cyst hydatid in the detailed evaluation. Anti-echinococcus IgG and IgM was performed with ELISA and found positive. No other lesion was detected in lungs and liver. albendazole 400 mg twice a day was initiated and substantial regression observed after three months. Atypical and sustained infections made us think of primary immunodeficiency disorders. Immunoglobulin subgroups were as follows: IgA: <1 mg/dL (70-400), IgG:1451 mg/dL (700-1600), IgM:223 mg/dL (40-230). Similar results were found in two weeks apart. IgG subgroups were normal.

**Conclusion:** Recurrence and atypical positions of infections should direct the physicians to consider primary immunodeficiency disorders and referral to immunology clinics should come into question.

## 1528 | Diagnosis of common variable immunodeficiency for patient with suspected celiac disease: Case report

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**Introduction:** Common variable immunodeficiency (CVID) is primary immune deficiency with significant hypogammaglobulinemia and dysregulation of the immune system leading to defective T-cell activation and proliferation. Usually, CVID manifests with recurrent bacterial infections; whereas, various autoimmune disorders can also develop in about 20% of these patients. The most common gastrointestinal symptom is intermittent or persistent diarrhea, and it occurs in 50% of immune deficiency patients.

**Case description:** 31 year-old male was firstly admitted to gastroenterologist due to intermittent diarrhea, abdominal pain and reactive lymphadenopathy. Celiac disease was suspected as genetic test showed HLA DQ8 (HLA-DQA1*03 and HLA-DQB1*0302), histological evaluation of duodenum biopsy provided picture of lymphoid hyperplasia and Marsh IIIA variant. However, laboratory testing for celiac disease showed very low amount of antibodies against transglutaminase. Gluten free diet for almost one year was ineffective as patient had a continuous problem of gaining weight due to chronic diarrhea. Additional questioning revealed recurrent respiratory tract infections with a need of antibiotics more than two times/year during last decade. Lymphocyte phenotyping by flow cytometry showed that CD3, CD4, CD8, CD19 are in normal ranges, but amounts of all immunoglobulins are low: IgM <0.22 g/L, IgG 2.53 g/L and IgA 0.09 g/L. Based on clinical symptoms and immunological evaluation diagnosis of CVID was confirmed, and replacement therapy with subcutaneous immunoglobulin (400 mg/kg/month) was initiated. After six months of treatment patient affirmed reduction of gastrointestinal symptoms; he gained 12 kg of weight, has no more infections and stable sufficient level of IgG (7.9 g/L).

**Conclusions:** This clinical case shows the importance of immune testing for primary immunodeficiency in all subjects (despite age) with unusual symptoms of autoimmune and/or infectious disorders. CVID may have manifestation of various symptoms, which can lead to misdiagnosis, as well as inadequate treatment.

## 1529 | Reversible secondary hypogammaglobulinemia related to anticonvulsant therapy in adult patients: A report of three cases

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**Case report:** Reduction of Immunoglobulin (Ig) levels related to anticonvulsant therapy that result in recurrent infections have been described. The objective of this study is to report three adult patients who evolved with hypogammaglobulinemia and normal lymphocyte populations after anticonvulsant therapy and normalization of Ig levels and improvement in clinical status after drug suspension. *Patient 1*: A 24-year-old man with absence seizures was treated with phenytoin. In a subsequent period of 12 months, he begun to present sinopulmonary infections and severe diarrhea. Ig levels (g/dL) were IgG:348, IgA:3, IgM:27. Monthly IVIG was indicated, as well as substitution of phenytoin with carbamazepine. Patient presented a progressive improvement in clinical status and Ig levels (IgG:749, IgA:160, IgM:93) normalized after a 48-month period following phenytoin withdrawal. *Patient 2*: A 46-year-old woman with left brachial palsy, Horner's syndrome and convulsive seizures requiring the use of carbamazepine. Six months later she developed chronic diarrhea, sinopulmonary infections and herpes zoster infection. Ig levels were IgG:450, IgA:14 and IgM:11. Monthly IVIG replacement was indicated as well as carbamazepine suspension. Three years later, IVIG infusion was suspended due to normalization of Ig levels (IgG: 892, IgA: 218 and IgM: 51.9). *Patient 3*: A 54-year-old man, alcoholic, evolving with seizures after alcoholic libation, was treated with lamotrigine. Six months after starting treatment he presented severe bronchopneumonia with no therapeutic response. On the occasion, Ig levels were IgG:234, IgA:26, IgM:4 and IVIG replacement was indicated. The patient evolved with absence of infections and progressive normalization of Ig levels (IgG:1094, IgA:75.4 and IgM 81.6) and nine months after, IVIG replacement was suspended.

IgA and IgM deficiencies related to anticonvulsant therapy that result in recurrent infections have been described whereas decreased serum IgG levels have been reported in a few studies and isolated clinical cases. The pathophysiological mechanisms of the hypogammaglobulinemia secondary to these type of drugs are not completely understood and several studies show the possibility of reversion after its suspension, mainly in childhood. We conclude that the reported disorders of immunoglobulin production were triggered by the introduction of anticonvulsants, evolving with less common complete remission after drug withdrawn in three adult patients.

## 1530 | Evolution of patients with hypogammaglobulinemia secondary to the use of Rituximab accompanied in a tertiary outpatient clinic

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**Introduction:** Rituximab (RTM) is a specific monoclonal antibody directed to B cells (anti-CD20). It is used to treat lymphoproliferative disorders and selected autoimmune disorders. Prolonged B cell depletion is associated with the risk of adverse effects, including hypogammaglobulinemia, increased risk of infections, failure to develop immune responses after vaccination and neutropenia.

**Objective:** To evaluate the evolution of patients with hypogammaglobulinemia secondary to the use of RTM in the Clinical Immunology and Allergy Service of HC FMUSP.

**Method:** Retrospective study with review of medical records and laboratory exams of nine patients who underwent MTR and presented hypogammaglobulinemia in the years 2004-2017.

**Results:** In our sample, all patients who progressed to hypogammaglobulinemia were receiving lymphomas. There is no immunoglobulin dosage record prior to treatment. Of the 9 cases, mean age was 52 years (4 men and 5 women), 2 lost follow-up, and 1 of them also presented neutropenia. Seventeen patients who continued in follow-up required IVIG replacement, due to infectious exacerbations, mainly pneumonia and sinusitis. The mean serum IgG dosage at the time of onset of IVIG replacement was 491 g/dL. The mean time between the first dose of RTM and the need for IVIg replacement ranged from 2 to 8 years, with an average of 5 years. The IgA dosage was used as a parameter for the recovery of hypogammaglobulinemia, and it was observed that only 1 of the 7 patients presented recovery of the condition up to the moment.

**Conclusion:** Given the data, we considered the immunoglobulin dosage to be important before initiating RTM treatment and periodically, in order to indicate the replacement of IVIg or IgSC in a timely manner avoiding complications such as potentially serious infections.

## 1531 | Myotonic dystrophy and hypogammaglobulinemia: Case report

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**Background:** Steinert's disease, also known as type 1 myotonic dystrophy (MD1), is the most common dystrophy of the adult. It is inherited with an autosomal dominant mechanism. It causes myotonia, progressive muscles atrophy, muscular weakness, and problems at the heart's conduction tissue and at the respiratory muscles. In patients with myotonic dystrophy, hypogammaglobulinemia is frequently described. The associations and the pathogenesis between those affections are not totally clear, but it is recognized an increased catabolism of the immunoglobulin in these patients. In most of the cases, hypogammaglobulinemia affects only the IgG class and does not become clinically manifest. However, replacement treatment is not always successful in these patients. We report the case of a patient with myotonic dystrophy and hypogammaglobulinemia.

**Case report:** A 44-years-old man with MD 1 came to our attention for a history of recurrent infections of the upper respiratory tract and persistent infection by Helicobacter pylori. At the laboratory tests, we documented low serum IgG levels (449 mg/dL), normal IgM and IgA levels and protective antibodies against tetanus consisting with the diagnosis of hypogammaglobulinemia. Due to the recurrent infections, he started replacement therapy with IVIg (0.4 g/kg/months), switched one year ago to facilitated subcutaneous Ig (fSCIg) with achievement of protective serum IgG levels (>600 mg/dL) and significantly reduction of infectious episodes.

**Conclusion:** Hypogammaglobulinemia is frequently reported in patients with MD1. In literature most of the cases described does not become clinically manifest, but in our case, the patient was symptomatic with recurrent infections. The replacement therapy with fSCIg showed both clinical effectiveness and safety.

## 1532 | Real-world experience of a novel, highly purified 10% liquid iv human immunoglobulin for the treatment of antibody deficiencies

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**Background:** Primary immunodeficiencies (PID) and secondary antibody deficiencies (SAD) are a heterogeneous group of diseases, which increase susceptibility to infection. The mainstay of treatment is immunoglobulin replacement therapy (IgRT), which is recommended by the UK Department of Health (DoH) for patients with PID and SAD who fulfil criteria laid out in the DoH Clinical Guidelines for Immunoglobulin Use (July 2011). A highly purified 10% liquid iv human immunoglobulin (Ig), with low levels of IgA, anti-A and anti-B haemagglutinins, factors XIa, XIIa, kallikrein and aggregates (I10E) was recently approved for use in the UK. Here I report our centre's experience in using this novel 10% I10E in three patients with antibody deficiencies.

**Case presentations:** A patient who presented in clinic with a first diagnosis of PID, was initiated on 10% I10E at 30 g infused every four weeks. After starting I10E, they experienced a decrease in the rate and frequency of infections, in line with expectations for IgRT.

A young patient on home therapy with a 20% subcutaneous Ig for PID presented in clinic with low trough IgG levels. Non-compliance was identified as the cause of these low trough levels and therapy was switched to 10% I10E at 40 g infused every four weeks in a clinical setting. Both the rate and severity of infections reduced and trough IgG levels normalised.

An older patient on IgRT for SAD was reviewed in clinic due to discontinuation of their current IgRT product. They were switched to 10% I10E at 20 g infused every four weeks. The efficacy and tolerability of I10E was comparable to their previous therapy.

A detailed analysis of patient, clinical and safety parameters associated with the initiation of 10% I10E will be presented, including infection rates, white cell counts, C-reactive protein levels, tolerability and infusion-related adverse events.

**Conclusion:** These cases highlight the real-world use of 10% I10E in two patients with PID and one patient with SAD. They show that I10E was well-tolerated and efficacious in one treatment-naïve, and two previously-treated patients.

## 1533 | Hereditary angioedema family testing status in the northern area of Spain

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**Background:** Hereditary angioedema with C1 Inhibitor deficiency (C1-INH-HAE) is a genetic disease caused by SERPING1 gene mutations. Often patients with C1-INH-HAE have been misdiagnosed before being diagnosed with C1-INH-HAE and suffer long delays in diagnosis.

**Objective:** To know the status of diagnosis of family members of patients with C1-INH-HAE in the Northern area of Spain and difficulties that arise for a correct and extended family tree

**Method:** Prospective study of families with one or more members with C1-INH-HAE followed in 7 hospitals in the northern area of Spain. A cohort of 105 patients from 28 families with C1-INH-HAE was evaluated for familiar diagnosis of C1-INH-HAE

One or several patients from the same family were chosen and were given a questionnaire to identify the total family members from the family branch affected by C1-INH-HAE that had been already studied (members with diagnosis of C1-INH-HAE and healthy members) and those that had not been previously studied. We also register the difficulties for obtaining these data.

Family members not previously studied and that consent to be contacted were asked for study of C1-INH-HAE. For C1-INH-HAE screening we use C4 blood levels

**Results:** We have studied 28 families with C1-INH-HAE, 24 (87%) type 1 and 2 (7%) type II; 13 families had all their known members already studied for C1-INH-HAE (50%): 12 families have all their members studied (42.8%), 18 families have 90% or their known members studied (64.2%) and 10 families had less than 50% of their total known members studied.

We have identified 85 members from 11 unrelated families that had not been previously studied for HAE, 10 healthy, 4 had low C4 levels and had presented symptoms of HAE; 1 had not presented symptoms of angioedema, had normal C4 levels, and low antigenic and functional C1-INH levels.

Difficulties for a complete family testing study have been: Family dispersion, scarce or no family relationship, do not wish to know their possible pathology

**Conclusion:** It is crucial to insist on the study of the relatives of patients with HAE. We propose to include a questionnaire to identify all patient's relatives at medical reviews of HAE patients.

## 1534 | Clinical and genetic profiles of patients with X-linked agammaglobulinemia from southeast Turkey

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**Background:** X-linked agammaglobulinemia (XLA) is characterized by absent or severely reduced B cells, low or undetectable immunoglobulin levels and clinically by extracellular bacterial infections which mainly compromise the respiratory tract. We aimed to analyze the clinical, immunologic and genetic characteristics of 22 children with XLA.

**Method:** Twenty two children with XLA from 12 unrelated families were enrolled in this study. Clinical and demographic features of patients, serum immunoglobulin levels, percentage of B cells and *BTK* gene mutations were reviewed retrospectively.

**Results:** We identified 12 different mutations in the *BTK* gene in 22 patients including 3 missense mutations, 4 premature stop codons, 3 splice-site mutations, 2 small nucleotide deletions. Eleven mutations had been reported previously including three missense mutations (c.1774T>C, c.1684C>T, c.83G>T), three premature stop codons (c.1558 C>T, c.753G>A, c.1573C>T), two splice-site (c.683-1G>A, c.1567-12_1567-9delTTTG) and two small nucleotide deletions (c.902-904_delAAG, c.179_181delAGA). Two novel mutations of the BTK gene were also presented and they included one splice-site mutation (c.391+1G>C) and one premature stop codon mutation (c.1243_1243delG). Six out of 12 mutations of the BTK gene were located in the SH1 domain, two in the PH domain, two in the SH3 domain and two in the SH2 domain. Three patients had a history of severe infection before diagnosis.

**Conclusion:** Our results show that mutations in Southeast Turkey could be different from those in the rest of the world, necessitating comprehensive studies in our country.

## 1535 | Vedolizumab treatment in patient with XLA, is it safe and efficient?

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**Background:** X-linked agammaglobulinemia (XLA) is caused by a B lymphocyte differentiation arrest associated with mutations in the *BTK* gene located on the long arm of the X chromosome. Patients with XLA are generally considered to have a low risk of autoimmune or inflammatory disease compared to other PID.

**Case:** A- 4 year old boy was admitted to our clinic with the history of recurrent respiratory tract infections. His all immunoglobulins were low (IgG <154 mg/dL, IgA <25.4 mg/dL, IgM <17.8 mg/dL) associated with the absence of B cells. His aunt cousin also had XLAA missense point mutation, c562C>T in exon 17 of the Btk gene was identified in both affected cousins. The patient was commenced on regular IVIG treatment every 3 weeks. At the age of 8, he suffered from intermittent fever attacks, abdominal pain and weight loss. Tests for giardia lamblia, clostridium difficile and cryptosporidium, noro virus or parasites were negative. MR-enterography revealed intra-abdominal fluid and thickened walls of his jejunum and cecum. Histopathological examination of the biopsy material obtained from terminal ileum, colon and cecum showed crohn disease. Initially, he was treated with prednisolone and infliximab. Because of the lack of response, infliximab treatment was switched to adalimumab. Terminal ileum was resected to relieve obstruction complication. Although he had been treated with adalimumab for 1 year, a significant improvement was not observed. Vedolizumab (Entyvio™), is a humanized monoclonal antibody $\alpha 4\beta 7$ integrin-receptor antagonist, was commenced. Induction dosing was 300 mg infusions at 0, 2, and 6 weeks followed by a maintenance phase at 8-week intervals. At the 6 month of the treatment, fever and

abdominal pain attacks reduced, while his weight and oral intake increased. No side effects were observed.

**Discussion:** Vedolizumab is effective for inducing and maintaining remission in adults with inflammatory bowel disease (IBD); however, there is limited pediatric data. This is the first immunocompromised child treated with vedolizumab. The symptoms of the patient receded and no side effect observed during 6 months of the treatment.

## 1536 | Wiskott Aldrich syndrome. Hypersensitivity to betalactams associated

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**Case report:** We present a case of Wiskott Aldrich syndrome. It is a well known genetic recessive disorder linked to the X chromosome which mainly affects male patients, typically during childhood. Its incidence is 1 in 250 000 males born alive and it is caused by the mutation of a gene that encodes the wiskott aldrich syndrome protein (WASp). Physiopathologically, the defect of this protein alters the immunological synapses at the site of interaction between lymphocytes and cells presenting the antigen. The resulting deficiency of T lymphocytes perturbs the homeostasis of B lymphocytes, reducing the number of mature B lymphocytes. Thrombocytopenia is caused by an increased clearance, during an ineffective thrombocytopoiesis. The possible phenotypic variants are 3: classical, X-linked chromosome thrombocytopenia, X-linked neutropenia. Eczema appears in 50% of patients during the first year of life with a typical atopic dermatitis clinic. Our patient has been sent to an allergological clinic in adulthood due to the presence of recent-onset generalized eczema. From infancy in treatment with gamma globulins ev at three-weekly intervals. In the past there have been reactions to gamma globulin infusion. A hypersensitivity reaction to betalactamic drugs (piperacillin/tazobactam) with rash during hospitalization for bronchopneumonia has occurred. There is a mild, clinically irrelevant thrombocytopenia, whereas neutropenia was well corrected by administration of growth factors (Filgrastim).The patient is in chronic therapy first with bactrim, then with atovaquone for trimethoprim hepatotoxicity. Moreover he is in chronic therapy with acyclovir. IgA values: 0.25, IgG 7.44, IgM 0.38. Normal values of the subclasses IgG 1 and 2, while IgG 3 reduced: 0.12. Numerous episodes of bronchopneumonia, with hospitalization (10). Numerous episodes of sinusitis. Two male cousins had a similar manifestation of immunodeficiency. Other two male cousins died in infancy without diagnosis. A survey using prick does not show any positivity for inhalant or food allergens. A patch test with standard series highlights only sensitization for dye. The eczematous lesions have been classified as an atopic eczema of the adult, associated with the syndrome. The history of hypersensitivity to betalactam is going to be investigated by RAST. Skin tests and challenges aimed at verifying the tolerability of cephalosporins and carbapenems have been already programmed.

## 1538 | A novel variant mutation identified in the STAT1 gene in a patient with fungal and sinopulmonary infections

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**Introduction:** Chronic mucocutaneous candidiasis(CMCC) is a heterogeneous collection of rare genetic disorders, typically characterized by noninvasive mucocutaneous candida infections and associated autoimmune manifestations. Gain-of-function mutations in signal transducer and activator of transcription(STAT1) have been shown to cause autosomal-dominant or sporadic cases of CMCC. Here we report a novel variant mutation in the STAT1 gene, identified through whole exome sequencing(WES).

**Case Presentation:** A 32 year old female presented with a history of undifferentiated connective tissue disease, antiphospholipid syndrome, stroke, mucocutaneous candidiasis in infancy, recurrent thrush, sinopulmonary infections and bronchiectasis with deteriorating pulmonary function. Her immune evaluation was remarkable for an elevated IgG(1880 mg/dL), and abnormal lymphocyte antigen studies with absent proliferative response to *Tetanus toxoid* although normal proliferative response to *Candida*. The remainder of her evaluation including IgA, IgM, IgE, complement studies, specific antibodies(to *Streptococcus pneumoniae*, *Haemophilus influenza B*, *Tetanus toxoid and Diphtheria*), lymphocyte subsets, lymphocyte proliferation to mitogens, was within normal range. HIV serologies and complete rare mutation analysis for cystic fibrosis were negative, nasal brushing for Primary Ciliary Dyskinesia was non-diagnostic. A fungal culture of a recent rash grew rare *Rhodotorula mucilaginosa*, additional skin biopsy revealed *Tinea versicolor*.WES was performed, revealing the heterozygous presence of the de novo c.1169 T>G likely pathogenic variant in exon 14 in the STAT1 gene and the heterozygous presence of two RBCK1 variants, c.1189 G>A and c.11 C>A of uncertain significance. The patient was subsequently treated with ruxolitinib.

**Conclusion:** To our knowledge, the de novo c.1169 T>G variant has not been previously reported as a pathogenic variant nor as a benign variant. In silico analysis predicts this variant is probably damaging to the protein structure/function. Missense variants in the same residues have been reported in individuals with STAT1-related disorders. Functional studies are needed to determine the actual effect of the c.1169 T>G change. This case report adds to the literature the identification of de novo c.1169 T>G variant with a clinical presentation of fungal and sinopulmonary infections in an individual with antiphospholipid syndrome and undifferentiated connective tissue disease.

## 1540 | DiGeorge syndrome in neonatal and infant children

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**Background:** Evaluation of clinical and morphological changes in children with DiGeorge syndrome.

**Method:** The retrospective study included 7 children with DiGeorge syndrome confirmed postmortem who were hospitalized at the Mother and Child Institute in the period 1991-2017. Children age was from 2 days to 5 months, including 2 children who died in the early neonatal period at the age of 2-3 days; the ratio of boys:-girls was 4:3.

**Results:** In this paper we present the clinical and morphological analysis of children with DiGeorge syndrome diagnosed post-mortem. Clinically were predominantly the generalized intrauterine infections or their development in the postnatal period.

The DiGeorge syndrome in pathomorphological investigation is characterized by thymus agenesia and parathyroid glands, sometimes with severe thymic hypoplasia. Samples taken from the thymus lodge consisted of connective tissue and adipose tissue. Peripheral lymphoid tissue, especially in the spleen and lymph nodes, was morphologically characterized by severe depletion of lymphocytes.

These children also had various stigmas of dysembriogenesis, such as low position of the auricles, hypertelorism, micrognathia, high palatine arches, palatoschisis and various congenital malformations, mainly heart defects.

**Conclusion:** The DiGeorge Syndrome is a severe primary immunodeficiency with parathyroid hypoplasia, which manifests at an early age with generalized infections, seizures and a high risk of death in the neonatal and infantile period.

## 1541 | Pulmonary infections in primary immunodeficiencies to children

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**Background:** The research the etiology of pulmonary infections to children with primary immunodeficiencies (PID).

**Method:** Study includes 10 children with PID, presenting syndromes of lung infection. The diagnosis of PID was confirmed by determining the IgA, IgM, IgG in the serum, CD lymphocyte populations. Immunological research of children with recurrent pulmonary infections, purulent pleural and lung complications, allowed diagnosis these PID syndromes: 4 children with Bruton agammaglobulinemia, 3 children with Luis Bar syndrome, 2 children Wiskott Aldrich syndrome and one child with DiGeorge syndrome.

**Results:** Children with Bruton disease were diagnosed by agammaglobulinemia, severe deficiency of IgA, IgM, IgG. These patients had severe lung purulent infection, empyema, purulent meningitis, osteomyelitis, mastoiditis, otitis. Bruton disease in a child occurred sepsis with multiresistant *Ps.aeruginosa* with death at the age of 8 years. Children with Luis Bar syndrome they had recurrent bronchitis, pneumonia and bronchiectasis. Two children with Luis Bar syndrome died to pulmonary sepsis caused by *Ps.aeruginosa*, MRSA, fungal infections. Wiskott Aldrich syndrome was confirmed in 2 infants 4-6 months through mutations of the WASP gene and trombocitopenie, hyperIgE, eczema, lung infection with *Pneumocystis jiroveci*, *S.aureus*, *Candida*. The child with DiGeorge syndrome died at the 1 age from pulmonary sepsis, due to nosocomial infections.

**Conclusion:** Primary immunodeficiencies in children evolves with pulmonary infections due to multiresistant pathogens.

## 1542 | Polymorphism of pulmonary manifestations in children with Louis bar syndrome

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**Background:** Evaluation of the pulmonary manifestations in children with Louis Bar syndrome.

**Method:** The study included 3 children with a diagnosis of PID Louis Bar. The children were examined clinically, radiological, immunological. In one of the children the molecular-genetic research identified the mutations in c.1564_1565del/p.(Glu Ilefs 522*43).

**Results:** Louis-Bar syndrome is a multisystem progressive disease with polymorphic manifestations which varies by age. The locomotor disability of these children is determined by neurological disorders, the exitus being caused by respiratory infectious and malignancies. The children involved in the study, had frequent episodes of respiratory infectious (bronchitis, pneumonia, atelectasis, empyema, lung abscess), ENT infections (otitis, mastoiditis, sinusitis), chronic pulmonary disease (pulmonary fibrosis, bronchiectasis). Index of death in this group is high (66.7%). In one of the boy, the pulmonary CT showed lymphadenopathy, later was confirmed Non-Hodgkin lymphoma, with subsequent death. Another child died from pulmonary and systemic infectious complications.

**Conclusion:** In children with PID Louis Bar clinical manifestations are dominated by polymorphic respiratory syndromes—pneumonia, pleurisy, abscesses, bronchiectasis, pulmonary fibrosis, malignancies, which determine the risks of death in childhood.

## 1545 | Nezelof syndrome in children: Morphological and immunohistochemical study

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**Background:** In this thesis we propose to present 6 patients diagnosed with post-mortem Nezelof syndrome and the morphopathological changes determined.

**Method:** The retrospective descriptive study included 6 children with Nezelof syndrome confirmed post-mortem who were hospitalized to the Mother and Child Institute between the years 1991-2017. The age of the children was up to 5 months. Material and methods of morphological research have served tissue specimen taken from all internal organs, including thymus, spleen, lymph nodes.

**Results:** In this paper we present the clinical and morphological analysis of children with Nezelof syndrome diagnosed post-mortem. Clinically were predominantly the generalized intrauterine infections or their development in the postnatal period.

At macroscopic examination all patients had thymic hypoplasia. Later on the microscopic study of the thymus specimens determined dysplastic changes, defined by the presence of concentrically arranged epithelial cells. In all patients, was determined the total lack of Hassall corpuscles and its predecessors. Besides the above-mentioned modifications in all specimens, there was no cortico-medullary segregation. Thymic parenchyma outside pseudorrhagia was made up of a reticular stroma with total lymphocyte depletion.

**Conclusion:** Nezelof syndrome is a severe primary immunodeficiency associated with thymic dysplasia and alymphocytosis, which is manifested early with generalized infections and major risk of death in neonatal and infant.

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## 1546 | Innate and adaptive immunity cytokines in nasal mucosa and blood serum of allergic rhinitis patients

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**Background:** The study was aimed to evaluate the cytokine profile in nasal secretion and blood serum in patients with seasonal (SAR) and perennial allergic rhinitis (PAR) with a potential for additional sensitization with microbial allergens.

**Method:** The inclusion criteria for AR were as follows: a diagnosis of AR for more than 2 years, the absence of nonallergic disorders of the nasopharynx, age of patients from 4 years to 60 years.*Control Group*: healthy volunteers at the age of 3-43 years without any allergic disorders at examination.In order to evaluate the innate and adaptive immunity, the cytokine profile of blood
serum (IL-4, IL-10, and TGF-$\beta$) and nasal secretion (TSLP, IL-1$\beta$, TNF-$\alpha$, and GM-CSF) was determined. To determine TSLP, TGF-$\beta$, IL-10, and GM-CSF concentrations, enzyme-linked immunosorbent assay kits were used (eBioscience, Bender MedSystems, R&D Systems, MN, USA).

**Results:** We have noticed a significant correlation ($r$ = 0 46, $P$ = 0 014) between the TSLP concentration in nasal secretion and as- IgE level to *Staphilococcus aureus* enterotoxin (allergen component m80) in patients with PAR. There was a significant correlation ($r$ = 0 56, $P$ = 0 008) between TSLP and GM-CSF cytokine concentrations in nasal secretion of these patients.There was a significant correlation between TSLP cytokine concentrations in nasal secretion and those in as- IgE to the allergen component m3 of *Aspergillus fumigatus* in the patients with SAR ($r$ = 0 43, $P$ = 0 023). GM-CSF cytokine is produced by upper airway epithelial cells in an allergic inflammation. There was a significant correlation ($r$ = 0 58, $P$ = 0 007) between GM-CSF concentrations in nasal secretion and those in as-IgE to the allergen component d1 of *D. pteronyssinus* in patients with PAR.

**Conclusion:** Staphylococcal superantigens might be one of the stimuli of local TSLP hyperproduction by the epithelium. There was a significant correlation between GM-CSF concentrations in nasal secretion and the intensity of sensitization to a staphylococcal enterotoxin (SEB) in the patients with AR. SEB is one of the polyclonal T cells activators, which may account for increased concentrations of cytokines such as GM-CSF locally within the system of mucosal immunity. The patients with AR and additional high sensitization to SEs demonstrated a higher TNF-$\alpha$ production profile due to macrophage and Tcell activation by these toxins.

## 1547 | Evaluation of circulating osteopontin level as potential biomarker of allergic asthma in patients with Caucasian and South-East Asian ethnicity

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**Background:** Osteopontin (OPN) is a pleomorphic cytokine known to influence a wide range of immune cells; allergic asthma was previously associated with high circulating OPN levels. In the present study, we aimed to verify if OPN may qualify as biomarker of activated immune response in allergic patients belonging to two different ethnic groups: Caucasians and South-East Asians.

**Method:** Serum OPN levels were measured by ELISA test (Human Osteopontin Duoset, R&D Systems) in a series of 121 Italian adult patients affected by extrinsic asthma, allergic rhinitis, Hymenoptera venom allergy, food allergy, allergic contact dermatitis and IgE mediated hypersensitivity to beta lactams. 116 healthy subjects served as controls. 576 ethnic Chinese subjects were recruited at the National University of Singapore (NUS) as cross-sectional cohort of an ongoing epidemiological study on the national prevalence of allergic diseases, and OPN levels were detected by Luminex (Milliplex Map, Merck) and ELISA assays (R&D Systems).

**Results:** In the Italian cohort, OPN levels were significantly higher in cases compared to controls ($P$ = 0.0010 by the Mann-Whitney test). Statistically higher OPN levels were found in asthma ($P$ = 0.0269) and food allergy ($P$ = 0.046) groups in comparison to controls. No significant differences were found ($P$ = 0.597) between Singaporeans with lifetime asthma and healthy controls, only the highest OPN levels were heterogeneously found to correlate with asthma. However, a strong gender effect was shown, in both cases ($P < 0.0001$) and controls ($P < 0.0001$), with males presenting higher OPN levels in comparison to females. Consequently, we checked the mRNA expression levels of OPN gene (SPP1) with Illumina chips in whole blood of males and females, and no difference was found

($P < 0.05$). Several experiments with Western Blots and different gel types were performed to verify if possible post-transcriptional/post-translational modifications of OPN could explain these findings.

**Conclusion:** OPN seems to be a promising biomarker for current, active allergic asthma in Caucasians even though technical difficulties, due to OPN intrinsically disordered structure, the complex enzymatic metabolism, and the low circulating levels, significantly affect the experiments. Further studies are needed to confirm these data.

## 1548 | Mortality, intubation, and healthcare cost in patients with allergic bronchopulmonary aspergillosis in a hospital setting: A nationwide study

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**Background:** ABPA is a complex hypersensitivity reaction to Aspergillus fumigatus that colonize in airways, it is almost exclusively seen in patients with asthma or cystic fibrosis(CF). This study is to estimate hospitalization outcomes and healthcare cost of hospitalized patients with ABPA.

**Method:** We conducted the study using data from National Inpatient Sample(NIS) from 2010 to 2014. Diagnosis were identified using ICD-9-CM codes. Hospitalization with a primary diagnosis of ABPA and hospitalization with a primary diagnosis of acute respiratory failure/acute and chronic respiratory failure/respiratory distress/asthma/CF and a secondary diagnosis of ABPA were included. The study population was divided into groups including ABPA with asthma, and ABPA with CF. Mortality and intubation rate were the primary outcomes; length of stay and total hospitalization cost(adjusted to cost in 2014 based on medical care CPI) were secondary outcomes. Student t-test and Chi-square were used for univariable analysis, linear and logistic regression were used for multivariable analysis.

**Results:** A total of 6308 hospitalizations with ABPA were included, with 2896 hospitalizations with ABPA and asthma, and 2793 hospitalizations with ABPA and CF. The overall mortality rate was 0.82% (95% CI: 0.44%-1.50%), the mortality for ABPA with asthma was 0.69% (95% CI: 0.26%-1.83%) and for ABPA with CF was 0.56% (95% CI: 0.19%-1.63%). The overall intubation rate was 4.83% (95% CI: 3.77%-6.18%); the intubation rate for ABPA with asthma was 5.51% (95% CI: 3.91%-7.72%) and 84.0% were early intubation (<3 days); the intubation rate for ABPA with CF was 1.95% (95% CI: 1.13%-3.35%) and 36.6% were early intubation. The overall mean length of stay(LOS) was 8.7 (95% CI: 8.0-9.3) days, while the LOS for ABPA with asthma was 5.6(95% CI: 5.2-6.1) days and the LOS for ABPA with CF was 12.1 (95% CI: 11.1-13.0) days. The overall total cost was 147 million USD, the total cost for ABPA with asthma was 33.4 million USD with a mean of 12 069, while the total cost for ABPA with CF was 101 million USD with a mean of 38 005.

**Conclusion:** Mortality among hospitalized patients with ABPA is low<1%. Intubation rate is relatively low, intubation, especially early intubation (<3 days), is more common in patients with asthma. Although ABPA is not a common disease in inpatient population, it does have a high health care cost and despite lower intubation rate, patients with ABPA and CF generally have a longer hospital stay with a higher hospitalization cost.

## 1549 | Frequent exacerbations of bronchitis with wheezing in adults: Is it possible to predict and prevent asthma?

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**Case report:** Frequent episodes of bronchitis, accompanied by wheezing and dry with a prolonged duration in adults, the clinical course may be similar to bronchial asthma.

The aim is to assess the risk of asthma in adult patients with 2 or more episodes of acute bronchitis per year, had a prolonged duration and accompanied by a dry wheezing.

For 5 years in two regional clinical pulmonology centers were observed in 46 patients (19 men and 27 women) with average age 34 ± 6.8 years. Each had at least 2 episodes of acute bronchitis per year, which was accompanied by prolonged cough and presence of wheezes. Average number of acute episodes per year was 3.2 ± 0.8.

In the course of the observation the patients were divided into 2 equal groups. The first group consisted of 23 persons treated in acute episodes of the disease symptomatic therapy, including inhaled β2-agonists short-acting short course. In the second group to the corresponding treatment added montelukast 10 mg per day lasting for 1 month. In all cases of exacerbation had a viral nature. Held in the period of remission of allergic sensitization, the survey revealed. Starting from the first year of follow-up all patients were vaccinated against influenza annually.

By the end of the fifth year of observation in the first group in 5 cases was diagnosed of bronchial asthma—4 cases easy persistent asthma and 1 case moderate. The diagnosis was exhibited in accordance with the GINA criteria. In the second group, the diagnosis of bronchial asthma were exposed to 1 patient (hazard ratio of 0.18).

Prospective observation suggests that the use of anti-inflammatory potential antileukotriene medicines in complex therapy of recurrent acute episodes of bronchitis accompanied by a dry wheezing in adults may be a factor preventing the development of asthma. For more conclusive results require more extensive research.

## 1553 | Expression of chemokine receptors CXCR3 and CCR5 is up-regulated on NK and NKT cells of patients with chronic obstructive pulmonary disease

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**Background:** Chemokine receptors play an important role in regulating the migration of T lymphocytes, monocytes and neutrophils from the peripheral blood into inflamed tissue, such as lung. However, little is known about their expression on natural killer (NK) and natural killer T (NKT) cells in patients with chronic obstructive pulmonary disease (COPD). Therefore the aim of the study was to determine the chemokine receptor profile of peripheral blood NK and NKT cells of COPD patients.

**Method:** For analysis of lymphocytes subtypes the flow cytometry method was used. The study population consisted of 57 smokers with COPD, 12 healthy smokers and 12 healthy non-smokers.

**Results:** We observed an increase in blood NK cells expressing CXCR3 receptors in smokers with COPD compared to healthy smokers ($P = 0.003$) and healthy non-smokers ($P < 0.001$). The percentage of NKT cells containing CXCR3 receptors was also significantly higher in blood of smokers with COPD compared to healthy smokers ($P = 0.021$) and healthy non-smokers ($P < 0.001$). COPD smokers had significantly higher proportion of $CCR5^+$ NK cells than smokers without COPD ($P = 0.002$) and healthy non-smokers ($P < 0.001$). Increased proportion of blood NKT cells expressing CCR5 on their surface was observed in smoking COPD patients compared to healthy smokers ($P = 0.002$) and healthy non-smokers ($P < 0.001$). There were no significant changes in the percentage of $CXCR3^+$ and $CCR5^+$ NK and NKT cells between healthy smokers and non-smokers. In addition, no differences were seen in the proportion of NK and NKT cells expressing CXCR4, CXCR6, CCR6 and CCR7 among all studied groups.

**Conclusion:** Our findings indicate smoking-independent alterations in expression of chemokine receptors CXCR3 and CCR5 on blood NK and NKT cells in patients with COPD.

## 1554 | IL-26 as a new biomarker of inflammation in obese and non-obese COPD patients

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**Background:** Th17 cells participate in antibacterial protection in the pulmonary tissue, contributing to the accumulation of neutrophils and macrophages in inflammation. Interleukin-26 (IL-26) participates in the development and maintenance of inflammatory process being a member of the IL-10 cytokine family expressed by T-cells, mononuclear cells, natural killer cells (NK). This study assesses the levels of IL-26 in induced sputum in COPD patients stratified by body mass.

**Method:** 58 patients with COPD in stable condition (GOLD stage 2) aged 40-70 years old, smoking history of ≥10 pack-years, were studied. BMI of patients were divided into 2 groups: obese (n = 31) (BMI—30.0-39.9 kg/$m^2$) and non-obese (n = 17) (BMI—18.5-24.9 kg/$m^2$). Ten subjects with normal lung function and BMI were the control group. The level of IL-26 assessed in induced sputum (pg/mL) was measured using an ELISA (RayBiotech®). Serum levels of CRP were measured using the "Vector-Best" (Russia Federation). Spirometry was performed according to American Thoracic Society and the European Respiratory Society (ATS/ERS) guidelines.

**Results:** Obese COPD patients had significantly increased concentrations of IL-26 compared with healthy subjects and non-obese COPD patients by 2.6 fold (139.0 ± 85.4 pg/mL vs 53.15 ± 18.5 pg/mL) ($P < 0.008$) and 1.15 fold, (139.0 ± 85.4 pg/mL vs 120.6 ± 60.15 pg/mL)($P < 0.04$), respectively. Non-obese COPD patients had higher levels of IL-26 by 2.3 fold compared with healthy subjects (120.6 ± 60.15 pg/mL vs 53.15 ± 18.5 pg/mL) ($P < 0.008$). IL-26 levels correlated with BMI ($r = 0.31$; $P = 0.02$), serum CRP levels ($r = 0.35$, $P = 0.007$), FEV1 ($r = -0.39$; $P = 0.002$) and FEV1/FVC ($r = -0.29$; $P = 0.02$).

**Conclusion:** The levels of IL-26 in induced sputum were greater in obese COPD patients than non-obese COPD patients and healthy subjects. IL-26 may serve as a biomarker for determining inflammation in the lung tissue in both obese and non-obese COPD patients.

## 1556 | The value of immune factors in monitoring the risk of patients with interstitial lung disease developing into lung cancer

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**Background:** Interstitial lung disease (ILD) presented to patients with a higher risk of development of lung cancer. This research evaluated the diagnostic effect of serum immune factors, which estimated the risk of ILD patients developing into lung cancer.

**Method:** The studied included 262 lung cancer patients, 220 ILD patients and 57 healthy individuals. Detection of the level of serum immune factors including C3, C4, IgA, IgG, IgM, C-reactive protein (CRP), ceruloplasmin (CER) and Rheumatic factor (RF) was carried out for each studied subject.

**Results:** Among these three groups, the level of CER in lung cancer patients (0.35 ± 0.10 g/L) was significantly higher than that in ILD

patients (0.31 ± 0.25 g/L) and healthy individuals (0.25 ± 0.04 g/L) ($P < 0.05$). Meanwhile, the levels of C3 and C4 in healthy individuals, which are 1.70 ± 0.29 g/L and 0.27 ± 0.34 g/L respectively, were both significantly higher than that in lung cancer patients (C3: 1.04 ± 0.26 g/L, C4: 0.24 ± 0.09 g/L) and ILD patients (C3: 0.97 ± 0.25 g/L, C4: 0.21 ± 0.09 g/L), (C3: $P < 0.05$, C4: $P < 0.05$). Results from optimal scaling demonstrated that lung cancer was closely associated with immune factors including CRP, CER, C3 and C4 (Cronbach's Alpha = 84.7%).

**Conclusion:** For ILD patients, when the level of CRP and CER is increased and the level of C3 and C4 is decreased simultaneously, the risk of the development of lung cancer should be considered for these patients.

## 1558 | Impact of endurance training by elite athletes on immune cell subpopulations and vitro secretion of immunoregulatory cytokines

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**Background:** Prolonged strenuous endurance exercise may impact cytokine production by PBMC which leads to immune dysregulation The influence of different types of sports (bobsled, biathlon and bullet shooting) on immune cell subpopulations and pro- and anti-inflammatory cytokine synthesis was assessed.

**Method:** 153 elite athletes of both sexes specializing in bobsled, biathlon and bullet shooting were examined. Studies were conducted on athletes in the pre-competition period of sports training. The main subpopulations of mononuclear cells in peripheral blood (PBMC) were assessed by flow cytometry (FC-500,Beckman Coulter, USA). Cytokine concentrations (IL4, IL 6, IL 10, IL 18 and IFNγ) were assayed by ELISA.

**Results:** Among PBMC subpopulations, endurance exercises impacted the number of NKT and activated T cells with NKT cell numbers greater in male bobsledders vs bullet shooting and biathlon (42.4% and 44.3%, respectively). The number of activated T cells ($CD25^+$) was greater in bullet shooting and bobsleigh athletes vs the biathlon group (34.9% and 22.7%, respectively). In female athletes the number of $CD25^+$ cells in the shooting and bobsled groups was greater by 46.1% and 25.5%, respectively vs the biathlon group ($P < 0.05$). Increased IL-10 occurred in bobsleds in comparison to bullet shooting and biathlon: 32% and 80% in male and 70.5% and 83% in female, respectively ($P < 0.05$). The concentration of IL-18 in male bobsledders and biathlon was 30% and 34% greater, respectively, compared with bullet shooting ($P < 0.05$). Serum concentrations of IFNγ in male as well as female athletes showed an increase of 41.6% and 39.5%, respectively vs biathletes ($P < 0.05$). Increased IL-4 occurred in the male biathlon group by 39.7% and 13%, respectively, vs the bullet shooting and bobsleigh athletes ($P < 0.05$). IL-6 was increased in the male biathlon group, compared to bullet shooting and bobsledders by 76.7% and 70.3%, respectively ($P < 0.05$).

**Conclusion:** Prolonged endurance exercises impacts secretion of pro- and anti-inflammatory cytokines in athletes of different sport specializations. Concentrations of studied cytokines did not exceed reference values perhaps due to specialized sport nutrition, which may restore immune function during endurance exercises.

TUESDAY, 29 MAY 2018
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IMMUNOLOGICAL AND CLINICAL OUTCOMES OF ALLERGEN IMMUNOTHERAPY

## 1561 | Network-based approach for identifying suitable biomarkers for oral immunotherapy of food allergy

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**Background:** Oral immunotherapy (OIT) is a promising therapeutic approach to treat food allergic patients. Recently, we have shown that the use of a mixture of short-chain- and long-chain fructo-oligosaccharides (scFOS/lcFOS) improves the efficacy of OIT in cow's milk and peanut allergic mice. However, concerns with regard to safety and long-term efficacy of OIT remain and there is a need to identify novel biomarkers (panels) that predict, monitor and/or evaluate the effects of OIT. Here we present a method for the selection of candidate biomarkers by using the computational approaches Bayesian networks (BN) and Topological Data Analysis (TDA).

**Method:** Data were used from scFOS/lcFOS diet-supported OIT studies performed in 2 independent cow's milk allergy (CMA) and 2 independent peanut allergy (PNA) experiments in mice. First, a subset of the data was used for learning the data structure and their interactions in terms of a BN. This BN was used to compare the key parameters in both experimental food allergy models. Finally, the relations within the dataset in combination with the BN were explored to identify and rank candidate biomarkers for the effect of OIT by applying TDA.

**Results:** The BN was able to predict the efficacy of OIT in the CMA and in the PNA model with 82% and 80% accuracy respectively, thereby identifying a set of 5 parameters (allergen-specific IgE and IgG1, body temperature, mMCP-1, earswelling) being key in the mechanisms involved in both scFOS/lcFOS-aided OIT food allergy models. The TDA zoomed in on the full set of 67 previously analyzed parameters and identified clusters of biomarkers closely linked to biologically relevant clinical symptoms but also unrelated and redundant parameters within the network. Taken together, this enables the prioritization of candidate biomarkers. Moreover, the TDA indicated differences between PNA and CMA models in how the data are related to each other.

**Conclusion:** Here we provide promising bioinformatics methods to compare mechanistic features between two different food allergies and to determine the biological relevance of biomarker (panels) of OIT for food allergy. We have shown that the key drivers that influence PNA and CMA are similar, but that these phenotypically similar diseases show mechanistic differences in their subnetworks. These new insights provide excellent starting points to generate new hypotheses to explain why CMA has a different disease pattern than PNA and to select biomarkers that are useful in future clinical studies.

## 1562 | Functional and immunoreactive levels of igg4 correlate with clinical responses during the maintenance phase of house dust mite immunotherapy

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**Background:** The relationship between clinical outcomes and functional responses of allergen specific IgG4 and IgE (sIgG4, sIgE) during immunotherapy is unclear.

**Method:** This study involved 83 patients with allergic rhinitis and/or asthma, of which 52 received a 156-week course of *Dermatophagoides pteronyssinus* (Der p) subcutaneous immunotherapy (SCIT), and 31 received only medications (controls). Symptom and medication scores (SMS), forced expiratory volume in one second ($FEV_1$), airway responsiveness to histamine bronchoprovocation (AHR), Der p sIgG4 levels, Der p sIgE levels and the serum inhibitory capacity against Der p sIgE facilitated allergen binding to B-cells (IgE-FAB) were determined during the updosing (week 0, 4, 12 and 16) and maintenance (week 52, 104, 156) phase of SCIT.

**Results:** SCIT patients had significant improvement in SMS from week 52 to 156 compared to medication-treated control subjects ($P < 0.05$). Levels of Der p sIgG4 in SCIT patients showed a significant increase from week 12 to 156 ($P < 0.05$). Serum obtained from SCIT patients significantly inhibited Der p sIgE binding to B-cells (IgE-FAB) after 16 weeks ($P < 0.01$). Significantly lower levels of Der p sIgE were observed in SCIT patients after 52 weeks ($P < 0.05$). A significant relationship was demonstrated between SMS and IgE-FAB or Der p sIgG4 during the maintenance phase according to linear regression analysis. IgE-FAB had a significant association with AHR only at week 156.

**Conclusion:** Der p sIgG4 level and serum inhibitory capacity against Der p sIgE binding to B-cells (IgE-FAB) are associated with clinical efficacy in the maintenance phase rather than the updosing phase of SCIT. Immunologic tolerance can be induced with SCIT when maintenance phase is achieved.

## 1563 | Basophil activation is driven by the predominant major allergen in AIT treated grass pollen allergic patients: A comparison of BAT using grass pollen extract and recombinant Phl p1 and Phl p5

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**Background:** Grass pollen allergy is a common condition in temperate climate zones. Phl p1 is considered the primary sensitizing allergen of grass pollen, while sensitization to Phl p5 often reaches high levels of allergen component specific IgE later in the course of grass pollen allergy. Allergen specific immunotherapy is an effective treatment of allergic rhinoconjunctivitis and changes in basophil sensitivity may reflect the clinical efficacy.

**Aim of the study:** To study basophil reactivity and sensitivity to grass pollen extract and the major grass pollen allergens Phl p1 and Phl p5 in grass pollen allergic patients 4 years after completion of 3 years of grass pollen SCIT

**Method:** Five grass pollen allergic patients who had completed a 3 year course of SCIT in 2013 and still reported good symptom control during grass pollen seasons were contacted. 100 μL of heparinized blood was incubated with 10 log dilutions of grass pollen extract, recombinant Phl p1 and Phl p 5 respectively, stained with CD193 and CD63, hemolyzed, then analyzed by flow cytometry. Basophils were identified as $SSC^{low}$ $CD193^{high}$, and CD63 was used as an activation marker. Reactivity was confirmed by anti-IgE as a positive control.

**Results:** In 4 patients, basophil reactivity and sensitivity was comparable for grass pollen extract and recombinant Phl p5, while Phl p1 only caused a lower basophil activation. In one patient, recombinant Phl p5 did not cause any basophil activation, while Phl p1 elicited an even higher sensitivity and reactivity than grass pollen extract.

**Conclusion:** In 4 patients, basophil reactivity was comparable for grass pollen extract and recombinant Phl p5, while Phl p1 only caused a minor basophil activation. In one patient, recombinant Phl p5 did not cause any basophil activation, while Phl p1 elicited an even higher sensitivity and reactivity than grass pollen extract. Reactivity of extract and the main sensitizing components correlated, while sensitivity did not.

## 1564 | In vitro assessment of hypersensitivity to allergen before and after allergen immunotherapy with whole blood basophil histamine release assay

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**Background:** Several immunological changes including decrease in quantity and hypersensitivity of basophils and mast cells have provided the effectiveness of allergen immunotherapy (AIT). The purpose of this study was to estimate the whole blood basophil histamine release (WBBHR) assay to evaluate the histamine release (HR) before and after AIT in terms of efficacy of allergen immunotherapy.

**Method:** Seven patients with allergic asthma or rhinoconjunctivitis sensitized to birch pollen confirmed by clinical history and positive skin-prick test results were involved in the study. Patients received first time preseason subcutaneous (s.c.) or sublingual (s.l.) AIT. WBBHR assay in these patients was performed 7-10 days before and 7-10 days after AIT. Heparinized whole blood samples (8 mL) of each patient after substitution of plasma with PIPES buffer were incubated one hour at 37°C with different concentrations of birch pollen extract (T3) in U-shape 96-well micro-titer plates. After incubation plates were centrifuged and supernatants from each well of the plate were directly analyzed for histamine content by reversed-phase high performance liquid chromatography with electro-spray ionization mass-spectrometry (RP-HPLC-ESI-MS). Results were expressed as ng/mL released histamine. Sensitivity (limit of quantification) was 5-7 ng/mL. To compare results of histamine release in patients before and after AIT data were calculated as area under the curve (AUC) values.

**Results:** In contrast to pre-immunotherapy activity of blood basophils there were significant decreases in HR induced by T3 extract after AIT. According to AUC values all patients demonstrated decrease in HR after AIT in compare to HR before AIT in a range of 25%-65% demonstrating a decrease of hypersensitivity to birch allergens. Analysis of basophil HR in patients received s.c. or s.l. The asthma and rhinoconjunctivitis symptom scores during and after pollination season decreased significantly and showed correlation with histamine release by T3.

**Conclusion:** Basophils have the potential to play an important role in the early clinical improvement of AIT which may be a result of the decreased IgE-mediated histamine releasability during AIT. Speed and simplicity of the performance makes the WBBHR assay employing RP-HPLC-ESI-MS a useful laboratory tool for the preliminary assessment of the efficacy of AIT.

## 1565 | Immunotherapy with the recombinant B cell epitope-based grass pollen allergy vaccine BM32 induces a biphasic allergen-specific IgG1 and IgG4 response

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**Background:** Immunotherapy with the recombinant B cell epitope-based grass pollen allergy vaccine has been shown to reduce symptoms of grass pollen allergy in a multicenter, double-blind, placebo-controlled study. Aim of this study was to investigate the levels and kinetics allergen-specific IgG responses in a double-blind, placebo-controlled phase IIb combined field and exposure chamber trial studying the effects of three, four and five pre-seasonal injections of BM32 as compared to placebo.

**Method:** A quantitative ELISA assay based on purified human monoclonal allergen-specific $IgG_1$ as well as $IgG_4$ antibodies as standards was developed to measure allergen-specific $IgG_1$ and $IgG_4$ concentrations induced by AIT with BM32.

**Results:** We found rises in levels of both tested allergen-specific IgG subclasses in the actively but not placebo-treated patients. Phl p 1- and Phl p 5-specific $IgG_1$ levels up to 83 μg/mL and 784 μg/mL, respectively and Phl p 1- and Phl p 5-specific $IgG_4$ levels of up to 468 μg/mL and 1423 μg/mL, respectively were measured in BM32-treated patients. Five pre-seasonal injections induced the highest allergen-specific IgG levels. Interestingly, allergen-specific $IgG_1$ and $IgG_4$ antibodies showed a biphasic response with early rises of allergen-specific IgG1 which declined quickly after the pollen season and a delayed but very sustained allergen-specific IgG4 response.

**Conclusion:** Treatment with BM32 induces a biphasic allergen-specific IgG response consisting of an early IgG1 and a sustained allergen-specific IgG4 response which may be responsible for early and sustained protection against allergic symptoms.

## 1566 | T reg $CD4^+$ $CD25^{high}$ in peripheral blood in patient with grass pollen allergy during sublingual specific immunotherapy SLIT

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**Background:** Specific subcutaneous immunotherapy is known for years. However, not every patient feel a clinical improvement after this treatment. Because of that, other routes of administration of immunotherapy, and parameters of effectiveness of immunotherapy are searched.

The aim of this study was to evaluate T reg $CD4^+$ $CD25^{high}$ in peripheral blood in patients with grass pollen allergy during sublingual immunotherapy SLIT.

**Method:** We examined 27 adult patients, aged 20-41, 13 female and 14 male. Patients were qualified to SLIT after confirmation of allergy- by skin prick tests, specific IgE and nasal provocation tests. We determined T reg $CD4^+$ $CD25^{high}$ from blood sampling of those patients (by flow cytometry method), before the SLIT, after reaching the maintenance dose, before the grass pollen season, during the grass pollen season, and after one year of SLIT.

**Results:** During SLIT the percentage of T reg $CD4^+$ $CD25^{high}$ increase after reaching the maintenance dose, then it decreased before and during the grass pollen season, and again increase after one year os SLIT. We observed, that in the group with significant improvement of symptoms, T reg$CD4^+$ $CD25^{high}$ decreased during grass pollen season, comparing to group without clinical improvement.

**Conclusion:** SLIT as a method of immunotherapy influence on levels of T reg $CD4^+$ $CD25^{high}$ cells. The observed decreased levels of these cells during the grass pollen season might be consider as a prognosing marker of clinical improvement.

## 1567 | T reg $CD4^+$ $CD25^{high}$ from peripheral blood during subcutaneous specific immunotherapy (SCIT) for grass pollen

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**Background:** Specific immunotherapy is the only causal method for grass pollen allergic rhinitis. However, we don't observe in every patients satisfying clinical effects. Because the treatment of allergic rhinitis takes 3-5 years, and is quite expensive, everyone is constantly looking for a perfect parameter, which may prognose the effectiveness of specific immunotherapy (SIT).

The aim of this study was to evaluate T reg $CD4^+$ $CD25^{high}$ lymphocytes from peripheral blood in patients during subcutaneous specific immunotherapy (SCIT) for grass pollen .

**Method:** We examined 99 adult patients (36 female, 63 male), age 18-60, who undergo SCIT for grass pollen allergy. We have done skin prick tests and specific IgE in those patients. Additionally, we confirmed the allergy by nasal provocation tests. We have determined lymphocytes T reg $CD4^+$ $CD25^{high}$ from blood sampling from those patients, with flow cytometry method: before immunotherapy, after reaching the maintenance dose of SCIT, before and during the grass pollen season, and after one year of SCIT.

Our control group was represented by 12 adult healthy volunteers.

After one year of SCIT we divided patients into two groups- with and without clinical improvement.

**Results:** In allergic patients we have observed decreased levels of T reg $CD4^+$ $CD25^{high}$ compared to control group before the start for SCIT. During immunotherapy, the percentage of T reg $CD4^+$ $CD25^{high}$ increased after reaching the maintenance dose, however it did not reached the level of healthy volunteers. Again, levels of T reg $CD4^+$ $CD25^{high}$ decreased before and during the grass pollen season, and increased after one year of SCIT. We compared also patient with significant improvement of clinical symptoms, and without. And we observed that the level of T regs $CD4^+$ $Cd25^{high}$ decreased during pollen season in improved group, and increased in the group without clinical improvement.

**Conclusion:** In patients with grass pollen allergy, during the grass pollen season, decrease of T reg $CD4^+$ $CD25^{high}$ cells might be considered as a prognosing marker for effective subcutaneous immunotherapy- clinical improvement.

## 1568 | Changes in gene expression as a marker of treatment efficacy in during grass pollen allergen specific immunotherapy

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**Background:** Allergen Specific Immunotherapy (SIT) is the only causative treatment in allergic rhinitis and asthma. Although widely used, its mechanism remains unknown. The aim of the study was to define the profile of gene transcripts, which change significantly their expression during build-up phase of SIT.

**Method:** The study group consisted of 23 allergic to grass pollen patients obtaining SIT in the out-patient clinic in Allergology Department of University Clinical Center in Gdansk. Analysis of 15 (selection based on studies up to date) transcripts expression was performed in whole blood samples taken before SIT (sample A) and after reaching the maintenance dose (sample B). The results were compared with the group of 25 healthy volunteers with negative allergy history (sample C). Results were normalized using 18s rRNA and calibrated to commercial total mRNA reaching Relative Quantification. RQ comparison was performed with Wilcoxon and U Mann Whitney tests. The correction for multiple testing was performed with Duncan's multiple range test. K nearest neighbors algorithm was built using genes with significant expression change. Training examples were sample A and C. Then, the model was tested on sample B and compared with ACS pre and post results.

**Results:** In the group of patients treated with SIT gene expression analysis revealed significant change in IFNG expression ($P = 0.03$) (comparison between sample A and B). Comparison between samples A and C showed significantly different expression in genes: AFAP1L1 ($P = 0.006$), COMMD8 ($P = 0.001$), PIK3CD ($P = 0.027$), and TWIST2 ($P = 0.0003$). Duncan's multiple range test confirmed difference between sample A and C for COMMD8 ($P = 0.004$) and also revealed new significant difference in TBX21 in samples A and B ($P = 0.035$; in Wilcoxon's test $P = 0.08$). K nearest neighbors algorithm was built based on IFNG, PIK3CD, COMMD8 expression.

**Conclusion:** The results of the study indicate, that there is a significant change in the expression of a few genes during the build-up phase of SIT. It may be suspected, that this change contribute to the mechanisms involved in the building tolerance to allergen. K nearest neighbors algorithm may be useful for SIT efficacy prediction.

## 1569 | Regulation of cytokine thymic stromal lymphopoietin (TSLP) in modulating TGF-ß1-induced interstitial inflammation and cellular fibrosis

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**Background:** Thymic stromal lymphopoietin (TSLP) has previously been linked to allergic inflammatory diseases, tissue fibrosis and organ dysfunction. It remains unclear, however, whether TSLP plays any role in the occurrence of renal fibrosis, so this study investigated that underlying mechanism.

**Method:** An in vitro fibrosis model was established by treating normal rat kidney fibroblast (NRK-49F) cells with transforming growth factor-β1 (TGF-β1), after which the levels of various fibrogenic markers (e.g., fibronectin) and downstream fibrogenic signal proteins (e.g., smad 7) were investigated. Also, TSLP shRNA was used to silence the effects of TSLP, while an ELISA was conducted to evaluate the fibronectin secretions.

**Results:** The level of fibronectin in the NRK-49F cells was dose- and time-dependently increased by the administration of exogenous TSLP ($P < 0.05$). TSLP also significantly increased the level of fibrosis signaling, in addition to inducing a marked decrease in the down-regulation of Smad7. Interestingly, the application of TSLP shRNA caused a dramatic reversal of the TGF-β1-induced cellular fibrosis while simultaneously leading to the suppression of fibronectin and fibrogenic signal proteins.

**Conclusion:** Taken together, these observations provide insights into how extracellular matrices develop and could lead to potential therapeutic interventions for the suppression of renal inflammation and fibrosis.

## 1571 | Effects of two years treatment with the recombinant B cell epitope-based grass pollen allergy vaccine BM32 on allergen-specific B and T cell responses

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**Background:** BM32 contains recombinant fusion proteins of non-allergenic peptides from IgE-binding sites of the four major timothy grass pollen allergens Phl p 1, 2, 5 and 6 and PreS protein from the Hepatitis B virus as a carrier. In a multicentre, double-blind, placebo-controlled trial, 181 grass pollen allergic subjects were treated for two years either with BM32 or placebo. Here we investigated in detail the effect of immunization with BM32 on allergen-specific T and B cell responses.

**Method:** Peripheral blood mononuclear cells (PBMCs) obtained during the study from 35 subjects treated in the Vienna centre (BM32: n = 25, placebo: n = 10) were investigated regarding proliferation using $^{3}H$ thymidine incorporation and cytokine production in response to various recombinant allergens at 9 different time points. Grass pollen allergen-specific IgE, $IgG_1$ and $IgG_4$ levels were determined by ImmunoCAP and ELISA.

**Results:** A significant increase of allergen-specific $IgG_1$ and $IgG_4$ levels was found in the BM32- but not in the placebo group in both years (year1 > year2) after treatment. There was no difference regarding T cell proliferation in response to Phl p 1 and Phl p 5 after first grass pollen season between actively and placebo-treated patients whereas proliferation in particular of Phl p 1-specific responses seemed to be blunted in the active group in the second year. No significant differences regarding allergen-specific Th1, Th2 and tolerogenic (i.e., IL-10) cytokines were observed between BM32- and placebo-treated patients.

**Conclusion:** The findings indicate that the BM32 induces high levels of allergen-specific blocking antibodies which may reduce allergen-specific T cell proliferation but does not induce significant increases of regulatory cytokines in T cells.

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TPS 56
MECHANISMS IN FOOD ALLERGY

## 1572 | The ligand of the major peach allergen Pru p 3 is presented to iNKT cells

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**Background:** Lipids transported by allergenic proteins have been demonstrated to play a crucial role in the sensitization phase of allergy. Pru p 3, the major allergen from peach fruit, is an nsLTP (non-specific lipid transport protein) that carries a ligand recently identified in our research group as a hydroxyl derivative of the alkaloid camptothecin bound to a phytosphingosine tail. For its participation into allergy sensitization events, the ligand activates immune responses through CD1d-mediated presentation. The CD1d receptor protein is a member of CD1 molecules that present lipids and glycolipids to the immune system. The family member CD1d is specifically recognized by the T-cell receptor (TCR) of invariant natural killer T-cells (iNKT).

**Method:** The interaction between the ligand of Pru p 3 and CD1d was studied through maturation inhibition assays of moDCs and immunohistochemistry in epithelial cells. Co-localization with iNKT cells was demonstrated by using the ligand of Pru p 3 loaded onto the CD1d Dextramer commercial system. In silico analyses were carried out by combining structural alignments with available structures of complexes involving CD1d and TCR receptors, docking calculations, and energy minimizations. Protein-ligand interactions and electrostatic potentials of the complexes with the ligand of Pru p 3 were computed on the corresponding optimized structures.

**Results:** Our in vitro results obtained by means of immunohistochemistry and cellular activation assays revealed that the ligand of Pru p 3 is loaded onto CD1d and is present in the interaction of CD1d with TCR. These results are complemented with *in silico* studies of structures and physicochemical properties of the CD1d-ligand and CD1d-ligand-TCR complexes. The crucial interaction known to activate TCR involves hydrogen bonds between amino acids from the receptor and hydroxyl groups in headgroups of the lipids. In our CD1d-ligand-TCR structure, this key interaction happens to occur at the same spatial location as that in other well-known lipid antigens.

**Conclusion:** The ligand of the major peach allergen Pru p 3 is loaded onto CD1d and thus presented to the TCR of iNKTs. Therefore, the process of sensitization to Pru p 3 should be produced by iNKT-activation mediated upon presentation of the ligand loaded onto CD1d receptor.

## 1573 | The CD203c expression of unstimulated basophils indicates resistance to rush oral immunotherapy for food allergies

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**Background:** The cell surface expression of CD203c is an activation marker of basophils, typically when they are stimulated with allergens in vitro. Furthermore, the CD203c expression on unstimulated basophils may reflect the activation status of basophils in vivo, like spontaneous histamine release from basophils (Sampson HA, NEJM 1989). We hypothesized that unstimulated CD203c expression may reflect the hypersensitivity of the patient, thereby influencing the clinical outcome of oral immunotherapy (OIT).

**Method:** From May 2016 to April 2017, 30 patients underwent rush OIT for hen's egg, cow's milk and wheat in our department. All of the participants showed systemic allergic symptoms after eating <10 g of the target food in the oral food challenge. The starting dose was decided based on the threshold dose and the severity of provoked symptoms. In the rush phase of OIT under 12 days of hospitalization, patients repeated the intake of the target food with a 30% increasing dose 4 times a day unless allergic symptoms were not observed. The target dose of the rush phase was 20 g boiled egg white, 100 mL cow's milk or 100 g udon noodles, and the clinical outcome of each patient was evaluated based on the proportion of achieved/target dose at discharge. The basophil activation test (BAT) was performed using an Allergenicity Kit® (Beckman Coulter, Fullerton, CA) before and three months after rush OIT. Before rush OIT, the baseline mean fluorescence intensity of CD203c-PE (BMFI) was a median 26.3 (interquartile range 16.0-32.2), and the subjects were classified into low (lower quartile, n = 8), middle (n = 14) and high (upper quartile, n = 8) BMFI groups.

**Results:** There were no marked differences in the age, sex, total IgE titer, comorbidity of bronchial asthma and atopic dermatitis or the starting dose of rush OIT among the groups. All patients in the low-BMFI group achieved ≥100% of the target dose, whereas 28.6% of the middle-BMFI group and 50% of the high-BMFI group failed to achieve the target dose ($P < 0.05$).

**Conclusion:** A high BMFI of CD203c on basophils suggests some risk with OIT in the rush phase.

## 1577 | Allergy to shiitake mushroom

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**Background:** Shiitake mushroom (SM) (*Lentula edodes*) is an edible fungi native to East Asia. It is traditionally cultivated and used in many Asian countries and its consumption is increasing worldwide. Direct skin exposure to SM can cause cutaneous reactions, including allergic contact dermatitis and urticaria, while its oral intake may prompt "shiitake flagellate dermatitis" (SFD), which is a distinctive itching linear erythematous eruption. SFD is usually considered a toxic reaction to *lentinan*, a thermolabile polysaccharide that increases interleukin-1. We report 3 cases (P1, P2, P3) of shiitake flagellate dermatitis studied in our Centre.

**Method:** Skin prick tests (SPT) to environmental allergens—including moulds -, prick-by-prick and patch test with raw and cooked SM were carried out. Total IgE and specific IgE to mushroom, white mushroom and environmental moulds were also determined. A raw and cooked shittake mushroom extracts were prepared. Both extracts were analyzed in all the patients by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE).

**Results:** Skin prick tests, prick-by-prick, patch tests and specific IgE were all negative except for P1, who had positive prick-by-prick to raw Shiitake mushroom. SDS-PAGE IgE immunoblotting assays with the patient's sera revealed IgE-reactivity with proteins ranging from 16 kDa to 32 kDa for P1, P2 and P3.

**Conclusion:** We report 3 cases of shiitake flagellate dermatitis with demonstrated IgE-sensitization. Physicians should take into account that some cutaneous reactions considered as toxic might be allergic reactions.

## 1578 | Immune status in children with allergic diseases and different variants of vitamin d receptor gene polymorphism

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**Background:** Vitamin D receptor (VDR) is intracellulary located on the cells of the immune system and is involved in the immune response. The development of allergic inflammation is controlled by different genes, including the gene VDR. Aim of the study was to investigate serum markers of allergic inflammation in children with food allergy and different variants of VDR gene polymorphism.

**Method:** To study the immune status in children with allergic diseases and different types of vitamin D receptor (VDR) gene polymorphism 130 children (66 boys and 64 girls) aged 1.5-16 years were examined. 25-OH vitamin D, IL-16, IL-17, BAFF, TGFβ1 and sCD134 serum levels were measured by immunoassay method. To genotype rs731236 (*Taq1*), rs1544410 (*Bsm1*) and rs2228570 (*Fok1*) VDR SNPs real-time PCR with melting curve analysis were used.

**Results:** Significant differences in genotypes and alleles frequency distribution between children with allergic diseases and population were revealed. The frequency of allele A, homozygous A/A and heterozygous G/A genotypes in site BsmI were significantly increased in children with allergic diseases compare population (OR=1.81, $P = 0.04$; OR=2.03, $P = 0.05$ and OR=1.8, $P = 0.05$ respectively).The investigation of IL-16, IL-17, BAFF, TGFβ1 and sCD134 levels in the sera of children with allergic diseases showed activation of various immune factors with pro- and anti-inflammatory activity, as well as T and B cells. A reduction in the level of TGFβ1 in serum in children—carriers of heterozygous A/G markers Fok1 VDR gene on the background of low levels of 25-OH vitamin D were revealed.

**Conclusion:** FokI site VDR gene polymorphism may indirectly influence on TGFβ1 synthesis in allergy diseases development.

## 1579 | Influence of vitamin D on antibody response against food extracts in Afro-descendant Colombian children

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**Background:** Allergic diseases such as asthma, rhinitis and food allergy have increased in recent decades in tropical countries. The tropics has climatic, environmental and ecological peculiarities that allow us to emit several hypotheses that could explain this phenomenon. In one of them, it is postulated that the increase of the sensitization to food, is due to the presence of lower serum levels of vitamin D, product of the adoption of a western lifestyle, with lower sun exposure, which in its turn diminishes the immunomodulatory action of this vitamin at intestinal level, favoring the sensitization against food antigens. We evaluate differences between the titers of serum antibodies against food antigens between two populations with African ancestry but different environment (rural vs urban) and investigate the influence of vitamin D levels.

**Method:** An observational, cross-sectional and descriptive study was carried out on 200 Afro-descendant children living in San Basilio de Palenque (Rural) or in the city of Cartagena, Bolivar (Urban). The sensitization was determined by a positive skin prick test to allergen extracts, including foods, and, specific IgE, IgA and IgG4 to egg, milk and peanut extract, as well vitamin D, were measured by ELISA.

Antibody and vitamin D titers were correlated by Spearman's test and comparisons between groups were done using the Wilcoxon rank sum test. A $P < 0.05$ was considered significant.

**Results:** Atopy was more prevalent in the urban population (24% vs 7%, $P < 0.001$). However, none participant tested was positive for food allergens. Regarding vitamin D levels, these were found to be higher in the rural population compared to the urban group ($P < 0.001$). Among the antibodies analyzed, only IgE against peanut showed differences, which were higher in rural population ($P < 0.001$) as well as those of IgA to peanut, which were higher in the urban population ($P < 0.001$). We observed only a significant correlation between peanut specific IgE (Rho 0.2127259, $P < 0.005$) and IgA (Rho -0.342434, $P < 0.001$) response and vitamin D.

**Conclusion:** In our study, we found differences between the peanut specific IgE and IgA response in urban and rural populations. The correlation between the levels of specific IgE and IgA to peanut and vitamin D, suggest that this vitamin may influence peanut sensitization in this population, besides other components like diet and genetic and environmental factors.

## 1580 | Evaluation of inhaled allergen sensitivity in patients with food allergies younger than two years of age

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**Background:** The frequency of sensitivity to inhaled allergens and their effects on the disease activity of infants with food allergies are currently unknown

**Method:** From January 2012 to December 2016, patients who were diagnosed with food allergies before 24 months of age were tested for inhaled allergen sensitivity via skin prick test at our center were included in our study. Skin prick test was performed with the following antigens: food (cow milk, egg white and yolk, wheat, peanut, fish, and soya bean), house dust mite (Dermatophagoides farina (DF), Dermatophagoides pteronyssinus (DP)), animal and insect derived allergens (cat, dog, cockroach [Blatella germanica]), mould (aspergillus fumigatus, Cladosporium species [Cladosporium cladosporium, Cladosporium herbarum], and Alternaria alternata). an increase of 3 mm's or higher (compared to negative control) was accepted as a positive result.

**Results:** A total of 473 infants were diagnosed with food allergy (IgE-mediated and mixed type) at our center during the study period, 305 of these patients underwent prick test for inhalant sensitivity, and 220 (64.9% male) of these were younger than 2 years of age. The study group was comprised of 286 (64.9% male) patients. Median age of prick test application was 8.2 months (interquartile range: 2-10), among these patients, 5 had DP (1.7%), 5 had DF (1.7%), 4 had cat (1.4%), 1 had dog (0.4%), 5 had mould (1.7%), and 1 had cockroach (0.4%) allergy.

**Conclusion:** Sensitivity to inhaled allergen were found in 14 of 292 (4.9%) patients with food allergy. Therefore, we believe that inhalant sensitivity should be evaluated in these patients. There is also a requirement for further studies to identify the influence of inhaled antigens on the disease activity of patients with allergic conditions.

## 1581 | Energy metabolism is altered in patients with severe allergic phenotype using metabolomics

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**Background:** Food allergy has dramatically increased in prevalence in the last decades. This has created a burden for health and economical systems. Some areas from Spain are characterized by a high level of grass pollen exposure, in particular in the western part. In this area, severe profilin food allergic reactions are relatively frequent. The underlying mechanisms of this phenotype are still unknown. These patients represent an outstanding clinical model to study looking for inflammatory biomarkers that might offer new diagnosis strategies. Metabolomics offers a novel approach to potentially study hundreds of metabolites within a single biological sample, which can provide an informative measure of multifactorial diseases.

**Method:** In this study, we aimed to perform the metabolic profiling of severe profilin mediated food allergic patients looking for biomarkers that might both, predict the prognosis of the disease and understand the molecular mechanisms of inflammation underneath. Other allergic patients (mild and moderate) and non-allergic were recruited in the study as comparative groups. The allergic patients class was predicted using a mathematical algorithm from non-allergic vs severe model

**Results:** Plasma samples from non-allergic subjects, mild, moderate and severe allergic patients were measured using gas chromatography coupled to mass spectrometry (GC-MS). The samples were from 4 different hospitals in Spain covering the areas with the highest pollen exposure. The metabolic profile was composed of 95 metabolites for each sample. Results after the statistical analysis showed differences between the groups. Firstly, a clear reduction of several

carbohydrates and pyruvate was observed in the severe group compared to the rest of allergic groups. In addition, an increment in lactate was noticed. These metabolites were closely associated with the energy metabolism. Other metabolic changes included increased levels of fatty acids such as myristate, palmitate and laureate. These fatty acids might be precursors of arachidonic acid, a key molecule in inflammation. Finally, alterations in some amino acids and adenosine were found

**Conclusion:** Results showed an increase of lactate, reduction of pyruvate and carbohydrates in severe group, suggesting the activation of Warburg metabolism. Further evaluation of detected metabolites might result in new ways of stratifying allergic patients

## 1582 | Detection of a digestion-resistant peptide of ara h 2 throughout absorption, transport, and distribution in sensitized and non-sensitized germ-free c3 h/hen mice

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**Background:** The cellular mechanisms by which food allergens are absorbed by the small intestine, transported across the gut epithelial barrier, and distributed throughout the body are largely unknown. In addition, the differences between sensitized (S) and non-sensitized (NS) individuals in their capacity to absorb, transport, and distribute antigen, remain unestablished. Ara h 2 is one of the most potent peanut allergens and digestion resistant peptides (DRP) of Ara h 2 have been discovered. These peptides represent a novel approach to tracking digestion and uptake of allergens in vivo.

**Method:** To evaluate these critical processes, 22 five-week old germ-free C3H/HeN mice were split into two groups; 12 were intraperitoneally sensitized to the peanut allergen Ara h 2 and 10 remained NS. Upon reaching 8 weeks of age, mice were intragastrically challenged with purified Ara h 2. Mice were harvested in two groups: 30-minutes and 60-minutes post-gavage. Upon harvest, the left lobe of the liver was collected and sera were removed. Sera and livers were evaluated for DRP-Ara h 2 using an in-house quantitative sandwich enzyme-linked immunosorbent assay (ELISA). A sample of the proximal small intestine was monitored for DRP-Ara h 2 using immunohistochemistry (IHC) and for mast cell degranulation using Toluidine blue stain.

**Results:** Sensitization does not have a large effect on the concentration of allergen present in the sera or liver. However, S mice allowed to digest Ara h 2 for 60-minutes were more likely to display tissues positive for detection of DRP-Ara h 2 than NS mice at the same time point.

**Conclusion:** There is drastic biological variation among mice in their capacity to absorb and transport allergens. The ELISA used in these analyses proved effective in the quantitative detection of DRP-Ara h 2 in both liver and sera samples, while IHC provided inconsistent results for the detection of DRP-Ara h 2 in tissues. However, in positive IHC samples, staining was indicative of paracellular transport across the epithelial barrier.

## 1583 | Eczema induces a high ovalbumin-specific IgE/IgG1 ratio and affinity maturation during the lactation period

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**Background:** Recent articles have revealed that ingestion of foods induces oral tolerance and cutaneous sensitization induces food allergy. Relationships with levels of immunoglobulin subclasses, affinity of allergen-specific IgE, and development of food allergy have also been indicated. However, relationships with levels and affinity of specific immunoglobulins and eczema during early infancy remain poorly understood. Therefore, the present study aimed to elucidate these relationships.

**Method:** This study enrolled women who visited Naruto Hospital (Tokushima prefecture, Japan) in late pregnancy and their children. Blood samples and information on skin condition were taken every 2 months from neonate to 6 months old. Egg white and milk allergen-specific immunoglobulin subclasses and affinity of ovalbumin (OVA)-specific IgE levels were measured using the densely carboxylated protein (DCP) microarray with 20 μL of serum.

**Results:** This study included 84 infants whose parents agreed to join this study. Of these, 42 infants (50%) were diagnosed with eczema by 6 months old. Egg white (EW) and milk-specific IgG4 were detected in a few subjects at 6 months old. However, these specific IgE and IgG1 were detected in some subjects at that time EW- and OVA-specific IgE levels and IgE/IgG1 ratios were significantly higher in participants with eczema than in those without eczema at 6 months old. Moreover, subjects with high OVA-specific IgE/IgG1 ratios showed higher affinity OVA-specific IgE antibodies than subjects with low OVA-specific IgE/IgG1 ratios. These results were not reflected in milk-specific IgE levels. The milk-specific IgE level differed between breast feeding and formula-fed infants, with no difference in the IgE/IgG1 ratio.

**Conclusion:** Eczema contributed to high EW- and OVA-specific IgE levels and IgE/IgG1 ratios. High OVA-specific IgE/IgG1 ratios involved high affinity OVA-specific IgE antibodies. However, the milk source during early infancy had no effect on the specific IgE/IgG1 ratio with eczema. These results suggest different sensitization routes provoke different results in levels and affinity of immunoglobulins.

## 1584 | Purification and characterization of naturally occurring post-translationally cleaved Ara h 6, an allergen that contributes substantially to the peanut allergome

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**Background:** The 2S albumin Ara h 6 is one of the most important peanut allergens. A post-translationally cleaved Ara h 6 isoform has been described in the past but had not been characterized in detail, nor had its relevance for peanut allergy been investigated.

**Method:** Post-translationally cleaved Ara h 6 (pAra h 6) and intact Ara h 6 (intact Ara h 6) were purified from Virginia type peanuts and the cleavage site was mapped using high-resolution mass spectrometry. Biochemical characteristics were determined by SDS-PAGE, UV absorbance spectroscopy, far UV CD spectroscopy, and immunochemical reactivity of both forms of Ara h 6 was compared by IgG immunoblotting and IgE-ELISA using sera from individuals sensitized to peanut. Reversed-phase liquid chromatography was applied to study the occurrence and abundance of pAra h 6 in various peanut types.

**Results:** Compared to intact Ara h 6, pAra h 6 lacks a 5-amino acid stretch, resembling amino acids 43-47 (UniProt accession number Q647G9) in the non-structured loop. Consequently, pAra h 6 consists of 2 chains; a N-terminal chain of approximately 5 kDa, and a C-terminal chain of approximately 9 kDa, held together by disulfide bonds. Intermediate post-translationally cleaved products, in which this stretch is cleaved but not removed, are also present. The secondary structure and IgE-binding of pAra h 6 resembles that of intact Ara h 6, indicating that the loss of the non-structured loop is not critical for maintaining conformational IgE-epitopes. Both forms of Ara h 6 were reactive with several commercially available IgG antibodies. The peanut cultivars Runner, Virginia, Valencia, and Spanish contained pAra h 6 at equivalent levels, suggesting pAra h 6 is a consistent and important constituent of the peanut proteome.

**Conclusion:** A post-translationally cleaved form of Ara h 6 is abundant in the main peanut market types, and has IgE-binding comparable to intact Ara h 6. This should be taken into account when Ara h 6 is investigated in peanut-containing products.

## 1585 | Release of major peanut allergens from their matrix at various pH and at saliva conditions; Ara h 2 and Ara h 6 are quickly bio-accessible

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**Background:** The oral mucosa is the first immune organ that encounters allergens upon ingestion of food. Peanut is often consumed in solid form, and it is not known if peanut allergens are released from the food already in the mouth. We set out to investigate the solubility of individual peanut allergens at conditions that mimic the first exposure site, i.e. the mouth.

**Method:** Light roast peanut flour was suspended in buffers of various pH mimicking saliva. Protein concentration was measured in supernatant, and release of major allergens Ara h 1, Ara h 2, Ara h 3, and Ara h 6 was assessed by SDS-PAGE. Also, the allergen profile of un-dissolved material was assessed.

**Results:** Peanut protein solubility is poor in the pH range 3-6, while at low pH (1.5) and at moderately high pH (>8), the solubility is higher. At all conditions tested, there was a substantial amount of un-dissolved protein. This indicates that the pH range of saliva, between 6.5 and 8.5 in healthy individuals, may be critical for the release of peanut protein from its matrix. In this pH range from 6.5 to 8.5, Ara h 2 and Ara h 6 are readily released, while Ara h 1 and Ara h 3 are poorly released. Increasing the pH from 6.5 to 8.5 slightly increased the release of Ara h 1 and Ara h 3, but still the recovery was low (approximately 20% for both Ara h 1 and Ara h 3) compared to that of Ara h 2 and Ara h 6 (approximately 100% and 65%, respectively). This remarkable difference in extraction kinetics suggests that Ara h 2 and Ara h 6 are the first allergens an individual is exposed to upon ingestion of peanut-containing food.

**Conclusion:** Based on our observations, we conclude that the peanut allergens Ara h 2 and Ara h 6 are quickly bio-accessible in the mouth upon ingestion of peanut. This new insight may contribute to the understanding of the extraordinary allergenicity of Ara h 2 and Ara h 6 compared to other peanut allergens.

## 1586 | Old drug, new tricks; Control of unremitting symptoms in non-IgE mediated cow's milk allergy using Ketotifen

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**Background:** In proven cases of non-IgE mediated cow's milk allergy clinical response can be partial even when treated with amino acid formulae e.g pain in infants. Residual intestinal symptoms can be related to ongoing nerve hypersensitivity, changes in microbiome or motility disturbance. Mast cells are thought to play crucial role in non-IgE mediated food allergy. Ketotifen is a first generation H1 antihistamine which has mast cell stabilising properties with pain blocking and anti TNF-a effect. Hence ketotifen could have important role in symptom resolution where diet elimination has not been successful. We aim to find out effectiveness of ketotifen to unresponsive/partially responsive symptoms such as pain in non-IgE mediated cow's milk allergy infants.

**Method:** Children who presented to single specialist centre over 11 years had their case notes reviewed retrospectively. Inclusion criteria were those children with confirmed non-IgE mediated cow's milk allergy by elimination of cow's milk with improvement of symptoms and worsening of symptoms on reintroduction of dairy. Where symptoms partially responded e.g pain, ketotifen was used at 0.5-1 mg once at night for 4 weeks and symptoms were reassessed. Statistical analysis was performed using R v3.3.3 with significance was set at $P = 0.05$.

**Results:** 1031 patients were identified with 675 patients excluded due to unconfirmed non-IgE mediated allergy. Of the 358 case (206 males, age 3-50 months), atopic co-morbidities were found in 62% children. Common symptoms were abdominal pain (51%), vomiting (47%), back arching (37%), constipation (35%), bloating (33%), food aversion (29%) and diarrhoea (26%). We compared the children who had symptom improvement on ketotifen and cow's milk elimination against children who improved on cow's milk elimination alone. Significant difference of symptom improvement was found with abdominal pain; 69% using Ketotifen compared to 53% who did not use Ketotifen ($P = 0.026$). No significant difference of symptom improvement noted with back arching: 79.5% vs 76.32% ($P = 0.68$), sleep disturbance: 74.3% vs 62.71% ($P = 0.128$) and vomiting: 86.21 vs 82.93% ($P = 0.555$). 2% children experienced minor adverse effects of Ketotifen.

**Conclusion:** Elimination diets are mainstay management option for children with non-IgE mediated food allergy. Despite this, significant proportion of children continue to have debilitating symptoms leading to poor quality of life. We have found the use of ketotifen in this subgroup of patients beneficial.

## 1587 | Closing the pandora's box: A single center, retrospective, epidemiological study of gluten associated morbidity

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**Background:** In recent years, the gap between the prevalence of self reported and diagnosed gluten associated disease has dramatically increased. The exact reason to explain this phenomenon remains elusive.

**Method:** We retrospectively analyzed serological markers of all patients in whom markers of celiac disease (anti-tissue transglutaminase IgA; tTGIgA) and wheat allergy (specific IgE directed against wheat; WIgE) have been analyzed in our laboratory between 2010 and 2016.

**Results:** A total of 3548 analysis for tTGIgA have been performed for a total of 2965 patients during the study period (2010, 2012, 2014, 2016). 128 patients showed at least once a positive tTGIgA. Among these, 11 had a negative result at first testing, and were positive at the second (n = 10) or third testing (n = 1). Despite an increasing number of tTGIgA requests, the number of positive results decreased. WIgE were rarely requested but were positive in about 45% of tested sera (Table 1a and 1b).

**Conclusion:** The amount of laboratory requests for tTGIgA has increased, while those for WIgE remains stable and is rare. Wheat allergy seems to be rarely investigated in our center and may deserve more attention.

Table 1a

| | 2010 | 2012 | 2014 | 2016 |
|---|---|---|---|---|
| Total no. of tTGIgA analysis | 731 | 884 | 960 | 973 |
| Total no. of new patients | 691 | 717 | 775 | 782 |
| Mean age (Interval) | 26 (0-99) | 28 (0-93) | 31 (0-97) | 29 (0-95) |
| No. of positive tTGIgA (% positive sera) | 64 (8.7) | 58 (6.6) | 47 (4.9) | 34 (3.5) |
| New patients with positive tTGIgA | 48 | 35 | 25 | 20 |

| Table 1b | 2010 | 2012 | 2014 | 2016 |
|---|---|---|---|---|
| Total no. of WIgE analysis | 18 | 21 | 18 | 19 |
| Total no. of new patients | 18 | 18 | 16 | 17 |
| Mean age (Interval) | 19 (1-49) | 23 (1-79) | 17 (1-50) | 20 (1-62) |
| No. of positive WIgE (% positive sera) | 9 (50) | 11 (52) | 8 (44) | 8 (42) |
| New patients with positive WIgE | 9 | 8 | 6 | 6 |

## 1588 | Improvement of eosinophilic enteritis after therapy with omalizumab

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**Case report:** Eosinophil-associated gastrointestinal disorders (EGIDs), including eosinophilic gastroenteritis (EoG), are a inflammatory diseases, characterized by gastrointestinal symptoms and eosinophilic infiltration. Patients with EoE have an increased incidence of allergy, with increased IgE mediated food and inhalant sensitivities. Use of either a targeted food allergen avoidance approach (based on allergy testing) or untargeted approach (based on food allergen avoidance) results in the resolution of eosinophilia in the gastrointestinal tract of 50%-70% of adult. We describe a case of a 27-year-old patient diagnosed with eosinophilic enteritis, associated to protein-losing enteropathy. The patient experienced severe diarrhea, nausea, vomiting and weight loss, that caused a severe dysproteinaemia and electrolytes abnormalities. An upper and lower endoscopy was performed, showing an ulcerative ileitis. The histological pattern was characterized by eosinophilic infiltration of ileum and duodenum>40 HPF. She presented also high levels of total IgE (800 K/UI), high serum tryptase (20 μg/L, n.v. ≤9.0) and sensitization to the lipid transfer protein (LTP) of peach. The patient was prescribed to a six-food elimination diet (SFED) and underwent high doses of oral and intravenously corticosteroids, but a satisfactory therapeutic response was not achieved. We hypothesized that IgE has a role in the mechanism of AEG and that blocking IgE would have improved disease symptoms and reduced allergic inflammation, as measured by a decrease in intestinal tissue eosinophilia. We started off-label administration of omalizumab 300 mg/month subcutaneously, the same dosage schedule used in allergic asthma and, by other authors, in eosinophilic gastrointestinal disease after achieving informed consent by patient. Except for an exacerbation of symptoms occurred 9 months after starting the therapy, when a further endoscopy, showing a gastrointestinal eosinophilic infiltration>50 HPF, was performed, a significant improvement of both gastrointestinal and cutaneous symptoms was observed during therapy, together with a normalization of laboratory parameters. After 30 months a clinical remission of disease was obtained and administration was stopped. Although a histological remission during the first few months of treatment was not obtained, in a subset of AEG patients, IgE plays a role in the pathophysiology of the disease and that anti-IgE therapy with omalizumab may result in disease remission.

## 1590 | Fullerene C60 reduces the allergic inflammation in food allergy mouse model

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**Background:** A food allergy (FA) is an abnormal immune response to food. The signs and symptoms may range from mild to severe. They may include itchiness, swelling of the tongue, vomiting, diarrhea, hives, trouble breathing, or low blood pressure. Food allergy is becoming increasingly common. Fullerene C60 has the unique electronic properties making it an attractive candidate for allergic diseases therapy. The main purpose of our research was to assess therapeutic effect of fullerene C60 in a mouse model of FA.

**Method:** New efficient method for producing a water-soluble fullerene C60 has been developed. FA experimental model was induced in Balb/c mice by the intragastrical (IG) OVA administration after subcutaneous (SC) sensitization. Fullerene C60 was administrated IG once a week, or twice a week, or daily. OVA-specific antibodies were assessed by ELISA. Splenocytes cytokine production upon OVA in vitro stimulation was detected by ELISA. Samples of jejunum of the small intestine were removed for histological examination immediately after the last IG allergen administration.

**Results:** It was shown that OVA-specific IgE and IL-5 level were significant decreased in groups treated with water-soluble fullerene C60. The greatest effect was observed in mice receiving fullerene C60 daily. The IFN-gamma level was significantly higher in IG C60-treated groups. The histologic analysis of jejunum of the small intestine samples showed that C60-therapy improved the histologic picture. The greatest effect was observed in mice receiving fullerene C60 daily too.

**Conclusion:** Taken together, these results demonstrate that the water-soluble fullerene C60 exhibits a significant anti-inflammatory effect in a mouse model of FA, and possesses a high therapeutic potential.

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NEW INSIGHTS INTO FOOD ALLERGY AND ANAPHYLAXIS

## 1592 | Fish-chicken syndrome mimicking exercise anaphylaxis

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**Background:** A 47-year-old male reported eight episodes of anaphylaxis after exercise. All the ingested food eight hours before each episode was analyzed. Before each episode, he had always eaten chicken or turkey meat, and he tolerated these foods without exercising. In one of the episodes the patient had taken a tablet of dexketoprofen a few hours before. Since several years, he referred chest tightness after eating some fish (emperor, salmon and whiff), however he tolerated others. The patient denied having eaten fish before any of the episodes of anaphylaxis.

**Method:** Commercial skin prick tests (SPTs) and prick by prick tests (PP) with all food ingested and fishes were performed. Tryptase, total serum IgE (IgE) and specific IgE (sIgE) (ImmunoCAP. ThermoFisher Scientific, Uppsala, Sweden) to the foods involved were determined. A controlled oral provocation test (OPT) with dexketoprofen was performed.

**Results:** SPT was positive to tuna extract (3 mm) and negative (0 mm) for the rest of fish extracts. It was also negative for chicken meat extract and other foods tested. PPs were positive for raw and cooked turkey meat (3 mm), raw and cooked tuna (6 and 8 mm), raw emperor (11 mm), raw and cooked whiff (9 and 8 mm) and raw hake (18 mm). PPs were negative to raw and cooked chicken meat. IgE was 700UI/mL and tryptase 2.95 ng/L. sIgE was slightly positive to hake, cod and chicken meat. Dexketoprofen OPT was negative. At that moment, we recommended the patient to avoid chicken and turkey, as well as the fishes which he had symptoms with. Since then, he has not suffered any new episode of anaphylaxis despite exercising daily. Protein extracts from turkey meat, tuna, emperor, salmon, hake and whiff were prepared and analyzed by SDS-PAGE. SDS-PAGE IgE-immunoblotting assays were carried out and revealed IgE-reactivity with a 25 kDa protein band in turkey meat extract, and other high MW bands (47, 55, 60, 70 and 97 kDa). A complete inhibition of the 25 kDa band was observed with emperor, salmon and whiff extracts in SDS-PAGE IgE-immunoblotting-inhibition. No inhibition of the other bands was observed.

**Conclusion:** Recently, triosephosphate-isomerase (28 kDa) has been identified as a new chicken meat allergen. This allergen could be responsible for the cross-reactivity between bird and fish meat and the episodes of anaphylaxis after exercise in our patient. The triosephosphate-isomerase has not been implicated previously as a cross-reactive allergen involved in the fish-chicken syndrome.

## 1593 | Co-factor enhanced food allergy: Allergens and co-factors involved

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**Background:** Recently the concept of *Co-factor Enhanced Food Allergy* (CEFA) was established and the allergens more frequently involved were determined. Our aim was to characterize patients from our department with CEFA.

**Method:** Retrospective analysis of medical records from patients diagnosed with CEFA, referred to our department, between 2012 and 2017. Diagnosis was established based on clinical history, skin tests, oral food challenge (OFC) and specific IgE (sIgE) to molecular allergens usually involved.

**Results:** Twenty-three patients were included, 61% male, median age 30 years (IQR 12.5), 48% atopic, 30% asthmatic. Non-specific lipid transfer proteins (nsLTP) were implicated in 70% (n = 16) and ω-5-gliadin in 30% (n = 7). Eighteen (78%) patients referred anaphylaxis in the reaction with co-factor, 7(22%) urticaria/angioedema, 2 had both depending on the co-factor.

All patients in which ω-5-gliadin was the allergen involved had anaphylaxis in the presence of co-factor, with tolerance to wheat without it.

In patients in which nsLTP was the allergen involved, 12 (75%) had anaphylaxis in the presence of co-factor. Reaction with co-factor was more severe than without in 13 (81%) patients; 4 patients had no previous history of reaction and subsequently tolerated the culprit food. Only 1 patient had anaphylaxis in the absence of co-factor; the remaining presented oral allergy syndrome and/or urticaria.

Exercise was the main co-factor, present in 22 patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) were the only co-factor in 6 patients; all of them had anaphylaxis, 4 with allergy to ω-5-gliadin, 2 to nsLTPs. All subsequently tolerated the NSAIDs involved.

**Conclusion:** nsLTP*s* and ω-5-gliadin were the most frequently involved allergens in CEFA, with exercise being the most frequent co-factor. NSAIDs were relevant co-factors, even when ω-5-gliadin was the allergen involved. Several patients subsequently tolerated culprit foods and NSAIDs, difficulting the diagnosis and further emphasizing the importance of a correct cofactor evaluation. Molecular allergens had an important role in the diagnosis, avoiding unnecessary OFC. Information about co-factors must be included in all patients with allergy to nsLTPs and ω-5-gliadin.

## 1594 | Allergy to wheat-dependent exercise-induced anaphylaxis (WDEIA) proteins, without? 5-gliadins as responsible

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**Background:** The second well-characterized form of allergy to wheat proteins is wheat-dependent exercise-induced anaphylaxis (WDEIA), with the ω5-gliadins (part of the gluten protein fraction) being the major group of proteins which are responsible, but other forms of food allergy have also been reported, with the proteins responsible including gluten proteins, CM proteins and non-specific lipid transfer proteins.

**Method:** The patient was a 38-year-old man who visited the hospital with acute urticaria just eat bread before run (30 minutes). According the components of bread. it was formed by a mixture of wheat, rye and barley. With a history (for several years) of episodes of severe urticaria after intake a mixture of cereals and/or different kinds of beer.

**Results:** Prick test and specific IgE with wheat, rye and barley were negative and the proteins from allergenic extract from these cereals, and also the gliadins and glutenins fractions were transferred onto a PVDF membrane to carried out a Western blot technique with the patient's serum. The patient's serum recognized several proteins from wheat and millet gliadins not compatible in molecular mass with a ω5-gliadins.

**Conclusion:** The association of w5 gliadin as responsible for the symptoms produced after the intake of products containing wheat and exercise is well referenced but in the case of this patient could have other proteins involved as triggers of their symptoms.

## 1595 | Food-dependent exercise-induced anaphylaxis in 17-year-old adolescent male

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**Background:** Food-dependent, exercise induced anaphylaxis (FDEIA) is an anaphylactic condition that develops in patients who ingest specific food followed by exercise. A variety of foods have been described to be the cause including shellfish, wheat and vegetables. The mechanisms of FDEIA is believed that exercise increases allergen absorption or decreases threshold of mast cell. The investigations such as skin prick test or specific IgE for food are useful because food sensitization is demonstrated. However, a challenge test including ingestion of suspected food followed by exercise is the only method to diagnose this disease.

**Method:** We report a case of FDEIA in a 17-year-old adolescent male.

**Result:** He presented with generalized urticaria and hypotension after eating a barbecue buffet which was one hour followed by playing taekwondo. After treatment with intramuscular adrenaline, antihistamine and systemic steroid, his condition was improved. The barbecue buffet consists of many kinds of food including shrimp, squid, salmon and pork meat which were previously tolerated. He had no past history of anaphylaxis or drug allergy. He was referred to our allergy unit for investigation. We performed skin prick test with food allergens and many kinds of fresh foods that he ate on that day and the result was positive to shrimp (6 mm. in diameter). Three-day challenge protocol was set up a month after recovery and we used aspirin as a cofactor. On the first day, Open challenge for 500 gram of shrimp was administered and the result was negative. On the second day, exercise challenge test based on the American thoracic society guideline was also negative. However, on the last day, he developed generalized urticaria five minutes after the same exercise challenge test which was 1 hour preceded by aspirin intake and 500 gram of shrimp ingestion. But his vital signs appeared to be stable. The patient was administered intramuscular adrenaline and antihistamine with full recovery. He was strongly advised to avoid shrimp for 4-6 hours before exercise and carry an adrenaline autoinjector.

**Conclusion:** The-three day challenge protocol is a definite tool to confirm the diagnosis of FDEIA. A correct diagnosis is important to avoid unnecessary restricted diet.

## 1596 | Food dependent exercise induced anaphylaxis in peach allergic patient—Case report

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**Background:** Most important peach allergens are Pru p 1, responsible mainly for oral allergy symptoms and Pru p 3 (LTP), responsible for a wide range of symptoms, including anaphylaxis. Characteristically in allergy to Pru p 3 symptoms may exacerbate in presence of cofactors, such as exercise, alcohol, NSAIDs.

**Case report:** Patient, 25 year old female, was admitted to the Clinic of Allergology because of recurrent anaphylaxis of unknown cause. Symptoms started in 2016 and appeared on average ones a month, in a form of severe lip and eyelids edema, followed by whizzing, dyspnea and generalized urticarial. They were linked with

consumption of different types of food (pancakes with cream cheese and fruit, peach, Chinese dish, sandwiches—all eaten on other occasions without symptoms) and co-occurring physical exercise (dancing, shopping, walking).

During diagnosis we performed SPT with inhaled and food allergens (Allergopharma), prick by prick tests with peach, banana, apple, pear and bread. We established the concentration of allergen specific IgE (peach, wheat flour, peanuts, hazelnuts) and the level of IgE specific to allergen components (ImmunoCap ISAC).

We performed exercise provocation test and open food challenge with peach.

**Results:** SPT were negative with all tested food and inhaled allergens (inc.egg; milk; cocoa; tomato; carp; apple; banana; strawberry; rye flour; wheat flour; peanuts; hazelnut; citrus, D. farinae; D. pteronyssinus; grass; weeds; clad. herbarium; alt. tenuis; dog; cat; poplar; hazel; alder; birch; mugwort).

Prick by prick tests were positive with fresh peach. Concentration of peach specific IgE was 0.55 kU/L. In ImmunoCap ISAC we found elevated levels of IgE specific to LTPs from different allergen sources (Jug r 3 - 1.3; Pru p 3 - 0.8; Pla a 3 - 0.6; Tri a 14 - 0.5 [ISU-E]).

Open food challenge with a medium size peach was negative. Exercise provocation test without allergen exposition was negative. Exercise provocation test after eating a medium size peach concluded with severe lip and eyelids edema, followed by whizzing, dyspnea and urticarial. Patient received adrenaline 0.5 mg im, steroids and antihistamines with good clinical effect.

**Conclusion:** Patient was diagnosed with food dependent exercise induced anaphylaxis (FDEIA) due to LTP allergy. She was advised to eat peeled fruit and vegetables, avoid cofactors of allergic diseases and carry rescue set (adrenaline, steroids and antihistamines).

## 1597 | Food-dependent effort-induced anaphylaxis: Four cases reports

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**Background:** Food-dependent exercise-induced anaphylaxis (FDEIA) and wheat-dependent exercise-induced anaphylaxis (WDEIA) or is a rare and possible fatal disorder

Cases reports: We report 1case of FDEIA and 3 cases of WDEIA.

Case 1:24-year-old woman with intermittent severe allergic rhinitis and food allergies since childhood. In the last 7 years she registered weekly episodes of FDEIA (urticaria, angioedema, wheeze, drop of BP) especially when during effort and after alcohol intake. Prick tests were positive for grass pollen, mugworth, ragweed, dust mites, celery, soy, sesame, pistachio, mango, honey and shellfish. She followed 3 years of subcutaneous immunotherapy for grasses pollen. The FDEIA episodes frequency and severity diminished during it. Provocation test for celery and mango were positive, for alcohol, soy, sesame, pistachio, honey and shellfish were negative.

Case 2:23-year old man with a 7-year history of acute gluten induced urticaria, recently developed 2 episodes of WDEIA (flushing, severe urticaria and angioedema, wheeze) when he went for gym. Skin test was highly positive for wheat flour and dust mites, in vitro tests for 5 omega gliadin and wheat-specific IgE were positive. Food challenge for wheat was positive. He followed oral immunotherapy for wheat. The WDEIA episodes were rare and mild.

Case 3:30-years old female with mild allergic rhinitis and controlled asthma, with WDEIA (urticaria, angioedema, wheeze, drop of BP) in the last 3 years. Skin tests showed positive results for wheat flour, dust mites and dog hair. Omega-5 gliadin and wheat specific IgE were high, but the provocation test for wheat was negative meanwhile combined wheat and effort provocation test was positive.

Case 4:52-years old female with mild allergic rhinitis, who developed WDEIA (nausea, choking sensation, wheezing, angioedema and urticariae) in the last 5 years. Each episode followed a meal, exercise and antibiotic drug therapy intake. She had positive prick test for wheat flour and house dust mites, positive omega-5 gliadin specific IgE, negative specific IgE for antibiotics. Provocation test alone for wheat and antibiotics was negative. Only a combination of food, exercise and antibiotics induced anaphylactic episodes.

Conclusion: Even the diagnosis is mainly clinical in FDEIA, provocation test is an important tool for diagnosis, avoidance and finding cofactors.

## 1598 | The molecular diagnostic in food-dependent exercise-induced anaphylaxis—Case report

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**Case report:** Food dependent exercise-induced anaphylaxis (FDEIA) is a clinical syndrome characterized by sequential food intake and physical exertion. The pathomechanisms of FDEIA remain largely unknown. A reliable gold standard procedure to diagnose FDEIA has not been established yet. Thus, the diagnosis of FDEIA can be challenging, especially when traditional diagnostic work-up is not concordant with the medical history.

25-year-old female athlete, otherwise healthy, experienced three episodes of FDEIA following running sessions. Two reactions were preceded by intake of salad containing lettuce, tomato and sunflower seeds and the third one occurred after eating celery salad. The patient denied occurrence of any symptoms with physical exertion or food ingestion alone. Physical examination and blood testing did not reveal any abnormalities. The differential diagnosis was performed. In skin prick test and specific serum IgE antibodies sensitization to house dust mite, grass and mugwort were found. The SPT and specific IgE assay to culprit and most common food allergens

were negative. The molecular diagnostic has been applied (Faber, CAAM, Rome, Italy). The test scored positive for Art v, Blo t, Der f, Der p, Eur m, Lol p, Phl p. No positive results for available food molecules including celery, tomato, sunflower seeds and lettuce were found.

The detection of culprit food in FDEIA is of crucial meaning as the syndrome can be life-threatening. The molecular diagnostic has been applied already in diagnosis of wheat-dependent exercise-induced anaphylaxis (WDEIA) proving ω-5-gliadin sensitization in the majority of the cases. As the presented case did not reveal sensitization to culprit food in traditional allergy tests the molecular diagnostic was performed. This test did not show sensitization to culprit food either. However, not all of the molecules are available in molecular assays yet. Cross-reactivity reaction to mugwort and grass has to be considered. The pathophysiological components of physical exertion has to be taken into consideration as well.

This could contribute to the assessment of reasonability of molecular approach in diagnostic work-up for FDEIA and to the establishment of standardized protocols for diagnosis and management of that syndrome.

## 1599 | A case of wheat-related exercise-induced anaphylaxis

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**Case report:** Food allergy to wheat is rare in adults, often reported in exercise-induced anaphylaxis. Food-Dependent Exercise-Induced Anaphylaxis (FDEIA) is a form of food allergy induced by exercise. FDEIA symptoms can include urticaria/angioedema, respiratory and gastrointestinal manifestations and hypotension/shock.

A 61-year-old male patient presented to the emergency department, was admitted after an episode of hives, hypotension and loss of consciousness. His consciousness was restored after treatment with epinephrine, glucocorticoids as well as fluids, and thereafter, the patient reported that the anaphylactic episode occurred when he started rapidly walking 1 hour after eating a slice of pizza. He mentioned that the offended food was tolerated always when it was not followed by a physical exercise. Review of his past medical history and family one were non-contributory with respect to this episode. The allergy skin prick testing for common foods revealed a positive response only to wheat, while and other laboratory test values were within normal ranges. The patient is discharged after instructions on the use of epinephrine auto-injector. He was also advised to avoid wheat containing products up to 6 hours prior to physical exercise.

Our case demonstrated that FDEIA can be characterized by the onset of anaphylaxis soon after physical exercise, when preceded by the ingestion of the responsible food. Avoidance of the combination of the exposure to respective allergen and exercise is the most efficient precautive measure toward subsequent FDEIA episodes.

## 1600 | Residual exercise-induced allergic reactions after successful rush oral immunotherapies for milk and wheat

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**Background:** Milk and wheat allergies are common in Japanese children, and many specialized institutes have been conducting rush oral immunotherapy (ROIT) in patients with persistent milk and wheat allergies. Although ROIT is effective in increasing the tolerable dose as long as ingestion is continued (i.e. desensitization), patients often suffer from exercise-induced allergic reactions (EIARs) after consuming the target food. Furthermore, the frequency, severity and duration of residual EIARs are unclear.

**Method:** We conducted ROIT for 55 children (median 8.7 years old) with milk allergy and 46 children (median 6.8 years old) with wheat allergy during 2010-2015. After 5-12 days of the rush phase in the hospital and a slow-increasing phase at home, patients consumed the maintenance dose (6.5 g milk protein or 5 g wheat protein). After at least three months of the maintenance phase without allergic symptoms, we conducted an exercise provocation test (EPT) after eating the target food. If the EPT was positive, we repeated it after a couple of years to check for remission. The presence or absence of EIARs was based primarily on the results of EPTs but also on the clinical history in some cases.

**Results:** As of December 2017, 44 milk- and 41 wheat-allergic patients were able to continue ingesting the maintenance dose (desensitization). In these patients, 38 milk- and 38 wheat-allergic patients underwent the first EPT at a median of 635 (228-2538) days after ROIT, and the result was positive in 19 (50.0%) and 19 (50.0%) patients, respectively. Among these EPT-positive patients, 10 milk- and 9 wheat-allergic patients conducted a second EPT at a median of 504 (119-1120) days after the first EPT. The result of the second EPT was positive in 7 milk- and 7 wheat-allergic patients. In addition, clinical histories of EIARs were subsequently observed in 4 milk- and 4 wheat-allergic patients after negative results on an EPT. Altogether, 19 (43.2%) milk- and 21 (51.2%) wheat-allergic patients still had EIARs even after getting desensitization as of December 2017.

**Conclusion:** Patients with persistent milk and wheat allergy often have residual EAIRs even after three to five years of desensitization due to the administration of successful ROIT.

## 1601 | Anaphylaxis caused by omega-5-gliadin initially diagnosed as idiopathic anaphylaxis: A case report

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**Case report:** We report the case of a 59-year-old man who experienced two episodes of wheat dependent exercise induced anaphylaxis, initially diagnosed as idiopathic anaphylaxis.

First episode: The patient woke up in the morning and drove to his resort. While driving, he ate a piece of cheese and ham pie. When he arrived, he walked some meters to the garden and started feeling pruritus and dizziness. He lost consciousness and recovered by himself. He was carried to hospital where his vital signs were normal.

The patient has a history of atrial fibrillation and has been on flecainide BID and aspirin at noon for the last four years.

A month after the first episode he visited an allergist. Skin prick tests to aeroallergens and prick to prick tests to the ingredients of the pie were negative. Tryptase levels were within normal limits and skin biopsy was negative for mastocytosis. An endocrinology workup was also negative. The patient was prescribed an epinephrine autoinjector and was asymptomatic for eight months.

Second episode: That morning he had a cup of milk and two slices of toast for breakfast and started working in the garden. Two hours later he experienced pruritus and urticaria and fell unconscious. His wife had to administer two epinephrine autoinjectors before he regained consciousness. After the second episode it was decided to start treatment with omalizumab.

Two months later he experienced an episode of urticaria while working in the garden. He could not recall what he had eaten before.

Based on history, we thought that a cofactor might contribute to the occurrence of anaphylaxis. We performed skin prick tests with peach (LTP) and gliadin, allergens associated with food dependent exercise induced anaphylaxis in our region. The test to gliadin was positive. Specific IgE in serum to omega-5-gliadin was also positive, while specific IgEs to all LTPs tested were negative. The patient was advised to avoid wheat and has been asymptomatic ever since.

Cases diagnosed with idiopathic anaphylaxis may actually be cases in which the culprit allergen has not been identified. Detailed history and extensive workup may contribute to the successful management of these patients.

Written informed consent has been obtained from the patient.

## 1602 | Wheat-dependent exercise-induced anaphylaxis (WDEIA) and NSAIDs: Clinical history is crucial

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**Case report:** Food-dependent, exercise-induced anaphylaxis (FDEIA) is defined as the occurrence of anaphylaxis when exercise takes place within a few hours of the ingestion of a specific food. Wheat is the most commonly reported allergen in FDEIA overall, being wheat-dependent exercise-induced anaphylaxis (WDEIA) the best-studied form of FDEIA. Cofactors and augmenting factors mostly involved in anaphylaxis are, apart from exercise: NSAIDs, alcohol, estrogens and other drugs.

**Background:** A 49-year-old white female without personal or family history of atopy was referred to our outpatient clinic. She had experienced several anaphylactic reactions to NSAIDS (ibuprofen, diclofenac, paracetamol, metamizole) in the previous 5 years. She had been diagnosed of non-allergic hyperreactivity to NSAIDs in another center. She also experienced episodes of facial edema, pruritus and dyspnea related to the ingestion of wheat-containing food and exercise, with and without taking NSAIDs. She eats regularly cereals, fruits (including peach), vegetables and nuts. She can exercise on an empty stomach.

Method: We performed skin prick tests (SPT) with commercial extracts of common aeroallergens, fruits, nuts, cereals, latex, Anisakis, profilin (Pho d 2), polcalcin-enriched date palm, peach nsLTP (Pru p 3) and determination of total and specific IgE (sIgE) to pollens, cereals, fruits, nuts, latex and O-5-gliadin. After obtaining informed consent, we performed single blind oral challenge tests up to the total cumulative doses with: ASA (1000 mg), diclofenac (87.5 mg), paracetamol (2000 mg) and metamizole (2012 mg). The patient rejected performing exercise tests and oral challenge test with ibuprofen.

Results: SPT showed positive results to wheat, Anisakis, D. Pteronyssinus, D. Farinae, Olea europaea pollen, Cynodon and nsLTP. sIgE was positive (> 0.35 KU/L) for: Anisakis, peach, hazelnut, rye and omega-5- gliadine. Serum tryptase: 3.58 μg/L, total IgE: 123 KU/L. Oral provocation tests were negative.

Conclusions :We present a case clinically compatible with WDEIA with NSAIDs intake as augmenting factor. This case emphasizes that a carefully and thoroughly taken medical history is of crucial importance, otherwise WDEIA can easily be unrecognized. As a result, non-allergic hyperreactivity to NSAIDs could be excluded and the diagnose of selective allergy to arylpropionic acids was made. Exercise challenge test could not be performed in our case.

## 1603 | Initial report of the first multicenter prospective web-based registry of anaphylaxis in Korea

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**Background:** To collect precise and standardized data and provide disease control strategy, we have developed the first multicenter prospective web-based registry of anaphylaxis in Korea, including all ages. Here we report the initial data from the registry.

**Method:** The case report form was developed by experienced allergists, and the web-based registry was established in cooperation with a professional medical software team. Twenty-two departments from 16 hospitals took part during the first year (Nov 2016—Oct 2017).

**Results:** The number of anaphylaxis cases registered was 358. The age of registered patients ranged from 2 months to 83 years, and 66% were less than 18 years old. In children, foods (85.7%) were the most common cause of anaphylaxis followed by drugs (6.8%), whereas in adults, drugs (54.5%) were more common than foods (31.4%). The most common food triggers were eggs (27.1%), milk (15.8%), and walnut (7.9%) in children, and shrimps (21.1%), wheat (15.8%), and crab (7.9%) in adults. Among drug triggers in adults, antibiotics (50.0%) were the most common cause followed by NSAIDs (16.7%), and H2-blockers (13.6%). The onset time was≤10 minutes in 48.6%. In children, home was the place of occurrence in more than half of the cases, whereas adults experienced anaphylaxis in out-of-home settings more often than children. Cofactors were present in 19%. Among the 289 cases registered via the emergency department of participating hospitals, epinephrine was administered in 66.8% (62.5% in adults, 69.8% in children) and the route of administration was IM in 90.8%, IV in 6.3%, both IM and IV in 2.1%, and subcutaneous in 0.7%. The number of epinephrine administration was single in 83%, twice in 13.5%, and more than thrice in 3.5%. (More detailed age-specific analysis will be released in near future.)

**Conclusion:** This multicenter prospective registry would provide a better understanding of anaphylaxis, and provide visionary modalities to improve the management and prevention of anaphylaxis in future. [Funded by the Korea Centers for Disease Control and Prevention (2016-E67001-00).]

## 1604 | A case of Kounis syndrome after chamomile tea consumption

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**Case report:** Kounis syndrome (KS) has been defined as an acute coronary syndrome that manifests as unstable vasospastic or non-vasospastic angina, and even as acute myocardial infarction. It is triggered by the release of inflammatory mediators following an allergic insult.

A 77-year-old woman with type II diabetes and hypertension, and unstable angina pectoris as cardiovascular risk factors, has consumed chamomile tea. Thirty minutes later, she developed generalized itching, skin rash, swelling of the face and the throat, chest tightness, dyspnea and syncope. The patient was transferred immediately to the emergency department, and sodium chloride, 50 mg prednisolone, 8 mg dexamethasone, 80 mg methylprednisolone, 5000UI heparin, 75 mg voltaren were intravenously administered along the subsequent 60 minutes under simultaneous treatment with oxygen therapy. An EKG examination is performed based on the patient disease's history, showing a 2.5-3 mm ST-depression on D1-D3 leads, 1 mm on V3, and 3.5 mm on the V4-V6 ones. In addition, 2.5 mm ST-elevation on the aVR and 1 mm on the V1 derivation was observed, associated by a negative T-wave on the V1, V2, and aVR leads. Blood tests revealed a normal troponin I level (of 0.07 ng/mL). Five hours later in the EKG was noticed: isolined ST-segments, and negative T waves on the D3, aVR, and V1 leads. Ultrasound examination revealed normal heart kinetics and function. Following the heart changes, the patient was administered sol. heparin 5000UI twice i.v., nebivolol 5 mg, plavix 75 mg, atorvastatin 80 mg,

monocinque 20 mg, ordinary insulin 10UI s.c., glargine insulin 20UI s.c., and sol. furosemide 20 mg i.v. The patient progressed favorably, and four days after the anaphylactic episode the EKG revealed a 0.5 mm ST-depression on leads V4, and V5, negative T-wave on aVL lead, and normalized one on the V3 one.

This case emphasizes the role of serious allergic reactions as cause of acute coronary syndrome in patients with altered coronary arteries and food intake as cause of Kounis syndrome.

## 1605 | Recall urticaria in two young patients with alpha-gal-syndrome after tick bites

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**Case report:** Patient A (m, age 25) had suffered from 7-8 anaphylactic reactions (hives, nausea, dyspnea and dizziness) within the past 15 months. All episodes occurred 3-5 hours after ingestion of red meat, once with alcohol as a co-factor.

All episodes started with a wheal measuring about 0.5 cm in exact the same spot where he had been bitten by a tick one year before.

Specific IgE to galactose-alpha-1,3-galactose (alpha-gal) was positive (2.55 kU/L). Skin prick testing using raw pork kidney suspension and intradermal testing with Gelafundin® 4% diluted 1:10 also showed positive reactions.

We performed an oral challenge with cooked pork kidney under careful monitoring being able to reproduce the recall urticaria as described above with a cumulative dose of 8 g pork kidney. We stopped the challenge and treated the patient with antihistamines and corticosteroids.

Patient B (m, age 22) reported on several anaphylactic reactions within the past 4 years with symptoms including abdominal pain, diarrhea, as well as dyspnea and loss of consciousness in one of the episodes. All episodes occurred several hours after ingesting food.

Furthermore the patient remembered a tick bite about 2 years before the first anaphylactic reaction, which repeatedly became inflamed and only healed completely over months.

Every episode started with pruritus and a wheal in the area of the former tick bite (in loco).

Specific IgE to galactose-alpha-1,3-galactose was positive (4.37 kU/L) as well as the skin prick testing with cooked pork kidney and intradermal testing with Gelafundin® 4% diluted 1:10.

This patient refused performance of oral challenge tests. An elimination diet of red meat for 12 months resulted in the absence of the symptoms as described.

The diagnosis of alpha-gal-syndrome with recall urticaria in loco was made in both cases. This symptom may also be useful in evaluating results of oral challenge tests as well as an important clinical sign in medical history.

## 1606 | Edible insects: Defining cross-reactivity and reducing allergenicity

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**Background:** Insects have gained interest as alternative nutrient source for humans and animals. However, being a "novel food" in the industrialized part of the world, several safety aspects, like allergenicity, need to be thoroughly addressed. In the present work we evaluated the cross-recognition of IgE from patients allergic to crustaceans, house dust mite or stable flies, using house cricket *Acheta domesticus* (AD), desert locust *Schistocerca gregaria* (SG) and mealworm *Tenebrio molitor* (TM). We further investigated changes of immune-recognition in terms of IgE-binding in differently processed insect extracts.

**Method:** Migratory locust *Locusta migratoria* (LM) was subjected to different extraction methods, enzymatic hydrolysis or thermal processing, whereas TM larvae (TML) were evaluated after different centrifugation modes and pH levels.

**Results:** We revealed that IgE from patients with crustacean allergy shows cross-recognition of *Acheta domesticus*, *Schistocerca gregaria* and stable flies. IgE from house dust mite allergic individuals binds to *Acheta domesticus* and *Schistocerca gregaria*.

Importantly, the cross-reactivity to LM can be deleted by enzymatic hydrolysis with different enzymes or heat treatment (cooking, autoclaving), but not by different extraction methods. Changes of pH and varying centrifugation steps are not sufficient to reduce IgE-binding to TML.

**Conclusion:** Our results show that patients allergic to crustaceans, house dust mite or stable flies-allergic patients cross-recognize desert locust and house cricket proteins, and crustacean-allergic patients also flies proteins. Furthermore, we confirm that the appropriate food processing method of insect proteins can reduce the risk of cross-reactivity for crustaceans- and house dust mite-allergic patients.

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## 1607 | Eosinophilic Esophagitis in a food allergy consultation: Characterization and comparison between children and adults

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**Background:** Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus. It's immunologically mediated and

characterized by symptoms related to esophageal dysfunction and esophageal mucosal infiltration by eosinophils (Eos).

**Objective:** Characterize patients (Pts) with EoE diagnosis and analyze the differences between pts with diagnosis at pediatric (Ch, <18 years old) and adult age (Ad, ≥18 years old).

**Method:** Observational retrospective study of pts diagnosed with EoE followed in our Department, from February 1st of 2009 to July 31st of 2017. Pts were divided in Ch and Ad, characterized according to demographic data, atopic background, symptoms, sensitizations [skin prick tests(SPT), Epicutaneous tests(EpicT)], serum total IgE and Eos, findings in upper digestive endoscopy (UDE) and biopsies. The correlation between food sensitization, clinical severity (visits to ER services or hospitalization due to complications of EoE, SClin) or severe histology (biopsy with Eo> 50 and/or microabscesses, SHist) was evaluated.

**Results:** 74 pts (81% male, average age 27 ± 17 years), 36 Ch and 38 Ad. The average age of symptoms onset and EoE diagnosis (years) was for Ch 7 and 9, for Ad 31 and 34, respectively. 96% Ch and 67% Ad were atopics. The most frequent symptoms of EoE were dysphagia (73%) and gastroesophageal reflux(46%) in Ch; impaction(85%) and dysphagia(46%) in Ad. 92% Ch and 71% Ad had aeroallergens sensitization. 77% Ch and 69% Ad had food sensitization. The most frequent positive tests were for Ch: SPT to milk(25%) and shellfish(19%), EpicT to shellfish(50%) and meat(19%); for Ad: SPT to milk(21%), fresh fruits and nuts both 18%), EpicT to shellfish(35%) and meat(13%). UDE showed: 65% striation and white plaques in 50% Ch; white plaques in 42% and esophageal rings in 35% Ad; 13% Ad but no Ch had stenosis. SHist (46%) was associated with SClin (35%), $P = 0.001$ in Ch; but this was not observed in Ad group [SClin(22%) and SHist(17%), $P = 0.5$]. There was no correlation between food sensitization and SClin or SHist in both groups($P > 0.01$). The average values of serum total IgE (KUA/L) were 653 in Ch and 458 in Ad; Eos were 679 and 413, respectively in Ch and Ad. There was no correlation between values of Eos and SClin or SHist.

**Conclusion:** We found, as expected, a predominance of males with EoE diagnosis. Ch were more frequently atopic and had aeroallergen and food sensitization. Impaction and esophageal stenosis were more frequent in Ad than Ch. SHist was associated with SClin only in Ch.

## 1608 | Eosinophilic esophagitis in children

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**Background:** Eosinophilic esophagitis (EE) characterized by chronic eosinophilic inflammation in esophageal mucosa is rarely seen in children.

**Method:** Three children with EE, boys aged 1.5-11 years, were assessed over 6 months to 3 years.

**Results:** 2 cases developed in infancy. One had dyspepsia and low weight gain in infancy soon after feeding began. Another had symptoms in infancy but not diagnosed until age 6 with dysphagia and esophageal stricture.. The third case was diagnosed at 11 years old after 2 episodes of food impaction in the esophagus beginning at age 9. All cases had allergic comorbid diseases including atopic dermatitis in all 3 and allergic rhinitis in 2. Skin prick tests were positive to several food allergens (cow's milk, egg protein) in 2, to dust mite in 2 and to pollens in 1. Serum total IgE levels ranged from 490 to 1039 IU/mL. Eosinophils in peripheral blood were elevated in all 3, reaching 10%-13%. Treatment included restricted diet and topical budesonide 1-2 mg daily depending with periodic endoscopic biopsy. In all cases clinical improvement occurred by one month of treatment, with endoscopic confirmation. Morphological improvement followed after 3-6 months of treatment. Side effects of medical treatment were not observed.

**Conclusion:** Clinical presentation of EE in children varies, partly depending on presenting age, with co-morbid allergic disease often seen. Duration of treatment with topical corticosteroids requires individualization as discontinuation of treatment may cause relapse of disease.

## 1609 | Clinical profile of eosinophilic esophagitis in children and adults

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**Background:** Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease limited clinically and pathologically to the esophagus, and whose prevalence is increasing. It is characterized by symptoms of esophageal dysfunction and, histologically, eosinophilic inflammation.

AIM: To evaluate clinical features and differences between children and adults suffering EoE.

**Method:** A retrospective review on databases of two centers, including 40 children and 40 adults with confirmed EoE in the last six years.

**Results:** The mean age at diagnosis was 10 years in children and 34 years in adults, more frequent in males (3:1). In the pediatric group, three had first-degree relatives with EoE and three had celiac disease. Two children had performed milk oral immunotherapy and five adults aeroallergens subcutaneous immunotherapy.

Most of them were atopics with sensitization to aeroallergens (77.5% of children and 82.5% of adults) and food allergens (75% of children and 82.5% of adults), without statistically significant differences. The most frequent foods were fruits and nuts in both groups. We found significant statistical differences in fruits (35% of children

and 57.5% of adults; $P = 0.007$) and cereals sensitization (5% of children and 47.5% of adults; $P < 0.001$).

In the clinical presentation we observed significant statistical differences in impaction (22.5% of children and 82.5% of adults; $P < 0.001$), dysphagia (42.5% of children and 77.5% of adults; $P < 0.001$) and abdominal pain (25% of children and 7.5% of adults; $P = 0.034$).

In the endoscopic findings children had more frequently exudates (92.5%; $P < 0.001$) and adults had esophageal trachealization (50%; $P < 0.001$). Significant statistical differences were found in the treatment with topical corticosteroids (30% of children and 77.5% of adults; $P < 0.001$) obtaining a variable positive response. 77.5% of patients in both groups received food elimination diet, 45% with four or more foods.

**Conclusion:** EoE presents differences in the sensitization profile, clinical manifestations and endoscopic findings according to the age of presentation. The response to pharmacological treatment is variable and a high percentage of patients receive food elimination diets. It is a pathology difficult to control, therefore new non-invasive techniques would be useful in order to facilitate its management.

## 1610 | Modulation of gut microbiota in patients with nickel allergy and IBS after diet and probiotics supplementation

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**Background:** Dietary modifications and increased antibiotic use have profoundly altered the co-evolved relationship between host and microbiota. Moreover in recent years, strong evidence of a possible relationship between modifications of the gut microbiota composition and development of Irritable bowel syndrome (IBS) has been collected. In sensitized subjects, ingested nickel (Ni) may induce gastrointestinal symptoms similar to IBS, in addition to typical systemic cutaneous lesions (systemic nickel allergy syndrome [SNAS]). The study aimed to evaluate the effects of probiotic supplementation, in addition to diet, in IBS and SNAS patients, in terms of modulation of faecal microbiota population, reduction of GI and cutaneous symptoms, increase of patient's quality of life and modification of gut dysbiosis.

**Method:** Forty patients aged between 18 and 65 years, affected by IBS, Ni sensitization and LTP sensitization were enrolled to evaluate gut dysbiosis. DNA extraction method (Next Generation Sequencing) with commercial kit (Microbiopassport®) was performed on stool samples. IBS patients were divided in two groups, according a gluten free diet prescription or a low FODMAPs diet prescription for three months. Similarly, (suspected) SNAS patients (confirmed by 5% Ni sulfate in petrolatum patch test) were prescribed a low Ni diet (100 μg/kg nickel content during the first four weeks and then up to 200 μg/kg up to three months). Two LTP (Lipid Transfer Protein) sensitized patients underwent a LTP free diet.

Gut dysbiosis was re-assessed after a fixed probiotic supplementation. A sex-age matched group of individuals without history of IBS, SNAS or any gastrointestinal disease was considered as control.

Gastrointestinal symptoms were evaluated using the visual analogue scale before and after treatment.

**Results:** At baseline, 31 out of 40 patients had an abnormal dysbiosis index [n.v. 0.070, 0.326]. Chi-square tests were performed, providing evidence of a clinically significant difference between patients and healthy controls ($P$-value <0.05 for both IBS and allergic patients). Dysbiosis values after 3 months returned almost to normal. Comparison of VAS scales after three months showed significant improvement of gastrointestinal symptoms.

**Conclusion:** Our preliminary findings suggest that probiotic implementation could be useful in patients with SNAS on a low-Ni diet to increase population diversity, which could contribute to restore the intestinal homoeostatic conditions.