

ABSTRACTS

SUNDAY, 18 JUNE 2017

LB TPS 01

ALLERGEN IMMUNOTHERAPY: FROM VACCINES TO EFFICACY AND SAFETY

1517 | The effect of azoximer bromide in treatment irritable bowel syndrome

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Introduction: Some evidence suggests that irritable bowel syndrome (IBS) is affected by the immune system. This study focused effect of Azoximer bromide in concert with Probiotics in treatment of IBS.

Objectives: Our study included 16 children treated by probiotic and azoximer bromide (study group), and 10 children treated only by probiotic (control group). Lymphocytes subset was analyzed by flow cytometric, phagocytic activity was assessed by latex article, IgE and serum cytokine were evaluated by ELISA. The intestinal bacterial microbiota was assessed by medical microbiologic method.

Results: The change of immune status in IBS patient is holistic description in our articles. After therapy in group study the percentage of all lymphocyte phenotype subsets, phagocytic activity, IgE, cytokine level and intestinal microbiota were near of healthy subjects compare with control group. In control group the mean percentage of CD3 and CD4 were less than in healthy subjects ($P < .05$), the mean percentage of CD8, CD16 and CD22 were more than in healthy subjects ($P < .05$). The mean level of IL-4 and TNF- α were significantly lower when compared with before therapy ($P < .001$). No significant difference between before and after therapy was observed in serum concentration of the mean level of IFN- γ , IL-1 and phagocytic activity. Intestinal dysbiosis is corrected after therapy in both groups.

Conclusions: Immunomodulator as Azoximer bromide when contributed with probiotic can to elicit or amplify an immune response in patient have suppressed immune system

Probiotic is a prescription medication for treatment of irritable bowel syndrome and in addition for correct immune status may be prescribed azoximer bromide.

1518 | Sublingual immunotherapy in treatment of perennial allergic rhinitis with or without allergic asthma

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Introduction: Sublingual immunotherapy is an effective treatment for perennial allergic rhinitis with or without allergic asthma (1), however real-world data on adverse effects, adherence and clinical outcomes are not commonly reported (2). Here we summarise patient-reported symptoms, adherence and adverse effects from using sublingual immunotherapy to perennial allergens, in a single specialised allergy centre in London, UK

Objectives: Online questionnaire responses from 44 patients (37 adults, 7 children) receiving sublingual immunotherapy with perennial allergens were collated as part of a service evaluation. Questionnaires were administered prior to initiation of immunotherapy, and then at monthly intervals. This project was not funded by the pharmaceutical industry.

Results: Products used varied according to patient and clinician preference, and were manufactured by Allergy Therapeutics, UK, and Immunotek, Spain. Treatment was initiated and supervised according to the manufacturers' instructions. Routine premedication was not used.

Three patients (6.81%) reported local symptoms during the first 14 days, that resolved with antihistamines. There were no adverse events reported. Adherence levels were high, and were confirmed monthly, with just one adult patient terminating treatment after one year due to personal reasons not related to treatment. All patients reported improvement in symptoms on average after 3.2 +/- 0.3 months with reduction in nasal and ocular symptoms frequency of asthma exacerbations.

Conclusions: Analytics of the received data showed improvement in nasal ocular and asthma symptoms, reduction in medication score after three months of treatment, that continued during the three year course. Assessment of patients' progress post treatment is ongoing.

(1) Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen) *Allergy*. 2008;63 (Suppl 86):8-160.

(2) Wheatley LM, Togias A. Allergic Rhinitis. *The New England Journal of Medicine*. 2015;372(5):456-463. <https://doi.org/10.1056/nejmcp>.

Proportion of patients reporting symptom improvement.

Month	Number of patients	%
1	2 adults; 1 child	6.82
2	13 adults; 4 children	38.3
3	30 adults; 6 children	81.8
4	35 adults; 7 children	95.4

1519 | Real life study on the therapeutic criteria and adverse events in the course of sublingual allergen immunotherapy in 150 patients with allergic rhinitis and asthma

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Introduction: Allergen immunotherapy is the only etiological treatment of atopic diseases and the only available disease modifying approach which makes its implementation in everyday practice very important. The use of the subcutaneous route is well established for more than a century but at the same time restricted by the high frequency of local and systemic adverse reactions. It is well known and generally accepted that all these disadvantages are not characteristic for the sublingual route of administration (SLIT). However good quality real-life evidence on that matter is scarce.

Objectives: The study is designed to assess the type and frequency of adverse reactions in patients with allergic rhinitis and asthma in the course of SLIT in an everyday clinical setting. The aim of the study is to estimate 1) the proportion of patients experiencing at least one systemic adverse reaction, 2) the incidence rate of systemic reactions in a real life setting and, 3) the possible risk factors involved in these reactions.

Material and methods: Patients, 145, women (43, 29.7%) and men (102, 70.3%), referred to the outpatient clinic of a major private hospital in Sofia, Bulgaria, for a suspected IgE-mediated allergic disease were included. Patients were diagnosed with an atopic disease on the basis of their medical history, SPT results and serum specific IgE levels. Upon meeting the criteria for starting SLIT, they were put on a regimen with the actual allergen extract (Stallergenes, Antony, France). Appointments were made for regular visits to doctor's office. Patients were instructed to contact their doctor as soon as they experienced whatever kind of an adverse event.

Results: On the basis of medical history, several atopic diseases were identified: atopic dermatitis (1.4%), asthma (32.4%), conjunctivitis (82.8%), rhinitis (99.3%). 125 (86.2%) persons were identified as sensitized to pollen. Sensitization was clinically significant in 116 (90.6%) patients. In 62 (84.95%) patients sensitization to house dust mites (HDM) was found. Sensitization was clinically significant in 52 (71.2%) patients. Adverse reactions were 20/145 (13.7%). Local reactions were 17/145 (11.7%) and systemic—2/145 (2.06%). The most

common local reactions were twinkling, itching, redness in oral cavity (106.7%), edema in oral cavity (60%).

Conclusions: Our data confirm on the basis of real-life evidence that SLIT is a safe AIT regimen. Adverse reactions are predominantly local, mild with low seriousness; systemic reactions are moderate, grade I and II.

1520 | A novel H4R-based epitope vaccine screening by phage display peptide library change the unbalance of the Th1 /Th2 in an allergic rhinitis model

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Introduction: Histamine receptor 4 (H4R) was suggested as a new therapeutic target because of its wide expression on almost all the immune-related cells.

Objectives: To construct a vaccine based on histamine receptor 4 and evaluate its therapeutic effect on the allergic rhinitis.

Results: FNKWMDCLSVTH, the 12 peptide named as P-FN12, could decrease the allergic symptoms such as sneezing and nasal rubbing. It also elicited increased levels of IFN- γ , IL-2 but decreased levels of IL-6, Th1 /Th2 cells ratio in the PBMCs cultures.

Conclusions: P-FN12+CTB@Lipo could suppress Th2 response and enhanced induction of Th1 in an allergic rhinitis model.

1521 | Preseasonal grass pollen SLIT in at risk individuals confers protection from epidemic thunderstorm asthma

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Introduction: Epidemic thunderstorm asthma in Australia is triggered when ryegrass pollen (RGP) grains rupture in storm moisture releasing respirable 3 μ m starch granules impregnated by major allergens. Thunderstorm downdrafts draw granules to ground level mimicking aerosol challenges. Susceptibility to thunderstorm asthma is conferred by RGP allergy, which affects >20% of people in south-east Australia. Asthma risk correlates with the elevation of specific IgE in serum. Last November, a springtime thunderstorm in Melbourne triggered the most devastating recorded thunderstorm asthma event worldwide. In a city of 4.5

million, emergency services were overwhelmed by 10,000 hospital presentations. Nine people died.

Objectives: From 2014-2016, we performed an investigator-initiated study (NCT02014623) of sublingual desensitisation for seasonal allergic rhinitis (SAR) in RGP allergic patients using a commercial five-grass tablet. Our aim was to determine efficacy of a four-month (June-September) pre-seasonal regimen, with the short duration to improve adherence. Treatments were concluded before the RGP season (October-December) to reduce risk under local conditions of sudden and extreme pollen loads augmented by local wind patterns. Twenty three participants completed 2-3 years of treatment prior to November 2016. This provided a serendipitous experiment to examine the protective role of prior immunotherapy in the face of extreme thunderstorm asthma.

Results: As anticipated, treatment reduced SAR symptoms (mean reduction in rhinitis symptom Visual Analogue Score 52 ± 29 mm, $P < .001$) with consistent changes of immunological efficacy: specific serum IgG₄ rise (median 0.37 g/L to 1.16 g/L, $P < .01$) and increased proportions of CD4⁺CD25⁺Foxp3⁺ Treg (2.9% to 6.1%, $P < .001$) and CD4⁺CD45RA⁺Foxp3⁺iTreg (3.8% to 6.4%, $P < .01$) after treatment, as determined by in vitro stimulation of PBMC with RGP extract. Controls on medical therapy showed no change. During and after the thunderstorm event, 5/23 participants described mild asthma symptoms, but none experienced a flare requiring emergency presentation or systemic corticosteroids. This was despite elevated mean RGP serum specific IgE (52.7 ± 38.4 IU), and 8/23 having documented asthma.

Conclusions: Pre-seasonal immunotherapy in high-risk individuals protects from unpredictable epidemic thunderstorm asthma. This has profound public health implications for such devastating events which are likely to increase with climate change.

1522 | Clinical research on the sublingual immunotherapy in mite-sensitized patients with allergic rhinitis

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Introduction: To evaluate the clinical efficacy and safety of sublingual immunotherapy (SLIT) in mite sensitized patients with allergic rhinitis (AR). Its compliance and related factors were also particularly analyzed.

Objectives: A total of 320 patients from Hangzhou First's hospital with moderate-to-severe AR were enrolled in this study. All patients were divided into two groups: SLIT group and SLIT associated with endonasal glucocorticosteroids. The grade of symptoms and signs, adverse events, as well as patient's adherence to the treatment, were carefully recorded and analyzed during the two years' sublingual immunotherapy. Statistical analysis was performed using SPSS software.

Results: A total of 43 patients in first group and 27 patients in second group were withdraw from the therapy group and the rate of compliance respectively were 73.1% and 83.1%. After the whole period of treatment, both two groups' grade of symptoms and signs were significantly failed. During the course of treatment, no severe general reaction happened.

Conclusions: The SLIT is effective and safe in mite-sensitized patients with AR. In the early stage of SLIT, association with endonasal glucocorticosteroids can raise the compliance.

1523 | Intra-seasonal initiation of the SQ-standardised grass sublingual tablet is well tolerated when applied by allergy specialists and allergologically experienced general practitioners

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Introduction: Intra-seasonal start of treatment (IS) with the SQ[®] grass sublingual (SLIT) tablet (GRAZAX[®], ALK, Denmark) has been previously demonstrated to be well tolerated if applied by allergists. Objective of our study was to investigate tolerability of IS comparing patients treated by allergists and allergologically experienced general practitioners (GPs).

Objectives: In a non-interventional, open-label, observational study, data on IS with the SQ grass SLIT-tablet were recorded in patients who started administration within grass pollen seasons by allergists and GPs in Germany. Adverse events (AEs) were recorded by the physicians at first administration and at the end of the 1 to 3 month observation period, and AEs and daily administration of the tablet in patient diaries for the first 14 days.

Results: A total of 198 patients were treated with the SQ grass SLIT-tablet within the study, 179 patients by IS (140 by allergists and 39 by GPs) and 19 patients post-season; average treatment period was 47 days. AEs related to IS were recorded in 43.6% of patients, and in 31.8% at first administration; no relevant difference between allergists and GPs were observed. In the subgroups of patients treated by allergists and GPs significant differences were observed for age (means \pm SD: 28.8 \pm 14.4 vs. 34.1 \pm 13.4 years, $P = .0191$), bronchial asthma (38.5% vs. 17.1%, $P = .0043$), concomitant allergies (69.2% vs. 48.6%, $P = .0223$), application of diagnostic tests for grass pollen allergy (61.5% vs. 90.0%, $P < .0001$), use of symptomatic medication in the previous grass pollen season (82.1% vs. 62.1%, $P = .0198$), concomitant treatment of other diseases (15.4% vs. 5.7%, $P = .0467$) and anti-allergic premedication at first administration (15.4% vs. 2.9%, $P = .0026$).

Conclusions: The intra-seasonal start of treatment with the SQ grass SLIT-tablet in patients routinely treated by allergists or allergologically experienced GPs was well tolerated although patient characteristics were different with respect to age, proportions of patients with asthma and concomitant allergies, symptomatic medication use in the previous grass pollen season and concomitant treatment of other diseases, and confirmed the safety profile from a previous placebo-controlled clinical trial and data from a previous real-life study on intra-seasonal start performed by allergists.

1525 | Patient's perceptions of using two types of sublingual immunotherapy

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Introduction: In the autumn/winter of 2015/16 due to unforeseen circumstances we had to change the manufacturer of the sublingual immunotherapy (SLIT) treatment we were using to treat children with grass and tree pollen driven allergic rhinitis (AR). It is not common practice to change the SLIT product during the treatment programme, which is a duration of three years. The primary outcomes of treatment with SLIT are safety and efficacy. Efficacy is associated with compliance, which is enhanced by acceptability. This forced change of treatment gave us an opportunity to compare both products, within the same patient group for acceptability.

Objectives: A retrospective evaluation of patients who had received both SLIT products was undertaken. Patients were in their second or third year of treatment and thus had taken both SLIT products and could compare their experience of both treatments. Parents were asked their experience of; side effects while taking SLIT; the taste of both products; parental perceptions of efficacy; conventional medication taken during the pollen season.

Results: We received 99 responses to our questionnaire. Most children (54%) were in their 2nd year of treatment with 66% taking both tree and grass SLIT. 45% preferred the taste of the new product, 34% had no preference. 63% experienced no side effects of the new treatment, of those who did the majority (67%) experienced oral pruritus. 22% required a daily antihistamine and 4% reduced the dose of the SLIT to prevent side effects. 80% continued to take conventional treatment for allergic rhinitis, and many parents (72%) felt there was a definite improvement in their child's symptoms. Only 11% felt there was no improvement.

Conclusions: Despite changing manufacturer during the treatment programme there was a perception by parents that SLIT was working. The new treatment was accepted by patients, with many

children preferring the taste of the new treatment and experiencing minimal side effects. Further studies would be useful to compare the efficacy of SLIT in terms of quality of life, symptom and medication reduction when treatments are changed midway through a programme of treatment.

1526 | Suitability of the facilitated antigen binding-assay for evaluation of treatment success in birch and grass pollen immunotherapy

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Introduction: Currently, the facilitated antigen binding (FAB)-assay is discussed as one potential surrogate marker for monitoring successful allergen immunotherapy (AIT). The assay measures binding of allergen-IgE-complexes to B-cells. When sera from patients undergoing AIT are applied, binding to B-cells is often inhibited, which is proposed to be associated with treatment success.

In the present work, the FAB-assay was performed with 69 sera of a double-blind randomized multicenter clinical trial. Included were patients with dual allergy (birch and grass) that were either treated with grass (n=34) or birch (n=35) pollen allergoid, one group served as the control for the other group. Effects of AIT were assessed by measuring nasal symptoms upon grass and birch pollen exposure in an environmental challenge chamber with each allergen before and after 9 months of AIT. All sera were measured in the FAB-assay blinded with grass and birch pollen extract (GPE, BPE) as well as with the most relevant single allergens Phl p 1, Phl p 5 and Bet v 1 in two concentrations.

Objectives: The aim of this work was to evaluate if the FAB-assay is suitable to determine treatment success on single patient basis in birch and grass pollen IT. Specific and unspecific FAB-assay inhibitions were analyzed.

Results: About ¼ of patients receiving grass pollen allergoid, showed an inhibition after AIT with GPE. Vice versa also about ¼ of patients receiving birch pollen allergoid showed inhibition after 9 months of AIT with BPE. The remaining patients showed no inhibition and are suggested by the assay as potential non-responders. As expected, when investigating patients receiving birch allergoid with the FAB-assay with GPE and in reverse, up to 90% showed no inhibition after 9 months. The application of single allergens resulted in slightly less specific and slightly more unspecific inhibitions.

Conclusions: With regard to the treatment and control group, the FAB-assay with BPE and GPE revealed a specific treatment effect. Interestingly, this effect was slightly decreased when applying the single allergens. In a next step, FAB-assay results will be compared to the clinical parameters, especially to evaluate if patients that are suggested by the FAB-assay as non-responders are also with other parameters non-responders.

1527 | Development of an ELISA-based surrogate assay for measuring blocking IgG induced by ait

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Introduction: The induction of allergen-specific blocking IgG antibodies which inhibits patients' IgE binding to the allergen is a major mechanism in successful allergen specific-immunotherapy (AIT).

Objectives: We have developed an ELISA-based surrogate assay for measuring the capacity of IgG induced by AIT in a given patient to block the very same patients allergen-specific IgE binding. The assay was evaluated using sera from grass pollen allergic patients who had been treated with the recombinant grass pollen vaccine BM32 consisting of carrier-bound non-allergenic grass pollen allergen peptides from the four major grass pollen allergens Phl p 1, Phl p 2, Phl p 5 and Phl p 6 or with placebo. Blood samples were collected before (baseline visit), during the entire study period and after 2.5 years of treatment. Plasma samples were obtained and a heat inactivation procedure involving heating treatment at 56°C for 1.5 hours has been used for inactivation of the IgE antibodies. ELISA plate-bound rPhl p 1, 2, 5 and 6 mix was pre-incubated with the heat treated plasma containing only IgG antibodies and then exposed to untreated patients' plasma from baseline visit containing allergen-specific IgE. Bound allergen-specific IgE was detected with anti-human IgE antibodies and the mean percentage of inhibition of IgE binding was calculated as: % inhibition of IgE=100 – (OD different visits/OD baseline visit) x 100.

Results: Induction of allergen-specific blocking IgG antibodies inhibiting patients' IgE binding to the allergen was clearly detectable. Our results demonstrated that heat treatment at 56°C for 1.5 hours destroys IgE antibodies without destroying the activity of allergen-specific blocking IgG antibodies produced during the course of AIT. Sera from BM32-treated patients but not from placebo-treated patients strongly inhibited allergen-specific IgE binding and the inhibitory capacity of blocking IgG antibodies remained detectable even 2.5 years after treatment.

Conclusions: The described surrogate ELISA assay will be useful for measuring the induction of truly IgE-blocking IgG antibodies in the course of AIT.

1528 | Treatment with a 300 index of reactivity (IR) 5 grass pollen tablet is associated with long-term relief of allergic rhinitis: a retrospective real-life dataset subgroup analysis

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Introduction: A retrospective study was conducted aiming to assess long-term efficacy of grass pollen sublingual immunotherapy (SLIT) tablets in allergic rhinitis (AR), their impact on asthma onset and progression of asthma. This abstract provides outcomes of subgroup analysis related to long-term efficacy of patients receiving 300IR 5-grass pollen tablet in AR.

Objectives: In a retrospective analysis of a German national longitudinal prescription (Rx) database (IMS LRx), two cohorts of patients with grass pollen AR were selected: active treatment (AT) and control (CT) groups. The primary endpoint was long-term efficacy of grass pollen SLIT tablets in AR assessed with the change from the year preceding index date in Rx of AR symptomatic medications to the period after treatment cessation. Total number of Rx per time period were summed and divided by the length of the time period. Linear regression was used to compare changes over time in rescue symptomatic AR medication use in the 2 groups. Confounding variables (gender, age group at the index date, main prescriber, asthma status at the index date and the length of the analytical time period) were corrected in all analyses. Sensitivity analysis was conducted to assess long-term efficacy in the subgroup of patients receiving 300IR 5-grass pollen tablet in AR.

Results: Among the 1,466 patients receiving the 300IR 5-grass pollen tablet, the median yearly treatment duration is 5.5 months. The average number of 300IR 5-grass pollen tablet group treatment courses is 2.8, slightly lower but close from AIT duration of treatment recommended by Guidelines. A significant long-term effect in improvement on the progression of AR after treatment cessation compared with CT group was observed: linear regression analysis RC [95% CI]=−0.202 [0.245-0.158]; *P*<.001. This reduction was slightly stronger than the one observed in the overall grass pollen SLIT tablet group, and persisted all over follow up period lasting from 2 to 5 years after treatment cessation.

Conclusions: The 300IR 5-grass pollen tablet has reinforced its clinical claim of long-term effect on allergic rhinitis after treatment cessation.

1529 | Comparison of immunogenicity of the recombinant B cell epitope-based grass pollen vaccine BM32 with allergen extract-based SCIT

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Introduction: Recently we have engineered a recombinant hypoallergenic vaccine comprising peptides from 4 major timothy grass pollen allergens (Phl p 1, 2, 5 and 6), fused to the PreS protein domain of hepatitis B virus, entitled BM32. The goal of this study was to compare three monthly injections of BM32 with standard treatment courses of 4 commercial subcutaneous allergen-extract-based vaccines regarding the induction of allergen-specific blocking antibodies in rabbits.

Objectives: Rabbits were immunized with BM32 and four allergen extract-based commercial vaccines. Levels and kinetics grass pollen allergen-specific IgG responses and the ability of these antibodies to inhibit allergic patients' IgE binding to grass pollen allergens were studied by ELISA, and their ability to inhibit T cell reactivity by T-cell proliferation assay.

Results: Three injections of BM32 induced grass-pollen allergen-specific protective IgG responses in rabbits which were comparable or better than those induced by multiple injections of allergen extract-based vaccines. BM32 was the only vaccine inducing IgG antibodies capable of inhibiting allergic patients IgE binding to the major grass pollen allergen Phl p 2.

Conclusions: Our data indicate that AIT with BM32 requires only few injections to induce protective allergen-specific IgG antibodies which promises more convenient AIT schedules as compared to allergen extract based vaccines. This work was supported by grants from the Christian Doppler Research Association, Vienna, Austria, Biomay AG, Vienna, Austria and the Austrian Science Fund (FWF), project F4605.

1531 | Effect of immunotherapy with total body bacterial extract inactivated in the prevention of infections in upper airways in patients with partial IgA deficiency

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Introduction: Selective IgA deficiency is the most common type of primary immunodeficiency. The infectious diseases of the respiratory

system are the most prevalent clinical manifestations in individuals with this immunodeficiency and, to date, there is no specific treatment for this pathological condition.

Objectives: We evaluated the use of sublingual immunotherapy with bacterial extract total body inactivated in a five patients with partial IgA deficiency presenting numerous recurrent episodes of upper airway infections. The extract was composed of total inactivated body of *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Moraxella (branhame) catarrhalis*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Streptococcus gordonii (S. mitis)* and *Streptococcus pyogenes*. The concentration used was 2 X 10⁹ colony forming units (CFU)/mL.

Results: After 12 months of clinical follow-up we observed a significant reduction ($P < .01$) in the number of episodes of respiratory infections and a reduction of antibiotic prescription.

Conclusions: The results suggest that the use of immunotherapy with total body bacterial extracts may be an important tool in the prophylactic treatment of upper airway infections in patients with partial IgA deficiency.

1532 | Influence of combined allergen-specific immunotherapy on immune status of patients with pollinosis with sensitization to the pollen and domestic allergens

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Introduction: With the purpose to evaluate efficiency of treatment with combined Allergen-specific immunotherapy, clinical studies of patients were performed on the base of municipal allergology center of the city Dnipro (Dnipropetrovsk, Ukraine).

Objectives: 29 patients with pollinosis with sensitization to the pollen and domestic allergens aged from 18 to 55 years (average age—36.0±1.89) including 16 women and 13 men were a subject of supervision. Patients were examined before and after combined Allergen-specific immunotherapy by the modified methodology. IL-4, IFN- γ , CD4, CD8, IgE indexes were used as efficiency criteria. For statistical analysis of data, license program STATISTICA v.6.1 was used. Taking into account the law of distribution, quantitative indexes were presented as a mean value and standard error ($M \pm m$) or median and quartiles (Me [LQ; UQ]), and for their comparison corresponding criteria of Student's test and Wilcoxon Pairs Test (T) in dynamics were applied

Results: The analysis of the obtained results testifies that after combined ASIT a reliable change of indexes of cellular link of the

immune system and cytokines profile was marked: increase of relative content of subpopulations of T-cell, expressing receptors CD4 (from 37.6 ± 1.04 to 50.4 ± 2.93 $P < .001$) and CD8 (from 23.4 ± 1.24 to 38.4 ± 3.63 $P < .001$), decline of level of IL-4 (from 4.25 ± 0.36 pg/mL to 3.15 ± 0.26 pg/mL; $P < .01$) on the background of increase of producing of IFN γ (from 4.20 ± 0.57 pg/mL to 6.61 ± 0.69 pg/mL; $P < .05$). Dynamics of level of general IgE in the blood serum was positive as well, this was manifested by its reliable decline from 243.7 [$105.9; 678.6$] pg/mL to 184.8 [$108.5; 407.6$] pg/mL ($P < .05$).

Conclusions: Modified combined ASIT testifies to switching of immune answer from Th-2 to Th-1 cells.

1534 | A treatment with 300 index of reactivity (IR) 5-grass pollen tablet is associated with a reduction of asthma onset and a reduction of its progression

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Introduction: A retrospective study was conducted aiming to assess long-term efficacy of grass pollen SLIT tablets in allergic rhinitis (AR), their impact on asthma onset and progression of asthma. This abstract focuses on a subgroup analysis related to long-term efficacy of 300IR 5-grass pollen tablets on new onset of asthma and its progression.

Objectives: In a retrospective analysis of a German national longitudinal prescription (Rx) database (IMS LRx), two cohorts of patients with grass pollen AR were selected: active treatment (AT) and control (CT) groups. The secondary endpoints were occurrence and progression of asthma, estimated from Rx of Guidelines-recommended medications. The presence of asthma was defined as at least two prescriptions of these medications in the same year or in two successive calendar years. Asthma progression was estimated by tracking Rx of long-acting β -agonists (LABAs), combinations of LABAs and inhaled corticosteroids (ICS), methylxanthines, leukotriene antagonists and depot formulations of systemic corticosteroids, SABAs and ICSs. The occurrence of asthma was analysed as a binary (yes/no) variable. Structures of analyses of the occurrence and evolution of asthma being linear and logistic regressions respectively. Sensitivity analysis was conducted to assess long-term efficacy in the subgroup of patients receiving 300IR 5-grass pollen tablet in AR.

Results: Among patients receiving 300IR 5-grass pollen tablet 21% had asthma at index date ($n=304$). The sensitivity analysis, conducted in the subgroup of patients receiving 300IR 5-grass pollen tablet without asthma at index date (78%), showed a significant effect on asthma onset during full analysis period (OR [95%CI]=0.676, [0.499-0.915]; $P=.011$), treatment period (OR [95%CI]=0.685, [0.484-0.969], $P=.033$), and was still positive after treatment cessation (OR [95%CI]=0.565, [0.319-1.002], $P=.051$). In patients with asthma at index date ($n=304$), progression of asthma was improved by 24.6% ($P=.013$) during treatment and by 15.2% after treatment cessation ($P=.0503$).

Conclusions: The 300IR 5-grass pollen tablet significantly reduces the risk of asthma onset and reduces the progression of asthma in asthmatic population in comparison with the control group. This demonstration of the impact on asthma reinforces the value of the 300IR 5-grass pollen tablet.

1535 | Quantitative measurement of allergen-specific IgG1 and IgG4 during immunotherapy with the recombinant B cell epitope-based grass pollen allergy vaccine BM32

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Introduction: Allergen-specific immunotherapy (AIT) is an allergy treatment with disease-modifying and long-lasting effects. The induction of allergen-specific blocking IgG antibodies interfering with the allergen-IgE interaction represents a major mechanism of AIT and there is thus a need for methods allowing the exact quantification of allergen-specific IgG responses.

Objectives: To measure the concentrations of allergen-specific IgG₁ and IgG₄ induced by AIT with the recombinant grass pollen allergy vaccine BM32 quantitative ELISA systems were developed using purified human monoclonal antibodies specific for grass pollen allergens to build up standard curves.

Results: For quantification of grass pollen allergen specific IgG₁ a purified human monoclonal Phl p 2-specific IgG₁ antibody and for IgG₄ measurement a purified human monoclonal Phl p 5-specific IgG₄ were used for the preparation of standard curves with a linear range from 50-1350 ng/mL. Purification of monoclonal antibodies from cell culture supernatants was done via affinity chromatography with the corresponding antigen (either Phl p 2 or Phl p 5) bound to NHS-Activated Sepharose™ 4 Fast Flow to purify functional antibodies. The ELISA assays were checked for reproducibility showing a

mean intra-assay variation for the IgG₁ measurements of 12% and for the IgG₄ quantification of 8%. The mean inter-assay variation was calculated after the quantification of Phl p 1 and Phl p 5 specific IgG₁ and IgG₄ levels during the analysis and found to be 21% for IgG₁ detection and 18% of IgG₄. Using the quantitative ELISA assays for measuring allergen-specific IgG₁ and IgG₄ concentrations we found that AIT with BM32 induced Phl p 1- and Phl p 5-specific IgG₁ levels up to 83 µg/mL and 784 µg/mL, respectively and Phl p 1

and Phl p 5-specific IgG₄ levels of up to 468 µg/mL and 1423 µg/mL, respectively.

Conclusions: We therefore conclude that the ELISA systems using human monoclonal allergen-specific IgG₁ and IgG₄ antibodies as standards can be used to quantify allergen-specific IgG₁ and IgG₄ levels induced by AIT and that AIT with BM32 induces high levels of allergen-specific IgG antibodies.

SUNDAY, 18 JUNE 2017

LB TPS 02

FOOD ALLERGY IN CHILDREN: FROM EPIDEMIOLOGY TO MANAGEMENT

1536 | “Allergen safe” food in the roadside small restaurants in 11 cities across Europe, Thailand & India—differences in practice, perception & legislation: An observational study

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Introduction: The lack of allergen awareness among food handlers (FH) may lead to significant health risk for the consumers with food allergy across the world.

Objectives: This study explored the heterogeneity of allergen awareness amongst small restaurants in the light of government legislation.

Results: 116 small restaurants from EU, Norway (European Economic Area), Thailand & India were randomly selected for this project. The number of restaurants included were from Newcastle in the UK (n=7), Valencia (n=6) & Barcelona (n=8) in Spain; Rome (n=9) in Italy; Vienna (n=11) in Austria, Corfu (n=11) in Greece, Stavanger (n=8) in Norway, Pattaya (n=11) & Phuket (n=16) in Thailand and New Delhi (n=12) & Calcutta (n=17) in India. Big food chain restaurants were not included in this study. The data was collected for allergen alert posters & allergen information on the menu card; their perceived ability to supply allergen free food with confidence; the acceptance that allergen avoidance requires bi-directional communication & is a shared responsibility with the consumers; as well as awareness of any government food label legislation about allergen information. The data was collected over two years (2014-2016). (See Table 1 for result summary)

Conclusions: There is an observed degree of heterogeneity in the awareness of allergen safe food & food label legislation across the included countries. This poses a potential health risk for tourists and the consumers with food allergy. Complete lack of awareness of food label legislation regarding allergen information in Thailand, partial lack of awareness in EU countries & absence of government legislation in India is concerning. The use of allergen alert posters for better bidirectional communication, the inclusion of allergen in the menu card and reassuring allergen safety through legislative implementation by the food safety agencies need urgent attention across the globe.

Observations	European Union n=52	Norway (EEA) n=8	Thailand n=27	India n=29
Allergen alert posters & Allergen information displayed in the menu card	18 (35%)	7 (87.5%)	0 (0%)	0 (0%)
Perceived ability to supply allergen free food with confidence	21 (40%)	7 (87.5%)	15 (55.5%)	20 (69%)
Agree that allergen avoidance is a shared responsibility	36 (69%)	8 (100%)	16 (59%)	9 (31%)
Awareness of government legislation	39 (75%)	8 (100%)	0 (0%)	No such legislation

1537 | Anaphylaxis to food in children up to 3 years

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Introduction: Anaphylaxis is a severe, potentially life-threatening, systemic or generalized immediate hypersensitivity reaction to repeated contact with the allergen, that was previously well-tolerated. Symptoms can be mild, moderate or severe. A proper diagnosis can be difficult, especially in infants and small children. In the group of the youngest children the most often it is caused by food.

Objectives: The analysis of anaphylactic reactions in children hospitalized in the Department of Pediatrics, Allergology and Gastroenterology, and under the care Outpatient Allergy Clinic in the period from 01.01.2015 to 31.12.2016.

Results: In years 2015 and 2016, 2029 children aged 0-3 years were hospitalized in the Department, including 411 (20.2%) of allergic disease. Anaphylactic reactions after food intake were observed in 18 patients (0.89%). In this group there were 13 (72%) boys and 5 (28%) girls. The mean age of the child at the time of an anaphylactic reaction was 15.6 ± 10.1 months. The most common clinical manifestations were: urticaria with angioedema in 13 children, urticarial in 4 children, vomiting in 7 children, difficulty in breathing in 3 children, rhinitis, conjunctivitis, coughing and anxiety in 1 child. 10 children (55%) had a positive family history of atopic diseases. As a

possible cause of the symptoms parents most often indicated the consumption of milk or milk-rice porridge introduced as a new food to your child's diet or consumed in a random manner. Sensitization has been demonstrated in all children. Most were found allergic to milk (n=15), β -lactoglobulin (n=14), α -lactalbumin (n=9), casein (n=8), egg protein (n=5), egg ovalbumin (n=4), peanut (n=3), hazelnut (n=2), rice (n=2), apple (n=3), citrus, peach, carrot, potato, soybean, wheat flour, serum albumin bovine and almond after 1 child.

Conclusions:

1. The incidence of anaphylactic reactions in children up to 3 years of age rated at 0.89% of children hospitalized due to allergies.
2. The most common allergy symptoms included skin lesions and vomiting.
3. The primary cause of allergic reactions was cow's milk.

1538 | Anaphylaxis induced by tree nuts in preschool age children

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Introduction: The incidence of anaphylaxis is increasing in preschool age children, being food the major culprit. In this age group, the commonest implicated foods are cow's milk and egg. Nevertheless, severe reactions to tree nuts have been increasingly reported.

Objectives: Characterization of children referred to our Immunology Department due to food induced-anaphylaxis related to tree nuts ingestion in preschool age.

Results: Material and methods: We have included retrospectively 20 children [current mean age 8.7 (SD \pm 3.1) yrs, 65% male] with clinical history of anaphylaxis induced by ingestion of tree nuts, confirmed by allergological work-up investigation. Sensitization to nuts was assessed by *in vivo* skin prick tests (extracts, Bial-Aristegui[®]) and/ or *in vitro* tests (specific IgE, ImmunoCAP, ThermoFisher[®]).

Results: The mean age of the first anaphylactic episode was 3.2 (\pm 1.2) yrs (2 to 5 years); in 13 children the first episode occurred during the first 3 years of life. The tree nuts implicated were: cashew in 9 children, walnut in 6, pine nut in 4 and hazelnut in 2 (in one child walnut and hazelnut). In 75% of them, the reaction occurred at the first contact with the implicated food; none had previous diagnosis of tree nut allergy. Regarding the place of the reaction, 15 occurred at home, 4 in a restaurant and 1 on the beach. We have identified cross-reaction with other nuts in 18 children, and peanut sensitization in 8 children. The most frequently reported symptoms were mucocutaneous (100%) and respiratory (75%), followed by gastrointestinal (55%). In 90% of the episodes, symptoms

appeared within the first 30 minutes after exposure; 19 (95%) children were admitted to the emergency department, although only 45% were treated with epinephrine. The majority (90%) had personal history of allergic disease, 45% with asthma. To all children an auto-injector epinephrine device was prescribed.

Conclusions: In our pediatric population, cashew and walnut were the most implicated tree nuts in preschool anaphylaxis. Most of the reactions occurred at home. In all cases an underneath IgE mediated mechanism has been proven. Reactions occurred upon exposure to minimal amounts of tree nuts, demonstrating the high potency of these allergens. Almost half of children also had peanut sensitization. Epinephrine was underused, as reported by others. Potential life-threatening tree nut allergy may occur early in childhood and adequate management should be undertaken.

1539 | Single dose food challenge with milk significantly accelerates tolerance acquisition in milk allergic infants

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Introduction: Children with IgE mediated cow's milk allergy (CMA) will tolerate unheated cow's milk sooner if they tolerate and are exposed to incremental amounts of baked milk products. We noted an apparently higher than expected rate of full tolerance in CMA babies after they had taken part in a study of a single, low dose exposure to unheated cow's milk.

Objectives: We report on the unexpected outcomes of children with CMA who completed the IFAAM single dose study.

Method: Twenty-three new referrals with CMA were given, at their first visit, a single dose of 1.5 mg milk protein in a dessert matrix. All parents were advised to use the 12-step MAP milk ladder at home. Telephone follow up was undertaken at the end of the study to assess if tolerance was 50% complete, 100% complete, or unsuccessful.

Results: 9/23 (39%) had achieved 50% tolerance by 6 months and 11/23 (48%) by 12 months. 3/23 (13%) had achieved 100% tolerance by 6 m and 7/23 (30%) by 12 m. 4/23 (17%) had demonstrated no signs of tolerance by both 6 and 12 months.

Conclusions: Children receiving a medically supervised single dose of 1.5 mg unheated milk protein at diagnosis attain partial and full tolerance of unheated milk faster than is reported in the literature. It is uncertain if this is an immunological effect or simply reflects rapid access to expert help and increased parental confidence to implement the advised programme of graded exposure to milk. A formal, randomized trial is needed to confirm this opportunistic observation and explore possible mechanisms for the observed effect.

1540 | Novel smartphone based interactive system to prevent food allergy in school

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Introduction: As most school provides lunch group meals for all students in Korea, students with food allergies are at risk of exposure to their own allergenic components contained in school meal. Each school provided food allergen labelling of school meal to the student's parents every month, and this information can be checked at the web page of National Education Information System (NEIS) of ministry of education. However, parents often do not check food allergen labelling, and even also in parents of students with food allergies. Although there have been increasing event related to food allergies, no active intervention to prevent food allergy existed in school itself.

Objectives: We aimed to develop a smartphone application called "food allergy alert" to prevent adverse allergic events from school group meals.

Results: Students with food allergies can input their name of school and choose their own allergenic components among 13 food allergens prescribed by the Food and Drug Administration. Then, the application automatically downloads the monthly student's school meal table including food allergen labelling throughout parsing the web server of National Education Information System. Students with food allergy can easily checked the daily school food including allergy labelling with the app. The app alarmed 'food allergy alert' at specified time when allergenic components contained in daily school meal. Parents can receive the allergy alert if they download the app and match their sibling's information. Homeroom teacher can review the allergenic profiles of students with food allergies and also receive the 'food allergy alert' of students with food allergy in the class.

Conclusions: We developed the smartphone-based novel interactive system to prevent food allergy accidents in school. Student with food allergy and their parents easily check the food allergy labelling and can avoid exposure to allergenic foods. Homeroom teacher can also easily provide appropriate intervention to prevent food allergy accident in school. We are planning to apply this system in elementary school and test the usefulness and feasibility of this application.

1544 | Food allergy profile and its influencing factors in children from schools in Hortaleza District, Madrid

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Introduction: n/a.

Objectives: To analyze the food allergy profile and factors influencing food allergy in children from schools in Hortaleza District, Madrid.

Material and Methods: A structured questionnaire on allergen-free diets based on specialist report, was administered in 49 schools in this District during the 2015-2016 school year. Data recorded included sex, age, asthma history, type of school, presence or absence of both polysensitization (sensitization to 2 or more food groups) and epinephrine prescription. Frequencies were computed in February 2017. The Bonferroni correction was used to account for multiple comparisons. The relationship between food variables and epinephrine prescription were determined by cross-tabulation, with Monte Carlo estimation of exact *P* values (SPSS V23).

Results: 110 male and 106 female children were evaluated with no differences observed in sensitization to different food groups. Epinephrine prescription and asthma history were also observed in general, but polysensitization was significant in male children, (*P*=.037). By age group, children under 6 years of age have higher egg and milk sensitization (*P*<.000); of these, only 8 and 10 children under 3 years present egg and milk allergy, respectively. On the other hand, children over 6 years present fruits (*P*=.032) and nuts (*P*<.000) allergy. No differences by age groups were observed in terms of epinephrine prescription, history of asthma, or presence of polysensitization, in the whole sample. It was observed that 68.75% of polysensitized children have epinephrine prescribed, *P*=.021 (31.25%, of monosensitized children). 76.47% of the polysensitized children are also asthmatic, (compared with 23.53% (*P*=.004) of monosensitized children). In those children with epinephrine prescription, being asthmatic is related (*P*<.0000); this prescription is also related to polysensitization, *P*=.034). The only food group that shows a significant relationship with epinephrine is legumes (*P*=.025). In children with food allergy to two different food groups that represents 51.35%, the most frequent food allergy combination for egg allergy is sensitization to milk and nuts; for nut allergy, sensitization to egg; for milk allergy sensitization to egg; and for fruit allergy, sensitization to nuts. A relationship between type of school attended and allergy profile was observed.

Conclusions: The food allergy profile in the group of children with epinephrine prescription, highlights consistent features in this study.

1546 | Implementation of EAACI Food Allergy Guidelines 2014 and National Russian Recommendations 2015 in 36 cities of Russian federation

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Introduction: Cow's milk protein allergy (CMPA) is a public health issue in children whose quality of life is strongly affected by the effective management.

Objectives: The objective of the study is the assessment of implementation of the international and national guidelines on prevention and management of food allergy in children under 1 year in routine pediatric practice.

Results: In 2016 we surveyed 1292 pediatricians in 36 biggest cities of 7 regions of Russian Federation and received 1693 questionnaires about management of babies with CMPA. First episode of CMPA was registered at 2.79 [SD 1.56] months. At the first visit to pediatrician mean age of babies with CMPA symptoms was 4.05 [SD 2.51] months. The following symptoms dominated: allergic rash 58.38% (atopic dermatitis was diagnosed in 46.81%, urticaria—4%, dryness, desquamation 11.57%), skin and associated gastrointestinal symptoms—in 35.77% and isolated gastrointestinal symptoms in 5.19%. Severe CMPA symptoms were registered in 6% of babies. In spite of the fact, that allergy was in family history in 69% babies, the partial hydrolyzed whey formulas (PHWF) were used for prevention of allergy in only 33% babies in total (from 28% and 29% in Volga and Ural Region up to 45% and 40% in South and North-West Region respectively). Correct diet with extensive hydrolyzed formulas (EHF) and amino acid formulas (AAF) according to the national and EAACI guidelines on food allergy management was prescribed to 7.49% of babies (7.33% EHF and 0.16% AAF) after the symptoms had appeared. In other 92.67% dietotherapy was inadequate with partial hydrolysis formula (34.93%), repeated switches between different base formulas with nonhydrolyzed protein (52.51%), goat milk or lactose free formulas (2.77% and 0.98%). Allergy immunotests were performed in 14% of babies. Well educated pediatricians prescribed correct diet for babies with CMPA—EHF in 93.03% and AF in 5.37%, other formulas—1.59%.

Conclusions: As we showed previously adequate diet, recommended by qualified pediatricians and allergologists was effective for CMPA therapy and reduced pharmacological and financial load on babies and their families. Our study strongly supports the beneficial effect of educational programs based on EAACI and national guidelines in parents and routine pediatric practice.

1547 | Goat's milk allergy in children under specific oral tolerance induction protocol for cow's milk allergy

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Introduction: Specific oral tolerance induction (SOTI) is a highly promising novel form of desensitization in children with severe cow's milk protein allergy. In this study we report cases that presented with allergic reactions to goat milk (GM) and sheep's milk (SM), following completion of SOTI to cow's milk (CM).

Objectives: Fifteen children (11 boys) aged 4.1-11 years (mean aged: 6.8 y±1.9) with persistent food allergy to CM, were included in this study. All children completed the protocol, while in one child anti-IgE was introduced during maintenance phase due to severe uncontrolled asthma.

Results: The mean time to SOTI completion was 15 (ranging from 13 to 42) months. All children were able to incorporate CM products, including cheese and yogurt, into their diet, following completion of the protocol. 4 out of 15 (26.6%) children presented IgE mediated allergic reactions after exposure to GM products. Two children had anaphylactic reaction during open food challenge (OFC) performed in the Unit to mixed goat and cow's milk cheese. Two more children reported IgE mediated reactions on regular follow-up, one anaphylactic and the other oral allergy syndrome and urticarial, during consumption of yogurt and cheese, which contained GM and SM. Skin prick test to GM in these patients was significantly larger compared to CM (mean maximum wheal size GM: 18.3±0.6 and CM: 6.3±1.5, P=.009). When reviewing the files of 207 children during the last 3 years that had gradually introduced CM following OFC, only 2 (0.96%) presented IgE mediated reactions to GM.

Conclusions: Children successfully completing SOTI to cow's milk present increased rates of allergic reactions to goat and sheep dairy products. It is plausible to consider either introduction of goat and sheep milk products following allergy evaluation or alternatively introduce parallel to cow's milk, with SOTI protocol, goat's milk in this population.

1548 | Allergy to cow's milk associated with allergic dermatitis and chronic diarrhea

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Introduction: Allergy to cow's milk (CM) is one of the most common causes of allergies in childhood producing multiple organic disorders such as eczema, diarrhea, vomit, respiratory disorders and other manifestations associated with food allergies.

Objectives: We studied 14 3 years old children diagnosed with allergic eczema, chronic diarrhea and cow's milk allergy by clinical history (atopic background); type of feeding (maternal, artificial); age of the beginning of the symptoms; time passed between the cow milk ingestion and appearance of symptoms (dry skin, itching, vesicles, exudation), and frequency increasing in stool (volume amount of liquid). Prick Test was performed with cow milk standardized protein extracts (Casein, A-lacto globulin, B-lacto globulin). A Histamine concentrate (1 mg/mL) was used as positive control, resulting positive 5 mm papule, and Saline Solution was used for negative control, giving non papule as result. Serum IgE and Specific IgE to Cow Milk in International Units milliliters were quantified by enzyme bioassay. We consider Diarrhea volume above 10 g/Kg/day.

Results: All of the 14 children studied presented atopic family antecedents, eczema and chronic diarrhea symptoms after cow milk dietary supplement. As a result, 5 children manifested some symptoms 1 year of life, and 9 of them during the 1 year. Ten from the 14 children analyzed revealed moderate Specific CM IgE levels and the other five showed low levels. 8 of the 14 children presented Alfa Lacto globulin Positive Prick Test and Negative Beta Lacto globulin and Casein, and 6 indicated all prick test positive. The Seric IgE levels were above 100 UI/mL. Symptoms (dry skin, itching, vesicles, exudation), and frequency increasing in stool (volume and amount of liquid). Prick Test was performed with cow milk standardized protein extracts (Casein, A-lacto globulin and B-lacto globulin). A Histamine concentrate (1 mg/mL) was used as positive control, being considered positive a 5 mm papule, and Saline Solution was used for negative control, giving non papule as result. Serum IgE and Specific IgE to Cow Milk in International Units milliliters were quantified by enzyme bioassay. We consider Diarrhea volume above 10 g/Kg/day.

Conclusions: According to these results, it is possible to determine that cow milk is present in the allergic eczema and chronic diarrhea of smaller children up to 3 years old, and that its replacement could improve the clinical sintomatology of the patient with prescribed medication.

1549 | Food intolerance and food allergy in children in Lviv region (Ukraine)

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Introduction: Food allergy has been increased in recent years in the world. True food allergy is less prevalent than commonly perceived. Up to 40% of individuals or parents think that they or a family member has a food allergy and 20% avoid particular foods because the food may possibly contain an allergen. However, only 1-6% of persons test positive on full evaluation, which may include double-blind placebo-controlled food challenges.

Purpose of the reported research was to study prevalence of food intolerance and food allergy in children in Lviv region (Ukraine).

Objectives: A questionnaire survey for the prevalence of food intolerance and food allergy in Lviv region was conducted in 1245 children. 140 of this group of children performed estimation of circulating IgE antibodies in the blood serum ("R-Biopharm AG"; Germany) and skin testing for immediate-type sensitivity by skin-prick tests ("Immunolog"; Vinnytsia, Ukraine) for domestic, epidermal, food, fungal and pollen allergens in Lviv City Children's Clinical Hospital.

Results: The average age of the first allergic reaction was 1.20 +/- 3.45 years.

61 (43.57%) children presented with skin manifestations (eczema, urticaria, angioneurotic oedema, other rashes), 53 (37.86%) children with gastrointestinal symptoms (vomiting, diarrhoea, colic, abdominal pain, failure to thrive), 26 (18.57%) children with wheeze.

The most common allergens causing food allergy were in order milk (24%), eggs (18%), wheat (12%), peanuts (8%), and soybeans (3%).

The most common place where allergic reaction developed was the patient's own home, followed by fast food restaurants, places visited, restaurants, and schools. In patients' own homes, fast food restaurants (buffet), places visited and schools.

Conclusions:

1. The most common allergens in Lviv region are milk, eggs, and wheat.
2. In structure of food allergy development most patients (44%) have skin manifestations, 38%—gastrointestinal symptoms and 19% children with wheeze.
3. Research allowed to determine the peculiarities of sensitization of different age-dependent children's groups for allergen and to confer the testing indexes in vivo and in vitro.
4. As possible food allergies can cause anaphylaxis, it is necessary to provide precise information for consumers regarding packaged and processed foods.

1550 | Severe Brazil nut anaphylaxis in a 3-year-old boy

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Introduction: The growing consumption of tropical nuts in recent years has increased IgE-mediated hypersensitivity. In Brazil nut (BN) allergy, storage proteins are the most clinically relevant allergens. Some cases of cross-reactivity have been clinically described as well.

Objectives: We report a 3-year-old boy referred to our Allergy Department after a severe anaphylaxis due to BN ingestion. No previous contact with BN was recalled by the parents. Respiratory symptoms attributable to aeroallergens or atopic dermatitis were not present.

Thirty minutes after eating a bit of BN the patient had gastric pain and vomiting followed by cough, eyelid edema, and generalized urticaria so they visited the Emergency Room (ER). At the ER uvula and facial edema and generalized urticaria were observed. He was initially treated with oral corticosteroids and oral antihistamines with improvement. However, 90 minutes later the facial edema and urticaria worsened and wheezing dyspnea appeared. He was then treated with intramuscular adrenaline, intravenous corticosteroids and inhaled β_2 agonists. He was hospitalized and discharged 48 hours later. The patient was advised to avoid all nuts, to carry with him an adrenaline autoinjector and was referred to Allergy.

Prior to this episode, he had consumed pistachios, sunflower seeds, almonds, hazelnuts, walnuts and chestnuts with good tolerance

Results: A diagnostic workup was carried out, involving skin prick test (SPT) with a panel of commercial peanut, tree nuts and seed extracts, prick-prick (PP) with fresh BN, specific IgE (ImmunoCAP, Thermo Fisher Scientific) to different nuts and oral food challenges (OFC).

1. SPT to commercial extracts of almond, hazelnut, peanut, chestnut, walnut, pine nut, sunflower seed, pistachio, coconut, LTP (Prup3) and profilin were negative.
2. PP with BN was positive (mean wheal 5 mm), and PP with hazelnut and walnut were negative.
3. ImmunoCAP to BN was 382 KUA/L, hazelnut 1.10 KU_A/L, walnut 0.46 KU_A/L and baseline tryptase 5.3 μ g/l. All the remaining nuts scored negative (<0.35 KU_A/L).
4. Open OFT with walnut and hazelnut were negative.

Conclusions: This is a selective Brazil nut allergy in a small child whose first reaction was a severe biphasic anaphylaxis.

The presence of specific IgE to hazelnut and walnut had no clinical relevance and can be the result of IgE cross-reactivity with BN.

1551 | Tolerance to hazelnut cocoa spread in hazelnut allergic children

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Introduction: Hazelnut allergy is one of the most common nut allergies. Previous in-vitro studies have shown that hazelnut allergens are heat-resistant.

Objectives: To assess tolerance of hazelnut cocoa spread (processed hazelnut) in children with sensitization or a positive history of IgE mediated allergy in hazelnut in the preceding 3 years. Children included were assessed by sIgE (ImmunoCAP) and SPTs to hazelnut. Maximum wheal diameter was recorded. We performed food challenges (FC), open and double-blind placebo-control to assess tolerance to hazelnut cocoa spread (4% hazelnut).

Results: 11 hazelnut allergic children (mean age: 8.9 ± 4.2 years, 4 girls) were included in the study. 7 children presented with convincing history of IgE mediated reaction following hazelnut consumption (2 severe anaphylactic, 1 mild anaphylactic, 1 angioedema, 2 urticarial and 1 oral allergy syndrome). These children had positive sIgE values (mean values f17: 6.7 ± 9.2 , Cora14: 4 ± 4 , Cora9: 1.5 ± 2) and skin prick test to hazelnut (wheal diameter: 8.3 ± 2.1 mm), as their history revealed allergic reactions to hazelnut. The other 4 were found sensitized during evaluation with positive sIgE values (mean f17: 3.4 ± 4.7) and skin prick test to hazelnut (wheal diameter: 9.5 ± 4.1 mm). All FC were negative. The total amount of hazelnut cocoa spread that children consumed during the food challenge depended on the sensitization of the patient (high risk children were offered smaller amounts). Mean total quantity was 42.5 g (1.7 g hazelnut). Following challenge, children were instructed to consume the same quantity on a weekly basis. 2 out of 11 children, 2 years after the challenge tolerated raw hazelnut (mean total quantity: 6.65 g), following negative FC.

Conclusions: Hazelnut allergic children tolerated hazelnut cocoa spread. It is plausible that fragmentation and heating, during spread production may reduce the nut's allergenicity. Tolerance to hazelnut spreads increases the variety of, already limited, food choices of hazelnut allergic children.

1552 | The nutcracker study: specific IgE to Ara H 2 as part of a 2-step model for the diagnosis of peanut allergic in egg allergic children

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Introduction: Peanut allergy affects 1-2% of UK children. The association between egg allergy and sensitisation to peanut is well recognised. Existing peanut skin prick (SPT) and peanut-specific IgE tests (SpIgE) are poor in predicting clinical peanut allergy. Approximately 22% of peanut-sensitised children have peanut allergy. Ara h 2 has been proposed as a more sensitive test in distinguishing between peanut allergy and tolerance.

Objectives: To examine the diagnostic value of Ara h 2-SpIgE in the diagnosis of peanut allergic in peanut-sensitised egg-allergic children who have never consumed peanut.

Results: 101 peanut-sensitised, egg-allergic children attending a tertiary allergy clinic were prospectively recruited between January 2015 and June 2016. SPT diameters to peanut, peanut- and Ara h 2-SpIgE antibody levels were measured. Children were subject to a peanut challenge (OPC) and then allocated to either the Peanut Tolerant or Peanut Allergic group. Children with test results above the positive predictive value of ≥ 8 mm or ≥ 15 kUA/L were allocated to the Peanut Allergic group without being subject to an OPC.

All 101 children had both egg allergy and a history of eczema. 70 (69%) children were diagnosed as Peanut Allergic. 39 children were subjected to an OPC; 31(79%) of whom proved to be peanut tolerant. 54/70(77%) peanut allergic children had SPT and peanut-SpIgE levels above the positive predictive values. Mean test values for peanut SPT and peanut- and Ara h 2-SpIgE concentrations were all higher in allergic children.

Receiver-operator curves identified optimal cut-off values of 6 mm (sensitivity 84%; specificity 80%) for peanut skin prick testing, 0.39 kUA/L (sensitivity 79%; specificity 93%) for Ara h 2-SpIgE concentrations and 1.08 kUA/L (sensitivity 81%; specificity 57%) for whole SpIgE testing.

Conclusions: Peanut SPT and whole-peanut specific IgE concentrations were poor discriminators between allergy and tolerance. The negative predictive value of the peanut SPT was useful as a first-line step in predicting peanut tolerance. Ara h 2-specific IgE concentrations should be measured in preference to peanut-specific IgE concentrations. Ara h 2 was the best predictor of peanut allergy, but had greater clinical utility as part of a two-step approach in conjunction with skin prick testing to peanut. When used in isolation, specific IgE concentrations to Ara h 2 were unable to replace the need for oral provocation challenge for the majority of egg-allergic, peanut-sensitised children.

1553 | Health-related quality of life of food allergic children compared to general population and other diseases in south-western Europe

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Introduction: To date, only one study has compared health-related quality of life (HRQL) in food allergic patients to general population and other chronic diseases. Previously published data in a Dutch population were compared to a prospective food allergic cohort using CHQ-CF87. HRQL was impaired only in adults and in teenagers with food allergy, but not in children, with an intermediate magnitude between diabetes mellitus and other pathologies.

Objectives: Our aim was to compare HRQL of food allergic pediatric patients with other allergic diseases, or with chronic diseases with an impact on food diet and general population, all prospectively included at the same time in a same catchment area in South-Western Europe. Generic HRQL questionnaires (CHQ-CF87) were completed by pediatric patients aged 8-17 followed in a tertiary care center: 135 with food allergy, 94 asthmatics, 70 diabetes mellitus, 50 obese, 19 with eating disorders, 18 with inflammatory bowel diseases and 463 healthy controls recruited in schools. Specific HRQL questionnaires (FAQLQ) were completed by food allergic patients at the same time.

Results: Food allergic patients reported poorer general health perception ($P < .048$) but less pain, better mental health, behavior and family activities than general population. Others chronic allergic diseases had overall a worse global HRQL compared to food allergic patients. Significant correlations were found between FAQLQ-TF total score and the General Health, Mental health, Emotional and Physical Functioning scores of CHQ-CF87 and between FAQLQ-CF and the Bodily Pain and Emotional scores of CHQ-CF87 (Spearman's correlation). Within the 8-12 food allergic group, higher FAQLQ scores—and so lower HRQL—were significantly associated to controlled asthma co-morbidity (57/91 children) in multivariate analysis ($P = .004$).

Conclusions: Even if specific questionnaires are more suitable to precisely evaluate HRQL impairment in food allergic patients, generic HRQL questionnaires used in a prospective manner show impairment in general health perception of pediatric food allergic patients. Nevertheless HRQL impairment in food allergy seems to be less important compared to pathologies involving the field of food or allergy but associated with daily treatments or daily perception of the disease. Asthma co-morbidity, even controlled, is moreover related to worse specific scores in food allergic children aged 8-12 and should lead to specific management and educational programs.

1554 | A complex diagnosis for a complex evolution

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Case report: Food allergy is now recognized as a worldwide problem. Research on allergenic food proteins and immunologic responses has moved to a molecular level hence tremendous progress has been made in our understanding of food-based allergic disorders. The present clinical case of complex food allergy is such an example.

A baby first seen in a pediatric allergology appointment due to an extended urticarial rash episode after being fed for the first time with rye bread at six months of age. From his medical history we highlight a surgical intervention due to hypertrophic pyloric stenosis. The first analytic evaluation showed: 11.3% eosinophilia, total IgE 78.4 kU/L and specific IgE for cereal mixture 4.33 kU/L. An eviction of gluten containing cereals was recommended. At nine months of age, one hour after eating banana for the first time, he developed an

intense urticarial rash in the thoracic region with rapid generalized progression. The specific IgE for banana was 5.66 kU/L and negative for latex. A molecular allergen study was carried out using the ImmunoCAP[®] ISAC technique that revealed (ISU-E): Tri a 14 (LTP) 6.5 and kiwi Act d 2 (TLP) 1.6. SDS-PAGE Immunoblotting showed an IgE binding band of 20 kDa in kiwi extract, and IgE-bands of 20 kDa and 30 kDa in banana extract. Banana extract was able to inhibit IgE-binding to 20 kDa-band from kiwi in Immunoblotting-inhibition assay. By in-gel digestion and mass spectrometry analysis of the 20 kDa-bands of kiwi and banana we were able to identify the proteins as Act d 2 and Mus a 4 both proteins belong to the family of Thaumatin-like proteins (TLP) of kiwi and banana respectively.

Although the ImmunoCAP[®] ISAC technique has revolutionized our understanding of food allergy and its specifications, we must not forget to consider other specific tests in some complex cases. They can assist us in contextualizing the clinical relevance of sensitization and improving our capacity to advise and treat our patients.

SUNDAY, 18 JUNE 2017

LB TPS 03

ANAPHYLAXIS, VENOM AND DRUGS

1556 | Specific IgE sensitization to honey bee venom and auto-injector adrenaline prescriptions for Japanese beekeepers

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Introduction: Honey bee stings are an occupational hazard for beekeepers and often lead to allergic reactions. Furthermore, approximately 40% of Japanese forestry workers have specific (s) IgE to Hymenoptera venom. Recently, we reported that around 6-33% of Japanese outdoor workers with sIgE positivity to Hymenoptera venom received prescriptions for adrenaline auto-injectors. Only 23-57% of such workers who had experienced systemic reactions to a Hymenoptera sting with a positive result of sIgE to Hymenoptera venom had been prescribed adrenaline auto-injectors. However, honey bee stings and the prescribing of adrenaline auto-injectors for affected workers have not been surveyed in occupational settings.

Objectives: We conducted a survey of beekeepers in Japan to examine the presence of sIgE to honey bee venom and the number of adrenaline auto-injectors prescribed.

The participants included 113 Japanese beekeepers (104 men, 9 women) between 2015 and 2016. All participants completed questionnaires and underwent peripheral blood tests on the same day. The questionnaire was administered by an allergist and included the following items: experience of a honey bee sting, systemic reaction to a honey bee sting according to Mueller grading system, adrenaline auto-injector prescription given, and adrenaline auto-injector carried. An adrenaline auto-injectors were prescribed to 3 subjects with Mueller grade I (14 subjects total), 0 in grade II (2 subjects total), 2 in grade III (3 subjects total), and 5 in grade IV (16 subjects total). Positive results for sIgE to honey bee venom were defined as values ≥ 0.1 IU_A/mL.

Results: The quantity of sIgE to honey bee venom was positive results in 77.9% (88 out of 113 subjects). We found that approximately 11% (12 out of 113 subjects) of Japanese beekeepers with sIgE to honey bee venom and 29% (9 out of 31 subjects) who had experienced systemic reactions to a honey bee sting and showed sIgE to the venom were prescribed adrenaline auto-injectors. Moreover, 33.3% (3 out of 9 subjects) of beekeepers usually carry auto-injectors during work, regardless of the presence or absence of systemic reactions to honey bee stings.

Conclusions: This study suggests that the owners of the cooperative should consider obtaining adrenaline auto-injector prescriptions for beekeepers who have sIgE Ab to honey bee. In addition, beekeepers should be educated about regularly carrying adrenalin auto-injectors.

1557 | Anaphylaxis in the Greek pediatric population

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Introduction: Anaphylaxis is an acute, potentially life-threatening hypersensitivity reaction, occurring in all age groups; however, elicitors and clinical characteristics of the disease in pediatric settings require further investigation.

Objectives: To present data on frequency, elicitors, clinical manifestations and emergency treatment of anaphylaxis from a tertiary Allergy Unit, in Greece. We analyzed data on a Greek pediatric population, retrieved from the European Registry of Anaphylaxis (NORA), from 2011 until March 2016. An on-line questionnaire, specifically designed for the study was used to record information.

Results: Data from 108 children, (1 month-18 years, mean aged 4.56 (95%CI 3.87-5.25), 74 males (68.5%) were analyzed. Cases mainly occurred at home (49.1%), with the majority (66.7%) occurring within 10 minutes following exposure. 44 patients (42.6%) had a previous reaction to the same allergen, while 19.6% had severe symptoms. The reported symptoms were cutaneous (86.1%) respiratory (75%), and gastrointestinal (50.9%). Food allergens were the most prevalent elicitor factor (88/108 cases, 81.5%), followed by insect venom (10/108 cases, 9.3%). Preschoolers were most likely to present anaphylactic reactions (74.1%, of all cases, 52.5% graded as moderate), while 58.8% had concurrent atopic dermatitis. 80% of the venom-associated reactions occurred at school age (6-12 years), where the main concomitant disease was allergic rhinitis (57.7%). We recorded only 2 anaphylactic reactions in adolescents, both of grade III severity, one of which was related to venom allergen and the other was unknown. Cow's milk (27.3%), wheat (14.8%), hen's egg (12.5%), and peanut (5.7%), were the most frequent triggers across all ages. Cashew (5.7%), walnut (3.4%), and fish (2.3%) were exclusively reported in preschoolers, while pine nut allergy (2.3%, mostly grade III) was only reported in school aged children. Only 15.6% (7/45) of lay-treated received adrenaline in respect of 59% (36/61) of professionally treated.

Conclusions: In the pediatric population of Greece, the predominant trigger of anaphylactic reactions is food, which seems to be in concordance with the anaphylactic data throughout Europe. Reactions with some persistent allergens were only observed in young children, suggesting efficient avoidance. Only mild to moderate reactions were noted. There were no grade IV reactions. Of note

remains the underuse of epinephrine in the community as a first aid treatment for anaphylaxis.

1558 | Severe abdominal pain in anaphylaxis

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Introduction: Subcutaneous immunotherapy (SCIT) is an effective treatment of allergic rhinitis and asthma, able to reduce symptoms, need of medication and with a disease modifying effect. However, these benefits may be overshadowed by the injection-related systemic reactions that may include anaphylaxis.

Abdominal pain is not uncommon in anaphylaxis. However, its severity may be underestimated, and it can be a therapeutic challenge.

Objectives: Case report: We report a 37-year-old woman who came to our unit to start grass pollen SCIT with a non-modified extract following a cluster schedule.

Thirty minutes after the second dose of the first cluster she presented rhinitis, and an oral antihistamine was given. The reaction progressed with neck and flexures itching erythema and mild abdominal pain, and intravenous (iv) antihistamines and corticosteroids were given. She was hemodynamically stable, but the pain was very severe and was described as intermittent uterine cramps. She was then given intramuscular (im) adrenaline, together with iv hyoscine butylbromide and paracetamol. Since the pain did not resolve 40 minutes later a second dose of im adrenaline, together with iv dexketoprofen and corticosteroids were administered. An abdominal ultrasound performed showed a hemorrhagic ovarian follicle without complications.

Results: The pain continued for about 2 hours, then slowly disappeared and the patient was discharged asymptomatic some hours later. No late reaction was reported.

A few weeks after the reactions the patients started SCIT with a modified (depot) grass pollen extract that has been well tolerated.

Conclusions: Gynecological symptoms as uterine cramps and their consequences (i.e. metrorrhagia or hemorrhagic follicle) are uncommon but possible in anaphylaxis and they are not easy to manage since they do not respond well to adrenaline as gastrointestinal pain does.

1560 | Limited clinical utility of a panel of routine honeybee venom components

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Introduction: Previous reports suggest the usefulness of rApi m 5 and rApi m 10 IgE testing for diagnosis of honeybee venom allergy. We sought to evaluate the diagnostic utility of this testing in a routine clinical laboratory setting.

Objectives: In this prospective multi-centre study, we included 88 patients with established honeybee venom (HBV) allergy. Diagnosis of HBV allergy was based on history, skin test results, and allergen-specific IgE levels to HBV. IgE reactivity to rApi m 1, rApi m 5 and rApi m 10 was analysed by ImmunoCAP (CAP) and to rApi m 1 with Immulite (LITE) immunoassays. We also included 41 healthy control subjects.

Results: The diagnostic sensitivity of rApi m 1, rApi m 5 and rApi m 10 CAP panel was 84.1% and this was lower than rApi m 1 LITE alone, which showed the diagnostic sensitivity of 87.5%. The diagnostic sensitivity of rApi m 1 alone was only 71.6% ($P=0.009$). Overall, 14 patients that tested negative for rApi 1 with CAP were positive with LITE rApi m 1, but none of the patients that tested negative with LITE rApi m 1 were positive with CAP rApi m 1. The specificity of rApi m 1, rApi m 5 and rApi m 10 CAP 97.6%, 100% and 97.6%, respectively, and the specificity of rApi m 1 LITE was 95.1%.

Conclusions: The clinical utility of the commercially available panel of HBV allergen components is limited, due to low diagnostic sensitivity.

1561 | Clinical characteristics of anaphylaxis by honeybee venom in north china

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Introduction: Venom allergy is significantly underestimated in China. Venom-specific IgE may not provide accurate clinical reactions.

Objectives: To investigate the clinical characteristics of honeybee venom anaphylaxis. From 2011 to 2016, we retrospectively analyzed anaphylaxis cases induced by honeybee sting. According to systemic manifestations post honeybee sting, the patients were classified into four grades. Patient residence and exposure types were analyzed. To evaluate the role of venom allergen components sIgE test in distinguishing dual allergy from cross-reactivity preliminarily.

Results: Gender ratio male: female was 12:18; median age 35 years old (27, 38). 70.0% (21/30) of patients live in BTH (Beijing-Tianjin-Hebei) region; 23.3% (7/30) in urban areas, 76.7% (23/30) in rural areas. Grades of systemic reactions: I (6/30), II (8/30), III (12/30) and IV (4/30). There were three exposure types: natural (2/30), occupational (26/30) and iatrogenic (2/30). 86.7% patients were beekeepers. sIgE level of i1 (honeybee venom): 12.80 (2.80, 33.50) kUA/L. 19 of 30 patients finished i208 (phospholipase A2), i3 (wasp venom) and i209 (antigen 5) tests. In the patients who had dual positive results to both i1 and i3, 7 of 8 patients' i209 <0.10 kUA/L, only one patient was dual allergy to both honeybee and wasp venom whose i209=8.03 kUA/L. 33% (10/30) of patients presented with large localized reactions before onset of system symptoms 3-12 months of being stung.

Conclusions: Occupational exposure is the most common cause of honeybee venom anaphylaxis in North China. Allergen components sIgE is a useful diagnostic parameter in determining dual venom allergy.

1562 | Hymenoptera venom immunotherapy in a pediatric group

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Introduction: Venom immunotherapy (VIT) is effective in Hymenoptera venom allergy, although data regarding the pediatric age is sparse.

Objectives: To evaluate a group of pediatric patients submitted to hymenoptera VIT in our Immunoallergology Department, including the safety and efficacy of this procedure.

Material and Methods: A retrospective analyses was performed, concerning an eight-year period (1999 to 2016). Demographic data, atopy, allergic diseases, comorbidities, VIT protocol used and its safety and efficacy were assessed.

Results: The study population included 9 patients, 3 were females; median age of 12 years (6-14 years). Severe systemic reactions occurred in all patients (6 had grade III reaction and 3 had grade IV, according to Mueller classification of systemic reactions); 4 were sensitized to aeroallergens and 3 had allergic rhinitis; 5 patients lived in rural areas and 4 had beekeepers in the close family. Specific IgE to *Apis mellifera* (Api), *Vespula vulgaris* and *Polistes dominus* (Pol) were positive in 8, 6 and 3 children, respectively, and skin testing to bee and wasp venoms were positive in 8 and 1 patients, respectively. Eight patients were submitted to bee VIT (3 with a rush protocol and 5 with an ultra-rush protocol) and 1 to Pol VIT (ultra-rush protocol). Five of

the 8 bee VIT patients ended their treatment (VIT duration ranged from four to eleven years); in the others, the process is ongoing. During the build-up phase, two patients submitted to the rush protocol presented adverse reactions (1 had bronchospasm and 1 extensive local reaction) and 1 patient submitted to the ultra-rush protocol had rhinitis. All patients reached the cumulative dose of 100 µg. During the maintenance phase, 2 patients had an extensive local reaction and one had rhinitis. Seven patients were re-stung and only one developed generalized urticaria and bronchospasm, which led to a raise in the maintenance dose to 200 µg. After VIT had been concluded, 2 patients were re-stung with no systemic reactions.

Conclusions: These data, although concerning few patients, showed that VIT in a pediatric population is safe and prevents recurrences of systemic reactions after subsequent insect stings.

1563 | Tryptase behaviour during venom immunotherapy associates with the risk of adverse reactions

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Introduction: Tryptase levels have been associated to VIT severe adverse reactions. The decrease in tryptase level during VIT has been related to tolerance to insect stings and VIT efficacy.

Objectives: We investigated the changes in serial serum tryptase during the build-up phase of VIT to analyse its relation to the presence of adverse systemic reactions (ASR) during VIT.

Serum tryptase was serially measured the first day of immunotherapy in patients diagnosed with venom hymenoptera allergy who underwent VIT in a cluster schedule: before the first dose of VIT and 90 minutes after the last dose. Adverse reactions to VIT were recorded during the first year of treatment.

Results: Hundred and fifty patients received 160 treatments. Twenty five (15.6%) developed ASR with VIT. Severe reactions, grades 3 and 4, were 6.25% of the total VIT. Tryptase was measured on the first day of IT in 158 treatments; level decrease after the 4 doses of IT (Tryptase post-IT), compared to the level before the first dose that same day (Tryptase pre-IT), in 81% of the treatments. Mean basal tryptase value was 4.87 µg/L ± 4.43 (range 0.9-51.9 µg/L). There was no significant association between ASR and basal tryptase levels. In 16 (64%) out of 25 patients who developed ASR, tryptase post-IT the first day of VIT was higher after the 4 doses, than tryptase pre-IT. Mean tryptase increase was 26.5%. Only 5 out of 16 patients experienced ASR that first day; in 4 of them the ASR was grade 1.

In patients without ASR, tryptase decreased 6.8%. A statistical relation between an increase in tryptase level the first day of IT (OR 20.48; 95% CI 6-40.6; $P < .001$) was found, and was independent of the day and severity of the ASR and was also independent of the basal tryptase value.

Patients with a tryptase post-IT value higher than pre-IT had a rate of ASR of 53%, compared to 7% in those with an equal or lower value ($P < .001$).

Conclusions: The increase of tryptase on the first day of IT is an independent variable strongly related to a high risk of suffering SAR with VIT. It is independent of the day of the SAR, the severity of the reaction, and regardless of the basal tryptase value.

1564 | Basophil activation test is a useful ancillary test in peri-operative anaphylaxis

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Case report: Anaphylaxis to neuromuscular blocking agents (NMBA) is a major diagnostic challenge. Intradermal tests (IDT), although standardized and reliable, are not infallible. Drug provocation tests are the gold standard in hypersensitivity testing, but their utility is limited by the risk of systemic reactions. Here we present a case of anaphylaxis to rocuronium, which presented a diagnostic conundrum, resolved by using the Basophil Activation Test (BAT). Patient has consented for this publication. Mrs D presented for resection of an incidental thymoma. On induction she developed moderate hypotension with urticaria. Serum tryptases during this episode were within normal limits and morphine sIgE was negative. Initial IDT was positive for rocuronium, equivocal for cisatracurium, and negative for vecuronium, atracurium, propofol, fentanyl, cefazolin and chlorhexidine. However, her subsequent anaesthetic induction with propofol, fentanyl and vecuronium resulted in urticaria without minimal hypotension. Repeat IDT was negative to NMBAs, including rocuronium. To clarify this situation, a provocation test was scheduled with graded doses of induction agents (propofol, fentanyl and rocuronium). This provoked an urticarial reaction to rocuronium. In view of the non-diagnostic nature of the previous two IDTs, NMBA BAT was organized to find a safe alternative for future anaesthetics.

The results of the BAT are as follows: (Drugs- CD63 activation%) rocuronium-14.3, vecuronium-4.2, atracurium-1.6, cisatracurium-1.6, suxamethonium- 1.1 (see table)

These results are consistent with the clinical pattern noted with the two anaesthetic episodes. In a recent review of its clinical utility, BAT was found to have a specificity of 93-100% in patients with proven NMBA anaphylaxis. In addition, due to its good negative predictive value, BAT may have an important complementary role in

identifying cross-reactivity and safe alternatives in these patients. In conclusion, BAT is a useful alternative to provocation tests in complex cases with indeterminate IDT or sIgE results. In our case we will use BAT to base safe recommendations for alternative agents for this patient's future anaesthetic episodes.

Drugs	CD63 activation%
Positive Control	93
Negative control	0.4
Rocuronium 500 µg/mL	14.3
Vecuronium 500 µg/mL	4.2
Atracurium 500 µg/mL	1.6
Cisatracurium 500 µg/mL	1.6
Suxamethonium 500 µg/mL	1.1

1566 | Cefixime induced fixed drug eruption in an adolescent

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Case report: Fixed Drug Eruption (FDE) is characterized by single or multiple round oedematous erythematous-violaceous plaques that can develop in a few hours or days after exposure to the causative drug. Subsequent use of the same drug leads to recurrence of the lesions at the same site. FDE is well recognized with many drugs including antibacterial agents, non-steroidal anti-inflammatory drugs, barbiturates, antimalarials, however cefixime related FDE is reported only a few in the literature.

Sixteen years old male patient followed by nephrology department with a diagnosis of chronic kidney failure, vesicoureteral reflux and neurogenic bladder referred to our pediatric allergy department with a complaint of eruption. He was under treatment with cefixime for urinary tract infection for four days. There was no history of any other drug intake prior to the eruption. In patient's physical examination itchy, irregular bordered, non-tumorous violet colored 5×8 cm eruption under umbilicus, red colored 2×2 cm eruption on the lateral side of left popliteal fossa and 12×8 cm eruption on the medial area of right thigh were observed. Blood tests were normal but urine tests revealed 7 leukocytes per site. The patient stated that he had also used cefixime three months ago, which caused similar eruptions in the same area, and those lesions regressed in 2-3 weeks when he discontinued the drug. Keeping in view the nature of lesions and recurrence of reactions following the use of the same drug, a diagnosis FDE was made and the patient advised to avoid the use of

cefixime. Patch test was applied to the lesional skin and upper back with 10% concentration of cefixime two months later, however the results were negative even though reaction reactivated after reuse of the same drug. Eruptions in thigh area did not regress completely after drug cessation and subsided with residual hyperpigmentation. To our knowledge this is the third case reported in the literature, which describes fixed drug eruption by cefixime use in children. Re-exposure of the patient with cefixime after 3 months later induced acute flare on residual lesions however patch test results were found negative. This result emphasize that although patch tests are commonly used, oral provocation tests remain as gold standard tests in the diagnosis of FDE.

1567 | Successful desensitization in a patient with hypersensitivity reaction to laronidase

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Case report: Mucopolysaccharidosis I (MPS I) is a rare, recessively inherited, lysosomal storage disorder caused by deficiency of the enzyme α -L-iduronidase. Scheie syndrome is the least severe form of MPS I. Patients can be diagnosed in the adolescent age group. Enzyme replacement therapy with laronidase is the best treatment option in Scheie syndrome and is generally well tolerated by patients. Anaphylaxis and other immediate hypersensitivity reactions to laronidase are very rare. Immediate hypersensitivity reaction to laronidase and successful desensitization with laronidase have only been described in two pediatric patients. We herein report the first of case a severe immediate hypersensitivity reaction to laronidase in an adult patient with MPS-I disease, who was successfully treated with a laronidase desensitization protocol.

Table 1. Desensitization protocol for laronidase IV (6500 U=13 vial): solution preparation

	Volume	Concentration	Total amount of drug in each solution
Solution 1	250 mL (25 mL Sol 2+225 mL SS)	0.26 U/mL	65 U
Solution 2	250 mL (25 mL Sol3 +225 mL SS)	2.6 U/mL	650 U

(Continues)

Table 1 (Continued)

	Volume	Concentration	Total amount of drug in each solution
Solution 3	250 mL (100 U/mL laronidase 65 mL) +185 mL SS)	26 U/mL	6500 U

Table 2. Protocol for intravenous desensitization with laronidase

Step	Solution	Rate, mL/h	Time, min	Amount per step, mL	Administered dose, U	Cumulative dose, U
1	1 (0.26 U/mL)	2.5	15	0.625	0.1625	0.1625
2	1 (0.26 U/mL)	5	15	1.25	0.325	0.4875
3	1 (0.26 U/mL)	10	15	2.5	0.63	1.1175
4	1 (0.26 U/mL)	20	15	5	1.26	2.3775
5	2 (2.6 U/mL)	5	15	1.25	3.25	5.6275
6	2 (2.6 U/mL)	10	15	2.5	6.5	12.1275
7	2 (2.6 U/mL)	20	15	5	13	25.1275
8	2 (2.6 U/mL)	40	15	10	26	51.1275
9	3 (26 U/mL)	10	15	2.5	65	116.1275
10	3 (26 U/mL)	20	15	5	130	246.1275
11	3 (26 U/mL)	40	15	10	260	506.1275
12	3 (26 U/mL)	45	339	232.5	6.045	6551.1278

Target dose: 6500 U, Total time: 504 minutes

1568 | Challenge is needed to obtain accurate diagnosis in allergic reactions to low-molecular-weight heparins

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Case report: Allergic reactions to low-molecular-weight heparins (LMWH) are uncommon. The most frequent form of presentation is localized dermatitis. Heparins may act as haptens by binding to dermal and/or subcutaneous structural proteins. Molecular weight discriminates high molecular weight (10-20 kDa), low molecular weight (4-6 kDa) and ultra low molecular weight heparin (1.7 kDa). Some of their functional groups are nearly identical and therefore cross-reaction among heparins could be expected. Consequently, in patients with allergic reaction to a LMWH, identification of a safe alternative anticoagulation is essential. Fondaparinux, a synthetic pentasaccharide with a molecular weight of 1.72 kDa, has been proposed as a safe and effective alternative.

Patients and methods: We present 3 cases of late pruritic localized erythema and eczema after injection of LMWH for the prophylaxis of deep venous thrombosis and/or treatment of thrombophlebitis: case 1 after injection of bemiparin, case 2 after enoxaparin and case 3 after enoxaparin and tinzaparin. Prick and intradermal skin tests with nadroparin, tinzaparin, enoxaparin, dalteparin, bemiparin and fondaparinux with immediate and late (48-96 hours) lecture were made to the three patients. Provocation was carried out with heparins that exhibited negative result in cutaneous tests.

Results: All patients showed at least one positive skin test for LMWH and had presented localized eczema. Prick testing was negative for all substances. In contrast, reactions to intracutaneous testing with concentration of 0.01% were positive at 48 hours for nadroparin, tinzaparin, enoxaparin, dalteparin, and bemiparin in case 1, for nadroparin and dalteparin in case 2, and for bemiparin in case 3. Provocations with nadroparin, tinzaparin, enoxaparin and dalteparin were positive in case 1. Provocation with tinzaparin was positive in case 2. Intradermal tests as well as subcutaneous challenge with fondaparinux were negative in all the three patients.

Conclusions: Although skin tests can help to identify alternative anticoagulation, accurate diagnosis relies on challenge. Some patients that exhibited negative skin tests with LMWH, experienced localized eruption at the injection site when administered. Fondaparinux demonstrated to be a safe alternative in the three patients.

1569 | A rare case of angioedema to different antihypertonic drug classes due to possible hypersensitivity to drug additives

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Case report: Background: Drug allergy can be distinguished into primary allergy and drug intolerance. In addition, there are upcoming cases with allergies to drug excipients. To distinguish the latter from a real allergy to active components is difficult; the only tests available are skin prick tests and oral provocation tests.

Case Report: After a cardiological checkup, the patient was prescribed to start antihypertensive therapy due to newly diagnosed hypertension. On behalf of the cardiologist's recommendation, the GP started the treatment with a sartane. After the second day the patient developed an angioedema of the lips about 3-4 hours after drug intake. No dyspnea or further allergic symptoms, the edema was resolving after oral anti-allergic treatment within 4 hours. The sartane was stopped immediately. One week later the GP started another treatment with a calcium antagonist of which on the second day, she developed an angioedema of the tongue. No dyspnea, but

need of anti-allergic treatment immediately, which helped to clear symptoms within an hour. The patient's history is negative for further allergies or other diagnosis. The allergic work up did not show a sensitization to eliciting drugs in the skin prick test nor could we find abnormal blood results (8 complement, tryptase).

In a more detailed investigation of the excipients, we found both tablets containing cellulose and magnesium stearate. The further work up contains skin prick test to carboxymethyl cellulose and magnesium stearate and open challenges with food additives and if all negative a challenge with an alternative antihypertensive drug.

Discussion: The reaction to calcium antagonists besides ACE inhibitors in this case opens the possibility of a hypersensitivity to excipients and not the effective drug as a cause of angioedema. AAs it is potentially affecting and lifesaving treatment, it is very important to gain more knowledge about it. Even if there is no sensitivity to an excipient found, we still think it is a very important case showing a big gap of knowledge in this field.

1570 | A new penicillin allergy diagnosis in pregnancy at Groote Schuur Hospital, Cape Town, South Africa: Could this be a hormonal phenotype?

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Case report: Introduction: Penicillin antibiotics are frequently used to treat infections in South Africa without establishing a causative organism. This results in many patients being unnecessarily labelled as being penicillin allergic, especially when faced with a viral exanthem after initiation of penicillin for a trivial viral infection. This may lead to antibiotic resistance and unnecessary use of alternative broad spectrum antibiotics. In pregnancy, penicillin has shown to be the only effective treatment to syphilis infection. Induction of drug tolerance has become mandatory for managing pregnant women with penicillin allergy to avoid maternal and foetal complications. There has been no published literature on hormonal influence as a risk factor for penicillin allergy. We present a pregnant woman with syphilis and a presumptive diagnosis of penicillin.

Case study: A 25 year old Primigravid presented to her family doctor in October 2016 with a sore throat and dizziness. She was treated with amoxicillin 500 mg P.O 8 hourly for 5 days. She had an immediate reaction about 20 minutes after the 5th dose of amoxicillin. She experienced a morbilliform rash, vomiting, diarrhoea, palpitations and dizziness (no respiratory symptoms). She improved spontaneously within 24 hours, but revisited her doctor for the dizziness that was persistent. He decided to do a pregnancy test for the

persistent dizziness and to stop the amoxicillin, as the pharyngitis had resolved. The pregnancy test was positive, and the doctor advised her to avoid penicillin, as she was probably allergic to it. She subsequently had an Obstetric visit, where she was diagnosed with syphilis in pregnancy, TPHA 1:4 and treated with Azithromycin 250 mg stat (due to presumed penicillin allergy). The Obstetric department referred her at 25 weeks gestation to the Allergy and Clinical Immunology Department at Groote Schuur Hospital for desensitisation of penicillin in January 2017, in order to treat the syphilis. She gave a history of recurrent pharyngitis (3 times a year), which was usually treated with amoxicillin, last treated in June 2016. She had no relevant past medical and drug allergy history, past surgical history was an open reduction and internal fixation of an elbow fracture. Family history of drug allergy was positive as her father is presumed to be allergic to penicillin.

Physical examination: Extremities: slight pallor, no oedema. Vital Signs: Temp.36.2, pulse 78 bpm, BP 108/74 mm Hg, RR 16, SpO2 100% on room air. Skin: No rash. ENT: Normal. Chest: Clear to auscultation bilaterally. Cardiovascular: Normal S1, S2, no murmurs. Abdomen: SFH 26 cm.

Diagnostic tests:

Skin Prick Test:

1. Penicilloylpolylysin 0 mm negative.
2. penicilloate 0 mm negative.
3. Negative Control 0 mm negative.
4. Histamine 3 mm.

Intradermal Test:

1. Penicilloylpolylysin 0 mm negative.
2. Penicilloate 3 mm.

Specific IgE Amoxicillin <0.10 kU/L (Below detectable).

Ampicillin <0.10 kU/L (Below detectable).

Penicillin G <0.10 kU/L (Below detectable).

Penicillin V <0.10 kU/L (Below detectable).

CAST ELISA Amoxicillin 0 pg/mL (100 pg/mL sLT).

Penicillin V 0 pg/mL (40 pg/mL sLT).

Penicilloylpolylysin 0 pg/mL (110 pg/mL sLT).

Minor determinant mix 53 pg/MI (100 pg/mL sLT).

Management: She received 3 induction of drug tolerance procedures for penicillin using the protocol below, followed by a therapeutic dose of 2.4 million IU.

1st desensitisation: Delayed (3 hours) reaction with urticaria, resolved without medical intervention.

2nd desensitisation: Delayed reaction with urticaria post discharge, resolved spontaneously.

3rd desensitisation uneventful recovery.

Penicillin desensitisation protocol Modified from Sullivan TJ.¹

Discussion: Syphilis in pregnancy is an infection with widespread complications for both the infected woman and her foetus. The following complications have been associated with syphilis in pregnancy:

1. Maternal: hydramnios, abortion, and pre-term delivery.
2. Foetal: foetal syphilis, hydrops, prematurity, foetal distress and still birth.
3. Neonatal: congenital syphilis, neonatal death and late sequelae.^{1,2,3}

A 2010 survey found that 1.5% of pregnant women in South Africa presenting at public antenatal care clinics were infected with syphilis.⁴ In rural South Africa, adverse pregnancy outcome in women with syphilis is 12 times more common than sero-negative women.⁵ Treatment with penicillin in pregnant syphilitic women has been the mainstay of treatment in order to avoid maternal and foetal complications. A study revealed that an intramuscular dose of 2.4 Mu of benzathine penicillin prevented foetal infection in 98% of cases in 204 pregnant women with primary, secondary or early latent syphilis. Nevertheless, some recommend a second dose of penicillin to ensure effective treatment.⁶ In another study involving 180 syphilitic pregnant women in South Africa, women who were treated with 3 doses or less delivered infants with decreased birth weight, and had premature delivery, neonatal death and a syphilitic infant more frequently than those who were treated with a course of antibiotic for longer than 3 weeks.⁷ The 25 year old patient was treated with 3 doses of benzathine penicillin weekly, to ensure efficacy of treatment. She had to be desensitised before each dose because of the risk of loss of tolerance to penicillin. The patient was given a suboptimal single dose of Azithromycin to treat her syphilis, due to her presumed penicillin allergy. Azithromycin and ceftriaxone offer potential alternatives for penicillin-allergic women, but insufficient data on efficacy limit their use in pregnancy.⁸ Approximately 5-10% of pregnant women with syphilis report a history of penicillin allergy.⁹ There have been humoral phenotypes identified for penicillin allergy. Antigen-specific T cell clones isolated from such cultures were of the CD4+ or CD8+ phenotype and secreted heterogeneous patterns of cytokines upon antigenic stimulation (Brander *et al*, 1995). The skin is a target organ of drug-induced CD8 cells (Hertl and Merk, 1995). The majority of penicillin T lymphocytes, particularly if isolated from peripheral blood appear to be of the CD4 phenotype (Brander *et al*, 1995; Padovan *et al*, 1996). Functional Th1/Th2 dichotomy is likely to play a role also in the allergic phenomena induced by penicillins, in particular with a prevalence of Th2 responses in immediate hypersensitivity reactions and of Th1 responses in delayed allergic phenomena.¹⁰ Pregnancy has no effect on the number of CD4+ and CD8+ lymphocytes in the peripheral blood or on the ability of mononuclear cells to react in mixed lymphocyte culture or to respond to antigens or mitogens.¹¹ This could be some support for decreased in circulating Th1 cells and increasing Th2 cells in late pregnancy.^{12,13} Our patient has had amoxicillin 500 mg three times a day, for five days, to treat pharyngitis, at least three times a year without any allergic reaction. After conception, she developed a delayed reaction with features of IgE immediate reaction. This appears to be a mixed Th1/Th2 phenotype with delayed morbilliform rash, gastrointestinal and cardiovascular

symptoms simultaneously after 32 hours Amoxicillin 500 mg per os taken every 8 hours. Skin testing with the major determinant and penicillin G only (without penicilloate or penicilloate) may miss up to 20% of allergic patients, but data on this are conflicting.¹⁴ The patient had a negative skin test to penicillin major determinant antigen (Penicilloylpolylysin) and minor determinant antigen (penicilloate). The combination of a positive intradermal penicilloate and a weakly reactive cellular antigen specific test ELISA to minor determinant mix helped with diagnosis.

Conclusion: Penicillin is the golden standard antibiotic for the treatment of syphilis in pregnant women. Pregnant women with penicillin allergy need to be desensitised before each dose of benzathine penicillin. Skin prick test is the most reliable diagnostic test in determining penicillin allergy. There could, however, be a role in using additional specific test such as intradermal and cellular antigen specific test. Pregnancy could pose risk to developing penicillin allergy as seen in this patient that previously tolerated amoxicillin before conception.

1572 | The efficiency of venom immunotherapy and its positive correlation on pollen allergy

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Case report: During the period of two years of VIT of my observed patients, I verified that the first case: 12 years old; gender: female and second case: 26 years old gender male was allergic in: pollens and bee venom with anaphylactic allergic reaction. Specific IgE on pollens and hymenoptera venoms, with the parameters of to first patient:

Bee venom has fallen from 5-4; Alder pollen: 1-0; Birch pollen: 2-0; Hazelnut pollen: 2-1; Beech pollen: 2-0; Oak pollen: 2-1; Pine: 2-0; Rhizopus nigricans: 2-0; Grass mix: 3-1 and house dust from 2-0.

Second patient A.V. 25 years old, gender M allergic on pollens and bee venom after one year of VIT with Anallergo vaccine the parameters of Bee venom has fallen down: 6-3; beech pollen: 1-0; house dust mites: 1-0; grasses mix: 2-2 has remained the same.

MONDAY, 19 JUNE 2017

LB TPS 04

DERMATITIS AND OTHER SKIN CONDITIONS

1573 | Oral H1 antihistamines as 'add-on' therapy to topical treatment for eczema: A Cochrane systematic review

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Introduction: Oral H1 antihistamines (H1-AH) may improve disease severity in people with eczema mainly by reducing the principal symptom itch. Its use as adjuvant therapy together with topical agents may bolster the effect of treatment.

Objectives: We aimed to assess evidence for the efficacy and safety of oral H1-AH as 'add-on' therapy to topical treatment in adults and children with eczema. We searched databases, trial registers, conference abstracts and hand-searched bibliographies for eligible randomised controlled trials. We extracted and analysed data, performed risk of bias assessments and rated the quality of the evidence.

Results: Twenty-five studies (n=3266) met criteria for inclusion. 8 studied children (n=1941) and 17 adults (n=1325). 13 different H1-AHs were used. Duration of the intervention ranged from 3 days-18 months and results are described for short-, medium- or long-term interventions. 23 provided a measure of itch, 19 of adverse events, 17 physician-assessed signs and 11 of escalation of treatment. None measured quality of life. For 9 of the 13 H1-AH no evidence for efficacy in itch reduction was found. Effects were noted for fexofenadine and olopatadine based on 1 study each while for cetirizine and loratadine inconsistent results emerged. Safety assessments in 17 studies with 2985 participants found no evidence for increased risk of adverse events apart from a dose-related effect of cetirizine in 1 study. Most studies lacked sufficient information to judge whether the methods used, can eliminate threats to the studies' validity. The risk most frequently ascertained, related to attrition bias. Using the GRADE approach, we found the evidence to be mostly low or very low. Clinical diversity across studies did not permit pooling.

Conclusions: We found no clear evidence to establish that H1-AHs as add-on therapy are effective in the treatment of eczema but they appear to pose no concern for safety in standard doses. Given the quality of the included trials and their reporting, the wide clinical diversity in comparisons and that there were no opportunities for pooling results in meta-analyses, caution is needed in making specific treatment recommendations.

1574 | Neutrophil-lymphocyte ratio in pediatric atopic dermatitis patients

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Introduction: Atopic dermatitis (AD) is a chronic inflammatory skin disease and it affects nearly 20% of the pediatric population. Neutrophil-lymphocyte ratio (NLR) is a practical and easy to obtain method that reflects subclinical chronic systemic inflammation. This ratio was shown to be associated with non-allergic (hypertension, diabetes, cancer, psychiatric disorders) and allergic (allergic rhinitis, asthma) diseases. In recent years, AD has increasingly become recognized as a systemic disease rather than an only local disease in the skin based on non-lesional skin inflammatory changes, atopic march and metabolic, cardiovascular and other comorbidities.

Objectives: We aimed to evaluate the NLR in pediatric AD patients to understand if there is a subclinical systemic inflammation.

Results: Two hundred and seventy patients diagnosed with AD and followed in our department were recruited as the patient group and 70 patients with no allergic, infectious or other chronic diseases were recruited as the control group. NLR was calculated by dividing neutrophil count to the lymphocyte count in complete blood count analysis. SCORAD indices of AD patients were recorded and grouped as mild (<25), moderate (25-50) or severe (≥50). Patient and control groups were compared according to the NLRs. Also the three SCORAD groups' NLRs were compared. The mean age was 4.02±3.85 years in the patient group. Mean NLR was 1.06±1.28 in the patient group and 0.75±0.34 in the control group. The difference was statistically significant (P=.003). There were no differences in the NLRs between the three SCORAD indices groups.

Conclusions: In our study the NLR of the AD patients was higher than the controls. This may demonstrate the systemic inflammation in AD. Although the major pathomechanisms are the inflammation due to the abnormal immunologic response to the antigens and antibodies and the abnormal epidermal barrier function in the skin, the presence of the subclinical systemic inflammation should not be overlooked. Although there are many complex biochemical assays to detect the systemic inflammatory response in atopic dermatitis for underresourced and economically disadvantaged clinical settings, a practical and routine blood test including NLR may also reflect this systemic inflammation, so NLR may be an alternative test. Yet, further studies are needed in this field.

1577 | Atopic dermatitis as a risk factor to chronic urticaria in children: New insights in atopic march?

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Introduction: Chronic spontaneous urticaria (CSU) represents a chronic inflammatory skin disorder, with partly unknown pathogenetic mechanisms. Studies assessing risk factors related to the onset or persistence of the disease are lacking. Clinical experience often depicts a frequent overlap between atopic dermatitis (AD) and CSU since childhood.

Objectives: To evaluate potential associations of children's demographic and atopy-related characteristics in early childhood with the risk of presenting CSU.

Methods: We retrospectively studied records of children examined between 6/2014 and 8/2016 in the Allergy Unit of a tertiary Hospital in Greece. Demographic data included gender, personal and family atopic history, season of birth and cause of patients' visit. Diagnosis of AD and CSU was based on standard criteria according to the EAACI proposed guidelines. Univariate analyses and a binary logistic regression model (multivariate) were performed for the statistical analysis. Post hoc power analysis calculated data power.

Results: Data on 2261 children (age 1-16 years, 60.4% males) were recorded. 761 (33.7%) children had a positive history of AD or still active disease, while 51 (2.3%) were diagnosed as having CSU. In respect to patients with CSU (31 males, 60.8%), 30 (58.8%) reported a clinical history of AD (active or non-active disease). A likelihood ratio calculation indicated that patients with clinical history of AD had an odds ratio (OR) of 2.923 (95%CI [1.647-5.189]) regarding later onset of CSU ($P < .001$).

No statistical significance regarding the effect of gender ($P = .986$), patients' season of birth [465 (21.9%), 550 (24.3%), 656 (29%) and 560 (24.8%) in study population vs 15 (29.4%), 12 (23.5%), 16 (31.3%) and 8 (15.7%) in CSU patients, during winter, spring, summer and autumn respectively, $P = .373$] or family history of atopy [1212 (53.6%) vs 29 (56.8%), $P = .812$], on CSU was noticed. Post hoc analysis showed that statistical test achieved 94.4% power.

Conclusions: Data from our retrospective study are suggestive of an increased risk of AD on subsequent occurrence of CSU. This notion warrants further studying and questions new prospects in the "atopic march."

1579 | Hypersensitivity to natural rubber latex gloves among Albanian dental students: The role of exposure duration

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Introduction: Latex allergy is a common occupational disease among healthcare workers who use latex gloves.

Objectives: The aim of the present study was to determine the prevalence of allergy to latex gloves among dental students and the role exposure duration in latex allergy.

Results: In this prospective study, a total of 240 students completed a self-administrated questionnaire that comprised of a total of different items and gave information about the participants and their glove use, working habits and glove use, signs and symptoms related to glove use, precautions taken to minimize it, etc. The challenge and patch tests were performed through latex gloves, skin prick test with commercial extracts. The questionnaire items and diagnostic tests revealed that one-fourth of subjects were suspicious for latex gloves hypersensitivity. Their mean value for skin reactions like contact urticaria, irritant or allergic dermatitis was between 10% and 14%, while for non-cutaneous symptoms the mean value was under 5%. The average latex exposure (in hours) is estimated to be about 214 (± 71 , SE), with a maximum of 11500 hours. The correlation between studied variables and the time exposure to latex gloves revealed weak to moderate links with respect to reported latex allergy, eczematous reactions, hand erythema after glove wearing, irritant reactions during wash/washout procedures, concentration oscillations during usage of latex gloves, or dyspnea attack during latex exposure.

Conclusions: Because of relationship between allergic reactions to latex gloves and some medical histories during school practice, it seems to be necessary for pre-matriculation evaluation and periodic health surveillance of dental students.

1583 | Evaluation of natural products extracted from copaiba, native tree of Brazil, in the treatment of experimental atopic dermatitis in mice

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Introduction: Copaiba is a tree native to the Brazilian Amazon from which the oil-resin of copaiba is extracted. This oil has anti-

inflammatory property popularly recognized by natives of the region. One of its predominant constituents is the trans-caryophyllene molecule.

Objectives: To evaluate the therapeutic potential of copaiba oil and trans-caryophyllene isolated from oil in experimental atopic dermatitis induced by ovalbumin in Balb/c mice. After atopic dermatitis was established, the animals were divided into five groups: I (untreated disease), II (dexamethasone 0.1%), III (tacrolimus 0.1%), IV (copaiba oil) and V (trans-Caryophyllene). An anatomic-pathological study of the lesions was performed, as well as histochemistry for mast cell count.

Results: Despite a better picture compared to the untreated samples, lesions treated with dexamethasone and with tacrolimus showed, in total, diffuse mixed crust and inflammatory infiltrate in the papillary and reticular dermis, with occasional erosion; the tacrolimus-treated samples exhibited more intense inflammatory infiltrate compared to the other treated groups. On the other hand, none of the samples treated with trans-caryophyllene and copaiba oil presented erosion, crust or hyperkeratosis, occasionally exhibiting diffuse mononuclear inflammatory infiltrate in the dermis. In addition a significant reduction in the amount of mast cells was observed in copaiba oil treated mice.

Conclusions: Copaiba oil and trans-caryophyllene presented higher anti-inflammatory property when compared with dexamethasone and tacrolimus. Therefore, this Brazilian natural product has important therapeutic potential justifying the accomplishment of therapeutic studies in atopic dermatitis.

A 55 year-old lady was seen in clinic due to CSU. Interestingly she reported that many of her episodes were localised and occurred shortly after exposure to sunlight but during cold days only. She also reported symptoms in the summer when swimming in cold water only and occasionally when sitting next to a window with the sun shining through it. Symptoms usually resolve within 30 minutes without treatment.

Autoimmune, porphyrin screen and cold stimulation test (ice cube test) were negative. Subsequently, she was referred to a specialised Photobiology unit. Narrowband phototesting elicited urticaria only with 400 nm light. However when this testing was repeated on skin precooled with a crushed ice pack, urticarial reactions were induced on narrowband testing from 330 to 400 nm, which is an augmentation of the responses demonstrated on the initial phototest.

A diagnosis of SU augmented with cold was made and she was advised appropriately.

To the best of our knowledge this is the first well-documented case of SU augmented with cold. This case highlights the importance of a detailed history in identifying accurate triggers of CindU; here the main presentation was of SU but with a peculiar seasonal pattern. Physicians should be aware that triggers may vary and that concurrent triggers may be needed, in this case UV or visible light exposure and precooled skin. Awareness will result in adaption of tests based on each individual's history, correct identification of eliciting trigger (s) and individual trigger thresholds, thus enabling improved care provision to such patients with tailor made recommendations (avoidance of relevant triggers) to improve their quality of life.

1584 | Solar urticaria augmented with cold

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Case report: Chronic inducible urticarias (CindUs) are a subgroup of urticaria triggered by specific physical stimuli. In rare cases, two or more concurrent triggers are needed. Herein, we present a case of solar urticaria (SU) augmented with cold. SU is a rare CindU characterised by development of wheals upon exposure to ultraviolet (UV) and/or visible light; its prevalence among patients with chronic spontaneous urticaria (CSU) is 0.08%. The average duration ranges between 3-6 years. Accurate diagnosis is based on thorough clinical history and broadband and narrowband provocation phototesting with wavelengths of UVB, UVA and visible radiation from 300-600 nm, so as to confirm the working diagnosis and to determine the minimum urticaria dose (MUD) of the causal wavelengths eliciting a response.

1586 | Epidermolysis bullosa in newborn: A case report

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Case report: Introduction: Epidermolysis bullosa (EB) is a rare group of inherited skin disorders that manifests as blistering of the skin in the varying degrees of severity. Although the clinical features are multiple and varied, treatment still remains a major challenge. The exact prevalence of epidermolysis bullosa is unknown. In US mild variants have been estimated to occur as frequently as 1 per 50,000 births. The more severe varieties in 1 per 500,000 births annually. The incidence rates of EB by subtype were approximately eight per million live births for EB simplex. This disease is extremely rare in Latvia. A newborn female admitted to our hospital 11/10/2016 with blistering of the skin since birth. She was born 01/10/2016 at term from the first pregnancy, the first spontaneous delivery without any adverse perinatal events. The child's birth weight 3300 g, Apgar 8/9 points.

Objectives: Baby had blistering of the skin involving the hand fingers, the next day bullous elements were seen in gluteus areas. Later the baby had extensive blistering skin defects, bullous the serous fluid, skin damage was 90% of the total skin surface, including erosion in the mouth. Erosive surface slowly reduce after treatment to 30% of the total body surface area. Minimal trauma elicited new blisters.

Results: 12/10/2016 Skin biopsy: The picture corresponds to epidermolysis bullosa. Local therapy: skin care, daily baths with potassium permanganate, wound treatment with sterile normal saline, wound contact layer for the erosive surfaces, zinc oxide spray, for dry scabs emollient ointment. For oral mucosa the buckthorn oil, Extractum sanguinis, Chlorhexidine 0.02%, Methyluracil, Lidocaini hydrochloridum. Antibacterial therapy: IV Sol. Oxacillin for secondary infection. Pain management: IV or rectal Paracetamol. 26/10/2016:

febrility, Il-6 2117 pg/mL, CRP 61.08 mg/L. Diagnosis: Late neonatal sepsis. Th: Sol. Piperacillin/tazobactam. Consultants: neonatologist, dermatologist, pulmonologist, otorhinolaryngologist, genetics, pathologist.

Conclusions: Around 20,000 children are born in Latvia every year. In 2016 two newborns were with severe EB in Latvia, what was a challenge for our doctors because low incidence of this disease. The interdisciplinary team is required for pain management, skin care, nutrition, secondary infection treatment. We had financial and organize problems with the disease morphological and genetic investigation.

MONDAY, 19 JUNE 2017

LB TPS 05

RHINITIS, RHINOSINUSITIS AND CONJUNCTIVITIS

1587 | Interaction between allergic and neurogenic response to allergen, histamine and hypertonic saline after specific and non specific nasal provocation in subjects with seasonal allergic rhinitis

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Introduction: Nasal challenges lead to inflammatory and neurogenic response. Simultaneous analysis of the mediators of inflammatory, neurogenic and neural reflex response in patients with allergic rhinitis was not demonstrated previously.

Objectives: The study was done to evaluate the interaction of allergic, neurogenic and cholinergic reflex response by simultaneous measurement of substance P (SP) and tryptase release in nasal lavage and tears and challenge in patients with seasonal allergic rhinitis (SAR).

Results: A group of 25 SAR patients were submitted consecutive nasal provocations out of season. Patients were challenged with 500 B.U. of lyophilized allergen in water solution which was applied to both inferior turbinates. Histamine (80 mcg per nostril) was applied 24 hours, and 2% hypertonic saline (HTS) 72 hours after allergen, respectively. Subjective scores for nasal and ocular symptom scores and nasal lavages were taken before and after each challenge. Immediately after provocation Schirmer test was done bilaterally, VAS scores and nasal lavage were done 15 minutes after provocation. Nasal lavages were analysed for tryptase, eosinophil cation protein (ECP) and substance P (SP) and tears collected with Schirmer strips were analysed for SP. SP levels in nasal lavage did not show significant increase 15 minutes after the challenges. SP concentrations in tears increased significantly compared to baseline 5 minutes after non-specific challenges (from mean 0.35 pg/mL to 0.54 pg/mL after histamine, and to 0.57 pg/mL after HTS). SP levels in nasal lavage and tears after challenges correlated significantly after allergen ($\rho=0.53$, $P=.003$), histamine ($\rho=0.599$, $P=.0001$) and after HTS ($\rho=0.766$, $P=.0001$), respectively. Schirmer scores between the challenges also correlated significantly, but not with mediator concentrations. Tryptase after allergen correlated with ECP at 24 hours, but not with SP. SP levels significantly correlated with burning sensation in the nose, and SP in tears with ocular itch and nasal burning. Tryptase and ECP did not correlate with subjective response.

Conclusions: Response to different non-specific nasal challenges in patients with SAR out of season may not reflect the response to allergen in terms of correlation between subjective symptoms and severity of inflammation, however, it seems that neural cholinergic

reflex response and neurogenic inflammation are similar after different challenges. Impact of mast cells proteases on SP degradation should be considered.

1588 | MP29-02 treatment reduces cold dry air-induced nasal mediators and nasal hyperreactivity in patients with house dust mite allergic rhinitis

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Introduction: Nasal hyperreactivity (NHR) is a prominent feature of allergic rhinitis (AR), being present in 2/3 of patients. So far, no treatment was shown to reduce NHR in AR. Therefore, there is a need for better treatments and increased understanding of the mechanisms leading to NHR.

Objectives: In a double-blinded placebo-controlled trial, we evaluated the efficacy of four weeks intranasal treatment with MP29-02 (azelastine hydrochloride (AZE) and fluticasone propionate (FP)) on the reduction of mediators in nasal secretions and cold dry air (CDA)-induced NHR in 28 patients with house dust mite AR. In addition, the effect of AZE +/- FP on human mast cell (MC) degranulation, activation of murine dorsal root ganglion (DRG) neurons and transient receptor potential (TRP)A1 and V1 overexpressing cells was studied *in vitro*.

Results: MP29-02 reduced the levels of substance P and β -hexosaminidase in nasal secretions and CDA-induced nasal hyperreactivity 1 and 4 weeks after treatment. CDA-induced nasal symptoms were significantly decreased after treatment with MP29-02 and correlated with the reduction in NHR.

Azelastine potentially reduced MC degranulation, whereas no synergistic effect AZE/FP could be demonstrated. The combination of AZE/FP increased intracellular Ca^{2+} of TRPV1 but not of TRPA1 overexpressing cells. AZE or FP alone could not activate TRPV1. In addition, when AZE/FP was applied to murine DRG neurons, only the TRPA1⁺TRPV1⁺ double positive neurons were activated. Lastly, desensitization of neurons was observed after repeated applications of MP29-02, but this state did not affect the sensitivity to capsaicin.

Conclusions: This study shows for the first time that MP29-02 nasal spray reduced nasal hyperreactivity and improved cold dry air-induced nasal symptoms. In addition, nasal MC and neuronal activation decreased significantly after 4 weeks of treatment. MP29-02 reduced MC degranulation to the same extent as azelastine alone. Further studies on the synergistic effects of AZE/FP are needed to fully elucidate the interaction between MP29-02 and neuronal activation.

1589 | Impact of serum 25-hydroxyvitamin D3 levels deficiency upon the symptoms and anxiety of allergic rhinitis

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Introduction: Serum 25-hydroxyvitamin D3 (VD3) levels deficiency have been recently found to be responsible for allergic diseases such as asthma. But there is a lack of knowledge about VD3 levels deficiency status in the symptoms and anxiety of allergic rhinitis (AR). The objective of this work was to evaluate the relationship between VD3 levels and the symptoms and anxiety of AR.

Objectives: Forty subjects with allergic rhinitis proved by skin prick test (SPT) and 23 subjects with deviated septum alone were recruited. The four major symptoms including nasal itching, sneezing, nasal discharge, and nasal congestion were evaluated by VAS, anxiety was evaluated by State trait anxiety(STAI) and VD3 levels were measured. AR was classified according to the ARIA guidelines.

Results: Mean VD3 levels were 14.37 ± 4.1 ng/mL in the AR group and 28.36 ± 4.68 ng/mL in the control group. These differences among groups were statistically significant ($P < .01$). There were not any association between VD3 levels and allergen sensitivity by VAS ($P > .05$). S-AI score was significantly higher in AR patients than control group. There was correlation between VD3 levels and S-AI score in severe intermittent allergic rhinitis.

Conclusions: VD3 insufficiency/deficiency is common in AR group. There were not any association between VD3 levels and severity and duration of allergic rhinitis. Lower levels of VD3 are associated with worse anxiety in severe intermittent allergic rhinitis.

1590 | Fluticasone propionate and mometasone furoate are equally effective in restoring epithelial barrier defects in allergic rhinitis

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Introduction: A defective epithelial barrier function, accompanied with decreased tight junction expression has been demonstrated in allergic rhinitis. Intranasal corticosteroids protect epithelial barrier function by promoting the expression of tight junctions, though no data is available on which corticosteroid is the most potent.

Objectives: To compare the effect of different corticosteroids on nasal epithelial barrier function in allergic rhinitis.

The effect of fluticasone propionate (FP) or mometasone furoate (MF) on epithelial integrity of Calu-3 epithelial cells was evaluated by measuring transepithelial electrical resistance (TER) *in vitro*. *In vivo*, the effect of FP and MF on mucosal permeability for fluorescein isothiocyanate-dextran 4 kDa (FD4) was studied in a mouse model of house dust mite (HDM) induced allergic airway inflammation. Bronchoalveolar lavage for differential cell count and nasal mucosa for evaluating the expression of occludin and zonula occludens 1 were collected.

Results: Both FP and MF significantly increased TER of Calu-3 cells compared to medium control. Moreover, treatment with both steroids prevented IL-4 mediated decrease in TER *in vitro*. *In vivo*, FD4 permeability was significantly increased in mice challenged with HDM, which was associated with decreased expression of occludin and zonula occludens 1 and increased BAL eosinophils compared to saline challenged mice. Pretreatment of HDM challenged mice with FP or MF significantly reduced FD4 permeability compared to sham treated HDM mice. Treatment with both steroids decreased BAL eosinophilia and promoted the expression of occludin and zonula occludens 1 compared to sham treated HDM challenged mice.

Conclusions: FP and MF are equally effective in preventing/restoring epithelial barrier dysfunction in AR by promoting the expression of occludin and zonula occludens 1.

1591 | Saline could improve the quality of life in the pregnancy rhinitis

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Introduction: The main symptom of pregnancy rhinitis is nasal blockage and disappeared after childbirth.

Objectives: To investigate the function of the saline on the treatment of pregnancy rhinitis.

Results: 34% women were suffered from the pregnancy rhinitis, and VAS of nasal blockage decreased in saline group () compared with the control group ($P < .05$).

Conclusions: Saline could be helpful in the pregnancy rhinitis.

1592 | The clinical characters of the allergic rhinitis in North China for 5 years

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Introduction: The prevalence of allergic rhinitis was increased by more and more research.

Objectives: To investigate the main allergen of allergic rhinitis in north china in continuous five year study.

Results: Dust mite, ragweed and artemisia was most common allergen. The highest allergen combination group was the combination of ragweed and artemisia with obvious seasonal characteristics and xxxx

Conclusions: The Environmental management education of allergic rhinitis was necessary in allergic rhinitis treatment.

1593 | Rhinologic disease is a burden for a patient

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Introduction: The individual and socioeconomic burden of chronic rhinosinusitis (CRS) and allergic rhinitis have recently been

recognized. However, little is known about the health-related quality of life (HRQoL) of other rhinologic patients. The purpose of this study was to measure the general HRQoL in different rhinologic diseases.

Objectives: All adult rhinologic patients requiring specialist care at the Helsinki University Hospital were enrolled in this cross-sectional, questionnaire-based prospective study in February, May, August and November 2014. The patients were mailed a patient-history questionnaire and a validated, generic 15D –HRQoL questionnaire. The ICD-10 diagnosis and the data of possible obstructive sleep apnea (OSA) were collected from the electronic patient records after the outpatient visit. These data were compared to age-and-sex matched Helsinki-Uusimaa region population data on HRQoL which were obtained from a large national Health Examination Survey.

Results: Our study consisted of 337 patients. The mean age was 50.2 years and 50.4% of them were men. The total 15D score of the rhinologic patients (0.867) was significantly ($P < .001$) lower than that of the control population (0.909). Rhinologic patients scored statistically significantly lower in all other 15D domains except in moving. When comparing the five age-adjusted main diagnostic groups (CRS with or without nasal polyps, rhinitis, turbinate hypertrophy, and septal deviation), no significant differences were observed in 15D scores. OSA was found in 10.5% of rhinologic patients and these patients reported clinically and statistically significantly ($P = .002$) lower 15D scores than non-apneic patients (0.816 vs. 0.871), but the total 15D score of the non-apneic rhinologic patients was also lower than that of the control population (0.871 vs. 0.929, $P < .001$). Therefore, the OSA offered only a partial explanation for low HRQoL of rhinologic patients.

Conclusions: Rhinologic disease has a devastating effect on a patient's HRQoL irrespective of diagnosis. Doctors and other health-care decision-makers should make a great effort to diminish this burden.

1595 | Role of allergy in the management of patients subjected to adenoid hypertrophy and otitis media with effusion

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Introduction: Adenoid hypertrophy and otitis media with effusion are common diseases during childhood. Nowadays these diseases are treated by surgery and long term antibiotics. There are increasing evidences based on the role of allergy in pathogenesis of two mentioned problems. Increased relapse rate of symptoms following surgery in allergic patients are also reported. The aim of this research is to determine the prevalence of allergy in children with adenoid

hypertrophy and otitis media with effusion, and to evaluate the effect of intranasal steroid in these patients.

Objectives: A nonrandomized, prospective, cross-sectional study was conducted on 122 patients younger than 18 years old, diagnosed as adenoid hypertrophy or otitis media with effusion. Patients, who were atopic, referred to an allergist and evaluated for allergic sensitization. Sensitized patients undertook one month treatment with intranasal corticosteroid and oral antihistamine.

Results: Among 122 patients under investigation, 116 were reported to have AHT and 30 persons were subjected to OME. 38 (32.7%) of the patients with AHT and 9 (30%) of the patients with OME were clinically allergic. Among a total of 122 patients, 34 (28%) were reported to have clinical signs of allergy and higher levels of total IgE serum from its normal level (proportional to their age) considered atopic. These patients were asked to take skin PRICK test and twenty five of them accepted. Allergic sensitization (evaluated by skin PRICK test) was recorded in 11 of total 25 (44%) patients. The most common allergen sensitization was found to be Russian thistle. The mean AHT and OME Symptoms score decreased significantly after treatment ($P.v=.001, .007$). Response to treatment in patients with allergic sensitization was significantly higher than patients without allergic sensitization ($P.v<.05$).

Conclusions: According to the results of this study, in patients with the AHT and OME who had an elevated IgE and clinical allergic symptoms, implementation of the PRICK test is helpful in taking any decision regarding the medical treatment and prevention of unnecessary surgery.

Table 1: Correlation between positive PRICK test and response to treatment

PRICK test	Response to treatment		Total
	Yes	No	
Negative (-)	9(64%)	5(36%)	14(56%)
Positive(+)	11(44%)	0 (0%)	11(44%)
Total	20(80%)	5 (20%)	25(100%)

1596 | pH alteration of paranasal sinus mucosa

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Introduction: We studied alteration of the chemical aspects of sinus mucosa in rabbit. The purpose of the study is to determine the effects of the artificially induced mechanical obstruction on the physiopathology of the paranasal sinus mucosa, taking into consideration an experimental model on animals, with the alteration of the nasal air-flow.

Objectives: The study was performed on 20 New Zealand white rabbits, distributed into two equal groups. In the case of the first group of 10 experimental animals, we induced the model of

ipsilateral double obstruction, the opposite side being left intact as term of comparison. Thus we produced the mechanical obstruction of the nasopharynx at the level of the choanal orifices, as well as, the obstruction at the level of ostiomeatal complex. In the case of the second experimental group we induced the model of the double contralateral obstruction: the obstruction of the nasopharynx at the level of the choanal orifices and the contralateral obstruction of the ostiomeatal complex. The procedures were performed surgically under surgical microscope. We studied and determined the pH of the mucosa and microscopically anatomopathological changes of the paranasal sinus mucosa.

Results: The results of the study show that ostial occlusion and nasopharyngeal obstruction are responsible for alteration of maxillary sinus status mucosa with decreased statistical significant of pH followed by alteration of mucociliary clearance. The study determines the anatomopathological aspects of normal unobstructed sinus mucosa and the presence of inflammatory infiltrations, which are more accentuated tending to be chronic in the case of obstruction of the maxillary sinus at a level of ostiomeatal complex and nasopharynx (double ipsilateral obstruction).

Conclusions: The experimentally induced obstruction of the nasopharynx, similar to the presence of a mechanical obstacle in the nasopharynx, reduces the airflow in the nasal fossae and leads to morphopathological changes in sinus mucosa causing inflammation. The anatomopathological aspects of sinus mucosa in experimental animals are linked to the changes due to the locally induced sinus obstruction. The pH of maxillary sinus mucosa decreases significant after gas changing into the sinus with increased concentration of carbon dioxide.

1597 | Differential response of primary nasal epithelial cells vs. calu-3 cells to exogenous stimuli

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Introduction: Airway epithelial cells serve as the first site of contact to exogenous stimuli like dust, pollutants or microbes. Previous studies revealed an impaired epithelial barrier function in upper and lower airway diseases. Accordingly, studying the regulation of the airway epithelial barrier integrity by exogenous and/or endogenous factors has become of major interest to better understand the pathology of these diseases.

Objectives: To compare the barrier response of calu-3 and primary nasal epithelial cells to exogenous stimuli.

Primary nasal epithelial cells from controls (n=5) and the epithelial cell line, Calu-3, were grown in air-liquid interface (ALI) on transwell inserts for 21 days. Primary nasal epithelial cell or Calu-3 epithelial cell cultures were stimulated at day 21 with *Staphylococcus aureus* enterotoxin B (SEB) (0.1 µg/mL, 1 µg/mL, 10 µg/mL), House dust mite (HDM) extract (1 µg/mL, 10 µg/mL, 100 µg/mL), chitosan (0.06%) or fluticasone propionate (FP) (10^{-7} M). Epithelial integrity was evaluated by measuring transepithelial electrical resistance (TER), together with paracellular flux measurement of fluorescein isothiocyanate dextran 4 kDa (FD4).

Results: Stimulation of Calu-3 cells with SEB decreased epithelial integrity in a dose dependent manner, accompanied with an increased FD4 permeability. On the contrary, no decline in TER was measured when primary nasal epithelial cells were stimulated with SEB. HDM extract did not affect the integrity or permeability of Calu-3 epithelial cells. However, epithelial integrity in primary nasal epithelial cells was altered after stimulation with HDM extract, leading to an increased FD4 permeability. Chitosan disrupted barrier integrity whereas FP increased epithelial integrity both on Calu-3 and primary nasal epithelial cells.

Conclusions: Care must be taken when studying epithelial barrier integrity using epithelial cell-lines as it does not necessarily reflect the response in primary cells. We therefore propose to use, if available, primary epithelial cells as they contain more relevant information for a better understanding of the barrier function in different allergic diseases.

1598 | Effect of dexamethasone induced autophagy on senescence in nasal epithelial cells of allergic rhinitis

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Introduction: Autophagy is a lysosomal degradation pathway that is essential for cell survival, differentiation, and homeostasis. Autophagy has been implicated in many chronic inflammatory diseases, such as asthma. Whether autophagy plays a role in the inflammatory or allergic disease of the upper airways is completely unknown and deserves investigation.

Objectives: To investigate the effect of dexamethasone (DEX) on autophagy and senescence in nasal epithelial cell, and explore the mechanism of DEX in the treatment of allergic rhinitis. Nasal epithelial cells were derived from nasal inferior turbinate mucosa and were cultured from AR patients (AR group: 16) and normal nasal mucosa (control group: 10). MDC staining and Western blot were used to detect the level of autophagy before and after stimulation with DEX

in the two groups. The mTOR pathway related molecules were investigated by western blot.

Results: The level of autophagy in nasal epithelial cells was higher in the DEX-treated group than in the DEX-untreated group but lower than in control group ($P < .05$). A dose-dependent increase in the number of autophagic vacuoles was observed in the DEX-treated nasal epithelial cells, which was demonstrated by MDC staining. The expression of LC3 was significantly increased in DEX-treated group.

Conclusions: Autophagy is deficient in allergic rhinitis and DEX is positively regulated by autophagy in allergic rhinitis tissues. Attenuation of inflammation by restoring autophagy might be a therapeutic strategy for treating allergic rhinitis.

1599 | Administration of liposomal eye spray vs antihistamine eye drops in patients with allergen-induced conjunctivitis—A comparison between different mechanisms of action

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Introduction: Guidelines recommend the application of local antihistamines (AH) for symptomatic treatment of allergic conjunctivitis, but health-conscious patients may prefer alternative, non-pharmacological therapy for symptom relief. With liposomal eye spray (LS, Optima Pharmazeutische GmbH, Germany), a physical operating principle is available. The spray formulation contains phospholipid double-layer vesicles, which are used for substitution of phospholipids in the tear film. The spray is applied to the closed eyelids, and the liposomes migrate via the lid margins into the tear film and thereby protect the conjunctival mucosa.

Objectives: A prospective controlled non-interventional study in patients with a history of allergic rhinoconjunctivitis was conducted to compare the onset of action and symptom reduction of these two different treatment principles. Conjunctival provocation testing (CPT) was used as a model, simulating the allergen load during the allergen season, followed by the application of either AH eye drops or LS spray for relief of eye irritations. The onset of action of both treatment principles was compared by the patients' assessment of the irritation of the eye at 5 time points after applying either drops or spray. The effectiveness and tolerability of the treatment was rated by the patients by means of a visual analog scale (VAS) with VAS score ranging from *not at all comfortable* (0) to *well comfortable* (100). Effectiveness was additionally measured by objective digital analysis of the redness of the eye.

Results: Data was collected from 40 patients aged 20-62 years (65% female and 35% male) who underwent CPT in routine medical care. 20 patients decided to administer levocabastine as AH eye drops, and 20 patients preferred to use the LS spray. In 80% of the patients of both groups the onset of action was perceived within 0-2 minutes defined by the feeling of first relief after treatment. The mean value of effectiveness in VAS shows an overall increase in both groups, from 27.4% to 71.9% for LS spray and from 28.3% to 78.93% for AH eye drops. No significant differences in any parameters studied were found between the two treatment groups.

Conclusions: LS spray represents a viable non-pharmacological treatment option to AH eye drops for patients suffering from allergic conjunctivitis with a similar onset of action and effectiveness.

1600 | Acute sinusitis combined with orbital cellulitis and subdural empyema

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Case report: The orbital and intracranial complications of sinusitis have decreased, but remain potentially severe, even life threatening in subdural or intracerebral abscess. A high index of suspicion and prompt treatment are needed. We report a case of previously healthy 37-year-old male who presented with sinusitis combined with orbital cellulitis and subdural empyema. He was referred to the department of otorhinolaryngology for headache and right periorbital painful swelling for three days. He had fever and nasal symptoms of mucopurulent rhinorrhea and nasal obstruction. Orbital symptoms of periorbital erythema, swelling, and proptosis were accompanied. Nasal physical examination showed mucosal swelling and erythema with mucoid crust. Computed tomography with contrast demonstrated opacification of right ethmoid, maxillary, sphenoid and frontal sinuses with dehiscence in lamina papyracea. In addition, preseptal soft tissue infiltration and enhancement at periorbital area and enlargement of superior ophthalmic vein were noted, consistent with orbital cellulitis. Magnetic resonance imaging (MRI) of brain, orbit, and sinuses with contrast indicated diffuse meningeal enhancement along right frontotemporal lobe and heterogeneous enhancement of right periorbital area. He was admitted and broad spectrum antibiotics including ceftazidime, vancomycin, and ampicillin/sulbactam were initiated. On the fourth hospitalized day, endoscopic sinus surgery (ESS) was performed. Sinus mucosa was thickened and mucopurulent discharge was come out. Necrotic tissues were removed and sent to the department of pathology for biopsy. There was no fungal ball or polyp. Sinus irrigation was done with normal saline mixed with antibiotics (clindamycin). After ESS, nasal and orbital symptoms improved, but he still complained of a headache. Sinus bacterial culture showed no grown organism, and tissue pathology revealed non-

specific inflammation with necroinflammatory exudates. Repeated MRI revealed fluid collection at right frontotemporal lobe, which showed low T1 & high T2 signal intensity with adjacent enhancing dura, indicating subdural empyema. Craniotomy and abscess drainage were done by the department of neurosurgery. The patient was treated with intravenous antibiotic agents for 6 weeks after surgery. He recovered uneventfully, with no neurologic sequelae or residual abscess on follow-up MRI taken 2 month after operation.

1601 | Chronic rhinosinusitis associated with alpha 1 antitrypsin deficiency

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Case report: A 58 year old woman, past-smoker, was recently referred to our medical joint rhinology/ENT clinic for the management of difficult chronic rhinosinusitis with nasal polyposis. She also had recurrent ear infections with hearing loss and had bilateral hearing aids as well as a history of rhinosinusitis with nasal polyposis since adolescence. She underwent two FESS with benefit. She also had recurrent chest infections since late twenties for which she was on prophylactic azithromycin but recently required repeat hospitalisations and IV antibiotics, as well as fungal toe infections, recurrent cellulitis and alopecia totalis since adolescence.

In clinic, her PEFr was 170 L/min, FEV1 1.95 L (80% predicted) and FVC 2.7 L (94% of predicted) with no reversibility. On nasal examination, she had no mucopus or nasal polyps and she had open post-surgical cavities. There was finger clubbing and diffuse rhonchi on auscultation; a recent HRCT thorax showed widespread bronchiectasis. Exhaled NO was high for lower airways (108 ppb, NR 0-20 ppb), and low for upper airways (left nostril 199 ppb and right 245 ppb, NR 550-850 ppb) with no improvement after decongestant. She had no evidence of allergic sensitisations to environmental antigens, normal total IgE and mildly raised eosinophil count.

A possible diagnosis of primary immunodeficiency was considered in view of bronchiectasis, history of recurrent infections and autoimmune alopecia.

An immune workup was carried out. She had normal serum immunoglobulins and IgG subclasses, good baseline specific IgG levels to Tetanus, Haemophilus and Pneumococcus and normal lymphocyte subset counts. Autoimmune screen (ANA, ENA, anti-thyroid peroxidase Ab) was negative. Serum electrophoresis showed reduced alpha 1 zone, hence serum alpha 1 antitrypsin protein (A1AT) was measured and found to be undetectable, with a PiZ phenotype.

Alpha 1 antitrypsin is serpin encoded by SERPIN1A gene. It inhibits neutrophil elastase. Deficiency results in lung disease with recurrent infections, liver cirrhosis and panniculitis. Whilst rhinosinusitis is not typically thought of in association with A1AT deficiency [1], links

between defects in the gene and chronic polypoid sinusitis have been described [2]. Equally links between SERPIN1A mutations and severe chronic rhinosinusitis unresponsive to medical therapy have also been reported [3], which may underlie the ineffectiveness of medical treatment in this case.

This case highlights the need to consider A1AT deficiency as a differential diagnosis in cases of chronic rhinosinusitis refractory to medical therapy and especially if associated with lung disease.

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1603 | Atopy associated keratoconus: A case report

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Case report: Keratoconus is a condition in which the cornea assumes a conical shape as a result of non-inflammatory thinning of the corneal stroma. The cause of this condition is still unknown, but genetics, systemic diseases, atopy, eye rubbing, and contact lens wear all play role in keratoconus.

Case: A 20-year old woman with gradually visual loss of her left eye since 2 years ago is diagnosed as keratoconus by her

ophthalmologist. Since childhood, she complained about itchy and reddish of her eyes. Because of that, she vigorously rubbed her eyes. It happened intermittently and resolved without medication. No history of asthma, drug or food allergy, hair loss, oral ulcer, rash, photosensitivity, or tender joints. No abnormality found in physical examination except her eyes. There was high level of serum IgE (2277 ng/mL) and mild eosinophilia (827/ μ L). Her ANA IF test was positive (1:320) but negative on further examination. Skin prick test revealed positive sensitization with house dust mites (*Der. farinae*, *Der. pteronyssinus*, and *Blomia tropicalis*).

Discussion: Keratoconus is a progressive non-inflammatory corneal ectasia characterized by central corneal thinning, corneal scarring and protrusion. This conditions, becomes apparent in the second decade, can cause high myopia and irregular astigmatism affecting visual quality. Keratoconus is a multi-factorial disease and frequently associated with eye rubbing. This habit is related with atopy. Atopy is marked with increased IgE levels with the highest levels generally being seen in patients with atopic dermatitis, atopic asthma, allergic rhinitis and allergic conjunctivitis. Skin prick test provides evidence for sensitization and confirm the diagnosis of allergy. Atopy in this case is marked by increased IgE levels, and positive sensitization with house dust mites. The itch of atopy caused the patient to rub her eyes that can contribute to keratoconus. The management of allergy is important to reduce the frequency of eye rubbing and to slow down the progression of keratoconus.

Conclusion: Keratoconus is a multi-factorial disease that can cause visual impairment. Atopy may contribute to keratoconus via eye rubbing associated with the itch of atopy. The management of allergy is important in the treatment of keratoconus.

MONDAY, 19 JUNE 2017

LB TPS 06

FOOD ALLERGY: MECHANISMS, DIAGNOSIS AND MANAGEMENT

1604 | Dermatitis caused by ingestion of Chia seedsEntrala A¹; Tomas M¹; Bartolomé B²; Caballero M³; Quirce S¹¹Allergy Department, Hospital La Paz, Madrid, Spain; ²Roxall España, Bilbao, Spain; ³Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain

Introduction: *Salvia hispanica*, *Lamiaceae*, known as Chia and native to central and southern Mexico and Guatemala, is a plant whose seeds are a source of fiber, proteins and omega-3 fatty acids. It has been described a previous case of allergy to Chia in a patient who suffer an anaphylactic reaction.

Objectives: We reported a case of a 46-year-old male with a personal history of chronic rhinitis with sensitization to mites and pollens, consultation because for several months, coinciding with the introduction of Chia seeds in his diet, presents eczematous lesions, and itchy, in his hands, which disappeared spontaneously, after he stopped the intake of the seeds.

Results: The allergy study was performed by skin-prick tests, with positive results to cat dander, *Dermatophagoides pteronyssinus*, and pollens from *Platanus hispanica*, grass and *Cynodon dactylon*, being negative with the rest of common inhalants. Prick-to-prick test with Chia seed extract was positive (3×4 mm).

Total serum IgE was 521 kU/L and specific IgE (ImmunoCAP; kU_A/L) was positive to extracts from pollens of *Platanus hispanica* 39.3; oak 3.12; olive 4.01; cat dander 0.73; hazelnut 2.98; walnut 1.57; peanut 2.58; white bean 2.47; green bean 3.97; lentil 1; soybean 1.43; wheat 2.09; rye 11.1; maize 2.61; oregano 0.75; sesame 2.67; latex 1.25; rPru p 3: 5.44.

To study the allergens involved in the patient's allergy, crushed Chia seeds were defatted and extracted. The extract was subjected to different treatments: heated at 100°C for 15 minutes, reduced with 2-mercaptoethanol or digested with pepsin at 37°C for 30 minutes, and analyzed by SDS-PAGE and IgE-immunoblotting with the patient's serum. In absence of treatments, the patient's serum detected two allergens of molecular weights around 60 and 30 kDa, whereas after the reduction treatment two more allergens around 15 and 10 kDa were intensely detected. Heating and pepsin treatments of the extract did not affect the IgE reactivity of these two allergens, suggesting that a LTP could be involved in the patient's sensitization to Chia seeds.

Conclusions: We described a case of IgE-mediated reaction induced by Chia seeds with an atypical clinic (eczema/ dermatitis).

1605 | Wheat allergy: Beyond the diagnostic suspicion

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Introduction: Wheat is one of the most common foods in the Mediterranean diet. 27 wheat food allergens have been described, but the current commercial diagnostic tools only allow to determine two of them: Tri a 14 (Lipid transfer protein (LTP)) and Tri a 19 (ω -5-gliadin), which have been described as the main wheat allergens, closely related to cofactors.

Objectives: The aim of the study was to describe the clinical and molecular pattern of wheat allergy in our area.

Methods: Patients were selected when having a history of allergy after wheat intake and a demonstrated sensitization to wheat (by positive Skin prick test to wheat or gluten extract and/or sIgE to wheat >0.35 kU/L). Clinical manifestations, time until diagnosis, initial diagnosis and cofactors involvement were recorded, as results of skin prick test, and levels of total IgE, Tri a 14 sIgE, and Tri a 19 sIgE.

Results: 30 patients were selected, 16 men. Mean age: 43 [35.0-57.0] y.o. The first clinical manifestation was urticaria in 21/30 (70%) of patients. 19/30 (63%) had had at least one episode anaphylaxis, and gastrointestinal disorders (GID) were present in 6/30 (20%). 2 patients had asthma due to wheat flour handling and inhalation; one of them as an exclusive clinical manifestation. Cofactors were involved in 75% of patients (Non-steroid Anti-inflammatory drugs (NSAID): 25/30 (83.3%), exercise: 17/30: (56.7%) and alcohol 5/30 (17%). Only 7% had had the right initial diagnosis. The median time from the clinical onset until diagnosis was 3 years [2.7-4.3]. Wheat was the only culprit food in 28/30 (93%) of patients. The molecular sensitization pattern was: Tri a 19: 22/30 (73%), Tri a 14 (LTP) 6/30 (20%), no Tri a 14 nor Tri a 19: 2/30 (7%).

Conclusions:

- Wheat allergy is predominantly expressed as recurrent acute urticaria in our area. Urticaria is also the most frequent clinical onset.
- The involvement of cofactors is very frequent in wheat allergic reactions, although it is not mandatory.
- The vast majority of wheat allergic patients are sensitized to ω -5-gliadin and wheat LTP, being ω -5-gliadin the main allergen involved.
- In the differential diagnosis of spontaneous urticaria as well as chronic diarrhea, wheat allergy, mainly ω -5-

gliadin sensitization, should be evaluated, especially when a potential cofactor is identified.

1606 | Contribution of conformational and linear IgE epitopes to Ara h 2-specific IgE-binding

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Introduction: Ara h 2 is the most important peanut allergen. Hypoallergenic Ara h 2 derivatives with reduced IgE-binding capacities are promising candidates for specific immunotherapy of peanut allergy. However, little is known about the role of conformational vs linear IgE epitopes of this molecule. Therefore, we aimed to define the patient-specific epitope profiles of Ara h 2-specific IgE.

Objectives: An *in silico* designed Ara h 2 mutant, mtAra h 2, lacking surface-exposed loops that contain most linear IgE epitopes, and the wild-type protein (wt) were expressed in the baculovirus insect cell system. After protein purification from the cell culture supernatants purity of the proteins was verified by SDS-PAGE. Purified allergens were reduced with dithiothreitol and alkylated with iodoacetamide. Physicochemical characteristics of the proteins were determined by mass spectrometry, N-terminal sequencing and CD spectroscopy. IgE-binding was tested by direct and inhibition ELISA using sera of thirteen peanut allergic patients.

Results: mtAra h 2, wtAra h 2 and nAra h 2 displayed correct sizes, N-termini and the characteristic alpha-helical structure. Complete reduction and alkylation and the ensuing destruction of the secondary structure were verified by mass spectrometry and CD spectroscopy. In direct ELISAs, allergic patients' sera revealed up to 70% ($P < .05$) reduced IgE-binding to the mutant compared to nAra h 2 and a 40% lower IgE-binding compared to wtAra h 2 ($P > .05$). Reduced wtAra h 2 revealed patient-specific decreases in IgE-binding compared to native wtAra h 2 ($P < .01$) and nAra h 2 ($P < .001$). Relative amounts of IgE-binding to reduced wtAra h 2 (mostly linear IgE-binding epitopes) and the native mtAra h 2 (mostly conformational IgE-binding epitopes) showed a high extent of patient-dependent variability. The reduced and alkylated mutant showed almost no IgE-binding at all. Moreover, preincubation of the sera with the different reduced and non-reduced proteins confirmed the results of the direct ELISAs.

Conclusions: The obtained results indicate that both conformational and linear IgE-binding epitopes are important for Ara h 2 specific IgE-binding. Relative contributions of linear and conformational epitopes to Ara h 2 IgE-binding are patient-specific.

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1607 | Molecular diagnosis of peanut allergy

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Introduction: According to the National Institute of Allergy and Infectious Diseases in the United States allergy to peanuts it applies to 0.6% of the population and is the leading cause of anaphylactic reactions with fatal outcome. So far, everyday diagnostics of peanut allergy were skin prick tests and determination of the level of allergen-specific IgE. New possibilities of food allergy diagnostics provide molecular diagnostics, in particular ImmunoCAP ISAC. ImmunoCAP ISAC is an excellent method of diagnosis of peanut allergy it detects up to 6 different antibodies against components: Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8, Ara h 9.

Objectives: The study was conducted at the Department of Allergology, Clinical Immunology and Internal Medicine in Bydgoszcz. The study was retrospective. 136 adult, living in Poland were classified to study. The ImmunoCAP ISAC test was performed to all patients.

Results: Antibodies against components of peanut (*Arachis hypogaea*) were detected in 28 patients (20%). 25 patients (18%) showed specific IgE against Ara h 8 (range 0.5-85 ISU-E), 6 (4%) v Ara h 9 (0.6-21) and 1 (0.7%) v Ara h 1 (1.6) and Ara h 3 (0.6). None of the respondents were not detected antibodies against components Ara h 2 and Ara h 6.

Conclusions: ImmunoCAP ISAC test is a modern commercial test which is the right tool for the diagnosis of allergy to peanut. It allows you to pinpoint not only the source of allergies, but also to assess the risk of severe anaphylactic reactions and to explain the presence of cross-reactions.

1608 | Immunotherapy in food allergy: Can it change the course of the disease?

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Introduction: The first therapeutic choice for food allergy is avoidance of the responsible food, but when this approach is not possible a specific oral desensitization could be considered a good alternative.

Objectives: the purpose of the study was to evaluate if the acquired tolerance after oral immunotherapy in food allergy was transient or persistent.

Results: 13 patients affected by IgE-mediated food allergy: to cow milk (3 patients), to hen egg (3 patients), to cod fish (2 patients) to peanuts (1 patient) and to corn (1 patient) confirmed by a complete allergological workup and a double-blind placebo-controlled food challenge (DBPCFC), were treated with sublingual-oral desensitization. After the interruption of maintenance phase, the laboratory tests were performed and 12 of 13 patients underwent DBPCFC.

Oral specific desensitization was completed successfully in all the 13 reported patients. At different times after the end of treatment, they decided, on their own initiative, to stop the ingestion of incriminated food. A new food allergen re-exposure caused adverse reactions in 12 of 13 patients. The detection of specific IgE and IgG4, during the period of allergen avoidance, showed an increase or a stable level of specific IgE and a decrease of specific IgG4 in 8 patients.

Conclusions: According to our experience, the tolerance obtained through the desensitizing treatment is transient and so the regular allergen intake is necessary for its maintenance.

1609 | Basophil-derived interleukin-4 promotes epicutaneous antigen sensitization concomitant with the development of food allergy

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Introduction: Exaggerated TSLP production and infiltration of basophils are associated with the pathogenesis of atopic dermatitis (AD), a recognized risk factor for the development of food allergies. While TSLP and basophils have been implicated to promote food-

induced allergic disorders in response to epicutaneous sensitization, the mechanisms by which TSLP-elicited basophils guide the progression of allergic inflammation in the skin to distant mucosal sites such as the gastrointestinal tract are poorly understood.

Objectives: We sought to test the role of basophil-intrinsic IL-4 production in T_H2 sensitization to food antigens in the skin and effector food allergic responses in the gut.

Results: Epicutaneous food antigen sensitization is associated with the infiltration of IL-4 competent innate immune cells to the skin with basophils and eosinophils representing the predominant populations. In contrast to basophils, absence of eosinophils did not alter disease outcome. Co-culture of IL-4 competent basophils together with dendritic cells and naïve T cells was sufficient to promote T_H2 polarization in an IL-4 dependent manner *in vitro*, while absence of basophil-intrinsic IL-4 production *in vivo* was associated with reduced food allergic responses.

Conclusions: TSLP-elicited basophils promote epicutaneous sensitization to food antigens and subsequent IgE-mediated food allergy via IL-4. Strategies to target the TSLP-basophil-IL4 axis in patients with AD may lead to innovative therapies that can prevent the progression of allergies to distant mucosal sites.

1610 | Biomarkers associated to patients with a severe allergic phenotype using metabolomics

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Introduction: Food allergy has dramatically increased in prevalence in the last decades. This has created a burden for health and economical systems. Spain is a country characterized by high level of grass pollen exposure, in particular in the western part, which is associated with an increase in profilin allergy. In these areas of high exposure, profilin sensitized patients can develop severe profilin mediated food reactions. Knowing the underlying causes for this and looking for inflammatory biomarkers associated with these severe reactions offer new diagnosis strategies for severe respiratory phenotypes. New omics approaches are potent tools to understand and classify allergic phenotypes. Metabolomics is the process of describing the phenotype of an organism through the full measurement of metabolites present in the biological samples. Metabolites are able to describe the metabolic mechanism underlying in the most severe allergic phenotypes. These metabolites represent the convergence of gene expression and environmental exposure, and can provide an informative measure of multifactorial diseases.

Objectives: We propose to perform the metabolic profiling of severe profilin mediated food allergic patients looking for biomarkers that might predict the prognosis of the disease and to understand the molecular mechanisms of inflammation underneath. As comparative groups mild profilin reactors and non-allergic subjects are included in the study.

Results: Plasma samples from non-allergic, mild and severe allergic patients were measured using gas chromatography coupled to mass spectrometry (GC-MS). Samples were from 4 different hospitals in Spain covering the areas with the highest pollen exposure. A metabolic profile was composed by 106 metabolites for each sample after the chemical derivatization process including mainly small molecules such as amino acids, organic acids and single sugars. These metabolites were identified using Fiehn and NIST libraries with high match to each compound. Data was analysed using multivariate and univariate statistical tools. Results from the statistical analysis showed differences between the groups. Metabolites from energy metabolism and amino acids were found significantly correlated to the severity of the disease.

Conclusions: This present work demonstrates the capability of metabolomics for exploring new biomarker strategies. Further evaluation of detected metabolites might result in new ways to stratify and predict food allergic severe reactions.

1611 | Alpha-gal epitope on protein surface affects uptake and degradation in immature monocyte-derived dendritic cells

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Introduction: Internalization and degradation of antigens by dendritic cells (DCs) are important steps in determining whether an antigen will trigger the immune system and subsequently elicit an allergic reaction. Red meat allergy is characterized by an IgE response against the carbohydrate galactose- α -1,3-galactose (α -Gal), which is abundantly expressed on glycoproteins from non-primate mammals, followed by severe allergic reactions several hours after red meat consumption. The aim of this study is to reveal whether the presence of α -Gal epitopes on the protein surface can influence antigen uptake and processing in immature monocyte-derived DCs (iMDDCs).

Objectives: Bovine serum albumin (BSA) and BSA conjugated α -Gal (BSA- α -Gal) were labeled with Alexa Fluor (AF) 488. Peripheral

blood mononuclear cells were prepared from healthy blood donors and red meat allergic patients. iMDDCs were generated by 6 days of culturing of monocytes in the presence of human IL-4 and GM-CSF. For uptake analysis, fluorescently labeled proteins were added to iMDDC cultures in the concentration of 10 μ g/mL and 10⁶ cells were collected at various time points (1, 2, and 4 hours). The overall protein uptake in iMDDCs was monitored using flow cytometry, while analysis of sub-cellular features in relation to the uptake of proteins in a single cell was investigated using confocal microscopy.

Results: A constant increase of protein uptake over time was noted in iMDDCs from healthy blood donors. For all time points examined, the percentage of AF488 positive cells was 6 to 8 times higher among cells treated with BSA- α -Gal in comparison with cells treated with BSA. Protein uptake after 4 hours was also monitored in iMDDCs from red meat allergic patients. Here the percentage of uptake in cells treated with BSA- α -Gal was approximately 5 times higher in comparison to cells treated with BSA. After 4 hours of uptake, confocal laser scanning microscopy revealed intense green fluorescently labeled BSA- α -Gal scattered around the cytoplasm in many iMDDCs. In contrast, just one or two iMDDCs showed very weak green fluorescently labeled BSA scattered around the cytoplasm.

Conclusions: We show that α -Gal containing proteins have an increased uptake and a slower degradation compared to proteins lacking the α -Gal epitope. This difference in the uptake and degradation time of α -Gal containing proteins may contribute to the delayed symptoms that patients allergic to red meat experience after consuming red meat.

1613 | Evaluation of the primary sensitizer in galacto-oligosaccharide (GOS) allergy

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Introduction: Allergy to the prebiotic, galacto-oligosaccharides (GOS) results in anaphylaxis and appears to be confined to the Asian region. Being a pure carbohydrate, GOS is not likely to initiate adaptive immune responses and induce IgE.

Objectives: This study aimed to investigate for the primary sensitizer of GOS allergy by screening for IgE cross reactivity with common local allergens in the Singapore environment.

Results: ELISA for GOS specific IgE (developed in-house) and ELISA inhibition assay were performed to determine IgE cross-reactivity

between GOS and extracts of dust mites (*Blomia tropicalis* (Blo t), *Dermatophagoides pteronyssinus* (Der p)), mold (*Curvularia spp*), pollen (*Elaeis guineensis* (*E. guineensis*)), mosquito (*Aedes aegypti*) salivary glands and bromelain using sera from three GOS allergic subjects. All three GOS allergy subjects had specific IgE to dust mites (Blo t: 26–103 ELISA units; Der p: 7–15 ELISA units) but not the oil palm *E. guineensis* and fungi *Curvularia spp* extracts. Blo t extract showed high cross reactivity with GOS and to inhibit almost 100% detection of GOS specific IgE in all three sera. In contrast, Der p extract was able to inhibit GOS-specific IgE in 2 out of the 3 sera and the concentration of Der p extract required to achieve 50% inhibition was at least 10 times higher than the Blo t extract. One subject had specific IgE to *Aedes aegypti* (12 ELISA units), however mosquito extract inhibited only 10% detection of GOS specific IgE. Bromelain did not inhibit the detection of GOS specific IgE.

Conclusions: Our results suggest that house dust mite, *B. tropicalis*, may be one of the primary sensitizers for GOS allergy in Singapore and may explain the geographical limits of GOS allergy.

1614 | Anaphylaxis by a hidden allergen—A diagnostic challenge

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Introduction: During the last few years, it has been shown an average increase of food-induced anaphylaxis. Sometimes the culprit allergen is not clear.

Objectives: To describe a case of a 58-year-old woman who was referred to the Allergy Unit because of two separate episodes of anaphylaxis associated with the ingestion of a cookie.

Results: She immediately proceeded to develop periorbital edema, generalized pruritus and hives, swollen tongue and airway obstruction. She was treated with IM epinephrine, intravenous methylprednisolone and antihistamines at the Emergency department. Her vital signs were within normal range. There were no history of atopy, concurrent infections or triggering factors. Until allergologic study, she did not develop an elimination diet; she only avoided eating that nougat cookie named “Turrón Oblea Arcor®”. It contains glucose syrup, enriched wheat flour (iron, folic acid, thiamine, riboflavin, and niacin), sugar, roasted peanuts (10%), sunflower oil, hydrolyzed vegetable protein, salt, soy lecithin, bovine gelatin, sodium, citric acid and artificial flavor.

Skin prick testing to wheat flour, barley, rye, alpha amylase, sunflower seeds, cocoa, peanut, almond, pistachio, soybean, veal, profilin and LTP were negative. Total IgE 114, Wheat 0.41, rTri14: 0, rTri-a19: 0.01, egg white, yolk, OVA, OVM, peanut, soy, walnut,

sunflower seeds, gelatin, veal: 0 (KU/L). Prick-prick with additives: E322, E500ii, E330 as well as OFC were negative. Prick-prick with the culprit biscuit obtained a 3 mm papule, histamine 4 mm. Serum level for tryptase at baseline was at normal range: 4.67 mcg/L. Celiac screening was negative. SDS-PAGE immunoblotting under reducing conditions with extracts of biscuit, wheat and peanut was performed. Serum sample of the patient recognized several bands greater than 37 kDa and a band in wheat flour extract which molecular weight was between 50–75 kDa (probably a gliadin).

Conclusions: Wheat allergy could have several clinical manifestations. Cofactors are not always involved. In our case, it suggests that the culprit allergen could be a gliadin protein, Clearly not ω 5-gliadin, however it has been described only a few, so it could be an undescribed one, or controversially, one described for which we do not have detection methods still available.

1615 | Peanut allergens Ara H 1 and Ara H 2 and peanut lipids impact on the barrier function of human airway epithelial cells

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Introduction: The airway epithelium forms a barrier to protect the body from inhaled harmful substances. It has been reported that allergic reactions to peanut often occur after inhalation of airborne peanut allergens. Individuals with food allergies often suffer from allergic asthma. Hence, we aimed to find out whether and how the major peanut allergens Ara h 1 and Ara h 2 affect the airway epithelial barrier. Moreover, as peanuts contain about 50% lipids these might play a key role in the sensitization process together with the allergens. Therefore, we studied their potential effect on the human airway barrier.

Objectives: The human bronchial epithelial cell line 16HBE14o⁻ was cultured in a 2-chamber transwell system and treated with natural peanut allergens and/or lipids when cells reached confluence (transepithelial resistance TER >700 Ω cm²). Epithelial barrier integrity was evaluated by measuring the transepithelial passage of fluorescein isothiocyanate-dextran 4 kDa (FD4), 10 kDa (FD10), and 70 kDa (FD70) through the 16HBE14o⁻ monolayer, co-administered with allergens and/or lipids. Polarized 16HBE14o⁻ cells were exposed to fluorescently-labelled peanut allergens for 1 hour and analysed by confocal microscopy.

Results: We observed that both peanut allergens impacted on barrier function: Ara h 2 reduced TER by 45% in 16HBE14o⁻ cells after 6 hours ($P < .05$) compared to untreated control, and Ara h 1 reduced TER by 33% after 16 hours. However, cells exposure to Ara h 1 or Ara h 2 in the presence of peanut lipids resulted in an increased resistance after 16 hours (by 51% and 71%, respectively) compared to allergens alone ($P < .05$). We also measured a reduced FD4, FD10, and FD70 paracellular permeability when cells were treated with Ara h 1 or Ara h 2 in presence of peanut lipids, or with lipids alone, compared to untreated cells. Both allergens were detected within the 16HBE14o⁻ cell monolayer after 1 hour of exposure. Ara h 2 was also localized in proximity of the tight junction protein ZO-1.

Conclusions: Our data show that Ara h 1 and Ara h 2 impaired barrier function by decreasing TER in the 16HBE14o⁻ cells, and that the presence of peanut lipids provoked a resistance increase after 16 hours, which led to lower permeability. These effects might contribute to determine the amount of allergens passing through the 16HBE14o⁻ cell monolayer and, therefore, be crucial for the polarization of the immune response.

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1616 | Pru p 7 is a major allergen and a severity marker in peach allergic patients from Southern France

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Introduction: Molecular-based allergy diagnostics using currently available reagents falls short of identifying the culprit allergen in some peach allergic patients from Southern France.

Objectives: To describe the prevalence and clinical implications of Pru p 7 sIgE sensitization in patients from Southern France with confirmed peach allergy.

Methods: 109 patients attending allergology departments for suspected peach allergy were included. Diagnostic workup comprised anamnesis, skin prick tests with commercial extract and fresh peach, specific IgE (rPru p 1, rPru p 3, rPru p 4, rPru p 7, MUXF3: ImmunoCAP, Thermo Fisher); peach oral challenge when necessary. Symptom severity was graded according to Muraro (Muraro *et al*, Allergy, 2007). Basophil activation test (Beckman Coulter, session TPS 24) with recombinant Pru p 7 was performed on 5 patients and sera of 6 patients were IgE tested with FABER[®] nanotest (CAAM, session TPS 42)

Results: Peach allergy was diagnosed in 74 (68%) patients. sIgE to Pru p 7 were detected (>0.1 kUA/L) in 58 (78%) peach-allergic patients and in 11 (31%) peach-tolerant patients (Table 1). Pru p 7 sensitization was significantly associated with increased clinical severity (Muraro 3), facial edema and cofactor implication (Table 2). Basophil activation test showed CD203c and CD 63 activation for Pru p 7 doses as low as 2.5 pg/mL. FABER nanotest confirmed Pru p 7 sensitization.

Conclusions: Pru p 7 has been reported as a major allergen in peach allergic patients from Spain and Italy, and seems to correlate with specific clinical presentations in Japanese patients. We have reported Pru p 7 as a major allergen in peach-sensitized patients from Southern France, mainly those with low sIgE to peach extract and devoid of sIgE reactivity to currently available peach component tests (Klingebl *et al*, Clin Transl Allergy, in press). We report here that Pru p 7 is associated with distinct, more severe and cofactor-related clinical presentations. A widely available test for Pru p 7 sensitization is needed for comprehensive component-resolved diagnostics and prognostic evaluation of peach allergy in Mediterranean patients.

Prevalence	Pru p 1	Pru p 3	Pru p 4	Pru p 7
Peach allergic 74 patients	15 (20%)	21 (29%)	12 (16%)	58 (78%)
Peach tolerant 35 patients	7 (20%)	14 (40%)	12 (34%)	11 (31%)

Clinical features and cofactors (number of patients)	Pru p 1	Pru p 3	Pru p 4	Pru p 7
MURARO I	2	4	3	7
MURARO II	2	3	0	5
MURARO III	1 (co-sensitized with Pru p 7)	3	0	35
Facial edema	2+3 co-sensitized with Pru p 7	5	3	30
Cofactors	1+2 co-sensitized with Pru p 7	1	0	21

1617 | Allergen declaration in non-prepacked food: The current European state and the unmet needs

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Introduction: The EU Food Information for Consumer Regulation (EU FIC) No. 1169/2011 made allergen information provision in non-prepacked foods mandatory in an attempt to increase the quality of life and to protect the health of food allergic and intolerant consumers. However, it left Member States (MS) free to provide on a voluntary basis further rules and guidelines for the means in which the allergen information is made available. This results in a non-harmonized approach in allergen labelling in the non-prepacked food industry despite a common EU legal basis.

Objectives: The main purpose of this study is to explore the innovations and limitations of the national measures and the challenges faced by the involved stakeholders when implementing the rules in practice. Secondary objective is to understand to which extent national measures are meeting the food allergic and intolerant consumer's needs. Remote, semi-structured interviews with key stakeholders across Europe were conducted and the transcribed data was used for thematic analyses.

Results: Fifteen interviews with patient's associations, governmental bodies and private organizations from ten MS were completed. The most positive impact of the EU FIC is the increase of awareness among food business operators (FBOs) on the topic of food allergy. However, this is not enough to protect the health of the targeted population as, in many cases, national measures lead to different interpretations and thus to different practices on allergen information provision which are, in many cases, suboptimal. Major gaps in the national legislations are the non-regulation of mandatory allergen trainings, the lack or absence of guidelines, the non-regulation of cross contamination, the absence of enforcement rules and the lack or absence of controlling activities. Best practices were identified mainly among those FBOs which are "big brands", members of FBOs associations and those which have contracts with patient's associations. In general, the preferred way of the food allergic and intolerant consumer for receiving allergen information was not in agreement with how the information is being provided in practice.

Conclusions: A joint of the regulatory bodies, patients and FBOs associations is urgently needed in each MS to create a stricter and widespread guideline; however, each category of FBOs should adapt particular specifications adjusted to their realities. Technological tools may become essential means to manage allergen information.

1618 | How useful is serum tryptase measurement during food allergic reactions: A prospective study of 52 peanut allergic adults

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Introduction: Serum tryptase is a mast cell activation marker and levels rise acutely during allergic reactions. There are limited data on acute tryptase levels in food allergic reactions. It is reported that tryptase is less likely to rise in food-induced anaphylaxis or in normotensive patients. The aim was to evaluate the usefulness of serum tryptase as marker in food allergic reactions.

Objectives: Serum tryptase levels were measured in 52 adults who underwent peanut challenges as part of the Thresholds Reactivity and Clinical Evaluation Study: 160 active and 63 placebo challenges. Tryptase levels were measured immediately at the onset of objective symptoms during peanut challenge and at 1 hour and 2 hours. Acute levels were compared to a baseline value obtained on the same day prior to peanut exposure.

Results: Tryptase levels >11.4 ng/mL (upper normal value) were only observed in 4/160 active challenges. All 4 cases were severe (anaphylaxis) and only 1/4 was hypotensive, the predominant symptom in the remaining 3/4 was severe dyspnoea. A rise relative to the baseline value was observed in 100/160 (63%) active challenges. The average rise (peak tryptase above baseline) was 35% across all reactions and 148% in the anaphylaxis group. Peak tryptase was correlated with severity with a correlation coefficient of 0.31 ($P=0.0005$). The anaphylaxis group showed a steeper rise in tryptase compared to the non-anaphylaxis group with peak levels occurring later at 2 hours.

Conclusions: Serum tryptase is correlated with severity in food allergic and non-hypotensive reactions. It is important to compare acute levels during a reaction to baseline readings, as a relative rise, even within the normal range, could be significant. Tryptase may peak later in food allergic reactions. We provide the largest series of sequential time course data for tryptase during adult food challenges.

1619 | How often a low risk allergy patient with a single food allergy should be followed up in clinic? Reviewing current practice on follow up appointments in allergy outpatient department

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Introduction: The need of reviewing current follow up practices in allergy outpatient departments is becoming urgent. The number of patients who don't attend (DNA) the outpatient allergy clinic is significant; this poses a risk to patient safety and puts a strain on resources. Ensuring that the right patient is seen at the right time is essential to tackle the demand for outpatient appointments. A new approach is needed to reduce DNA rates and improve patient monitoring.

Objectives: To create the profile of the DNA allergy patient and to identify ways to reduce the DNA rate, increase patient safety and use outpatient resources wisely.

Results: Six month data from a single weekly allergy clinic was used. 76 of a total of 296 patients did not attend their scheduled outpatient clinic appointment. 45% (n=34) were children aged 0-5 yrs and 55% (n= 42) were older children and adolescents 6-16 years. All children in the younger group were food allergic while in the older group, apart from food allergy (85%) airborne and venom allergy were also recorded. 46% (n=35) of the DNA patients had a single allergy with no risk factors and no adrenaline auto injectors (low risk patients) and 54% (n=41) suffered from multiple allergies and carried AAls (high risk). The low risk patients were seen in clinic 2 years prior to the missed appointment and the high risk ones were seen the year before to their appointment.

Conclusions: Within a six-month period, a quarter of the follow up appointments in an allergy outpatient department were lost despite using text message reminder to parents/patients. This could have implications in patient management as well as carrying a significant strain on resources. There are no agreed guidelines on the timeframe of allergy patient follow up. A follow up every 3-5 years for low risk patients is suggested by some centres; however this could compromise patients' care. We are proposing a 4 year follow up appointment for low risk allergic patients and a phone consultation every 2 years. This could reduce the patient DNA rate while maintaining adequate patient monitoring.

1620 | Anaphylaxis due to avocado with different sensitization pattern

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Case report: Background: Avocado allergy has been almost exclusively considered in the context of the latex-fruit syndrome. There are few cases reported of systemic reactions due to avocado outside of this condition.

Objective: We studied the case of a 41-year-old woman with seasonal allergic rhinitis and seafood allergy, who presented two episodes of allergic reaction immediately after avocado ingestion. She complained of oral pruritus, pharyngeal tightness along with abdominal pain, nausea and vomiting and perioral hives. She had no latex allergy symptoms and tolerated any fruit, including kiwi, banana and chestnut.

Materials and methods: Skin tests and specific IgE determination to aeroallergens, latex, food extracts and allergens were performed. Prick-prick tests to avocado, kiwi, banana, chestnut, as well rubbing and latex glove use test were carried out. Avocado allergens from Hass and Strong avocado varieties were studied by electrophoretic and immunochemical methods. Avocado extract of each varieties were separated by SDS-PAGE. Bound IgE antibodies were detected using biotin-conjugated anti-human IgE, and using Horseradish peroxidase. The protein-IgE junction was detected by chemiluminescence, following the manufacturer's recommendations (Amersham Biosciences, UK).

Results: Skin tests were positive to avocado and negative to the remaining fruits studied. Rubbing and latex glove use test ruled out latex allergy. CAP was positive to pollens, dust mites, rBet V 2 (0.54 kU/l), latex (0.97), peach (0.42), rPru p 4 (0.36), banana (0.38) and kiwi (0.40). Specific IgE to rPru p 3, rBet v 1, avocado and nut extracts were all negative. SDS-PAGE studies showed the typical protein pattern of avocado with multiple protein bands over 30-40 kDa, 60 kDa, 75 kDa. Other bands close to 100 kDa were also identified. Immunoblotting revealed IgE-binding proteins bands about 100 kDa with absence of recognition of the lower bands.

Conclusions: We present a patient with anaphylaxis due to avocado ingestion outside latex-fruit syndrome, which presents a different pattern of sensitization than those avocado allergens commonly implied (Pers a 1 and Pers a 4).

1621 | Anaphylaxis caused by linseed as a hidden food allergen

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Case report: Background; Allergy to linseed (*Linum usitatissimum*) has unfrequently been reported despite of its wide use in bread, laxatives and in a range of “health food” products. Linseed contains potent allergens which have not yet been characterized.

Material and methods: A 37-year old-woman, with pollinosis, complained of severe abdominal pain along with labial and facial angioedema, generalized urticaria, dysphonia, dysphagia, diarrhea, dizziness and hypotension immediately after the ingestion of a croissant which contained linseeds. She was fully recovered after being treated at the emergency room. She previously suffered another anaphylactic reaction after eating an unidentified bakery product but tolerated any other food, including cereals, nuts and fruits. Skin tests and specific IgE determination to aeroallergens and food allergens were carried out. Linseed allergens were studied by SDS-PAGE and IgE-immunoblotting.

Results: Prick tests were positive to grass and *Cupressus arizonica* pollens and negative to profilin, peach LTP, food, nuts, cereals (wheat, rye, rice, barley, oat and corn), enzymes, pectin, mustard, sesame, fruits, soy and legumes. A prick-prick test yielded strongly positive result to the croissant itself and linseed. Baseline tryptase levels were 3.94 mcg/l. Specific IgE by ImmunoCAP was positive to linseed (4.59 kU/l), and negative (less than 0.35 kU/l) to Pru p 3, Ara h 1, Ara h 2, Ara h 3, Ara h 9, Cor a 8, Bet v 1, Bet v 2, Ber e 1, cereals, fruit and nut extracts. Linseed immunoblot under non-denaturing conditions revealed IgE-binding proteins of 14-kDa, 27-kDa and 30-kDa. IgE-immunoblotting under reducing condition showed two 10-kDa and 16-kDa bands in the linseed extract.

Conclusion: We present a patient with anaphylaxis to linseed contained as an unexpected allergen in a bakery product. The presence of low-molecular mass protein bands in the Immunoblot and the absence of specific IgEs against LTP seems to lead to storage proteins as the responsible allergens in linseed, which seems to be a non-cross-reactive allergen to other seed and nut allergens. However, the presence of allergens from other protein families cannot be discarded. Linseed should be taken into account as a hidden food allergen because it is increasingly used and capable of producing severe allergic reactions.

1622 | An unusual case of positive SlgE to galactose-Alpha-1,3-galactose from south Italy

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Case report: A new form of delayed anaphylaxis has been observed due to IgE antibody directed at a mammalian oligosaccharide epitope, α -Gal.

In Italy, only two studies have been done therefore, we've decided to investigate if this oligosaccharide could be detected in South Italy. Serum sample of a 38-year-old man who was bitten by a tick while he was hunting was obtained. The tick was identified as *Ixodes ricinus* specie.

He was been bitten by a tick minimum 3 times/yr for almost 20 years during his lifetime. In 2016 he was bitten once on January, twice on December (with an interval of 20 days) and once in January 2017.

He has been eaten every kind of meat (pork, beef, lamb, chicken, rabbit, liver meat, etc) after all episodes of tick bit, without developed any early or delayed allergic symptoms. No previous history of anaphylaxis after the ingestion of red meat has been reported. No history of malignancy in therapy with cetuximab or other similar was reported. Positive history of seasonal rhinitis has been reported in the last year.

ImmunoCAP technique (ThermoFisher, Sweden) was used to measured slgE antibodies to α -Gal in the sera of the patient collected on December 2016 (20 days after the first tick bite of this month) and 1 day after the last tick bit (January 2017). For slgE, the cut-off used for a positive reactions was ≥ 0.1 kU_A/L.

slgE to α -Gal were 1.08 kU_A/L and 0.58 kU_A/L, respectively. slgE for pork, beef, lamb and milk were negative. Positive slgE were for Der pt 1.73 kU_A/L, Parietaria 16.7 kU_A/L and Cipresso 1.82 kU_A/L. Negative slgE were for Der f, Graminacee mix, olive, cat, dog and *Alternaria*. Total IgE was 53.8 kU_A/L. The day after the last tick bit, BAT with beef and cetuximab in different dilution, were performed and the results were below the cut-off ($\geq 15\%$ of activated basophils for food, and $\geq 5\%$ for drugs). (Fig 1.a, b) This correlated with the assent of clinical symptoms in this patient.

Risk factors like number of tick bites during the lifetime and recent tick bites, didn't show a higher value of positivity, as it has been described by Villalta et al.

For our knowledge, this is the first time that a case of positive α -Gal patient without symptoms, has been reported in Italy.

The frequency of the exposure to the tick bites and the amount of tick bites during his lifetime might have induced a sort of tolerance in this patient.

Dilutions ng/mL	% of activated basophils with beef
0.88	1.54
4.4	1.61
22	10.4
44	5.83

(Continues)

Table 1 (Continued)

Dilutions ng/mL	% of activated basophils with beef
Dilutions ng/mL	% of activated basophils with cetuximab
25	0
50	1.52
200	2.9
1000	2.88

TUESDAY, 20 JUNE 2017

LB TPS 07

AIRBORNE ALLERGENS AND AIR POLLUTION

1623 | Impact of outdoor molds on daily short-acting beta2 agonists (SABA) sales in central France area for 5 years

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Introduction: No time-series study has investigated the relationship between daily SABA sales and outdoor mold spore levels. The aim of this study was to assess the short-term relationship between outdoor mold spore exposure and SABA sales over 5 years (2010-2015) in an urban area (Clermont-Ferrand, 260 000 inhabitants) in central France.

Objectives: The relationship between daily changes in fungal spores (25 species) and daily changes in SABA sales obtained from the social security database was analyzed using generalized additive models, taking into account confounding factors such as air pollution, weather, pollens and days of the week.

Results: The relative risk: RR [95% CI Confidence Interval] of SABA sales in the whole population associated with an interquartile increase in mould concentration increased for *Alternaria* (Alt): 1.016 [1.001-1.031], *Aspergillus/Penicillium* (Asp-Pen): 1.013 [0.999-1.028], and *Cladosporium* (Cl): 1.039 [0.991-1.089]. When addressing the influence of gender and age, the relationship was significant only in boys 6 to 15 years for Alt: 1.066 [1.012-1.124] and Asp-Pen: 1.053 [1.021-1.085] and in males over 65 years old for Cl: 1.052 [1.001-1.106].

Conclusions: The association found between temporal changes in exposure to outdoor mould and daily SABA sales indicate that mould contributes to asthma and COPD morbidity in young boys and old males in the general population.

1624 | Towards developing personal allergy symptom forecasting system in Baltic states

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Introduction: The paper presents the just-accepted project for development of Personal Allergy SYmptom FOrecasting system (PASYFO) in Baltic States, which will start in April 2017. The project

is a Use-case demonstration downstream application of Copernicus Atmospheric Monitoring Service CAMS. The project will elaborate the working hypothesis that pollen exposure, being necessary for developing the allergy symptoms, is not a sufficiently accurate proxy to predict the severity of the individual reactions. Personalised approach is necessary, and a feasibility of personalised symptom forecasting has been demonstrated, providing that sufficiently detailed history of the symptoms is available.

Objectives: PASYFO will develop instrumentation for collecting the symptom records (expanding the existing Patient Hay Fever Diary, PHD, online system of MUW), handling the CAMS pollen data down-scaled using pollen computations of SILAM model (FMI) for Lithuania and Latvia. The project aims at a symptom forecasting system prototype added to EAN app (<https://www.polleninfo.org/AT/en/free-pollen-app.html>). The instrumentation design will be made in co-operation with clinical practitioners and allergy sufferers themselves. This tool will work in Lithuanian, Latvian and English languages.

Results: For the market trial phase, volunteers from Latvia and Lithuania will be engaged to provide their daily symptoms and evaluate the performance of the PASYFO system. At least 200 regular users, who entered the symptoms, will be subsequently surveyed to reveal their satisfaction with the tool and the forecasts. The system will be made for Lithuania and Latvia, which have all necessary prerequisites for the development, but the constructed system and business model will be made universal, thus allowing for straightforward replication to other parts of Europe.

Conclusions: The connection to actual pollen concentrations, not available from CAMS, will be ensured by using the in-situ regional pollen data reported by Siauliai University and University of Latvia.

1625 | Aerobiological, biogeographical, and meteorological features of the November 2016 fatal thunderstorm asthma event in Melbourne, Australia

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Introduction: Melbourne has experienced six of the nine thunderstorm asthma (TA) events previously reported in Australia. These episodes of TA all occurred in November during the spring grass pollen season; 1984, 1987, 1989, 2003, 2010 and 2011. On 21 November,

2016, Melbourne and Geelong (75 km to the south west), experienced the most severe TA epidemic of all 22 events reported globally. From 5 pm and throughout the night, emergency services received 2666 calls of which 962 were for breathing difficulty; 9900 patients presented to emergency departments of which over 4000 were recorded for respiratory symptoms; at least 30 patients were admitted to intensive care and tragically nine deaths may be attributable to this event (under investigation by state coroner; Preliminary Report of Inspector General Emergency Management).

Objectives: To describe the conditions associated with this TA event.

Results: A north/south storm front approached Melbourne from the west preceding the escalation of ambulance calls which commenced from the same region. Weather conditions of the day changed abruptly with the passage of a thunderstorm gust front into the urban area. Temperatures dropped rapidly from the mid 30 s to the low 20s °C. Winds changed swiftly from northerly winds to west or west-northwest winds with mean speeds between 45-60 km/h and gusts of 60 to 90 km/h. Relative humidity rose quickly behind the gust front to 70%-80%, persisting in this range throughout most of the evening. Remote sensing of greenness in the grassland cover of the rural region northwest of Melbourne over which the wind passed hours before the TA event, showed an anomalously high vegetation index. Extreme levels of airborne grass pollen (102 grains/m³, constituting 41% of total pollen) were recorded that day.

Conclusions: Like all previous TA events in Australia, in which 90%-100% of affected patients showed allergic sensitivity to grass pollen with a history of allergic rhinitis, high grass pollen exposure on 21 November appears to be a major contributing factor in this TA epidemic. However, co-exposure and sensitization to fungal allergens (*Cladosporium*) may be an additional contributing factor. TA events in Melbourne appear to be associated with elevated grassland biomass suggesting satellite remote sensing as useful component of a predictive model for grass pollen season severity that should be evaluated for utility in prediction and better management of TA events.

1626 | Sensitization to peach tree pollen in Madrid

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Introduction: The most relevant pollens in our working area (Madrid, Spain) are Grass, Olive tree and *Plantago lanceolata*. Other pollen of clinical relevance are *Cupressus arizonica*, Plane tree and

Salsola kali. These pollens share different proteins that behave as panallergens. Whether or not other pollens not present in our environment are also relevant remains to be determined. We studied the sensitization to Peach tree pollen in our patients. This pollen is not only a source of LTP but also may carry other proteins that cross-react with common prevalent vegetal allergens.

Objectives: A total of 411 subjects who came to our Allergy Unit reporting Rhinoconjunctivitis and/or Asthma were evaluated. The allergological work-up included: clinical history (seasonal symptoms and food allergy/tolerance) and skin prick tests with a panel of inhalant allergens that included house dust mites, molds, cat and dog dander, most relevant pollens (Cypress, Plane tree, Olive tree, Grass, *Plantago lanceolata*, mugwort and *Parietaria judaica*) and Peach tree pollen. In addition, the following molecular components were also tested: Pru p 3 (LTP) and Pho d 2 (Profilin).

Results: From the total group (age range: 3-73 y.o.; median age: 29.5) 65.3% were female and 23% were children (younger than 15 yo). The 83% of the patients had positive skin prick test to at least one pollen: Grass (66%), Olive tree (61%), *P. lanceolata* (60%), *C. arizonica* (40%), Plane tree (37%), *S. kali* (34%), mugwort (12%) and *P judaica* (11%). The 18% of them were sensitized to Profilin and 9% to LTP. Positive skin prick tests to Peach tree pollen were found in the 38% of the patients. The sensitization pattern analysis of those patients who were positive to Peach tree pollen showed: 90% were also sensitized to *P. lanceolata*, 88% of them to Grass pollen, 84% to Olive tree, 69% *C. arizonica*, Plane tree and *S. kali*, 27% mugwort, 23% *P. judaica*, 39% Profilin and 20% were sensitized to LTP. Only four patients with positive skin prick test to Peach Tree pollen had also fruit or vegetable food allergy: three of them Contact urticaria to Peach peel and the other one was allergic to legumes.

Conclusions: The sensitization to Peach tree, a pollen that is not prevalent in our area, may be explained by cross-reactivity with other inhalant or vegetal food allergens. Although one out of five patients was positive to Pru p 3, the clinical relevance of this finding must be established.

1627 | Diagnosis and treatment of allergic patients to tree pollen in Lviv region, Ukraine

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Introduction: The city of Lviv is located in the Pre-Carpathians area, characterized by predominance of deciduous and coniferous forests. Typical spices are beech, alder, hazel, birch, maple, ash, privet etc. The pollen of these trees has distinct allergic properties.

There is taxonomic dependence between closely related trees' species, which depends on the presence of homologous molecules that are not found in other unrelated species of trees. Molecular diagnostics of PR-10 (Bet v 1 homologues) family is important for our patients, as they are major *Fagales* allergens, in particular *Betulaceae* family often associated with the oral allergy syndrome (OAS). However, ash (*Fraxinus excelsior*) refers to the order *Lamiales* of *Oleaceae* family. Fra e 1, ash's major component and Ole e 1 are homologues, what is proved by almost identical IgE-binding profiles.

Objectives: To study sensitization of Lviv region patients to spring trees and analyze the efficiency of SLIT by "Spring Tree" mixture (Diater Laboratorios, Spain).

Object and methods: 286 patients (17-58 years, 55.9%—women and 44.1%—men) were involved in the study. SPT was carried out by extracts "Mixture of trees" (*Alnus glutinosa*=25.00%; *Corylus avellana*=25.00%; *Betula verrucosa*=25.00%; *Fraxinus excelsior*=25.00%) (Diater Laboratorios, Spain). The levels of specific IgE were performed by ImmunoCAP (Thermo Fisher Scientific, USA). SLIT was carried out with the "Spring Tree" mixture (*Alnus glutinosa*=25.00%; *Corylus avellana*=25.00%; *Betula verrucosa*=25.00%; *Fraxinus excelsior*=25.00%).

Results: 98.3% patients have positive (>3 mm) SPT to extract "Mixture of trees". Since the ash is also common in the region and we have a large number of patients with positive SPT to "Mixture of trees". A 77.0% of the patients were sensitized to birch pollen. We evaluated the efficiency of SLIT by visual analogue scale (VAS). The results revealed a significant decrease in the severity of symptoms in a study group after 1 year (83.1%) and 2 years (94.1%) of treatment.

Conclusions:

1. *Betulaceae* pollen allergens sensitization was 77%.
2. Ash sensitization is typical for patients of Lviv region, according to SPT it was as high as 31.9%.
3. SLIT by combined vaccine "Spring Tree" demonstrates high efficiency and safety for patients with sensitization to *Betulaceae* and *Oleaceae*.

1628 | Approaches to molecular diagnosis of allergy to pollen of weeds

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Introduction: Currently identified 35 weed pollen allergens that can play an important role in the development of allergic rhinitis, hay fever, asthma and food allergies.

Objectives: Materials and methods: The study involved 100 people aged 18-62 years with seasonal allergic rhinitis/conjunctivitis with exacerbation of clinical symptoms in the summer months. Patients performed skin prick tests to the standard panel with extracts of

pollen allergens from local sources of allergens ("Immunologist", Ukraine) determining the levels of total and specific IgE antibody class by ImmunoCAP. We determined five allergen markers for true sensitization to pollen of weeds and grasses.

Results: According to the results of prick test: at 50%—sensitization to various sources of allergens; 30%—monosensitization to weed pollen, 20%—monosensitization to grass pollen. The results determine IgE to the true components of *Artemisia* (Art v 1, Art v 3), *Ambrosia* (Amb a 1) and timothy (Phl p 1, Phl p 5) as follows: 20% of detected sensitization to *Artemisia* and *Ambrosia*, 30%—monosensitization to *Artemisia*, and 20%—monosensitization to *Ambrosia* pollen. Most (70%) patients with monosensitization to weed pollen have identified specific IgE for Art v 1 and/or Art v 3 and/or Amb a 1. False positive results of skin prick tests that indicated the co-sensitization to grasses and weeds can be explained by the presence of sIgE for cross-reactive markers profilin Phl p 12 and polcalcin – Phl p 7.

Conclusions: On the basis of skin prick tests and molecular diagnostics doctor takes a fundamentally different decision on the selection of extracts for specific allergen immunotherapy.

1629 | Respiratory symptoms associated with the inhalation of *Cladosporium*, *Alternaria* and *Aspergillus* mold spores in Zimbabwean patients

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Introduction: The inhalation of *Cladosporium*, *Alternaria* and *Aspergillus* mold spores is associated with respiratory diseases. These molds elicit both IgE and IgG mediated Immune complex diseases. The symptoms closely resemble asthma and rhinitis. The geographical distribution of the molds is influenced by climatic conditions with *A. alternata* predominantly in humid environments, *Cladosporium* and a worldwide distribution *Aspergillus fumigatus*. There were very few reports of the prevalence, pathogenicity and symptomatology associated with these mold spores in tropical African countries.

Objectives: We investigated the frequency of mold sensitization in a cohort of 900 patients tested for the presence of allergen specific IgE antibodies and correlated these with the resultant symptomatology.

Results: There were eighty mold-sensitized patients. Their ages ranged from 4-53 years (mean 22.72 years). Their respective allergen

specific IgE antibody sensitization was *Alternaria alternata* (9.34%), *Aspergillus fumigatus* (8.54%), and *Cladosporium herbarum* (1.8%). Other than molds, the predominant allergen sources were house dust mites (*D. pter* 41%, *D. farinae* 32%), animal hair (cat 21%, dog 17% and horse 6%), grass pollen (16%), tree pollen (10%) and mugwort pollen (7%). The symptoms were associated with rhinitis (sneezing, nasal blockage, nasal discharge, frontal/temporal headaches, anosmia), conjunctivitis and pharyngitis. Asthma related wheezing, nocturnal cough, shortness of breath were relatively infrequent. A battery of lung function tests was performed, and the average FEV1 and PEF for the group were respectively 86.65 and 79.4% of predicted values for age, BMI and ethnicity. Patients with asthma related wheezing and coughing had respective FEV1 and PEF values of 62.2% and 56.4%.

Conclusions: The results show differential sensitization to mold spores with *Alternaria* and *Aspergillus* being equally frequent and *Cladosporium* being rare in this African population. Sensitization affects the upper and lower respiratory tract. When there is lung inflammation, there is significant lung function compromise. Mold spore inhalation can be associated with severe pulmonary manifestations.

1630 | *Alternaria* spores counts during 2016 in Seville, Spain

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Introduction: Moulds allergy is known for more than two centuries. The reproductive particles of moulds, the spores, are responsible for allergic diseases. These spores experience regularly an atmospheric transport, which changes according to the geographical area, due to the environmental conditions. Mould allergy is suffered from 3 to 10% of general population. In Spain, Sensitization to *Alternaria* is estimated about 20%. We consider that exists a high prevalence of sensitization to *Alternaria* in our geographical area, especially in paediatric population. Therefore, it would be interesting to perform *Alternaria* spores counts in the area North of Seville during a year.

Objectives: Daily *Alternaria* spores counts were performed during 2016, using Burkard volumetric collector, model seven-day recording volumetric spore Trap[®]

Results: During 2016 the total *Alternaria* spores counts obtained were 5.332 spores/m³. May 20th was the day of major concentration (peak day) with 340 spores/m³. The seasons of the year with major spores counts were Spring and Autumn. During Spring, the

period of major concentration of atmospheric *Alternaria* spore was from April 18th to June 15th, especially May, from 13th to 24th. In Autumn the period of major concentration was from October 13th to November 3rd. The total *Alternaria* spores counts in months of major atmospheric concentration were: April 1, 213 spores/m³, May 2.476 spores/m³, June 552 spores/m³, October 339 spores/m³ and November 212 spores/m³.

Conclusions: Spring was the season when the major liberation of *Alternaria* spores took place in our area, being May the month in which we found the major concentration, besides the peak day. In Autumn we also got more spores counts than the rest of the year. Taking into account that we live in a high pollination area, sensitization to *Alternaria* might be a confusing factor in patients who, in addition, are sensitized to pollens, due to the fact that the high pollination period and the major *Alternaria* spores concentration occur at the same time. Therefore, it is important to perform *Alternaria* spores counts, just like pollen counts, in order to get a better diagnostic approaching.

1631 | Peach tree pollen is highly prevalent in areas with extensive peach cultivar

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Introduction: Relevant pollens in Mediterranean regions are grass, olive, Parietaria, plain tree and mugwort. In dry inner areas, Salsola and Chenopodium are also prevalent. Because in some regions there is also great extension of tree cultivars like peach no information is available concerning sensitisation to Peach tree pollen. It is heavy and sticky and not considered relevant in allergy.

Objectives: We studied a well defined population of 6000 inhabitants in a village with agricultural activities focused on peach and other rosaceas. Workers concentrate in direct and indirect activities peach. The approach was a prevalence study based in a population sample stratified by age. The study included: Clinical history and skin prick tests with a panel of inhalant and food allergens, Peach tree pollen, Pru p 3 and Pho d 2.

Results: A total of 1600 cases ranging from 3 to 90 years are included. Based on the overall prevalence, the highest sensitisation was to Olive (33% of population), grass (26%), Salsola kali (19%), Cupressus arizonica (17%), Parietaria (13%), Plane tree (10%) and mugwort (9%). The Peach pollen was 21%, being the third one in the prevalence. These differences were significant (P<.001). Analysed by 10 intervals of 6 years each (from 1 to 69 yo), the prevalence to

Peach pollen at the interval 1-6 years was 6% with a progressive increase in the following intervals reaching a maximum at 21-27 y.o. (47%) with a slow decrease in the following intervals being 4% at the 63-69 y.o. interval. This tendency behaviour was similar to the one observed with olive and grass pollen. From the total positives to Peach pollen, the 40% were Pru p 3 positive with a percentage of sensitisation that was increasing and decreasing in parallel to the one of Peach pollen. These differences were also significant ($P < .001$). The clinical entities reported by the patients were rhinitis (79%), followed by asthma (29%), urticaria (24%) and anaphylaxis (18%). Most of these patients were polysensitised to other pollens being olive and grass the most frequent.

Conclusions: Peach tree pollen sensitisations and allergy must be considered relevant in those areas with high extension of cultivars. This seems to be a source of sensitisation to Pru p 3 by inhalant route. Because most of the cases are polysensitised to other trees and plants that overlap in the season, the clinical relevance of Peach tree pollen must be established.

1632 | Allergy medications sales: An useful surrogate marker for pollinosis health impacts in Alentejo, Portugal?

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Introduction: The burden of pollen allergies has been increasing worldwide. Due to their environmental-related aetiology, management of the disease in a changing environment has proven challenging. Several strategies have been used aiming the monitoring of the disease health impacts with limited outcomes.

Objectives: The aim of this work was to investigate the association between the sale of antiallergic drugs with air allergenic loads and whether it constitutes a marker for health impacts of pollinosis in Alentejo, Portugal.

Results: Olive and Poaceae pollen and their major allergens Ole e 1 and Phl p 5 were obtained within the HIALINE project (2010-2011). The pollen was monitored using a 7-day Hirst type sampler and the indexes were determined by the standard methodology. Allergen load was monitored using a high-volume cascade impactor and specific allergens were quantified by specific ELISA. The medication sales data (2010-2011) were provided by CEFAR (Centro de Estudos e Avaliação em Saúde, Associação Nacional de Farmácias), and were divided into two groups: group 1 (G1: medication used throughout the year—histamine antagonists) and group 2 (G2: medication used in SOS—corticosteroids, β_2 agonists and a LTR antagonist).

Spearman's test was used in the correlation studies. Sales of anti-allergic medication are higher between March and June (<2-fold) for both groups compared to the rest of the year, corresponding to the Spring time in Alentejo region. The sales peaked in May, coinciding with pollen and allergen season peak.

Sales of G1 showed association with both Olea (0.735) and Poaceae (0.729) pollen and Ole e 1 (0.776) and Phl p 5 (0.505) allergens. Sales of G2 also correlated both with pollen (0.619 for Olea and 0.593 for Poaceae) and allergens (0.658 and 0.437 for Ole e 1 and Phl p 5, respectively). Correlation was stronger when the total pollen or allergen load was considered for G1 (0.744 and 0.627, respectively) and G2 (0.675 and 0.743, respectively).

Conclusions: In summary, it was observed that allergy drug sales positively correlated with airborne pollen and allergen loads; A stronger correlation was observed for G1, particularly when the total allergenic load is considered. These results suggest that the sales of G1 medication might be used as a surrogate marker of health impacts of pollinosis during the pollen season of highly allergenic species in Alentejo region, Portugal.

1633 | Spatial distribution of pollen-induced symptoms within a large Metropolitan area—A pilot study

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Introduction: Although cities, especially large cities, are a diverse mixture of urban environments and environmental conditions, often only a single pollen trap provides information about airborne pollen in the entire urban area. Notable differences in spatial distribution of three allergologically relevant pollen types for Central Europe (birch, grasses and mugwort) have been present in a novel survey focusing on pollen monitoring at 14 sites (at street level height) within a large metropolitan area—Berlin, Germany.

Objectives: Under these different exposure conditions, it is assumed that persons affected by pollen allergy could develop pollen-induced symptoms to different degrees within one city. An examination of the hypothesis is the main purpose of the study. Anonymously reported daily pollen-induced symptom data from Berlin area were extracted from the online-based self-documentation tool "Patient's Hay-fever Diary". The user overall total symptom (eyes, nose, airways) entries were associated to the nearest of 14 pollen monitoring sites on the basis of postal codes. From the resulting 14 user groups the weekly user symptom data were statistically compared with weekly pollen data of the corresponding monitoring sites using Kendall's Tau B.

Results: Higher amounts of monitored birch and grass pollen in the peripheral areas of Berlin were reflected in stronger symptoms of users located within suburbs than those located in the city centre. A statistically-based relationship between the varying presence of mugwort pollen in the air and the severity of symptoms could not be found on an intra-urban scale.

Conclusions: Grass and birch pollen data from a single inner city trap cannot serve as an adequate source of information and as an appropriate explanation of pollen-induced symptoms of allergy sufferers living within the suburbs and vice versa. In order to provide more detailed and reliable information about the exposure to allergenic pollen, pollen monitoring should be based on more than one pollen trap per city. Furthermore, the occurrence of higher quantities of mugwort pollen in the air is a local phenomenon, strongly associated with the presence/absence of those plants in the immediate vicinity, and cannot be adequately expressed in symptom data at a postal-code scale. Therefore, in this case appropriate placement of pollen monitoring traps within cities or the usage of personal pollen samplers would render more realistic data.

1634 | Diagnostic study of serum specific IgE vs skin prick test in diagnosing sensitization to house dust mites and cockroach allergens in patients with allergic asthma and/or rhinitis in Indonesia

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Introduction: Serum specific IgE testing has recently been introduced in Indonesia, but diagnostic test has not been performed to know its performance to detect common inhalant allergens in patients with respiratory allergy.

Objectives: The objective of this study was to obtain diagnostic accuracy of serum specific IgE testing in diagnosing allergen sensitization to selected inhalant allergens in respiratory allergic patients.

This was a cross-sectional study among patients with respiratory allergy and was part of a larger epidemiology study on specific IgE-sensitization in the Division of Allergy-Immunology, Cipto Mangunkusumo Hospital, Jakarta between September and December 2016. Specific IgE sensitization was measured using immunoblot method (Euroline[®], Euroimmun AG, Germany). Allergens tested were *Dermatophagoides pteronyssinus* (Der p), *Dermatophagoides farinae* (Der f), *Blomia tropicalis* (Blo t), and *Blattella germanica* (Bla g). The results were compared to the standard skin prick test. Diagnostic test were performed and include sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive and negative likelihood ratio (LR+ and LR-).

Results: A total of 101 patients were enrolled; 77 (76.2%) were women. Patients mean age was 38.8 years old. Based on SPT, sensitization was highest for Blo t (76.2%), followed by Der p (70.3%), Der f (69.3%), and Bla g (41.6%). Specific IgE-sensitization was highest for Der f (52.9%), followed by Der p (38.2%), Blo t (33.3%) and Bla g (10.8%). Der p allergen had 50.7% sensitivity, 90% specificity, 92.3% PPV, 43.5% NPV, 5.1 LR+ and 0.1LR-. Der f showed 71.4% sensitivity, 87.1% specificity, 82.6% PPV, 57.4% NPV, 5.5 LR+ and 0.3 LR-. Blo t allergen had 41.6% sensitivity, 91.7% specificity, 94.1% PPV, 32.8% NPV, 5.0 LR+, and 0.6 LR-. Bla g allergen had 23.8% sensitivity, 98.3% specificity, 90.9% PPV, 64.4% NPV, 14.5 LR+ and 0.8 LR-.

Conclusions: Serum specific IgE testing to common inhalant allergen in patients with respiratory allergy showed only low-to-moderate sensitivity, but high specificity. This new assay cannot be used for screening purposes and should be interpreted as an adjunct to the standard skin prick test in diagnosing allergy.

1635 | Study of aero-allergen sensitization in subjects with naso-bronchial allergy in a tertiary care centre from India

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Introduction: To study the pattern of allergen sensitization in patients with allergic rhinitis and asthma.

Objectives: We have analyzed retrospective data of 580 patients who underwent skin prick test for nasobronchial allergic symptoms at Narayana Hrudayalaya Hospital, Bangalore between June 2014 and March 2017. Ethical approval from the institutional committee was obtained. Data analyzed include, history, skin prick data and clinical examination details. Conditions were classified according to GINA (for asthma) and ARIA (for allergic rhinitis) guidelines. Skin prick test was performed using standardized allergens.

Results: Out of 580 patients, 338 (58.3%) were males. The male to female ratio was 1:1.4. The mean age was 23.9 ± 14.2 years. Fifty seven percent of patients were above 18 years of age and 43.1% were below 18 years. Allergic rhinitis (AR) and bronchial asthma (BA) was almost equally presented in patients (88.4% vs 88.3% respectively). Seventy-two percent of patients presented with both AR and BA. Family history of allergy was positive in 67.1%. Seventy-nine percent of patients were positive for at least one allergen tested and 42% had more than one sensitization (table 1). Sensitization was more in men than women. There was a positive co-relation between number of allergen sensitization and increasing age (P=.041).

Conclusions: Prevalence of sensitization was 79% in patients with nasobronchial allergy. The most common allergen being House dust mite mix (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) at 66.9%. The next most prevalent allergen is cockroach allergen at 47.2%. The prevalence of fungal and pollen sensitization were relatively low at 11% and 8.7% respectively. We present one of the largest data from India on pattern of allergen sensitization. The prevalence and incidence of allergy is rapidly growing in India, but the data remains scarce. To address the geographical differences and planning proper treatment strategies require a good descriptive study.

Sl.#	Allergen	Positivity n=580 (%)
1	House dust mite mix (<i>Dermatophagoides farinae</i> , <i>Dermatophagoides pteronyssinus</i>)	388(66.9)
2	Cockroach	274 (47.2)
3	<i>Alternaria alternata</i>	67 (11.7)
4	<i>Aspergillus</i> species (<i>Aspergillus fumigatus</i> , <i>Aspergillus flavus</i> and <i>Aspergillus niger</i>)	51 (8.7)
5	Grass pollens mix (<i>Poa pratensis</i> , <i>Dactylis glomerata</i> , <i>Agrostis gigantea</i> , <i>Phleum pratense</i>)	69 (12.0)
6	Others	137 (23.6)

1637 | Small and handy—The personal particle sampler

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Introduction: In many countries worldwide airborne pollen is monitored by stationary 7-day volumetric spore traps (Hirst type). This kind of trap and the method of pollen analysis of airborne samples are taken as a standard method of pollen monitoring among aerobiologists and allergologists. These pollen data are used for pollen forecasts, for diagnostics and for therapy of pollen allergies as well as backgrounds for pollen exposure of populations during clinical studies. However, pollen exposure of individuals varies permanently due to human spatial mobility. Therefore the nearest pollen station may not adequately reflect individual's pollen-induced symptoms. To gain more realistic data about pollen exposure of individuals a small personal particle sampler (PPS) was developed. The main aim of the study is the validation of the sampler against the standard pollen monitoring method (Hirst type).

Objectives: PPS works on the same volumetric principle as stationary traps—it sucks air through an orifice inside the device on an adhesive medium (stripe with silicon). The sampler is small and light—13 cm × 2 cm × 2 cm in size and 94 g in weight—equipped with a rechargeable battery, GPS and with the possibility to adjust sampling

intervals. A PPS (with flow rate of 4 L/min) was mounted on a standard volumetric pollen trap running parallel during 5 sunny days for 8 or 10 hours per day during the summer of 2016. Exposed stripes were stained and fully analyzed under a microscope with a 400× magnification.

Results: The first evaluation data of the PPS show appropriate correlations with data from a stationary volumetric pollen trap. In simultaneous measurements in ambient air the following ratios between PPS and stationary trap were determined: grass pollen 1 to 2.7, pine pollen 1 to 2.6, nettle pollen 1 to 3.8, *Alternaria* spores 1 to 2.3. The validation needs to be completed for further pollen types in order to be reliable.

Conclusions: An application of the PPS would bring most detailed information about the kind and concentration of certain pollen types which may affect a pollen allergic individual. In combination with symptom data and environmental conditions a better assessment of immunotherapy in field trials would be available as well as evaluating an individual's pollen threshold and therefore being able to accurately forecast an individual's symptoms.

1638 | Allergen production and demographic increase in *Dermatophagoides farinae* mass reared population

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Introduction: *Dermatophagoides farinae* is one of the most important responsible in House Dust Mites (HDM) allergy.

Objectives: A mass reared population of *D. farinae*, stock cultured for diagnostic tests and immunotherapy was monitored.

1. every ten days, the mite density and composition of population mainly considering the distribution of adult and immature stages was calculated;
2. at the same intervals, an SDS-PAGE electrophoresis was performed to evaluate the protein content in culture;
3. the ability of mites, immatures and adults, to move towards higher humidity level was ascertained.

Results: In laboratory at 25°C and 75% RH the population sensibly increased for 50 days by reaching the density of >35,000 *D. farinae*/g of culture. SDS-PAGE shows that Der f11 content is strictly correlated with population density.

Conclusions: The culture population process seems to influence the expression of some major Allergens as Der f11 and not of others as Der f1.

TUESDAY, 20 JUNE 2017

LB TPS 08

IMMUNOLOGY AND ALLERGOONCOLOGY

1640 | Allergooncology: folate receptor alpha as a therapeutic target in breast carcinomas using recombinant antibodies

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Introduction: Triple negative breast carcinomas (TNBC) represent a high unmet clinical need, for which no effective targeted therapies are available. This is partly because cell surface antigens suitable for antibody therapies are urgently required. We have identified the tumour-associated antigen folate receptor alpha (FR α) as a potential target in TNBC and we evaluated its clinical relevance, role in breast cancer progression and targeting with monoclonal antibody-based cancer immunotherapy. We derived new strategies of targeting and immune clearance using engineered antibodies with Fc regions conferring unique immune effector cell-polarizing properties against FR α -expressing cancer cells.

Objectives: FR α expression patterns were examined by transcriptomic studies using breast cancer patient samples, or by flow cytometry screening using cell lines. RNA-interference was used to deplete FR α for *in vitro* functional studies. The immunotherapeutic tumour cell killing effect of FR α -targeting MOv18 antibodies (IgG1 and IgE classes) were measured by multicolour flow cytometry-based assay, in addition to *in vivo* xenograft model.

Results: We demonstrated elevated FR α expression coupled with suppressed MTHFR (active folate) in basal compared to other breast carcinoma subtypes by interrogating the METABRIC database (N=1548), and confirmed these in our local King's College London sample collection (N=155), suggesting that cancer cells may overexpress FR α to overcome the low folate tumour environment. Knock-down of FR α on basal breast cancer cells led to reduction in cellular proliferation, colony formation and ERK activation. Furthermore, a monoclonal antibody (MOv18) recognizing FR α could engender cytotoxic and phagocytic mechanisms against basal breast cancer cells by using healthy volunteer and patient peripheral blood mononuclear cells as effectors. MOv18 treatment of TNBC orthotopic human xenograft-bearing mice was associated with immune cell engraftment and showed signs of restricted tumour growth.

Conclusions: Our results point to FR α as a promising target for TNBC immunotherapy with antibodies able to recruit human and patient immune effector cells against breast cancer.

1641 | Inhibition of nasal allergic remodeling by JNJ7777120

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Introduction: JNJ7777120, the specific antagonist of HR4, could inhibit nasal symptoms by single and repeated intranasal administrations

Objectives: In this study the role of JNJ7777120, the inhibitor of histamine receptor 4 (HRH4) in ameliorating inflammation and remodeling of allergic rhinitis in a mouse model were investigated.

Results: Compared with saline control group, treatment with JNJ7777120 significantly reduced accumulating of eosinophils and changing the Th1/ Th2 balance of inflammatory cells, subepithelial collagenization, and thickening of the nasal mucosa epithelium.

Conclusions: JNJ7777120 may play a protective role in remodeling in murine allergic rhinitis.

1642 | Release of neutrophil extracellular traps as a main trigger for asthma onset

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Introduction: Allergic asthma is an important Th2 associated immunopathology. Even if the pathology of the disease is well described, its aetiology is still largely unknown. Nevertheless, some environmental factors like viral infections and exposition to low doses of lipopolysaccharide (LPS) (also known as hygiene hypothesis) strongly increase the risk of disease inception. Interestingly, these two particular risk factors both induce a strong recruitment of neutrophils into the lung. Recently, scientists highlighted the ability of neutrophils to form neutrophil extracellular traps (NETs) composed of a network of extracellular DNA associated to anti-microbial peptides. NETs release (or NETosis) is an important component in organism defence against pathogen invasion but has also been identified as initiator of pathophysiological conditions like erythematous systemic lupus, gout and diabetes.

Objectives: In this study, we investigated the role of NETs as potential asthma inducers in specific pro-Th2 environmental risk factors like respiratory viral infections and low LPS doses exposures.

Results: First, we assessed the correlation between respiratory viral infection or low LPS doses exposure and NETosis using western blot and confocal microscopy analysis. An influenza A infection induced a strong NETs release between days three and seven after viral inoculation whereas exposition to low (100 ng LPS) but not to high (10 µg LPS) LPS doses also resulted in NETosis within 24 hours following the exposition. Then we developed two mouse models, a virus induced asthma model and a model of asthma promoted by exposition to low LPS doses. In these models, only previously infected mice or mice exposed to low LPS doses displayed all the characteristics of allergic asthma following sensitization and challenge to house dust mite (HDM). To test the role of NETs in asthma onset, we specifically inhibited NETosis in our models using three distinct NETosis inhibitors. When infected or low LPS doses exposed mice were treated with NETs inhibitors, all asthma key features were strongly decreased compared to non-treated mice. Finally, the mechanism whereby NETs led to a Th2 immune response was elucidated by analysing by flow cytometry the distinct subpopulations of lung dendritic cells (DCs) in our two mice models. We observed, during the NETosis phase, a recruitment of monocytic derived DCs (moDCs).

Conclusions: In conclusion, we have demonstrated an unexpected role for NETs in asthma onset by recruiting lung moDCs.

1643 | Specific IgE plasma levels for definite cat antigens correlates with total IgE in Russian patients with cat allergy

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Introduction: Today allergies to domestic pets are an urgent problem all over the world. The number of patients with cat allergy reaches up to 60% in some Eastern countries. Modern research methods allow us to determine the direct source of the allergy—an individual protein that causes the symptoms of the disease. But it is still poorly understood if there is any dependence of Fel d—sIgE levels on age, gender and total IgE.

Objectives: We aimed to investigate whether sIgE reactivity to three major cat allergens Fel d 1, Fel d 2 and Fel d 4 correlates with total IgE levels or with gender and age in patients suffering from cat allergy.

Results: A total of 174 patients suffering from cat allergy (93 males and 81 females) were enrolled. Individual allergens were obtained in

a recombinant form from *E. coli* (Fel d 1 and Fel d 4) or as a native protein purified from cat serum (Fel d 2). IgE and sIgE concentrations were measured using special microarray method developed in our laboratory. Sensitization to Fel d 1, Fel d 2 and Fel d 4 were considered significant when specific IgE level was ≥ 0.35 IU/mL. The mean age of the overall patient group was 17.3 years and a significant difference in age was observed between genders (males: 14.33 ± 14.26 years; females: 21.23 ± 15.21 years; $P = .0019$). We reaffirmed the results of previous works and showed that there were no significant differences in mean total IgE levels between the two sexes and age. But in contrast to some previous studies it was not detected any decrease of sIgE level with increased age. We found weak total IgE correlation with Feld1-sIgE (0.36, $P < .005$) and no correlation with Fel d 2-sIgE levels. For Fel d 4 such correlation was observed only in male group (0.37, $P < .05$). Also we found no correlation between sIgE to Fel d 2 and to other *Feline* antigens. There was weak correlation of Fel d 2-Fel d 4 sIgE levels, but when we considered the Fel d 2 or Fel d 4 positive groups separately this correlation disappeared. Also there was found significant correlation (0.33, $P = .0005$) of Fel d 1 and Fel d 4 sIgE levels, moreover in the group of Fel d 4 positive patients this correlation increased to 0.52 ($P = .0005$).

Conclusions: In conclusion, total IgE and Fel—sIgE levels did not depend on a patient age and gender. Total IgE production correlated with sIgE anti Fel d 1 and Fel d 4 (only in male group) but not with Fel d 2. So it seems that there is distinction between Fel d 2 and other Fel sIgE formation, what should be investigated more thoroughly.

1644 | Epithelial dynamics in IL-4-stimulated human nasal epithelial cells

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Introduction: The airway epithelial cells are frequently injured by inhaled toxicants because of the in the permanent contact with the external milieu. During wound healing, the epithelial cells at the edge of the wound transiently exhibit highly motile mesenchymal properties including disorganization of the actin cytoskeleton, defective tight junction (TJ) function, and altered cellular polarity. Importantly, they migrate collectively on exposed extracellular matrix (ECM) while maintaining E-cadherin-mediated attachment to follower cells behind the leading cells.

Objectives: Here, we focus on both constrained and unconstrained HNE cell monolayers that collectively become motile after IL-4

stimulation. IL-4, an essential mediator in Th2-driven allergic inflammation, appears to be critical in controlling airway epithelial cell migration and repair after injury by decreasing TJ proteins and cell-matrix adhesion.

Results: We first examined wound closure assay using primary human nasal epithelial cells (HNECs) cultured in the presence and absence of IL-4. IL-4 stimulation significantly accelerated wound closure in HNE cells. Surprisingly, IL-4-stimulated cells exhibited initial epithelial layer shrinkage and then uniform sheet migration. We also tested if IL-4 can induce collective migration in confluent HNE cell monolayers with no free leading edge. Surprisingly, IL-4 induced TJ defects, actin cytoskeleton remodeling, and continual swirling cellular motions. We found that periostin, which is an ECM protein to influence cell migration and ECM organization, was considerably up-regulated in IL-4-stimulated HNE cells. Furthermore, periostin-blocking antibodies inhibited IL-4-induced cell migration.

Conclusions: Taken together, these data suggest that periostin may be involved in collective cellular motion of IL-4-stimulated HNE cells through the E-cadherin-mediated cell adhesions.

1645 | Binding of the active vitamin A metabolite retinoic acid impairs immunogenicity of the major cows' milk allergen Bos D 5

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Introduction: The major cow's milk allergen Bos d 5 belongs to the lipocalin protein family. Lipocalins can bind hydrophobic ligands in their intramolecular pocket, which leads to modulation of Th2 responses.

Objectives: We investigated whether Bos d 5 when loaded with the active vitamin A metabolite retinoic acid (RA), would elicit differential immune responses compared to the unloaded state.

Results: By *in silico* docking an affinity energy of -7.8 kcal/mol and a dissociation constant of 1.7 μ M were calculated for RA into Bos d 5. Loading of RA to Bos d 5 could be achieved *in vitro*, as approved by ANS displacement assay. Loading had no effect on serum IgE binding in tolerant or challenge-positive milk allergic children. Bioinformatic analysis revealed that RA binds to an immunodominant T-cell epitope of Bos d 5, with the most important core residue K101-E112. In accordance, Bos d 5 suppressed the CD3+CD4+ cell numbers and IL-10, IL-13 and IFN- γ secretion from stimulated human PBMCs only when complexed with RA. This phenomenon was neither associated with apoptosis of T-cells nor with the activation of CD4CD25 Foxp3+ T-cells, but correlated likely with enhanced stability to lysosomal digestion.

Conclusions: Taken together, our data indicate that proper loading of Bos d 5 with RA, derived from organic cows' feed, may turn it non-immunogenic and thereby decide between tolerance and allergy.

1646 | Comparison of allergic airway inflammation induction potency of *Dermatophagoides farinae*, *D. pteronyssinus* and *Tyrophagus putrescentiae*

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Introduction: Features of mouse model for allergic asthma include airway hyperresponsiveness, excessive production of Th2 cytokines, and eosinophil accumulation in the lungs. *Dermatophagoides farinae* and *D. pteronyssinus*, house dust mites, are the major source of indoor allergens that can cause allergic asthma, rhinitis and atopic dermatitis. The storage mite, *Tyrophagus putrescentiae*, produces potent allergens commonly found in grain and hay.

Objectives: To compare allergic airway inflammation induction potency of *D. farinae*, *D. pteronyssinus*, and *T. putrescentiae*, Balb/c mice were sensitized with 10 mL of aerosolized extract (10 μ g/mL or 100 μ g/mL) of these three kinds of mites through air-compressing nebulizer in the chamber.

Results: In the methacholine challenge test, all of the mice sensitized to the three kinds of mites increased airway hyperresponsiveness, but *T. putrescentiae* sensitized mice had the highest airway hyperresponsiveness. In bronchoalveolar lavage fluid, total cell count and eosinophils increased the most in *T. putrescentiae* sensitized mice. In histology, immune cell infiltration, fibrosis, and mucus production increased in all of the mice sensitized to the three kinds of mites but increased the most in *T. putrescentiae* sensitized mice. Specific IgE increased most in mice serum sensitized with *T. putrescentiae*.

Conclusions: These results showed that *T. putrescentiae* has higher allergic airway inflammation induction potency in mouse than *D. farinae* or *D. pteronyssinus*. The mouse model used in this study would be considered as a useful model for future research of allergic asthma caused by storage mites such as *T. putrescentiae*.

1647 | A SHIP-1 antagonist does not increase CD63 upregulation of human blood basophils

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Introduction: IgE-mediated activation of basophils results in a bell-shaped dose-response. The decreased activation at supraoptimal stimulation is thought to be associated with SH2-containing inositol-5'-phosphatase 1 (SHIP-1). SHIP-1 may limit IgE-mediated activation by dephosphorylating the important second messenger phosphatidylinositol-3,4,5-trisphosphate (PIP₃). SHIP-1 phosphorylation is inversely related to IgE-mediated releasability of basophils and it is suggested that high SHIP-1 activity is distinctive in non-responder basophils. The SHIP-1 inhibitor 3- α -aminocholestane (3- α -AC) could increase the IgE-mediated immediate basophil response and potentially facilitate a response in non-responders.

Objectives: To clarify the role of SHIP-1 inhibitor 3- α -AC in the regulation of basophil IgE-mediated upregulation of CD63.

Results: Ten grass pollen allergic patients were recruited. Basophil reactivity and sensitivity were assessed by flow cytometry with CD63 as activation marker. The effect of 3- α -AC (1-60 μ M, 0-45 minutes) was analysed at individual suboptimal, optimal and supraoptimal grass pollen concentration. The activity measured at different conditions was compared to evaluate the maximal effect of SHIP-1 inhibition. Non-responder basophils of six patients were treated with 3- α -AC at optimal condition (10 μ M, 30 minutes). The maximal increase in reactivity was achieved at 10 μ M of 3- α -AC incubated for 30 minutes. At suboptimal stimulation the median reactivity increased from 27.5% to 44.9% CD63+ basophils (IQR: 34.7-68.2; $P=0.0153$). At optimal stimulation the median reactivity increased from 76% to 77.3% (IQR: 66.1-93.8; ns). At supraoptimal stimulation median reactivity decreased from 66% to 43% (IQR: 29.75-96.2; ns). The antagonist has no clinical relevance as the only reproducible, significant increase was observed at suboptimal allergen stimulation. At high concentrations (>60 μ M) of 3- α -AC, cells appeared to enter apoptosis which is a known feature of 3- α -AC. No increased response was measured in non-responder basophils of six patients.

Conclusions: SHIP-1 inhibition by 3- α -AC did not increase basophil activation. It questions whether 3- α -AC can be used to repress the activity of SHIP-1 in basophils.

1649 | Allergic immune- reactivity to Japanese cedar pollen in donors with different rates of pollen exposure

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Introduction: Japanese cedar pollen is one of the most common triggers for allergic rhinitis in Japan, affecting approximately 20% of the entire Japanese population. Two major allergens, Cry j 1 and Cry j 2, have been identified in Japanese cedar pollen. Additionally, iso-flavone reductase (IFR) was also isolated and reported as IgE target in JC-allergic patients.

Objectives: We compared the antibody and T cell response to JC pollen-derived extract and peptides in 3 study cohorts: 1. JC pollen-allergic patients who have lived in Japan for at least 1 year (LIJA); 2. JC pollen non-allergic patients who have lived in Japan for at least 1 year (LIJNA) and 3. JC pollen allergics who have never lived in Japan (NLJA).

Results: Immunological analysis of T cell responses was performed using isolated PBMC cultured with JC pollen extract and restimulated with peptide pools derived from Cry j 1, 2 or IFR. T cell reactivity was assessed by IL-5 and IFN γ production by ELISPOT. JC pollen-specific IgE titers were found to be significantly higher in the LIJA cohort vs the NLJA cohort. Similar trends were found for the magnitude of T cell reactivity. Interestingly in both allergic cohorts, T cell reactivity was most dominantly targeting peptides derived from the major allergens Cry j 1 and 2, and only very few T cell responses were detected against IFR. Furthermore, Cry j 1 and 2 were also found to be dominant targets for T cell responses from IgE negative patients (LIJNA). When comparing the exact peptide sequences found to elicit T cell responses, no clear differences were observed between cohorts.

Conclusions: Japanese cedar pollen is one of the major triggers for pollinosis in Japan and IgE sensitization to JC is also observed in non-Japanese individuals who have never lived in Japan. Characterizing the allergic response to JC pollen in cohorts from different geographical locations may give insights into sensitization origins and patterns of relevant cross-reactivity. These new findings may be of high relevance for the development of a more effective immunotherapeutic approach.

1650 | The adaptor molecule MyD88: an inhibitory pathway of the allergic response induced by *Aspergillus fumigatus* spores

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Introduction: *Aspergillus fumigatus* is one of the most ubiquitous of the airborne saprophytic fungi, found both outdoors and indoors. Every day, humans inhale thousands of *Aspergillus fumigatus* conidia. In immunocompetent host, these conidia are eliminated by the innate immune system and a protective inflammation through the generation of Th1/Th17 responses. But in immuno-compromised hosts, *Aspergillus fumigatus* can induce serious diseases like aspergillosis. However, this aggressive fungi species can also activate detrimental Th2 responses in the lungs leading to the development of an allergic inflammation in such hosts.

Objectives: The early events inducing the allergic inflammation induced by *Aspergillus fumigatus* are actually not defined. The immune activating properties of this fungus species have been investigated in an asthma murine model to determine which receptor, signaling pathway are activated by conidia and identify which cytokines are crucial in this model.

Results: A model of lung allergic inflammation based on the transfer of dendritic cells pulsed in vitro with *Aspergillus fumigatus* was developed. Bone marrow-derived dendritic cells (BMDCs) from wild type or deficient mice were stimulated in vitro with *Aspergillus fumigatus* conidia and then transferred into wild type mice by intranasal administration. Fourteen days after the transfer, all mice were challenged with conidia intra-nasally and the lung inflammations were analysed three days later. This fungus species induced a strong lung Th2 response with a high recruitment of eosinophils in broncho-alveolar lavages and an increase of Th2 cytokine mRNA in lung homogenate.

The transfer of BMDCs deficient for the expression of MyD88 induced a worsening of the allergic lung inflammation, which is specific of the *Aspergillus fumigatus* species.

Conclusions: These results indicate that the MyD88 pathway on BMDCs is able to control the allergic response generated by *A. fumigatus* via the recognition of compounds on *Aspergillus fumigatus* conidia.

1651 | Bacterial CpG-DNA prevents asthma by expanding lung interstitial regulatory macrophages from local and splenic reservoir monocytes

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Introduction: The hygiene hypothesis postulates that decreased exposure to environmental and commensal microbes increases the risk of developing asthma. While LPS was used as a proxy for bacterial exposures in many studies, its protective effects is uncertain. Another potential candidate for mediating the protective effects of microbes exposure is unmethylated CpG-DNA from bacteria as it prevents allergic sensitization and reverse established asthma in animal models. However, how CpG-DNA exerts these immunomodulatory effects remains unclear.

Objectives: In this study, we investigated, in mice, the role of CpG-DNA on immunoregulatory mechanisms in the lung particularly on lung interstitial regulatory macrophages (IM).

Results: We show that CpG-DNA has the unique ability to expand IM. Experiments in clodronate-treated, chimeric, parabiotic and splenectomized wild-type mice and mice lacking CCR2, a receptor required for classical monocyte mobilization from the bone marrow, unexpectedly demonstrated that CpG-DNA-induced IM (IM_{CpG}) developed from monocytes residing in the lung or recruited from the spleen independently of CCR2. Moreover IM_{CpG} were endowed with hypersuppressive properties and were able to protect against airway allergy even when mice were sensitized and challenged with high doses of allergens.

Conclusions: Our study thus sheds new light on how Mregs expand in the lung, explains why CpG-DNA has strong immunomodulatory effects, and provides a possible mechanistic basis for the hygiene hypothesis.

1652 | Facilitated allergen binding of venom allergens via CD23 mediated by CCD-specific IgE

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Introduction: Immune responses to xenobiotic N-glycan core structures from allergens and parasites are often associated with pronounced high affinity IgE and IgG reactivities. Cross-reactive carbohydrate determinants (CCDs) in insects, plants and helminths are constituted by modification of the conserved N-glycan core structure with α 1,3-linked fucose and—in plants and helminths only— β 1,2-linked xylose. CCDs represent the most frequently recognized epitope in allergic immune responses but their biological and clinical relevance as well as functional characteristics of CCD-specific antibodies remain elusive.

Objectives: In order to gain insights into the functional role of CCD-specific IgE and IgG antibodies we aimed for analysing the interplay of CCD-specific IgE with CCD-carrying allergens. We therefore differentially produced the glycosylated venom allergens Api m 2 and Api m 3 as either CCD-carrying or CCD-free glyco-proteins using variant lepidopteran cell lines. After verification of presence and absence of CCDs we assessed the interaction of the allergens with the CCD-specific IgE in ELISA, immunoblot and ELIFAB analyses.

Results: Recombinantly produced CCD-specific IgE exhibited pronounced interactions with CCD carrying venom allergens native Api m 1, rApi m 2 and rApi m 3, carrying one, two and three N-glycosylations with CCDs. The CCD-specific rIgE mediated facilitated antigen presentation of allergens with multiple glycosylations by binding of IgE/antigen complexes to CD23. In contrast, allergens with single glycosylation did not form complexes binding to CD23. Similarly the same glycosylated allergens, but without CCD, did not form complexes binding to CD23. Notably, CD23 binding of the complexes could be blocked by CCD-specific IgG.

Conclusions: Our study clearly suggests a role of CCD-specific IgE in facilitated allergen binding, allergen uptake and transport and thereby amplification of the allergic response. Our data also provide evidence for the relevance of valency in CCD-reactivity and shows for the first time that recognition of ubiquitous carbohydrate epitopes is equivalent to proteinic epitopes with implications for diagnostic and immunotherapeutic concepts.

1653 | Allergooncology: Functional evaluation of SF-25 IgE and IgG1 antibodies as novel candidates to activate human effector cells for cancer immunotherapy

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Introduction: Monoclonal antibody therapeutics for cancer have been designed with Fc regions of only one antibody class, namely IgG. Building upon previous studies, we hypothesize that the unique properties of the IgE class antibodies: a) the high affinity to their receptors and b) their natural retention in tissues, will result in greater efficacy in the treatment of solid tumours. SF-25 IgE, an engineered chimeric antibody, recognizes a tumour antigen expressed on the surface of tumour cells, with low or no expression on non-malignant cells and tissues.

Objectives: SF-25 IgE antibody was initially produced from the Sp2/0 hybridoma cell line. SF-25 IgG1 and IgE were then cloned in pVito1 vector, expressed in Expi293™ cells and purified through Protein A and kappa-select columns, respectively. The direct effects SF-25 IgE on tumour cells were tested via colony formation and MTS assays. Functional assays to compare the ability of SF-25 IgE and IgG1 to (a) bind to Ig receptors, (b) bind to SF-25 antigen on target cells and (c) induce antibody-dependent cell-mediated cytotoxicity (ADCC) and phagocytosis (ADCP) were analysed by flow cytometry.

Results: The variable heavy and light chain regions of the SF-25 clone were sequenced from the original hybridoma cells. IgE and IgG1 antibody versions were successfully cloned, expressed and purified. SF-25 IgE and IgG1 showed the same affinity to the SF-25 antigen on a panel of cancer cells. The IgE and IgG1 antibodies also bound Fc ϵ Rs and Fc γ Rs, respectively, on human immune primary cells and monocytic cell lines. The direct effects of SF-25 IgE were tested in isolation on multiple target cell lines, showing no effect on tumour cell proliferation nor their clonogenic ability. Among the three versions of SF-25 antibody (SF-25 IgE produced in Sp2/0 hybridoma, SF-25 IgE and IgG1 cloned in pVito1 vector), SF-25 IgE pVito1 seemed to have the most potent effect in mediating ADCC and ADCP *in vitro*. The two IgE SF-25 antibodies were superior to their IgG1 counterpart in mediating ADCC *in vitro*.

Conclusions: As hypothesized, functional comparisons between SF-25 IgE and its IgG1 counterpart showed the former to be more efficient in mediating ADCC *in vitro*. We have therefore selected the SF-25 IgE clone as a promising candidate to investigate the role of IgE antibodies in the tumour microenvironment. Further *in vitro* and *in vivo* studies are underway to evaluate this agent for its potential as a novel therapeutic tool for solid tumour malignancies.

1654 | Evaluating therapeutic IgE antibody toxicity using in vivo rat models and an ex vivo human basophil assay

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Introduction: Monoclonal antibody cancer therapeutics are of one antibody class, IgG. However, efficacy may be improved by the development of tumour-antigen specific IgE antibodies due to the superior tissue bioavailability and higher receptor affinity of this antibody class (allergooncology). MOV18 IgE was engineered to recognise folate receptor alpha (FR α), a tumour antigen expressed by up to 90% of epithelial ovarian carcinomas and other tumours.

Objectives: Given the lack of cross-reactivity of human IgE Fc with murine Fc ϵ R_s, and the similarity between human and rat Fc ϵ RI structure and distribution, the efficacy of MOV18 IgE immunotherapy was evaluated using surrogate rat MOV18 IgE and IgG2b chimeric antibodies in an immunocompetent syngeneic rat model. MOV18 IgE conferred superior efficacy compared with IgG in restricting lung metastases. This model also allowed toxicity assessments.

Results: No differences in clinical toxicities were observed between untreated, MOV18 IgE or IgG treated animals. No moderate or severe toxicity scores were observed in any animal group. Only mild piloerection, responsiveness and hunching toxicity scores were measured in both IgE and IgG treatment groups. Histopathological and haematological evaluations demonstrated no differences in off-target tissue and blood samples, respectively, from MOV18 IgE or IgG treated animals. Following the promising efficacy and toxicity profile of MOV18 IgE, this antibody is now the first IgE immunotherapy to be evaluated in man. Therefore, bespoke assays have been developed to evaluate safety of this novel immunotherapy throughout the first-in-class, first-in-man clinical trial. Basophil activation tests (BAT) are often used *ex vivo* to assess immediate type 1 allergic reactions and hypersensitivity to suspected agents such as allergens. We adapted and validated the BAT assay to monitor hypersensitivity of basophils from patients with cancer receiving MOV18 IgE treatment. A positive basophil activation response cut-off was determined to provide clear criteria for the detection of any activation of basophils by MOV18 IgE alone, or in combination with its target antigen, FR α , and anti-FR α IgG autoantibodies that may be present in patient whole blood.

Conclusions: To-date results indicate that MOV18 IgE does not activate basophils from healthy volunteers or from patients with cancer *ex vivo*. This assay is now being applied to support clinical safety observations during the Phase 1 study of MOV18 IgE.

1655 | Allergooncology: A TNF α /MCP-1/IL-10 axis is associated with tumour antigen-specific ige-dependent monocyte-mediated functions against cancer

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Introduction: Monoclonal antibodies (mAbs) are an established modality for cancer treatment. Clinically available mAb therapies are designed to be of the IgG class. We previously demonstrated that tumour antigen-specific IgE antibodies may engender superior and different effector functions to those triggered by IgG. Moreover, it has been shown that monocytes/macrophages, IgE Fc receptor expressing immune cells often found infiltrating tumours, may play important roles in the efficacy of anti-tumour IgE. However, the mechanisms by which these cells elicit IgE-mediated effector functions are insufficiently characterised.

Objectives: We aimed to investigate the mediators associated with tumour antigen-specific IgE anti-tumour functions *in vitro* and *in vivo*, and to dissect the conditions that induce these mediators.

Results: A tumour antigen-specific IgE antibody restricted the growth of lung metastases more effectively than the corresponding IgG in a syngeneic immunocompetent rat model of cancer. Bronchoalveolar lavage (BAL) fluid from animals treated with IgE demonstrated elevation of TNF α , MCP-1 and IL-10 compared with those given IgG. Flow cytometric evaluation of tumour-infiltrating macrophages extracted from IgE-treated animals also demonstrated elevated intracellular expression of these mediators. TNF α , MCP-1 and IL-10 were also detected in the supernatants of *in vitro* tumour cell cytotoxicity assays mediated by monocytes and tumour antigen-specific IgE. To delineate the conditions required to promote this IgE-mediated cytokine/chemokine signature, cell stimulation experiments were conducted. Cross-linking of IgE antibodies on the surface of monocytic cells resulted in upregulation of TNF α . In turn, stimulation with TNF α induced upregulation of MCP-1 by monocytes and tumour cells. Neither cross-linking of IgE or IgG antibodies, nor by stimulation with TNF α , MCP-1 or IL-4 were sufficient to induce upregulation of IL-10 by monocytes. However, IL-10 induced IL-10 upregulation by monocytes in an autocrine manner.

Conclusions: Monocyte-mediated tumour cell cytotoxicity induced by IgE antibodies involves stimulation of TNF α , MCP-1 and IL-10. Our findings provide early insights into the mechanisms by which IgE class antibodies can potentiate activation of effector cells against cancer and support the clinical development of this novel antibody class.

TUESDAY, 20 JUNE 2017

LB TPS 09

ASTHMA IN CHILDREN AND ADULTS

1657 | Manufacturers offer fake solutions for house dust mite allergic patients—An insight into market of bedding products with reference to current medical guidelines

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Introduction: House dust mite (HDM) allergen is a common allergen causing asthma and/or allergic rhinitis and patients with HDM allergy are advised to avoid or diminish allergen exposition. Pillows and duvets are believed to be significant source of HDM allergens, thus so-called “hypoallergenic bedding” products are typically recommended by many allergists. However, current evidence does not recommend any special bedding products in prevention of asthma (GINA).

Objectives: Since manufacturers of bedding products tend to overuse the terms of hypoallergenicity or allergy-friendly status of bedding we aimed to systematically review existing anti-HDM solutions on the market in the view of current evidence on HDM avoidance.

Results: Using shopping comparison website we systematically reviewed 35 most popular websites offering bedding products, and identified 210 pillows and 70 duvets. The data on anti-allergenicity, filling content, barrier encasing, encasing fabric, price, and medical product were analyzed. Majority of pillows (61%, 127/210) and duvets (74%, 52/70) have been advertised as anti-/hypo-allergenic. Down or feather fillings were found in 14% (30/210) of pillows and in 17% (12/70) of duvets and these products were less frequently advertised as antiallergenic—26% (8/30) and 41% (5/12) respectively. HDM-barrier encasings were found in 8% (16/210) of pillows and in 4% (3/70) of duvets. 4% (9/210) of pillows and 11% (8/70) of duvets were described as products for medical purposes.

Conclusions: Despite limited evidence for multi-component HDM allergen avoidance strategies that are complicated and expensive and offer no clinical benefit for HDM-sensitized patients the manufacturers massively advertise and sell their bedding products as anti-/hypo-allergenic.

1658 | Serum quantitative specific IgE level of house dust mites and its relationship with the severity of allergic asthma patients in Indonesia

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Introduction: House dust mites (HDM) are important inhaled allergens in allergic asthma. However, molecular diagnostic study using specific IgE to HDM allergens has not been done in Indonesia. In addition, quantitative specific IgE measurement has not been associated with asthma severity. The aim of this study was to know the IgE-sensitization of HDM allergens and the difference of specific serum IgE levels based on asthma severity.

Objectives: This was a cross-sectional study on adult allergic asthma patients who were invited for serum specific IgE testing and was part of a larger research in the Division of Allergy and Clinical Immunology, Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Asthma severity was defined based on Global Initiative on Asthma (GINA) 2015 criteria and were grouped as intermittent or persistent. Quantitative specific IgE testing was done on blood serum using a multiple allergosorbent test (Polycheck Allergy, Biocheck GmbH, Munster, Germany). The HDM allergens tested were *Dermatophagoides pteronyssinus* (*D. pteronyssinus*), *Dermatophagoides farinae* (*D. farinae*), and *Blomia tropicalis*. Differences between groups were tested using Mann-Whitney test.

Results: A total of 87 subjects were enrolled in this study; 69 (79.3%) were women. Mean patients' age was 40.2 years. Sixty-three (72.4%) patients had asthma and allergic rhinitis. Fifty-eight (66.7%) patients were classified as persistent asthma. The prevalences of sensitization were 62.1% *D. farinae*, 51.7% for *D. pteronyssinus*, and 48.3% for *Blomia tropicalis*. Significantly higher specific IgE levels in persistent asthmatic than intermittent asthma were shown for *D. farinae* (median 1.30 vs. 0.0 kU/L; $P=0.024$) and *B. tropicalis* (median 0.57 vs. 0.0 kU/L; $P=.015$), and tend to be higher for *D. pteronyssinus* (0.67 vs. 0.00 kU/L; $P=.066$).

Conclusions: Sensitization of HDM allergens is shown to be highest for *D. farinae* (62.1%), followed by *D. pteronyssinus* (51.7%) and *Blomia tropicalis* (48.3%). Specific IgE for *D. farinae* and *B. tropicalis* are higher in patients with persistent than intermittent asthma, whereas specific IgE for *D. pteronyssinus* tends to be higher in persistent asthma.

1660 | Clinical correlation of acute inflammatory marker in asthmatic children

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Introduction: Asthma is a chronic inflammation that can also be seen in childhood. Within ages of childhood; to assess the level of disease control while monitoring asthma; we wanted to investigate the role of white blood cells, platelet, mean platelet volume and eosinophil percentage which are inflammatory marker as an objective data.

Objectives: Demographical specifications, white blood cell amounts, eosinophil percentages, platelet amounts, mean platelet volumes, pulmonary function test results, skin prick test results and levels of asthma control of the patients were recorded.

Results: Between groups whose asthma under control and whose not under control, in terms of white blood cell amount and eosinophil percentage, statistical differences were found ($P=.001$) ($P=.003$). In terms of platelet amounts and Mpv levels no significant difference was found ($P>0,05$). When we grouped the patients with their atopy and asthma control levels; only difference was found according to logistic regression analysis of eosinophil percentage.

Conclusions: Our work showed that; the percentage of eosinophil can be used as a parameter for controlling asthma.

1662 | Patient with chronic asthma and treatment poor response associated to benzodiazepines chronic administration

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Introduction: We present the case of a 61-year-old male patient with asthma with morbid evolution. Patient was chronically treated with benzodiazepines because of insomnia problems. There are multiple causes of poorly controlled asthma. The most common pharmacological cause of asthma attacks are anti-inflammatory drugs. Subacute worsening by maintained treatment with benzodiazepines is not described in literature.

Objectives: Once the patient was diagnosed as suspected asthma with worsening in relation to benzodiazepines administration, we planned maintained oral challenge tests with respiratory function control prior to oral provocation and 7 days after maintaining drug daily doses. Previously we made sure that there were no other factors that could worsen the underlying pathology presented by our patient. We tested tolerance with three different benzodiazepines, with a time interval of one month between each provocation test.

Results: We observed significant decreases in FEV1 after tolerance tests with three different benzodiazepines: Clonazepam, diazepam and alprazolam. The patient was asymptomatic and with proper control prior to the provocation tests as well as after the successive recovery after each positive provocation.

Conclusions: We present the case of a patient with FEV1 significant fall after sustained doses of until three different benzodiazepines. We hypothesize that GABA receptors are involved in the observed phenomenon. It could be related to an increase in expression of a certain GABA_A receptor profile that upon stimulation by GABA agonist drugs would determine inflammatory cellular activation, mucus production and progressive bronchospasm and a infectious processes higher incidence.

1663 | The role of allergens in the progression of obesity and hyperglycemia in asthma patients

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Introduction: Asthma is one of the most common diseases. Statistics show a steady increase in morbidity, disability and mortality from disease worldwide. Set the influence of obesity and hyperglycemia on the threshold of allergic sensitization in patients with asthma

Objectives: A total of 23 patients with asthma uncontrolled flow in combination with obesity. We evaluated the clinical and laboratory data: FVC, FEV1, the level of total IgE and specific (sIgE to Ara h9, Gly m4, Tri a 19) by technique ImmunoCAP (Phadia), Body Mass Index (BMI) and waist-to-hip ratio (WHR).

Results: It was shown that the android type patients were older and had longer duration of a disease vs the patients with gynoid type obesity. HbA1c and HOMA-IR index reliably increased in patients with android type of obesity. Assessment of pulmonary function has shown that FEV1 %, FVC % in these groups were different as well. Among patients with android obesity type, FEV1 and FVC parameters were reliably lower than in the group with gynoid obesity type.

It was found out that all 23 patients had sensitization to food allergens. These indicators were distributed as follows: 5 patients from—Ara h9 averaged 2.03 ± 0.12 kUA/L ($P<.05$); 6 Gly m 4— 3.22 ± 0.14 kUA/L, ($P<.05$) 12 patients Tri a 19— 10.4 ± 2.1 kUA/L ($P>.05$), 9 of these patients were of android type of obesity (pic. 1). Reference level <0.1 . Positive correlations among the entire group of patients examined between the level of hyperglycemia and the level of sensitization to food allergens $r=0.72$ ($P<.05$), BMI $r=0.32$ ($P<.05$), and negative correlation with FEV1 $r=-0.42$ ($P<.05$).

Conclusions: The problem of glucose homeostasis disorder demand further study to pathogenesis clarification, diagnostic optimization and treatment. The solution to the problem of food and pollen allergy influence on disease progression is evident, however, for making detailed conclusions is important to research this group of patients.

1664 | Asthma control levels with the diagnostic-therapeutic-educational pathway IOEASMA: A study comparison through the periods 2007-2010 and 2008-2014

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Introduction: Asthma is the most frequent chronic disease in children and its prevalence has increased over the years. GINA guidelines suggest several key factors leading to optimal management of asthma: asthma control level monitoring, asthma education and pulmonary function assessment. The “Io e l’Asma” center developed a Diagnostic-Therapeutic-Educational pathway (PDTE)—“IOEASMA” to use in every day practice to manage asthmatic children and adolescents. This integrated care involves a multidisciplinary team of clinicians, therapeutic educators, nurses and primary care physicians. PDTE includes 3 clinical visits at 8-12 weeks intervals and 2 follow-up visits at 6-month intervals, with a primary care evaluation between the visits. After V1, patients and their parents also receive an educational course lead by healthcare professionals.

Objectives: To evaluate the level of asthma control at V1 (evaluation) with study comparison during 2 periods, 2007-2010 and 2008-2014.

Results: From 2007-2010, 262 pts between 6-17 years followed PDTE from V1 to V3 as well as the 2 follow-up visits. From 2008-2014, 935 <6 years and 1200 patients ≥6 yrs old.

Conclusions: 44% of pts 6-17 years (2007-2010) presented with asthma controlled at V1 decreasing to 35.4% in 2008-2014. 29.3% of 0-5 years resulted controlled, showing the difficulty to manage preschool children. This confirmed the increase and worsening of asthma management of patients arriving at V1.

	6-17 years (2007-2010)	6-17 years (2008-2014)	0-5 years (2008-2014)
Noncontrolled (%)	20.2	25.5	30.6
Partially controlled (%)	33.3	36.1	30.4
Controlled (%)	44	35.4	29.3
Missing (%)	2.5	3	9.7

1665 | Serum specific IgE-sensitization to inhalant allergens in asthma and allergic rhinitis patients in Jakarta, Indonesia

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Introduction: Serum specific immunoglobulin E (ssIgE) sensitization to common inhalant allergens has been studied in Indonesia. Accurate allergy diagnosis is important to prevent symptoms and to plan treatment in individuals with respiratory allergy.

Objectives: To evaluate specific IgE sensitization of common inhalant allergens in patients with asthma and/or allergic rhinitis in Jakarta, Indonesia. This was a cross-sectional study in patients with a history of respiratory allergy in Jakarta, Indonesia between September-December 2016. Patients aged 19-59 years were invited to undergo ssIgE testing at the Allergy—Immunology Clinic, Cipto Mangunkusumo Hospital, Jakarta. Patients were included if they showed at least one positive skin prick test (SPT) with environmental allergens. Serum specific IgE was assayed by using multiple allergosorbent method (Euroline® Euroimmun, RIDA® Alleisa Screen, R-Biopharm AG). Inhalant allergens tested were mites (*D. pteronyssinus*, *D. farinae*, *D. microceras*, *Blomia tropicalis*, *Tyrophagus putrescentiae*, *Glycyphagus domesticus*, *Acarus siro*); Bermuda grass, Timothy grass, grass mixed, acacia, Australian pine, pine mixed, maize, oil palm); German cockroach, cockroach mixed; cat, dog, mould mix. Serum IgE level more than 0.35 kU/L was considered positive.

Results: 100 subjects were enrolled in this study; 76 patients of them were women. 62% patients have both asthma and allergic rhinitis. The highest prevalence of IgE-sensitization was to *D. pteronyssinus* (62%), followed by *B. tropicalis* (58%), and *D. farinae* (53%). Altogether, dust mites comprised of 75% sensitization, followed by cat/dog (31%), cockroach (27%), pollen (24%), mould (6%). Almost all patients sensitized to cockroach, pollen, cat/dog epithelia and mould also co-sensitized with dust mites. 22% patients were negative to all allergens tested.

Conclusions: IgE-sensitization to inhalant allergens varies widely in respiratory allergic patients. House dust and storage mites are the highest allergens. Co-sensitization among dust mites and between mites and other allergens is also common. About one-fifth of the subjects do not show specific-IgE sensitization; this test should always be combined with SPT to diagnose allergy.

Allergen	n	%
<i>Dermatophagoides pteronyssinus</i>	62	62.0
<i>Blomia tropicalis</i>	58	58.0
<i>Dermatophagoides farinae</i>	53	53.0
<i>Dermatophagoides microceras</i>	51	51.0

(Continues)

Table 1 (Continued)

Allergen	n	%
<i>Acarus siro</i>	47	47.0
<i>Glycyphagus domesticus</i>	45	45.0
<i>Tyrophagus putrescentiae</i>	38	38.0
Cockroach, German	10	10.0
Cockroach mixed	22	22.0
Bermuda grass	3	3.0
Timothy grass	3	3.0
Grass mix pollen	8	8.0
Maize pollen	15	15.0
Acacia pollen	10	10.0
Pine mix pollen	10	10.0
Australian pine	2	2.0
Oil palm	1	1.0
Cat epithelia	17	17.0
Dog epithelia	19	19.0
Mould mix	6	6.0

1666 | A Delphi approach to development of standard questionnaire to investigate asthma in Korean children

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Introduction: Nowadays, the prevalence and disease burden of asthma have increased. So the need for early diagnosis and appropriate management of asthma is emerging. However, it is difficult to identify the diagnosis, symptoms and the prevalence of asthma due to lack of reliable investigating items.

Objectives: The purpose of this study is development of survey and manual in order to assess prevalence of pediatric asthma in Korea.

Results: We investigated surveys and related information that are utilized to assess asthma diagnosis and prevalence by Systematic Review. After then, Delphi survey was conducted on 20 Korean pediatric allergists in order to develop a standardized survey and manual in Korea. The process consisted of 3 serial rounds across 2 children

groups (less than 5 years old, greater than or equal to 5 years old). Each subsequent round narrowed investigating items for the decision of standard set about asthma prevalence, current asthma, and asthma aggravation. Lifetime asthma was defined as "ever doctor-diagnosed asthma" in all groups. Current asthma was defined as "treatment for asthma during the past 12 months" in all groups, and "doctor-diagnosed asthma during the past 12 months" was added to the greater than or equal to 5 years old group. "Wheezing, ever" was defined as "wheezing at any time in the past" and Current wheeze was defined as "wheezing in the last 12 months". Asthma aggravation was defined as "visited emergency room or admission due to asthma attack within the last 12 months" in all groups.

Conclusions: We concluded applicable nationwide definitions of "lifetime asthma", "current asthma" and "asthma aggravation" in Korean children by the Delphi survey.

1667 | Evolutionary particularities in respiratory allergy associated with Cystic Fibrosis in children

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Introduction: Respiratory allergy manifested as asthma and/or allergic rhinitis in children may associate a plurality of related comorbidities that customizes the evolution and treatment of each patient. Rare association with cystic fibrosis (CF) may create difficulties for proper diagnosis and therapeutic management.

Objectives: highlighting the evolutionary particularities and treatment in children with CF and respiratory allergic sensitization vs. patients with respiratory allergy without CF.

Results: From 342 children with respiratory allergy (7-18 years), 16 patients were identified with cystic fibrosis (group 1) and they had been compared with 16 patients without CF (group 2). The parents or legal guardian of the patients have given consent for the research to be published. Familial atopy: group 1-78%, group 2-85%; in both groups the patients had allergic sensitization; group 1 prevailed sensitization in the fungi rate. Bacterial respiratory infection rate: group 1-82%, group 2-63%; Group 1: moderate persistent bronchial asthma (BA) -7/11 cases, severe BA- 4/11 cases, allergic rhinitis (AR) only -5/11 cases; the rate of asthma exacerbations/year (> 3/yr): group 1-73%, group 2-54%; BA controller treatment: group 1-inhaled corticotherapy (ICS) and long action bronchodilator (BDI) -9/11 cases, ICS only -2/11 cases; group 2-ICS-only -7/11 cases, ICS and BDI long action-4/11 cases.

Conclusions: Cystic fibrosis complicates the management of asthmatic child from diagnosis, when BA can be ignored prioritizing CF, until treatment which should be correct individualized for improve prognosis and quality of life of the patients.

1669 | The effect of vitamin D on the clinical outcome of children with asthma and vitamin D deficiency

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Introduction: The wide effects of vitamin D on the innate and adaptive immune system, has attracted the attention of scientists in recent years. In this context, the effect of vitamin D on the incidence and severity of asthma has shown different results. The aim of this interventional study was evaluation of the effect of prescription vitamin D supplements to vitamin D deficient children with asthma

Objectives: In this study 62 children with asthma have vitamin D deficiency who were admitted to the tertiary referral hospital in Kurdistan province were examined. Serum levels of vitamin D, the severity of asthma and pulmonary function tests before and after administration of Vitamin D were calculated. Some indicators like Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and FEV1/FVC were measured. Serum level of vitamin D was measured by enzyme-linked immunosorbent assay. Data were analyzed using SPSS 15.

Results: The mean age of the examined samples was 10.69 ± 9.78 years. 39 patients (57.4%) were male and 29 patients (42.6%) were female. The average serum level of vitamin D before (18.21 ± 8.22) and after treatment (35.45 ± 9.35) had increased ($P < .05$). Also the disease severity and FEV1, FVC, and FEV1/FVC indicators were significantly improved after treatment ($P < .05$).

Conclusions: It seems that administration of vitamin D was able to control the asthma well. However duration of administration should be based on age, environmental factors and living conditions of under control children.

1671 | Tobacco cessation in asthmatic patients

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Introduction: Asthmatics who are cigarette smokers have worse respiratory symptoms, more comorbidities and are more likely to attend to urgency department with an attack of asthma than non-smokers with asthma. There are few Portuguese data about tabagism in asthma patients.

Objectives: The objective of this study is to characterize the asthma cases in a program of tobacco cessation, in terms of: tobacco consumption characteristics, reasons for smoking, nicotine

dependence, morbidity associated, factors that led to the decision of initiating the program, motivation for giving-up tobacco and types of therapeutic modalities.

Results: The authors selected asthmatic patients from a retrospective analysis of 200 clinical records of a tobacco cessation program, randomly selected from the total of patients in the program since January 2012. Patients with incomplete data in clinical records were excluded. The variables analyzed were: sex, age, age of initiation smoking, years of consumption, % of women who smoke in pregnancy and lactation, comorbidities, who smokes around, reasons for smoking, motivation to start the program, nicotine dependence score in the Fagerström Test (FT), motivation score in the Richmond Test (RT) and types of therapeutic modalities (educative, compartmental and pharmacologic).

A total of 18 asthmatics were identified, the average age was 44 years (minimum 27, maximum of 77 years). The average age for starting consumption was 13.6, and 26.25 was the average of the years of consumption. The asthmatics females were 27.8%, 60% of them smoked during pregnancy and 40% during lactation. Reasons for initiating the program were personal in 94%, medical advice in 50% and familiar guidance in 11%. For 50% of patients co-workers smoked too, for 38.89% friends did it too, and for 28% family smoked around too. The average score in FT was 6 and in RT was 8. All patients had educative and compartmental advice and 72% followed also a pharmacological strategy: 72.% nicotin gum, 50% varenicline, 17% bupropion and 11% nicotin patches. All patients reported comorbidities.

Conclusions: Understanding the factors that lead an asthmatic to initiate a cessation is crucial for the success of these programs. We also identified some interesting data that could be important when designing primary prevention programs (eg most women smoked during pregnancy). More studies should be done in this field as they could be a valuable tool for primary prevention and public health.

1672 | Evaluation of sensitization to Der P 1 and Der P 2 in a pediatric population of the north of Portugal

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Introduction: In Portugal, data on the role of Der p 1 and Der p 2 in patients with house dust mite (HDM) allergy are scarce. Allergen-specific immunotherapy (sIT) is the only treatment that improves symptoms, reduces the requirement of pharmacological therapy and modifies the natural history of the disease.

Objectives: With this study the authors aim to understand the local epidemiology and to clarify if the molecular assay of *major* allergens is advantageous in deciding and/or modifying the decision to initiate sIT in children sensitized to *Dermatophagoides pteronyssinus* (*Dp*) and with clinical indication.

The authors analyzed the clinical files of patients observed in the pediatric allergology appointment with asthma and/or rhinitis. Study period: January 2013-December 2016. Inclusion criteria: 1) positive prick-test to *Dp* 2) clinically relevant disease even though medicated. All patients were submitted to a blood assay for Der p 1 and Der p 2 using the CAP System (Thermo Fisher Diagnostics). Assay values ≥ 0.35 kUA/L were considered positive, divided into the following group values: low (0.35-0.7), moderate (0.7-3.5), high (3.5-17.5) and very high (>17.5). Statistical significance was set at $P < 0.05$ and analyses were conducted using SPSS (version 24.0).

Results: The clinical files of 279 patients were included—181 (64.9%) were male. Ages varied between 4-17 years old (mean: 9.45). Asthma was present in 199 children (71.3%) and rhinitis in 245 (87.8%). A family history of atopy was registered in 202 (72.4%) patients, 54 had mother and/or father with asthma. Eosinophils $\geq 4\%$ was presented in 145 children and 158 had increased total IgE values for age. Der p 1 and Der p 2 was < 0.35 kUA/L in 25 (10.4%) patients, 11 (3.9%) had low values, 37 (13.3%) moderate values, 54 (19.4%) high values and 148 (53%) very high values.

The value of Der p 1/ Der p 2 correlated with the size of the prick-test papule, the value of the eosinophils and the total IgE. No statistical correlation was found between Der p 1/ Der p 2 and the age of the patients, nor with the symptoms.

Conclusions: Der p 1 and Der p 2 are dominant allergens in our population. Der p 1/Der p 2 assay was simultaneous negative in 29 (10.4%) patients. Given the fact that currently marketed vaccines for *Dp* are standardized only for *major* allergens, there may be advantage in determining Der p 1/Der p 2 levels in patients with a positive prick-test and clinical indication for sIT prior to deciding initiating or not sIT.

1674 | Parental perceptions of salbutamol use and clinical response in children with asthma

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Introduction: The current recommended dose for inhaled salbutamol lies between 100-1000 mcg, indicating that children may receive a wide range in reliever dose. Salbutamol should start to work within minutes of inhalation and last between 4-6 hours. To date, no research could be identified which looks at the perception of response to salbutamol in children with asthma.

Objectives: An online questionnaire was used to assess parental perceived efficacy of salbutamol as reliever medicine in children. The survey was piloted before The Anaphylaxis UK emailed this to parents of children with asthma.

Results: 259 parents responded; 254 children had been prescribed salbutamol (range 1-17 years, mean age 10 years). The dose of prescribed salbutamol was wide with a small proportion of children exceeding 700 mcg. Overall, 33% of children reported an inadequate response to salbutamol with symptoms returning within an hour or no improvements reported. Of those requiring 300-600 mcg, 42% reported an inadequate response. Of those requiring >700 mcg, 74% reported an inadequate response. There was a significant inverse relationship between parental perception of response to salbutamol and actual dose administered ($P < .001$). The majority of parents (76%) of children who did not improve after >300 mcg salbutamol discussed this poor response with their doctor which often resulted in an alternative medication or increased dose being prescribed. Only 8% of parents were aware that genotype may influence salbutamol response.

Conclusions: There is wide variation in prescribed inhaled salbutamol dose in children. The perceived efficacy of salbutamol as a reliever medicine in children is suboptimal; over a third of parents feel their children show an inadequate salbutamol response, even with relatively large doses. As β_2 agonists remain the recommended first line treatment for acute asthma, there is a need to assess salbutamol dose-response in children with asthma and consider alternative relievers, such as ipratropium bromide or maintenance of stricter asthma control, for those reporting inadequate response to salbutamol.

1675 | Prevalence of asthma-like symptoms and allergic diseases in preschool children and risk factors

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Introduction: The prevalence of asthma and allergic diseases in children has increased in many countries over recent years. The prevalence and risk factors for asthma and allergic diseases have been studied extensively in school age children but there is little information about younger children.

Objectives: Objectives to estimate the prevalence of current asthma-like symptoms and current allergic diseases among preschool children and determine risk factors.

Materials and Methods: This study is cross-sectional. Parents of children aged 3-6 years living in five cities of Altai Territory, Russia were surveyed by questionnaire to find out the presence of asthma-

like symptoms and current allergic diseases. The International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire was used and added with the questions on risk factors. Three thousand two hundred parents of preschool children 3-6 years old answered the questionnaire.

Results: The prevalence of current asthma-like symptoms is 11.1%, current allergic rhinoconjunctivitis—7.5%, current atopic dermatitis—12.3%. Out of 3205 children 0.9% have diagnosed asthma, 3.0% have diagnosed allergic rhinoconjunctivitis, 7.9% had diagnosed atopic dermatitis. The burdened family anamnesis on allergic diseases increases risk of development the current asthma-like symptoms twice (OR=2.11, 95% CI=1.66-2.68), current allergic rhinoconjunctivitis by 2.8 times (OR=2.85, 95% CI=2.16-3.75), current atopic dermatitis by 4.6 times (OR=4.62, 95% CI= 3.69-5.77). The male sex increases risk of development current asthma-like symptoms by 2.6 times (OR=2.63; 95% CI=1.17-5.93), current allergic

rhinoconjunctivitis by 1.3 times (OR=1.35; 95% CI=1.03-1.76), smoking of parents on the first year of life of the child increases risk of development current asthma-like symptoms by 1.6 times (OR=1.61; 95% CI=1.15-2.24), breastfeeding duration less than 6 months increases the risk of development of current atopic dermatitis by 1.6 times (OR=1.62; 95% CI=1.26-2.09).

Conclusions: The prevalence of current asthma-like symptoms and current allergic diseases considerably exceeds the prevalence of medically verified diagnosis. Family history of allergic diseases, male sex, smoking parents and a short period of breast-feeding increases the risk of development of allergic diseases in preschool age.