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ABSTRACTS

SUNDAY, 18 JUNE 2017
TPS 01
ANIMAL STUDIES IN ASTHMA

0590 | Effect of costimulatory signal blockade on T cell responsiveness to glucocorticoid in vitro and in vivo

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Introduction: To investigate the role of helper T (Th) cells in steroid resistant (SR) asthma, steroid sensitive (SS) and resistant (SR) Th clones were selected in vitro, and then adoptively transferred into unprimed mice. Effect of CTLA4-Ig was analyzed both in vitro and in vivo.

Objectives: For in vitro evaluation, ovalbumin (OVA) reactive Th clones were cultured with antigen presenting cells and OVA in the presence of various concentrations of dexamethasone (DEX). Proliferative responses of Th clones were measured by ^{3}H-thymidine incorporation. For in vivo assessments, unprimed BALB/c mice were transferred with Th clones, challenged with OVA, and administered with DEX subcutaneously. Bronchoalveolar lavage fluid (BALF) was obtained 48 hr after challenge, and the number of infiltrating cells was differentially counted. CTLA4-Ig was administered through nasal inhalation or venous injection.

Results: SS and SR clones were selected based on the effect of DEX on the proliferative responses of antigen-stimulated Th clones. Airway infiltration of eosinophils and lymphocytes of mice transferred with SS clones were effectively inhibited by the administration of DEX. In contrast, those of mice transferred with SR clones were not significantly inhibited by DEX. Administration of CTLA4-Ig significantly suppressed the proliferation of DEX-treated SR clones in vitro, and the eosinophil infiltration of SR asthma model transferred with SR clones in vivo.

Conclusions: Steroid sensitivity of Th clones assessed in vitro was consistent with that of adoptively transferred asthma model assessed in vivo. Costimulatory signal mediated through CD28 is crucial for the induction of steroid resistance both in vitro and in vivo.

0591 | Regulation of allergic airway inflammation by adoptive transfer of IL -10-producing CD4^{+} T cells

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Introduction: Anti-inflammatory pharmacotherapy for asthma has mainly depended on inhalation of glucocorticoids, which non-specifically suppress the immune responses. If an anti-inflammatory cytokine, IL-10 can be produced by a specific antigen, asthmatic airway inflammation could be suppressed when the individuals are exposed to the antigen.

Objectives: Purpose of this study is to develop a cellular immunotherapeutics for atopic diseases using IL-10-producing CD4^{+} T cells. In this study, we experimentally evaluated a conventional protocol for antigen-induced proliferation of IL-10-producing CD4^{+} T cells, which are responsive to a specific antigen. It was assessed whether the induced IL-10-producing CD4^{+} T cells can be utilized for antigen-specific cellular immunotherapy. In addition, phenotype of the IL-10-producing CD4^{+} T cells was analyzed.

Results: 1) When spleen cells isolated from ovalbumin (OVA)-sensitized mice were cultured with OVA together with IL-21, IL-27 and TGF-β for 7 days in vitro, CD4^{+} T cells producing IL-10 in response to the specific antigen, OVA, was proliferated. 2) When the CD4^{+} T cells purified by magnetic beads were adoptively transferred to recipient OVA-sensitized mice followed by intratracheal OVA challenges, IL-10 was preferentially produced in the serum and bronchoalveolar lavage fluid (BALF) in vivo. OVA-induced increase in the number of eosinophils in the BALF was significantly suppressed by the adoptive transfer of CD4^{+} T cells. Histological analyses by staining the lung tissue with Periodic acid-Schiff revealed that mucus accumulation in the bronchial epithelium of the asthmatic mice was significantly decreased by the transfer of IL-10-producing CD4^{+} T cells. 3) By FACS analyses, it was found that most of the IL-10-producing CD4^{+} T cells were negative for Foxp3 and GATA-3, transcription factors of naturally occurring regulatory T cells and Th2 cells, respectively, but double positive for LAG-3 and CD49b, surface markers of inducible regulatory T cells, Tr1 cells.

Conclusions: Most of the induced IL-10-producing CD4^{+} T cells could be Tr1 cells, which respond to the antigen to produce IL-10, and effectively suppressed allergic airway inflammation. The induced Tr1 cells may be useful for antigen-specific cellular immunotherapy for atopic diseases.

0592 | Reduced susceptibility to allergic airways disease in BALB/C offspring following maternal therapeutic immunomodulator (OM85) treatment during gestation

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Introduction: Seminal studies of traditional farming families across Europe indicate that maternal exposure to benign environmental microbial stimuli whilst pregnant can potentially play a key role in mitigation of asthma risk in their offspring. The potential to harness this environmental phenomenon by therapeutically mimicking farm microbial exposure in pregnant women therefore presents a novel strategy in preventing the development of allergic disease in children.

Objectives: To investigate the therapeutic potential of an immune modulating agent (OM85) in protecting against development of allergic asthma in offspring via treatment of the pregnant mother, and to elucidate the cellular and molecular mechanisms that promote protection.

Methods: We employed a pregnant BALB/c mouse model. OM85 was given orally to pregnant BALB/c mice selected at random for the last half of gestation; controls were left untreated. All offspring were experimentally sensitised to ovalbumin and exposed to aerosol challenge. We determined bronchoalveolar lavage cellular and molecular profiles, airways tissue cellular responses and profiles via multicolour flow cytometry, IgE titres and airways hyperresponsiveness to methacholine.

Results: Sensitised and allergen aerosol challenged offspring from OM85 treated mothers had attenuated airways eosinophil infiltration and diminished methacholine responsiveness compared to equivalent offspring from non-treated mothers. Flow cytometric analysis identified a significant increase in $CD103^+$ conventional dendritic cells within peripheral lung tissue of sensitised and aerosol challenged offspring from OM85 treated mothers, but reduced expression of the activation marker MHC II. Furthermore, these offspring displayed increased $Foxp3^+$ regulatory T cells (Treg) within the tracheal mucosa, and their mucosal Tregs exhibited increased CD69 and CD152 expression.

Conclusions: The susceptibility to allergic airways disease in mice sensitised and aerosol challenged during the early post-weanling period is thus markedly attenuated by previous maternal OM85 treatment during gestation, and this effect appears associated with an increase in the frequency and functional capacity of regulatory cell populations within the airways mucosa. Our findings suggest that therapeutic treatment of mothers during gestation with immune modulating agents may be a viable strategy to promote fetal immune training in utero and improve the outcomes of allergic disease onset in later life.

0593 | Inhibiting activation of complement c5 attenuates airway hyperresponsiveness and allergic lung inflammation in a house dust mite induced model

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Introduction: In the airways of asthma patients, complement system activation occurs following allergen challenge. Activation of the complement system ultimately leads to C5 activation and generation of C5a. Signaling of C5a via C5a receptors has been demonstrated to either aggravate or attenuate airway hyperresponsiveness (AHR) and lung inflammation in various experimental asthma models. This pleiotropy role depends on the timing of inhibiting C5 activation. Whilst sensitized mice benefit from C5 activation inhibition following allergen challenge, blocking C5 activation prior to sensitization enhances both AHR and lung inflammation.

Objectives: In this study, we determined the effect of inhibition of C5 activation during the challenge phase in our clinically relevant asthma model on AHR and allergic lung inflammation. In particular, we studied how Thelper-2 cells (Th2) and innate lymphoid cells (ILC), pivotal effector cells in asthma, are affected in this setting.

Results: Intraperitoneal injection of a C5 blocking antibody (BB5.1) in house dust mite sensitized mice resulted in significantly decreased levels of C5a in bronchoalveolar lavage fluid, indicating inhibition of C5 activation. Moreover, mice treated with BB5.1 showed significantly lower AHR. While the number of Th2 cells in the lung was decreased, the number and composition of ILCs remained unchanged in this setting. Cells from lung draining lymph nodes produced less IL-4 upon restimulation with house dust mite. However, inhibiting C5 activation did not affect the production of Th2 related cytokines.

Conclusions: Inhibition of C5 activation during the effector phase of asthma attenuates AHR and is accompanied by lower numbers of Th2 cells in the lung.

0594 | Obesity promotes lung fibrosis through TGF-ß signaling in mice

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Introduction: Obese patients with asthma have severe symptoms and poor prognosis and respond poorly to conventional asthma medication. Some studies reported that the baseline level of transforming growth factor β (TGF-β) was elevated in high-fat diet fed mice. TGF-β

was also known to induce subepithelial fibrosis in asthmatic airways remodeling.

Objectives: The aim of this study is to evaluate the effects of TGF-β on obesity in a murine model.

Results: We generated diet-induced obesity (DIO) models by high fat feeding during three month. Then DIO and DIO-OVA mice were treated with TGF-β neutralizing antibody as a TGF-β blockade through the tail vein. Airway hyperresponsiveness (AHR), airway inflammatory cells from bronchoalveolar lavage fluid (BALF) were measured and TGF-β in lung homogenate were evaluated with ELISA. DIO model induce insulin intolerance and glucose intolerance. AHR and lung fibrosis were increased in DIO mouse compared to normal diet mouse. TGF-β level in lung homogenate was increased in DIO mouse, but inflammatory cells in BALF were not different between DIO and normal diet group. AHR and lung fibrosis of DIO model was attenuated by anti-TGF-β antibody.

Conclusions: These results suggest that TGF-β may play an important role in development of lung fibrosis and AHR by DIO in the murine model.

0595 | Evaluation of a murine allergic asthma model to study immunotherapy with purified Der p 1 and der p 2

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Introduction: The IgE response of the vast majority of house dust mite (HDM) allergic patients is heavily dominated by IgE against the major allergens Der p 1 and Der p 2. Current subcutaneous immunotherapy (SCIT) is performed with HDM extract-based products, but the use of purified Der p 1 and 2 has been proposed. Sensitization profiles in murine models do not typically reflect the dominance of Der p 1 and 2 sensitization as observed in man.

Objectives: To skew murine HDM sensitization more towards Der p 1 and 2 dominance and evaluate treatment with mixtures of purified Der p 1 and 2.

Results: Mice were sensitized with 5 μg HDM extract (whole culture extract, lot nr 15G10, Citeq BV, Groningen, The Netherlands) together with 2.25 mg alum at day 0 and 14 i.p. and were challenged with three 25 μg HDM intranasal challenges at day 39, 42 and 44. Mice were divided in different groups and received three subcutaneous immunotherapy administrations (d21, 23, 25) consisting of i) 100 μg HDM, ii) 98 μg Der p 1 with 2 μg Der p 2, iii) 90 μg Der p 1 and 10 μg Der p 2, iv) 67 μg Der p 1 and 33 μg Der p 2, v) No SCIT (PBS s.c.). We analysed airway inflammation, Th2 cytokine production, immunoglobulin production and airway hyper-responsiveness after i.n. HDM challenges.

Inhalational challenge with HDM extract induced a clear Th2 driven eosinophilic airway inflammation with HDM specific (s)IgE, but Der p 1 and 2 sIgE was not detected. The short SCIT protocol did not dampen the inflammation or airway hyper-reactivity. All s.c. treatments induced Der p 1 sIgE, but only Der p 1/ 2 mixtures with ≥ 10 μg Der p 2 induced significant Der p 2 sIgE responses. In concordance with that, Th2 cytokine secretion after ex-vivo re-stimulation of lung draining lymph nodes with Der p 1/ p 2 was increased after Der p 1/ p 2 SCIT but not after HDM SCIT.

Conclusions: Our study and published work has revealed that alum/i.p sensitization of mice with HDM extract does not result in a convincing IgE response dominated by Der p 1 and 2. Additional s.c. exposure to Der p 1 and sufficient Der p 2 is able to achieve sensitization resembling that in human. Our study with a short treatment protocol, followed by a high dose challenge did not result in an effective SCIT Future experiments will evaluate whether a prolonged SCIT protocol followed by a milder challenge will result in a suppressed Th2 driven airway inflammation.

0596 | Exacerbation of allergic responses including respiratory inflammation in Derp-induced allergic march in mice

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Introduction: House dust mites (HDMs) are the most important inhalant allergen in Korea due to the high prevalence of HDM allergy and IgE sensitization shown in Korean population. Allergic march known as the unique characteristic of allergic diseases have been studied so far, but murine model of allergic march by HDM allergen have not been established yet.

Objectives: In this study, we investigated allergic responses including airway inflammation in the murine allergic march model that induced atopic dermatitis followed by asthma by Korean HDM allergen. We used HDM allergen from cultured *Dermatophagoides pteronissunus* (*Der p*) that are indigenous to Korea. Atopic dermatitis was induced by repeated *Der p* exposure with DNCB (1,2-Dinitrochlorobenzene) on ear skin of mice. Asthma was then developed by *Der p* sensitization and challenge in lung. After last challenge, we investigated various allergic responses by the measurement of the level of total and specific IgE in blood, Th2-related cytokines in bronchoalveolar lavage fluid (BALF), cell infiltration in lung, and airway hyperresponsiveness.

Results: Plasma level of total and *Der p*-specific IgE were higher in the allergic march induced group than the asthma only induced

group as well as normal control. In the lung, the levels of IL-4 and IL-5 in BALF and cell infiltration including eosinophils in the lung tissue was significantly increased in allergic march induced group. Airway resistance and dynamic compliance by invasive measurement was significantly aggravated by the induction of allergic march. These results were similar or higher compared with positive control group that induced asthma with OVA, classical materials for murine asthma development.

Conclusions: In this study, asthma-related symptoms such as allergic inflammation and airway hyperresponsiveness were exacerbated by *Der p*-induced atopic dermatitis prior to asthma development. We demonstrate that our murine model could be helpful to improve researches for the progress of allergic march.

0598 | A specific combined n-3 and n-6 long-chain fatty acid supplementation exhibits anti-inflammatory effects in allergic asthma bronchiale

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Introduction: The increasing incidence of allergic *asthma bronchiale* in western societies demands new treatment alternatives to control especially the early disease phase and mild forms. Several species of n-3 and n-6 long-chain polyunsaturated fatty acids (LCPUFA) have been suggested to modulate chronic airway inflammation, predominantly fish oil associated eicosapentaenoic (EPA, C20:5n3) and docosahexaenoic acid (DHA, C22:6n3).

Objectives: The aim of this study was to investigate immune-modulatory effects of a synergistically combination of EPA, DHA and crop-oil based stearidonic (SDA, C18:4n3) and gamma-linolenic acid (GLA, 18:3n6) in a murine allergic asthma model.

Results: House dust mite-secrete sensitized mice were per-orally supplemented with a combination of EPA, DHA, GLA and SDA in a recall model. The fatty acid profiles of blood cell membranes and plasma were analyzed by capillary gas-chromatography. Lung function was determined and bronchoalveolar lavage as well as lung histochemistry were examined.

Mice with significant higher EPA and DHA levels and tendentiously higher SDA and GLA levels in plasma, blood, spleen and lung cells revealed an improved lung function and disclosed a reduced eosinophil-based inflammatory situation in the pulmonary alveolar and lung-tissue.

Conclusions: This study demonstrated that a specific combination of orally applied n-3 and n-6 LCPUFA reduced eosinophilic inflammation and improved lung function within allergic bronchoconstriction and therefore indicates an alternative treatment strategy against *asthma bronchiale*.

0599 | Respiratory epithelial CD93 expression is decreased by pulmonary allergic inflammation in murine model of asthma

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Introduction: CD93 exists as a membrane-associated glycoprotein on the surface of cells, including endothelial and myeloid cells, involved in the inflammatory cascade. It was existed a soluble form of CD93 (sCD93) as well as typical form of membrane bound. sCD93 is receiving renewed attention as a biomarker of inflammation in various inflammatory and immune-mediated diseases.

Objectives: In this study, we aimed to evaluate the potential of CD93 as a biomarker by identifying the association between asthma and CD93 in murine model.

Results: The murine model of OVA-induced asthma demonstrated important features of allergic asthma, including increases in eosinophil counts and Th2 (IL-4, IL-13) cytokines compared to the control group. Histopathological examination showed peribronchial and perivascular inflammatory cell infiltration and goblet cell hyperplasia in murine model of OVA-induced asthma. The levels of CD93 were decreased in lung tissues of murine model of asthma, by immunohistochemical stain, and the feature was consistent with the measurement of CD93 in lung homogenate by enzyme-linked immunosorbent assay, and Real time PCR. However the inflammation induced by lipopolysaccharide did not attenuated the epithelial CD93 expression.

Conclusions: These data showed that CD93 expression in respiratory epithelium was attenuated by allergic inflammation in murine model of asthma, specifically. We suggest possibility of CD93 as a biomarker in asthma associated with the Th2 immune response.

0600 | Cystatin from the nematode ascaris lumbricoides reduces inflammation in a mouse model of allergic asthma

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Introduction: Severe helminth infections are negatively associated to allergic diseases including asthma. In addition, the

immunomodulatory properties of parasite-derived components have been analyzed, raising the possibility of their use as anti-inflammatory molecules. We are currently studying the human and mouse immune response to *A. lumbricoides* components; among them, the recombinant cysteine protease inhibitor (rAl-CPI).

Objectives: To evaluate the immunomodulatory properties of rAl-CPI in a mouse model of asthma induced by the house dust mite *Blomia tropicalis* and also its effects on isolated human dendritic cells. For this, airway reactivity and inflammation were determined by whole body plethysmography and cell counting in bronchoalveolar lavage fluid (BALF) as well as regulatory T cells (Tregs) in spleen, as detected by flow cytometry. Interferon-γ, IL-4, IL-5, IL-10 and TNF-alpha were quantified in BALF and splenocyte supernatant. Total and specific IgE, IgG1 and IgG2a were measured in serum. Peribronchial and perivascular inflammation and goblet cell metaplasia were qualitatively assessed. Human monocyte-derived dendritic cells (HmoDCs) were treated with rAl-CPI, LPS or rAl-CPI plus LPS. IL-6, IL-10 and TNFα in cell-free supernatants and the expression pattern of surface molecules were quantified by ELISA and flow cytometry, respectively.

Results: The sensitized/challenged mice developed an extensive cellular airway inflammatory response, which was significantly reduced in the rAl-CPI treated group, particularly the perivascular/peribronchial infiltrate and the goblet cells/eosinophil number. Also, a significant decrease of Th2 cytokines and specific IgE antibodies was found in rAl-CPI-treated mice. rAl-CPI administration and rAl-CPI treatment were associated with a significant increase of Treg cells number and IL-10 levels. In vitro rAl-CPI showed a strong effect on HmoDCs diminishing the expression of HLA-DR and CD83 and inducing IL-10, which suggests an inhibition of their maturation.

Conclusions: Our findings suggest that rAl-CPI is an immunomodulatory molecule potentially useful in the prevention and treatment of the airway inflammation associated with asthma. Although its effects in the mouse are associated with greater expression of IL-10, other mechanisms, such as interference with the process of maturation of dendritic cells, may be involved and should be further studied.

0602 | A drosophila smoking model—an emerging model for transgenerational studies

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Introduction: Cigarette smoking is a well-known risk factor for the development and exacerbation of chronic inflammatory lung diseases such as bronchial asthma. In the meanwhile, epidemiological studies indicate that not only maternal smoking during pregnancy but also paternal smoking at early puberty is associated with a higher risk for childhood asthma. These findings imply that genetic and epigenetic changes caused by cigarette smoking are transmitted to the following generation(s). As transgenerational studies can hardly be carried out in humans, combined animal studies are required to unravel the mechanisms underlying these phenomena. Due to a short generation time, high fertility, ease of culture, and the availability of various genetic tools, the fruit fly *Drosophila melanogaster* is a very promising model to work with. Furthermore, it has already been successfully used in respiratory research to explore immune dysfunctions and remodeling processes of airway epithelial cells frequently observed in asthma patients.

Objectives: Our goal is to establish a *Drosophila* smoking model for subsequent transgenerational studies. So far, we have succeeded in generating a juvenile smoking model in *Drosophila* third instar larvae reflecting an antioxidant response phenotype.

Results: In this model, nicotine is degraded to the major metabolite cotinine after entering the body. Furthermore, in tobacco smoke exposed larvae as well as their isolated airways the expression level of *Cyp18a1* - a murine and human cytochrome P_{450} 1a1 (Cyp1a1) homologue - is markedly increased demonstrating that also in flies highly toxic tobacco smoke components such as poly-aromatic hydrocarbons are detoxified by cytochrome P_{450} homologues. While tobacco smoke exposure at the juvenile stage does not affect the survival rate of the emerged adult flies, the developmental time of tobacco smoke exposed male but not female larvae seems to be significantly delayed. The latter implies that tobacco smoke exposure modulates gender-specifically the expression profile of developmentally relevant genes.

Conclusions: Finally, using this *Drosophila* smoking model we hope to identify highly conserved genetic and epigenetic mechanisms particularly mediating parental smoke-induced alterations in airway epithelial cells. Ideally, these results should be extrapolated to mammalian systems to find novel targets and mechanisms involved in asthma pathogenesis that simultaneously have the potential to serve as therapeutic targets in humans.

0603 | Experimental model of neutrophilic allergic asthma

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Introduction: The aim of this study was to develop a mouse model of neutrophilic allergic asthma employing different types of lipopolysaccharides (LPS).

Objectives: BALB/c mice were divided into 5 groups. Group 1 was i.p. sensitized 3 times with 20 μg/mouse of ovalbumin (OVA) together with $Al(OH)_3$ (2 mg/mouse) and aerosol challenged with 1% OVA on days 41, 42, 43. Group 2 was s.c. sensitized 3 times with OVA (20 μg/mouse together with Complete Freund's adjuvant (CFA)

and aerosol challenged on days 41, 42, 43 with 0.1% OVA together with LPS obtained from *S. sonnei*. Group 3 and 4 were sensitized in the same manner like group 2 and aerosol challenged on days 41, 42, 43 with 0.1% OVA but together with LPSs obtained from *K. pneumonia* and *C. auroginosa*, respectively. Mice in group 5 (control) were sensitized and challenged with PBS. Twenty-four hours after the final challenge, airway hyperresponsiveness (AHR) was measured using whole body plethysmography. 48 hours after the final challenge bronchoalveolar lavage (BAL) was collected for white cells differential count and lungs were removed for histological examination. Serum anti-OVA IgE, IgG1 and IgG2a were detected by ELISA.

Results: AHR to increasing concentrations of methacholine in groups 1-4 was increased in compare to group 5. Anti-OVA IgE was at high level in all experimental groups in comparison to group 5. At the same time in groups 2, 3 and 4 anti-OVA IgE was significantly lower than that of group 1. Anti-OVA IgG1 and IgG2a levels were high in groups 1, 2, 3, 4 in compare to group 5. Analysis of cell composition of BAL in group 1 demonstrated an increase in eosinophils compared to control group 5, while groups 2, 3 and 4 demonstrated a significant elevated neutrophil and decreased eosinophil counts as compared to mice in groups 1 and 5. General presentation of allergic inflammation (in points) in the lungs of mice in groups 1-4 was more pronounced as compared to control group with significant bronchial epithelium hyperplasia and metaplasia. Peribronchial and perivascular infiltration with eosinophils observed in group 1 only while infiltration with neutrophils was significantly increased in groups 2, 3, and 4 compared to group 5 and group 1.

Conclusions: These data indicate that challenge of CFA-based sensitized mice with specific allergen together with different LPSs can lead to the formation of experimental neutrophilic pulmonary inflammation.

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TPS 02
ASTHMA, EDUCATION AND EPIDEMIOLOGY

0604 | What do patients with obstructive lung disease prefer about social media? a Latin-American multicenter study

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Introduction: Long term goals of management of obstructive lung diseases (OLD) are symptom control and risk reduction. It requires a partnership between patient and their health care providers

Objectives: To compare social media preferences between patients with OLD according to age and years of disease in Latin America, because of scarce availability of data in our region.

Results: 982 patients were enrolled in several countries Ecuador, Argentina, Mexico, Venezuela, and Peú. Mean age was 51.4 (SD 21.1). One third of patients (32%) were less than 40 years old. 57.3% were female, and one third (32.7%) reported having a university or post-graduated diploma. Mean time of diagnosis of OLD was 12.7 years (SD 13.9), and 59.9% reported having more than 5 years with disease. Most of the patients (62.5%) reported using SMS for any purpose at least once a week, followed by Internet (49.8%), Facebook (43.9%), and Email (41.8%). Interestingly, YouTube was reported to be used by 26.1% of participants. Twitter, LinkedIn and Skype were reported by around 15% of patients with OLD.

The most rated electronic media type for searching information about disease was Internet by 36.5%, followed by Email (11.4%) and Facebook (8.1%). Patients with OLD rated as interesting to receive information by SMS (54.4%), followed by WhatsApp (51.1&), and Email (38.8%). Finally, patients also reported as interesting to ask information about disease with their healthcare provider by SMS (69.9%), followed by WhatsApp (51.9%), and Facebook (32.4%). According to age, patients with less than 40 years old reported the highest rates of use social media for any purpose ($P < .001$). Furthermore, use of any electronic media type for searching information related with OLD was higher in youngest patients ($P < .001$), except by Email. Also, interest of receiving information by SMS was similar among age categories. Despite of youngest patients were more interested in receiving or asking information by Social Media, WhatsApp were more rated as interesting among older patients (>40 years old). Comparisons among years with disease showed that patients with more than 5 years with OLD rated being interested in asking information by WhatsApp (32.9% vs 18.5% in younger patients, $P < .01$).

Conclusions: Adherence and control programs could be developed according to age of patients. Subjects with <40 years old would communicate with their healthcare provider by almost all Social Media. SMS's reminders would be an alternative for all patients with >40 years old.

0605 | Corticosteroid phobia among parents of asthmatic children

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Introduction: Asthma is the most prevalent chronic disease among children; its prevalence and morbidity have been rising in recent decades. Pediatric asthma causes significant burden on families; allergen-avoidance measures, uncontrolled disease, and disease severity are the major predictors of cost of pediatric asthma in Turkey. Inhaled corticosteroids (ICS) are considered as a corner stone asthma controller medication that reduces asthma morbidity and mortality. Our aim was to address corticophobia in caregivers of asthmatic children and its impact on asthma management.

Objectives: Five hundred parents of asthmatic children aged 5-18 years were interviewed using structural questionnaire in this study.

Results: More than half of the parents (56.8%) told that they are afraid of using corticosteroids and most of the parents (82.6%) knew that the asthmatic drugs they use contain corticosteroids. 24.8% of parents made changes in their treatment regimen or stopped using the drugs due to corticophobia. 55.2% of parents had no idea about the side effects of corticosteroids. Only 12.6% of parents told that they were informed by their physicians about the effects of steroids. Any change in asthma treatment regimen due to corticophobia was found to be related with poor asthma control level of the child (p: 0.004).

Conclusions: The relationship between parental information given by the physician about steroids and better asthma control was highly significant ($P < .001$) so; physician and health providers should take more time to explain the importance of adherence to asthma treatment. This may extinguish fears about ICS.

0606 | Adaptation of education programmes for elderly patients with asthma

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Introduction: Elderly patients often experience more severe forms of asthma, while their levels of patient education and ability to self-manage asthma tend to be lower in comparison with other age groups. Adaptation of education programmes for elderly patients is needed for a more effective treatment and self-management of asthma.

Objectives: This research aimed to identify main issues of elderly patients' education: knowledge gaps and understanding of asthma self-management with the help of traditional and new approaches to patient education.

This study included 50 patients (age 64+) with bronchial asthma, who were treated in Saratov State Medical University Allergology Centre during 2014-2015; each patient completed Asthma Knowledge Questionnaire with a follow up assessment of their understanding of received information and recommendations.

Results: Collected data allowed to identify following factors which had an adverse impact on asthma control among elderly patients: lack of knowledge about asthma - 36%, inadequate self-management —56% and expectations (56% expected full recovery from their treatment); wrong inhalation techniques—56%, low compliance and adherence to therapy—60%; irregular pharmacotherapy—68%; fear of therapy adverse impacts—56%; no Asthma Action Plan—24%.

Elderly patients basic level of knowledge about asthma self-management was established from consultation with medical professionals—72% (92% of respondents trusted these recommendations, 8% were not able to establish trustful relations); 12% attended asthma school; 36% used printed and 12% - internet sources. The overall use of on-line information for this age group was very limited—29% (urban population—24%, rural—39%). In spite of high ownership of smartphones - 86%, respondents did not use SMS/text or other services; most of respondents were reliant on social networks rather than professional sites and other credible sources of information.

Conclusions: In this situation contacts with medical professional remains the most effective way of conducting elderly patient education. Introduction of on-line/mobile elderly patient education programmes should be backed up by a significant effort (probably in cooperation between medical professionals and telecommunication industry) to convert elderly patients into contemporary mobile/web-technology based education.

0607 | Assessment of level of knowledge about asthma by parents/caregivers of children with asthma, elementary school teachers and university students in Uruguaiana RS, Brazil

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Introduction: Asthma is one of the most prevalent chronic diseases in childhood and the main asthma guidelines consider the knowledge of the disease as one of the main pillars for its management and control.

Objectives: To evaluate the level of knowledge about asthma by parents/caregivers (P) of patients with asthma, primary school teachers (T) and students of university courses (S) in Uruguaiana, RS, BR.

Method: Participants of the study, P: 111, T: 177 and S: 299 (Medicine, Nursing, Physiotherapy, Pharmacy and Physical Education) who answered the questionnaire Newcastle Asthma Knowledge Questionnaire (NAKQ), (Portuguese validation)$_1$.

Results: Although parents had children with respiratory disease, mainly asthma, only 63% identified a symptom of asthma, higher among (T: 84%, S: 90%). To believe that smoking outside the home does not harm patients was pointed by P: (65%, T: 62%, S: 50%). Surprisingly (P: 83%, T: 92%, S: 65%) believe that children with asthma should not consume products with milk. Although most of them (P: 71%, T: 83%, S: 88%) know that there are medicines for symptom relief and crisis, minor portion (P: 45%, T: 45%, S: 33%) thought it should only be treated while with symptoms, although a significant portion of them (P: 79%, T: 72%, S: 75%) believes that inhaled medications can create dependence and they affect the heart (P:77%, T:87%, S:78%). Avoidance of physical activity was indicated by (P: 60%, T: 54% and S: 61%).

Conclusions: Despite the high prevalence of childhood asthma, we found that parents/ caregivers of children with asthma, as well as teachers and university students still have inadequate levels of knowledge to follow up these patients.

Reference:

1. Cidade SF, Rocada C, Costa DD, Rafael JG, Pitrez PM. Linguistic and psychometric validation of the questionnaire (NAKQ). Rev Ciên Méd 2016; 24(2):1-13.

Key words: Students, teachers, parents/caregivers, knowledge, asthma.

0608 | Higher mortality in adult-onset asthma: a 15 year follow-up of a population-based matched cohort

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Introduction: The increased prevalence of asthma and allergic diseases is a major public health problem affecting 1-18% of the population worldwide. A higher all-cause mortality in asthmatics has been shown previously but evidence on the prognosis of adult-onset asthma is very limited.

Objectives: The aim of the study was to examine all-cause and cause-specific mortality in Finnish adults with asthma compared to matched non-asthmatics, and to address the role of potential risk factors on mortality. A sample of asthmatic individuals over 30 years old were identified from national registers, and matched with one or two controls. Baseline information was obtained by a questionnaire in 1997, and study population was linked with the death certificate information of Statistics Finland from 1997 to 2013. The probability and differences of survival were calculated by using Kaplan-Meier method, and the log-rank test. Cox's proportional hazards regression models were applied to estimate crude and adjusted hazard rate (HR) for the effect of asthma. The effect of potential risk factors on mortality was studied by stratified analysis.

Results: During a mean follow-up period of 15.5 years, 255 deaths among 1127 asthma patients and 359 among 1956 non-asthmatics were observed. Asthma was associated with increased all-cause mortality (crude hazard ratio 1.27; 95% confidence interval, 1.08-1.49, $P = .003$ and this association was significant after adjustment for age, sex, smoking, education level, and BMI (HR 1.34, 1.13-1.57, $P < .001$). Asthma was also associated with increased mortality from chronic obstructive pulmonary disease (15.5, 3.63-66.1, $P < .001$), malignant neoplasms of respiratory organs (3.02, 1.36-6.71, $P = .006$), and cardiovascular diseases (1.53, 1.08-2.18, $P = .017$). Among asthmatics higher risk of death was significantly associated with age, smoking, and moderate and severe asthma symptoms. Obesity and female sex showed an association with a decreased risk. Only three asthma deaths were found in the whole group.

Conclusions: Asthma is associated with increased all-cause mortality, mainly smoking related chronic obstruction contributing to the excess mortality. Cardiovascular diseases and malignant neoplasms of the respiratory organs also contribute to the higher mortality.

0610 | Weather type influences the harmful effect of air pollution on asthma symptoms

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Introduction: Asthma has been known to be influenced by weather and air pollution. Spatial Synoptic Classification (SSC) which classifies daily weather into 6 categories: dry moderate (DM), dry polar (DP), dry tropical (DT), moist moderate (MM), moist polar (MP), and moist tropical (MT) is a useful tool for the research on the environment. We, therefore, explored relationships among synoptic weather-type, air pollution, and asthma symptoms in adults.

Objectives: The purpose of the present study was to investigate whether asthma symptoms are affected by weather type and air pollution.

Results: Forty nine asthmatic adults aged from 23 to 68 years living in Seoul, Korea, were enrolled as a panel and followed for 17 months between August 2013 and December 2014. Asthma symptoms including dyspnea, wheezing, nocturnal cough, and awakening at night were recorded on a daily basis. Exposure to particulate matter with a diameter less than 10 mm (PM_{10}) and nitrogen dioxide (NO_2) in each individual was estimated with time-weighted average of concentrations considering outdoor and indoor level of air pollutants and time activity of each individual. Daily weather was classified according to the SSC. Based on a generalized linear mixed model (GLMM), a total of 10 575 person-days of records were analyzed after controlling for cigarette smoke, age, and sex.

Among 6 weather types, the presence of any asthma symptom was more frequently found on DP days (16.3%, $P < .05$) and lower on MM (12.0%, $P < .05$) and MT days (10.3%, $P < .05$). The risk of developing asthma symptoms was increased by the exposure to PM_{10} on DM days [adjusted odds ratio (aOR) = 1.12; 95% confidence interval (CI), 1.03-1.22] and on MM days (aOR = 1.35; 95%, 1.17-1.55) and by NO_2 on DM days (aOR = 1.14; 95% CI, 1.03-1.25) and on MM days (aOR = 1.38; 95% CI, 1.11-1.73). With an increase in 10 $\mu g/m^3$ of PM_{10}, asthma symptom increased by 9.3% (95% CI, 4.9-13.8) on dry days and 9.0% (95% CI, 1.5-17.1) on moist days, whereas 10 ppb of NO_2 increased asthma symptom by10.9% (95% CI, 2.8-19.7 per 10 ppb) only on dry days.

Conclusions: Asthma symptoms in adults are aggravated on days with dry polar weather. Furthermore, the harmful effect of PM_{10} on asthma symptoms is significant both on dry and moist days, whereas the exposure to NO_2 increases the risk of asthma exacerbation only on dry days. Both weather type and air pollution should be considered for the proper management of asthma.

0611 | Endogenous and exogenous sex steroid hormones and asthma and allergy in women: a systematic review and meta-analysis

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Introduction: Female sex steroid hormones have long been implicated in the development and expression of asthma and allergy in women, but the underlying evidence has not been comprehensively synthesised.

Objectives: To synthesise the evidence on the impact of endogenous (puberty, menarche, menstruation, and menopause) and exogenous (hormonal contraceptives and hormone replacement therapy (HRT)) sex steroid hormones on asthma and allergy in women.

We searched 11 electronic databases from Jan 1990 to Nov 2015 for epidemiological and experimental studies. We assessed for risk of bias using the Effective Public Health Practice Project tool (for epidemiological studies) and the Cochrane Risk of Bias Tool (for experimental studies), and synthesised data using random-effects meta-analyses. The overall quality and strength of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results: Of 22 488 identified papers, 64 (57 studies) were included. All six experimental studies were judged to be at high risk of bias, and results were unclear. Of the observational studies, 80% were graded moderate risk of bias, the remainder high. Early puberty was a risk factor for asthma and allergy. Early and late menarche, irregular menstruation, menopause, and HRT use were associated with increased risk of asthma, wheeze, and allergic rhinitis. Key findings from pooled analyses were that early menarche was associated with increased risk of new onset asthma (odds ratio (OR) 1·49, 95% CI 1·14-1·94), as was ever use of any HRT (hazard ratio (HR) 1·37, 95%CI 1·22-1·54), past use (HR 1·41, 95%CI 1·22-1·63), current use (HR 1·48, 95%CI 1·22-1·78), and current use of oestrogen-only HRT (HR 1·85, 95%CI 1·50-2·28). Results for hormonal contraceptive use were unclear. Based on GRADE, the overall quality and strength of evidence was moderate for asthma and wheeze, low for allergic rhinitis, and very low for other outcomes.

Conclusions: Puberty, menarche, irregular menstruation, menopause, and HRT use appear to be associated with asthma and allergy in women, but high quality studies are lacking. Evidence on the use of hormonal contraceptives is unclear. Robustly designed longitudinal studies are required, as are studies investigating the underlying biological mechanisms.

0612 | Specific and generic questionnaires for the assessment of health related quality of life in adult asthmatics

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Introduction: Health related Quality of life (HRQoL) is recognized as one of the most important patient-reported outcomes in patients with asthma. As HRQoL provides additional information to asthma symptoms, severity and control, it has been of high interest. It is very important to identify the factors that affect it so as to provide multidisciplinary care to asthmatic patients.

Objectives: To identify clinical factors (atopy, asthma severity, smoking, obesity, type of treatment) that affect HRQoL. To compare the subscales between the disease specific ACQ, AQLQ and the generic SF36 and EQ5D questionnaires.

Results: 104 asthmatic patients (73.1% women, 26.9% men), aged 17-76 years (mean age: 47 years) previously treated in the Allergy Department of Laiko General Hospital, Athens were recruited. Information on sociodemographic and clinical characteristics were collected and atopy was identified with skin prick tests and Rast tests. HRQoL was assessed using asthma specific ACQ and AQLQ and generic SF36 and EQ5D questionnaires.

Methods: Patients were on stages I (9.6%), II (9.6%), III(30.8%), IV (34.6%) and V(15.4%).

Patients with allergic asthma (n = 72, 69.2%) and under immunotherapy (n = 46, 44.2%) presented better HRQoL in all 4 questionnaires. 20 patients (21.2%) were smokers and ex smokers (15 smokers, 5 ex-smokers).16 asthmatics were on treatment with omalizumab.

Asthma severity affected negatively HRQoL in all questionnaires except the SF36 where it affected only the mean Physical Component Summary (PCS) and had no impact on the mean Mental Component Summary (MCS). Smoking didn't have statistical correlation with HRQoL (maybe due to the small number of smokers) in most questionnaires and affected only the domain "Physical Activity" of SF36. Obesity affected negatively HRQoL in only some subscales of the questionnaires concerning Physical Activity (AQLQ domain "Activity Limitation" and SF36 domain "Physical Activity"). There was a significant correlation between disease specific and generic questionnaires.

Conclusions: Generic questionnaires SF36 and EQ5D are sensitive and accurate in measuring HRQoL in asthmatic patients.

Asthma severity affected negatively HRQoL. Obesity is also a factor that worsens HRQoL concerning the domain "Physical Activity". Asthmatic patients deserve having a good quality of life. Therefore

weight management and the optimum treatment (immunotherapy, biologics) where appropriate should be addressed in order to improve their quality of life.

0614 | Study of age of asthma symptom onset as a potential predictor of disease development and progression

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Introduction: Despite some clinical evidence, long-term studies aimed at testing the hypothesis that early age of asthma onset is a predictor of disease progression, are currently lacking.

Objectives: To investigate the differences in progression of asthma with childhood vs adolescent onset, and to study whether age of onset can be used to predict the course of the disease.

We evaluated 117 children born to mothers with asthma (observation period ≥ 7 years); 143 young patients with asthma (age 18-25 years): 100 patients with childhood (up to 12 years of age) onset of asthma, and 43 patients with onset in adolescence. In addition, we investigated 464 randomly selected adult asthmatic patients with long-term history of asthma. All patients underwent physical examination, pulmonary function testing, and total serum IgE evaluation.

Results: The results of observations of 117 children born to mothers with asthma showed that one-third of these children developed asthma by 7 years of age. "Childhood asthma" phenotype was significantly more common in those patients, whose mothers had developed asthma in childhood ($P < .05$). This phenotype was characterized by the presence of atopic dermatitis and food allergies in the early years of life, and mild asthma after the age of three.

Among young patients (18-25 years of age), milder asthma symptoms were found in males first diagnosed in childhood and early adolescence, while more severe symptoms correlated with female sex, and onset of asthma in late adolescence. However, even when these young patients had spontaneous remission, 80% of them retained bronchial hyper-responsiveness (positive bronchial provocation tests), and 25% had increased serum IgE levels.

Among 464 adult asthmatic patients with long-term history of asthma 20.8% of patients had asthma with onset in childhood and adolescence (8.5% and 12.3%, respectively). Male sex, atopy and early onset of asthma correlated with mild asthma symptoms (male to female ratio of 3:1). Asthma first diagnosed in adolescence was more severe, especially in women and people with intolerance to nonsteroidal anti-inflammatory drugs.

Conclusions: In order to help predict the course of asthma progression in a given patient, it is advisable to consider "childhood asthma" phenotype, characterized by onset in the preschool years, gender differences, family history of asthma, presence of atopic diseases. This phenotype in our study positively correlated with relatively favorable prognosis.

0615 | Non-atopic severe asthma—is it really always non-atopic? The IDENTIFY project

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Introduction: About 10% of all asthmatics suffer from severe allergic asthma, which is frequently caused by IgE hypersensitivity against perennial and/or seasonal allergens. Evaluation of these allergic sensitizations is inevitable for the treatment of severe asthma. However, allergy testing is often limited to the most frequent allergens and furthermore within the German reimbursement system, testing of only 8 allergens per quarter is paid for by health insurances. Thus, analyses of all relevant allergens are seldom carried out.

Objectives: The aim of this ongoing project is to gain data on sensitizations towards aeroallergens in severe asthmatic patients, in which no allergen could be detected in previous testings and who are therefore considered non-atopic. These data might help to identify the most frequent, as well as infrequent aeroallergens in asthma.

Methods: 35 local perennial aeroallergens (mites, fungi, animal epithelia and insects) are measured by specific IgE assessment in 600 severe asthmatic patients in Germany who had negative results in previous allergen tests by either Skin Prick Test or analyses of specific IgE. Furthermore, total IgE levels are determined and a general anamnesis is documented.

Results: In an interim analysis of 362 patients (62.4% females, mean age 53.4 y), 51.4% demonstrated at least one sensitization towards a perennial aeroallergen despite them being considered non-atopic before. According to GINA classification 84.2% of the patients were (partly) uncontrolled and 50.8% had ≥2 exacerbations in the past 12 months. A subgroup of 126 patients receiving oral corticosteroids as maintenance therapy (91.2% (partly) uncontrolled, 71.9% with ≥2 historic exacerbations) had a slightly higher rate of sensitizations (54.8%). Interestingly, a subgroup of 104 obese patients with BMI ≥30 (89.3% (partly) uncontrolled, 53.5% with ≥2 historic exacerbations) showed the lowest rate of sensitizations (47.1%). Overall, the most common sensitizations were found towards *Staph. aureus* Enterotoxin B and A (20.7% and 11.5%), *R. nigricans* (14.9%), *A. fumigatus* (14.4%), *D. farinae* and cat dander (11% each).

Conclusions: These results indicate a lack of diagnostics of sensitization towards aeroallergens in severe asthmatic patients. This suggests that the percentage of non-allergic asthmatics might be overestimated. The correct ascertainment of the allergic status is crucial to make optimal treatment decisions.

0616 | The challenges of living with severe asthma in Europe

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Introduction: To assess the impact of severe asthma on daily life (asthma control, activity, psychological aspects, treatment) in patients from six European countries

Objectives: Collection and analysis of data has been done from GFK Health on behalf of Novartis. Data were collected through an online survey between 12th July and 31st October 2016 on patients suffering from severe persistent asthma in six countries. 904 patients comprising of two age categories were enrolled: adult patients (≥18 years) and children (6-17 years old). Data for adolescent and pediatric patients were obtained through caregivers. Demographics are summarized in Table 1.

Results: Severe asthmatic patients are diagnosed by respiratory physicians (38%), general practitioners (33%), allergists (23%) and pediatricians (5%). On average, adults were diagnosed 15 years ago, adolescents 7 and pediatrics 3 years ago. According to patients knowledge 49% are non-allergic (no additional tests have been done). A big discrepancy was found between real-life control according to GINA guidelines (6%) and self-estimated control (46%). In the previous year 74% patients experienced exacerbations that required treatment from a healthcare professional (emergency room, ambulance, physician at home) and 32% had more than two exacerbations (11% three, 7% four, 3% five, 10% more than five). The most prevalent symptoms during the exacerbations were cough, wheezing (daytime and nighttime), persistent shortness of breath and breathlessness while lying down. An average period of 20 days of oral corticosteroids use was reported in the last 6 months. Asthma exacerbations were quickly resolved (54% within 24 hours) with appropriate medication. However, patients remained psychologically affected for prolonged time after the exacerbation (19% ≥ 1 week). Disruption of activities of daily living (88%), physical activities (84%) and sleep (97%) were reported. More than 50% believe that their professional lives are negatively affected.

Conclusions: Although asthma control is GINA's main goal, severe asthmatic patients are mainly uncontrolled with a poor quality of life as reflected in both their psychological profile and everyday activities. There is a strong disconnect between perceived and actual asthma control. More action should be taken to help severe asthmatic patients achieve control and live normal unrestricted lives.

0618 | Beta 2 agonists and doping

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Introduction: Beta 2 agonists have proven to be very effective bronchodilation agents and hence have been frequently applied therapeutically for symptoms' relief in asthma. The prevalence of asthma is higher in elite athletes than in the general population. Although few studies have found potential ergogenic effects for beta 2 agonists, questions remain.

Objectives: Our objective was to evaluate inhaled beta-2 agonists used in asthma treatment and their possible ergogenic effects in non-asthmatic competitive athletes with normal pulmonary function.

Sample composition and size per country

		Children asthma patients (Data captured through caregivers)			
	Adult Asthma Patients	Caregivers	Adolescents	Pediatric patients	Total
1. UK	n = 190	n = 29	n = 18	n = 11	n = 219
2. GERMANY	n = 170	n = 24	n = 14	n = 10	n = 194
3. FRANCE	n = 170	n = 30	n = 15	n = 15	n = 200
4. ITALY	n = 116	n = 10	n = 5	n = 5	n = 126
5. SPAIN	n = 115	n = 20	n = 4	n = 16	n = 135
6. PORTUGAL	n = 30	—	—	—	n = 30
TOTAL	n = 791	n = 113	n = 56	n = 57	n = 904
MALE (rate)	45%	33%	54%	56%	
FEMALE (rate)	55%	67%	46%	44%	

Results: We performed a systematic review in PubMed, ISI Web of Science and SCOPUS databases. The search criteria were for studies on the effect of inhaled beta-agonists on physical performance in human subjects. Reference lists were searched for additional relevant studies. Studies with subjects participating only in recreational sports were not considered.

32 studies were included. The inhaled substances were: salbutamol (n = 23), salmeterol (n = 5), formoterol (n = 5) and terbutaline (n = 3). Very high doses of salbutamol (800-1200 μg) were given in 6 studies. The athletes were each tested in a randomized double-blind placebo-controlled manner, mostly in a crossover design. The subjects were mainly endurance athletes such as cyclists, middle- and long-distance runners, cross-country skiers, triathletes, and swimmers.

At therapeutic doses no significant effects on performance were detected for the inhaled beta-2 agonists. Although salbutamol increased oxygen uptake, serum lactate and may be involved in gluconeogenesis, the majority of studies did not report any increase in performance even at supratherapeutic doses. However, in one study in swimmers, swim ergometer sprint performance and maximal voluntary isometric contraction were increased after the combined inhalation of salbutamol, salmeterol and formoterol.

Conclusions: There appears to be no justification to prohibit inhaled beta-2 agonists from the point of view of the ergogenic effects. Moreover, the improved lung function described cannot be regarded as ergogenic. However, some doubts persist regarding the use of high dose inhaled beta 2 agonists alone or in combination.

SUNDAY, 18 JUNE 2017
TPS 03
AEROBIOLOGY: AEROALLERGENS AND THEIR CLINICAL IMPACT

0619 | Molecular characterization, gene expression profile and histopathology of fungal spore causing allergies in southwestern Nigeria

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Introduction: Airborne fungal spores and pollen grains are ubiquitous both indoors and outdoors due to their sizes, predominance and aerodynamic properties which enhance their distribution. Fungal spores are associated with dysfunction of multiple system and organs such as respiratory, nervous, immune, haematological and skin.

Objectives: The aim of this research work is therefore to determine the seasonal variation of airborne fungal spores in two states in Nigeria. The Specific objectives are to:
collect, isolate and identify (culturally and molecularly) aero-spores from different locations in Lagos and Ibadan monthly for a period of eighteen months. To compare the effects of fungal spores on inoculated mice at different concentrations.

Results: A total of 44 spore types were identified. Genotypic identifications were accomplished through sequencing of amplified ITS1 and 4 of rDNA genes. The fungal strains identified belong to Ascomycetes, Deuteromycetes and Basidiomycetes. The results revealed lowest count during dry and maximum during the rainy season. *Aspergillus* was quite abundant in all the environments surveyed. The predominance of *Aspergillus*, *Curvularia*, *Alternaria*, *Cladosporium*, *Fusarium and Penicillium* in all the surveyed environments has been attributed to their ability to grow in various substrata. The mean relative gene expression values ranged from 18.95-31.28 for Actin, 17.38-26.77 for β tubulin and 19.74-30.63 for *P. oxalicum* and 30.22-37.56 for *P. citrinum*. All genes were significantly correlated to the Bestkeeper index ($P < .001$). Fungal spore inoculation was done intranasally on balb/b albino mice. Histopathology result for *Aspergillus flavus*, *A. penicilloides*, *Penicillium chrysogenum* and *P. citrinum* inoculated organisms on mice lung appear to be similar although with varying degrees of severity. All of them had intra-lesional unstained fungal hyphae. Pathologies include thickening of alveolar sepatae, which causes impairment in vascular exchange and/or respiratory movements. Hyperplasia of the bronchiolar epithelium was also observed. The hyperplasia is a response to the irritation caused by the fungal hyphae as well as an attempt to replace necrotic epithelial cells of the bronchioles.

Conclusions: Data on the abundance/prevalence of fungi species in the atmosphere of sub-Saharan Africa is limited which necessitated this study for forecasting the prevalence of allergenic fungi in the environment at various seasons.

0620 | Q. rotundifolia and p. hybrida pollen extracts induced basophil degranulation: study using a cell line expressing human FcERI

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Introduction: Currently skin prick test remains the favorite technology in allergy diagnosis to aeroallergens. These tests, however, cause discomfort to the patient. Several biochemical methods based on IgE analysis are available but have limited diagnostic power as biological response, hence elicitation of allergic reaction, is not predicted by these tests.

Objectives: The aim of this work was to investigate whether a basophil cell line expressing human high affinity IgE receptor (FcERI) is useful as a complementary tool for the evaluation of potential allergic reaction elicited by novel allergenic species.

Results: Pollen extracts from different species were prepared with ammonium bicarbonate buffer, lyophilized and stored at −80°C until use. A group of selected patients with known allergy to grasses selected to this study and sera was obtained under informed consent. Enzymoallergosorbent test (EAST) was performed to characterize immunoreactivity to *Dactylis glomerata*, *Quercus rotundifolia* and *Platanus hybrida* pollen. Batches of RBL-h21 cells, maintained in adherent culture, were sensitized with human sera (purified IgE was used as control) and were stimulated with pollen extracts or Anti-IgE antibody. Histamine release (%degranulation) was assessed using a ß-hexosaminidase assay.

All sera exhibited immunoreactivity against *D. glomerata*, *Q. rotundifolia* and *P. hybrida* in EAST test. Inhibition analysis evidenced cross-reactivity with *D. glomerata* in 60% (*Q. rotundifolia*) and 50% (*P. hybrida*) cases. Batches of RBL-h21 cells sensitized with pooled sera from specific (sPool) or cross-reactive (crPool) patients exhibited a selective and dose-dependent degranulation responses upon stimulation with pollen extracts in the range of 1-200 μg/mL. Maximal degranulation (>25%) was observed for 50, 120 and 62 μg/mL for *D. glomerata*, *Q, rotundifolia* and *P. hybrida* pollen extracts, respectively. Stimulation of sPool cell batches showed dose-response curves shifted towards lower concentrations (LOEC 6 and 12 μg/mL) when

compared to crPool (LOEC=24 μg/mL) for *P. hybrida* and *Q. rotundifolia*. Similar cell responses to *D. glomerata* were observed irrespectively of the pool group.

Conclusions: These results show that RBL-h21 cells sensitized with human sera exhibit specific and dose-dependent degranulation upon stimulation with pollen extract containing allergens suggesting this bioassay may constitute an useful tool both for research and/or diagnostics to evaluate potential elicitation of allergic reactions.

0621 | Effect of airborne formaldehyde on skin barrier in a mouse model

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Introduction: Formaldehyde is an indoor air pollutant that poses a significant danger to human health due to its toxicity. Although formaldehyde can irritate the skin, it is not known whether formaldehyde exposure could cause development of atopic dermatitis (AD). We aimed to investigate whether exposure to airborne formaldehyde causes AD-like lesion by inducing skin barrier dysfunction in a mouse model.

Objectives: Forty, 6 week-old female Balb/c mice were exposed to airborne formaldehyde in a chamber for 2 weeks. They were divided into 4 groups: (1) a normal control group with no exposure to airborne formaldehyde, (2) a group with exposure at 2 ppm, (3) at 8 ppm, (4) at 32 ppm for 4 hours a day, 5 days per week. Histologic changes were examined by hematoxylin and eosin (H&E) staining and Toluidine blue staining. The expression of filaggrin (FLG), sodium/hydrogen exchanger-1 (NHE-1) was compared between 4 groups by immunofluorescence staining. After incubation of splenocytes for 48 hours, cytokine levels were measured by ELISA.

Results: The thicknesses of epidermis and adipose tissue were significantly decreased in all formaldehyde exposure groups in a concentration-dependent manner, but dermal thickness did not change. Degranulated mast cells were more frequently found in formaldehyde-exposed groups. Protein expression level of FLG and NHE-1 was significantly reduced by the exposure to airborne formaldehyde in a dose-dependent manner. In the splenocytes, the expression of interleukin (IL)-4, IL-5, IL-13, IL-17, IL-22 and interferon-g significantly decreased by the exposure to formaldehyde.

Conclusions: Exposure to airborne formaldehyde induced skin barrier dysfunction by reducing expression of FLG and NHE-1 in normal Balb/c mice. However, histologic and immunologic changes by formaldehyde exposure to the skin were different from AD.

0622 | Distribution of aeroallergens on skin prick tests of atopic children living in akdeniz area

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Introduction: It is important to detect allergens that cause sensitization to decrease the morbidity of allergic diseases and to prevent or to delay the development of the disease in already sensitized patients. In this study, we aim to evaluate which aeroallergens cause sensitization in the allergic patients in Akdeniz Area, Turkey, as well as their frequency of occurrence.

Objectives: In this study the demographic properties, the diagnoses, total IgE levels, the sensitization against aeroallergens detected via EPT, the dates of application of the EPT and peripheric eosinophil counts at the time of EPT application are analyzed in 510 patients aged 2-18 years, between January '14 and July '15, who were admitted to Akdeniz University Pediatric Allergy—Immunology and Pulmonology Departments and Antalya Education and Research Hospital Pediatric Allergy - Immunology Department, presented with allergic history or diagnoses. All patients were applied EPT during their follow-ups and sensitivity against at least one aeroallergen was detected. The seasonal distribution of these aeroallergens is also analyzed.

Results: 1180 children were accepted for this study, to which allergic skin test were applied between January '14 and July '15. It was seen that 510 patients (43.2%) had positive response to at least one aeroallergen and 402 patients among them (78.8%) had positive response to more than one aeroallergen. 58.4% of the patients who has showed positive EPT were males and 41.6% were females. The most frequently detected sensitivity (69%) were against house dust mites. Second and third frequently detected sensitivities were against, respectively, tree pollen mix (54.9%) and grass/weed mix (52.5%). The other allergens were detected as, respectively, animal danders (45.3%), fungi mix (43.4%), herb/pollen mix (34.9%), cockroach (16.9%) and olea (6%). Further, by analyzing the seasonal distributions of allergens, it was seen that the most frequent sensitivity was against house dust mites in all seasons.

Conclusions: As a result, in allergic patients the prevention from specific allergens has an importance in eliminating and managing the symptoms. For this reason, the disclosure of the regional differences of sensitivity to one allergen is necessary.

0623 | Sensitization patterns to the common pollens in the city of Manila, Philippines

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Introduction: Allergic sensitization is a known risk factor for the development of atopic diseases. Grass and tree pollens are one of the most common triggers of allergic disease worldwide. The type of pollen species differ geographically according to climate and local species. This study identifies the specific patterns of pollen sensitization which may provide relevant clinical insight on the risk of allergy.

Objectives: The study aims to identify patterns of allergic sensitization to pollens among individuals in the city of Manila, to compare sensitization patterns and its association with atopy and to determine sensitization patterns in association with serum IgE levels.

This is a cross-sectional study prospectively conducted in Manila City from April to July 2016. Subjects aged 2-70 were included in the study. Standardized questionnaires in English and Filipino translations adapted from the International Studies of Asthma and Allergy in Children (ISAAC) validated for Filipino patient were used, Skin prick test to 15 pollen allergens were done and total serum IgE levels were extracted.

Results: Five hundred thirteen subjects were included. Of which 130 (25%) were atopic and 383 (75%) were non-atopic. One hundred twenty one (23.6%) were children and 392 (76.4%) were adults; 316 (62%) were female and 263 (51%) had a history of allergic disease. Sensitization to pollens were found in 25% of subjects.

Of the 130 atopic subjects, IgE levels were increased in 77-%.Twenty-eight percent were monosensitized and 49% were polysensitized. Sensitization was significant to the tree pollen *Mangifera indica* ($P = .005$).

Conclusions: *Mangifera indica* was identified as the most common allergen in the city of Manila. Sensitization was only significantly associated with asthma and allergic rhinitis. Sensitization was associated with elevated IgE levels. Other significant pollens such as *Acacia auriculiformis*, *Mimosa sp.*, *Amaranthus spinosus*, *Lanatana camara*, *Pilea microphyla* and *Chloris barbata* in different age groups may be also useful for selecting the allergen extracts to be added to skin prick test panels in our setting.

0624 | Aeropolinologic screening in patients with pollinosis

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Introduction: The clinico-epidemiological study revealed that Georgia is distinguished with diversity and frequency of allergic diseases, especially high rate of pollinosis caused by the acute factors of eco-geographical climate: air temperature, humidity and the variety of plants represented in the same region.

Objectives: We study aimed to establish specific IgE specificity in the patients with pollinosis among the population of west Georgia. In the study have been involved 89 patients (among them 44 males and 45 females) of different ages. I step—To detect allergenization degree, total serum IgE levels, specific IgE, using modern automated system - "Immuno CAP 100", were estimated in the patients. II step - Monitoring of aeropollutants concentration was conducted by using aeropolinometer "Burkard Trap". Results allowed us to divide 89 involved patients into two groups: I—the group contained 59 patients diagnosed with pollinosis while the II group comprised 30 patients suffering from other allergic diseases (atopic dermatitis, bronchial asthma).

Results: Identification of a particular allergen was carried out by investigation of allergen-specific IgE. In the patients with pollinosis of I study group, a specific positivity of specific IgE to the weeds (Wx2)—ambrosia, plantain, clasp/tarragon, atriplex—in 47 (68%) on average; tree dust (Tx9) - alder, lactarius piperatus, nuts, oak, willow - 21 (30%) on average; and cereals (Gx1) - festuca pratensis, lolium temulentum, timoti grass, poa - 19 (28%) on average was revealed. According to the study results, among the etiologic factors of pollinosis, the highest percentage comes on plant allergens-aeropollutants, which is proved by appropriate specific IgE positivity. The patients suffering from pollinosis were supplied with the data of aeropolinometer "Burkard Trap", developed by our clinic permanently updating calendar for distribution of aeroallergens in Imereti region, which reflects the concentration of blossoming plant-trees and atmospheric aeroallergens in the air at a given period of time. Increased concentration in blood indicates to the presence of atopic allergy reaction to inhalative allergens. "Immuno CAP 100" allowed us to specify/determine the presence of specific IgE to certain allergens in blood serum.

Conclusions: The high level of specific IgE to aeroallergens was revealed in the patients with pollinosis, the specificity of which was particularly strengthened by correlation with other allergens specific for the given region.

0625 | Common aeroallergens and food allergens seen among allergic children in the United Arab Emirates

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Introduction: The aim of this study is to determine the most common aeroallergen and food allergen via the skin prick test.

Objectives: The study design is retrospective cross-sectional. Data was collected from the results of 206 patients that have undergone skin prick test during 2013-2015 in the allergy clinic at the

University Hospital of Sharjah. Skin prick tests were performed with 15 aeroallergens selected based on the most common identifiable allergens in the region, and 27 individual food allergens according to patient history. A mean wheal diameter of at least 3 mm greater than the negative control was taken as positive. Analysis was conducted via SPSS version 21.

Results: The patients' ages ranged from 2 months to 16 years (84 males, 122 females). From our study population, 60.70% had allergic rhinitis, 46.10% had asthma symptoms, 26.20% had atopic dermatitis, and 26.20% had food allergy. Among the one's positive for aeroallergens, 85% were poly-sensitized and 15% were single sensitized. House dust mites showed the highest prevalence of sensitivity (D. Farinae 37.04%, and D. Pteronyssinus 36.51%), followed by cat dander (32.25%) and Feather mix (31.68%). The least common of all indoor aeroallergens was Cockroach (15.84%). Molds showed the following percentages: Alternaria 25.9%, Cladosporium mix 19.58% and Aspergillus mixture 17.46%. Russian thistle had the highest percentage of sensitivity (32.25%) making it the most prevalent outdoor aeroallergen in our study. Chenopodiaceae showed a prevalence of 26.73% followed by PhleumPart Timothy (20.63%) and Palm date (19.80%). The least common outdoor allergen was Bermuda grass 16.9%. The most common food allergens were peanut (48.15%), egg (46.25) and Cow's milk (40.74%).

Conclusions: In conclusion, the most common aeroallergen identified based on skin prick test in the allergy clinic in the UHS was house dust mites in all allergic diseases, which corresponds with the results of similar studies conducted in our region. Identifying allergens plays an important role in management, giving appropriate allergen avoidance and possible immunotherapy. The commonest allergic disease among our population was allergic rhinitis. The most common food allergen was peanuts, followed by eggs and then milk. Data on food allergy is scarce in the UAE and further studies looking at food allergy prevalence are needed.

Aeroallergen	% of sensitized patients
D. FARINAE	37.04%
D. PTERONYSSINUS	36.51%
ALTERNARIA	25.93%
PHLEUMPARTTIMOTHY	20.63%
CLADOSPORIUM MIX	19.58%
ASPERGILLUS MIX	17.46%
CAT DANDER	32.25%
RUSSIANTHISTLE	32.25%
FEATHERS MIXTURE	31.68%
CHENOPODIACEAE	26.73%
PALMDATE	19.80%
COCKROACH	15.84%
BERMUDA GRASS	16.90%
RABBIT HAIR	7.84%
HORSE HAIR	4.95%

0626 | Sensitisation and allergy patterns to inhalant and food allergens in a population from the Mediterranean area

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Introduction: Olive pollen is one of the most important causes of seasonal respiratory allergy in the Mediterranean basin, and peach is the main cause of vegetable food allergy. However, there is a lack of studies analysing the pattern of sensitisation and allergy of these allergens in this area.

Objectives: We determined the prevalence of sensitisation and allergy to olive pollen and peach in a population from southern Spain (Periana, Málaga). We estimated sample size stratified in 10 age intervals (1-90 y-old). A questionnaire and skin prick tests (SPT) to relevant inhalant and food allergens were performed.

Results: A total of 1396 individuals were included. One third was positive to at least one inhalant allergen and 5.9% to at least one vegetal food allergen. Almost one fifth (18%) were positive to olive pollen (CI: 16.4-20.5) and 2.1% to peach, being all of the latter also positive to Pru p 3. Around half (51%, CI: 48.9-54.3) of individuals reported rhinitis symptoms; 22.6% (CI: 20.6-25.1) reported asthma, and 40% (37.9-43.23) reported conjunctivitis. Clinical entities suggesting food allergy were reported by 8% of the cases (6.3-9.5), with urticaria and/or angioedema being the most common. SPT positivity to olive pollen in the first age interval was 18%, peaking to 29% in the third interval and decreasing progressively ($P < .0001$). No significant variation due to age was observed in SPT to peach and Pru p 3.

Conclusions: In a well-defined areas of high exposure to inhalant (olive tree pollen) and food allergens (peach), a relatively high proportion of individuals become allergic to olive pollen, particularly for those between 20-39 years old. Most of these tolerated peach.

0628 | Control of Fel d 1 levels in a cat allergen exposure chamber

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Introduction: Exposure to cats in an allergen chamber is a naturalistic means to assess responses to cat dander within a controlled

environment. However, control of Fel d 1 levels remain problematic with reported values varying by orders of magnitude within and between chambers possibly because cat dander is aerosolized by shaking blankets used by the cats. The aim of this study is to assess methods to ensure stable and consistent levels of Fel d1 for future cat allergen chamber exposure studies.

Objectives: The chamber, volume 520 ft^3 (14.7 m^3) was designed and built to accommodate two neutered cats and 1-2 subjects. Samples are obtained at 3 locations in the chamber using portable air sampling pumps (Gillian 5000) with glass fiber filters (Millipore), flow rate 4 L/min. Fel d 1 is quantified using ELISA (Indoor Biotechnologies). Samples will be collected daily for 15-minutes, to follow evolution of Fel d 1 levels and their similarity at different points in the room before and after shaking the cats' blanket. Chamber cleaning and air circulation as a means to control and homogenize allergen levels will be evaluated.

Results: Preliminary data from one sampling pump obtained for intervals of 15 minutes, after shaking the cat's blanket, showed a decrease in Fel d 1 levels from 39.7 to 12.3 to 9.2 to 4.4 ng/m^3 after 15, 30, 45, and 60 minutes, respectively suggesting this is sub-optimal to aerosolize cat dander.

Conclusions: The results of validating the chamber should allow controlled levels of Fel d 1 to be maintained in future cat allergy studies. Furthermore, the chamber may enable more accurate evaluations of efficacy of pharmaceutical interventions in cat allergy.

SUNDAY, 18 JUNE 2017
TPS 04
ALLERGY EPIDEMIOLOGY

0630 | Canine sensitization in Fel d 1 allergic patients

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Introduction: The main cat allergen, Fel d 1, a uteroglobin-like protein from the secretoglobin family, is an exception among mammal allergens, because in the majority of cases the main allergen is lipocalin.

Objectives: Establishing the frequency of canine sensitization in Fel d 1 allergic patients.

Results: 69 patients with a positive feline allergy diagnosis and 30 controls went through an allergological interview and a physical examination. The total IgE (tIgE) concentration of all patients as well as their allergen-specific IgE (asIgE) against feline and canine allergens and canine (Can f 1, Can f 2, Can f 3, Can f 5) and feline (Fel d 1, Fel d 2, Fel d 4) allergen components were measured (ImmunoCap). 61 patients had heightened levels of specific IgE to Fel d 1. In the same group, 30 patients had elevated levels of IgE against Fel d 1, but with no specific antibodies against Fel d 2 and Fel d 4. Within that group 19 had an isolated sensitization to Fel d 1 among the examined animal allergen components. Curiously, 11 patients had heightened levels of IgE against Fel d 1, no specific antibodies against Fel d 2 (albumin) or Fel d 4 (lipocalin), but at the same time were sensitized to canine allergens.

Conclusions: Among patients sensitized to felines, with heightened levels of specific IgE to the main allergen Fel d 1, but who do not have specific IgE to other feline components, the risk of a cross-allergy to other fur animals is still high.

0632 | Clinical impact of mosquito aedes aegypti in allergic respiratory diseases

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Introduction: Allergic reaction to *Aedes aegypti* is associated with saliva allergens introduced by mosquito sting. However, several allergens have been described in the body of this insect, suggesting its participation in the induction of allergic respiratory diseases.

Objectives: To investigate the clinical relevance of the *A. aegypti* mosquito in allergic rhinitis.

Results: Skin Prick Test (SPT) to whole body extracts of *A. aegypti*, *Blomia tropicalis* and *Dermatophagoides spp*, were performed in 29 patients with rhinitis and 12 healthy subjects (controls) residing at a tropical area of Colombia. All subjects gave informed consent for this study and were challenged with either 200 μL of saline or 1 mg *A. aegypti* extract/200 μL of saline. In addition, serum IgE, IgG and IgG4 levels to *A. aegypti* whole body extract was determined by ELISA. 18 patients with rhinitis (62%) were SPT positive to *A. aegypti*. All subjects in the rhinitis group except 2 were SPT positive to mite extracts. One control subject showed positive SPT to *A. aegypti*. Ten of eighteen (55.5%) allergic patients with positive SPT to *A. aegypti* were positive by nasal challenge test. Two patient with positive nasal challenge and SPT to mosquito extract was SPT negative to mites. None were positive with saline challenge test. In allergic patients the frequency of positive IgE, IgG and IgG4 levels to *A. aegypti* was 27.5, 69.0 and 28.0%, respectively.

Conclusions: *A. aegypti* can induce allergic rhinitis. Regardless whether sensitization to *A. aegypti* is by cross-reactivity with other allergenic sources like mites or not, the positive nasal provocation test indicates that IgE sensitization to mosquito is clinically relevant and could be induced not only by the mosquito sting but also for the inhalation of their proteins. The potential allergenic role of each *A. aegypti* protein should be further investigated.

Subjects n = 42

0633 | Prevalence of low diamine oxidase in patients with seasonal allergic rhinitis and cross food allergy

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Introduction: Recent decades were marked by a worldwide increase in the level of allergic diseases in general, and seasonal allergic rhinitis (SAR) in particular. Epidemiological studies have indicated that the prevalence of SAR in adult population across different

countries was 8-10%. Furthermore, according to the literature, the frequency of cross food allergy (CFA) in patients with seasonal allergic rhinitis (SAR) varies between 20 and 70%. This combined allergic pathology is linked to damage of the digestive system, which further leads to the absorption of incompletely digested food components and formation of hypersensitivity to food, house dust, epidermal and pollen allergens. Furthermore, a heavier version of the combined pathology results from the presence of the syndrome of low tolerance to histamine (SLHT). A hallmark of SLHT are low levels of diamine oxidase (DAO), which leads to excess histamine absorption from food and other sources. To date, there are no studies exploring the incidence of this syndrome in patients with SAR and CFA and so, the severity and prevalence of this combined pathology remains to be investigated.

Objectives: To examine changes in the level of DAO in patients with SAR with and without CFA. To examine the incidence of SLHT in patients with SAR with and without the CFA. We carried out an allergic survey of 217 Kyiv residents suffering from SAR and sensitization to tree pollen. The age of patients was between 18 and 55 years, with an average age of 36.2 $\pm$ 3.25 years. The diagnosis of SAR was defined based on symptom complains, allergic history data, allergy survey results (skin prick test, levels of total and allergen-specific IgE, as well as the content of allergen-specific IgE to recombinant allergens), clinical and instrumental examination of ear, nose and throat. Syndrome of the low tolerance to histamine was established on the basis of patient's specific complaints, analysis of questionnaires and laboratory examination data of the level of diamine oxidase.

Results: Low DAO levels in patients with SAR and CFA was determined at 10.5%, while in the group with SAR and without CFA it was only 1% (the difference was statistically significant at $P < .5$, t-criterion Student 3.16).

Conclusions: It appears that low DAO and SHLT occurs more frequently in cases of combined SAR and CFA pathology (10.5% vs 1% in SAR only group). This knowledge improve personalized approach to the elimination diet frequently prescribed to patients with SAR and CFA.

0634 | Overweight and obesity in school-age and adolescence are associated with airway obstruction—results from a population-based cohort study

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Introduction: Few large prospective studies have investigated the impact of body mass index (BMI) on lung function during childhood.

Objectives: The aim of the present study was to analyze the association between BMI status at 8 and 16 years, including changes in BMI status, and lung function at 16 years in the BAMSE population-based birth cohort.

Methods: A total of 2889 children were included in the analyses. Height and weight were measured at 8 and 16 years and categorized into thinness, normal weight, overweight, and obesity per International Obesity Task Force guidelines. Lung function was measured by spirometry at 16 years. Small airway function was assessed by impulse oscillometry at 16 years. Associations between BMI status (using normal weight as reference) and lung function were analyzed by linear regression.

Results: In cross-sectional analyses, both overweight and obesity were associated with higher forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1), but lower FEV_1/FVC (e.g. −3.5% [95% CI: −6.0; −1.0] and −4.3% [95% CI: −6.9; −1.8] in obese girls and boys, respectively, at 16 years). Further, both overweight and obesity were associated with higher airway reactance ($AX^{0.5}$) and frequency dependence of resistance ($R_{5\text{-}20}$), (e.g. 56.8 Pa/L*s [95% CI: 38.3;75.4] and 47.8 Pa/L*s [95% CI: 34.9;60.7] in obese girls and boys, respectively at 16 years). In longitudinal analyses, persistent overweight between 8 and 16 years was associated with lower FEV_1/FVC and higher $R_{5\text{-}20}$ and $AX^{0.5}$ at 16 years, compared to persistent normal weight.

Conclusions: In childhood and adolescence, both overweight and obesity, and particularly persistent overweight, were associated with evidence of airway obstruction, including effects on the small airways. However, lung volumes and flows were in general higher in overweight compared to normal weight children.

0635 | Associations between serum carotenoid and tocopherol concentrations and risk of asthma in childhood: a nested case-control study in Finland

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Introduction: The dietary antioxidant hypothesis proposes that the rise in asthma during the second half of the last century may partly be a consequence of decreased consumption of foods rich in antioxidant nutrients. So far, studies investigating the role of dietary antioxidants in asthma have remained conflicting. Whilst some data indicate that the role of antioxidants in childhood asthma risk may have a critical time window of effect, only a well-designed longitudinal cohort study can clarify this hypothesis.

Objectives: We investigated the age-specific and longitudinal associations between serum carotenoid and tocopherol concentrations

during the first 4 years of life and risk of asthma risk by the age of 5 years.

Based on a case-control design nested within a Finnish birth cohort, 146 asthma cases were matched to 270 controls on birth time, sex, genetic-risk, and birth place. Non-fasting blood samples were collected at the ages of 1, 1.5, 2, 3, and 4 years and serum carotenoids and tocopherols were analyzed. Parents reported the presence and age at start of persistent doctor-diagnosed asthma in the child at the age of 5 years. Data analyses were conducted using generalized estimating equations.

Results: In age-specific analyses, we did not find statistically significant associations between serum carotenoids and tocopherols and the risk of asthma. However, in longitudinal analyses, both lower and higher quartiles of α-carotene (1^{st} quartile vs 2^{nd}&3^{rd} quartile: OR 1.48, 95% CI 0.99-2.25; 4^{th} quartile vs 2^{nd}&3^{rd} quartile: OR 1.29, 95% CI 0.82-2.03) and γ-tocopherol (1^{st} quartile vs 2^{nd}&3^{rd} quartile: OR 1.50, 95% CI 1.06-2.12; 4^{th} quartile vs 2^{nd}&3^{rd} quartile: OR 1.23, 95% CI 0.82-1.86) borderline increased the risk of asthma.

Conclusions: Our findings do not support the suggestion that the increased prevalence of asthma may be a consequence of decreased intake of antioxidant nutrients. Moreover, we did not confirm any critical time window of impact of antioxidants on asthma risk. Replication of these findings in similar longitudinal settings will strengthen this evidence base.

0636 | Allergic diseases and vitamin D

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Introduction: Several studies have shown that vitamin D deficiency plays an important role in allergic diseases such as asthma, allergic rhinitis, and urticaria

Objectives: We researched the vitamin D levels in these diseases.

140 patients with allergic rhinitis (AR), urticaria (U) and asthma (A) who were referred to our outpatient clinic were included in the study.

The mean age of the patients was 41.76 ± 1.51 and the mean age of the control group was 49.7 ± 9.59. The patients were divided into 7 groups as AR (20), U (20), A (20), AR + A (20), AR + U, A + U (20) and AR + A + U (20). Vitamin D levels were measured in these patients. As a control group, vitamin D levels in 20 healthy subjects were measured.

Results: Vitamin D levels in patients with Asthma were 23.35 ± 21.14, in patients with AR were 22.08 ± 11.74, in patients with urticaria were 18.07 ± 6.20, in patients with asthma + AR were 18.83 ± 9.74 in patients with asthma + urticaria were 17.2 ± 11.34, in patients with AR + urticaria were 14.02 ± 7.22, in patients with asthma + AR + urticaria were 12.7 ± 6.18 and in the control group was determined as 28.85 ± 14.88.

Conclusions: As a result, vitamin D levels were found to be lower in AR + A + U patients group. $P < .005$.

0637 | Report of pilot study of prevalence of asthma, allergic rhinoconjunctivitis and atopic dermatitis in the pediatric age

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Introduction: The allergic diseases in childhood and adolescence have a high prevalence. So it's a major public health problem at both the national and the international level. In recent years, diseases allergic have increased according to some reports between the 20 and 50% in the general population. The Allergic Rhinitis has a high prevalence, affects up to 40% of patients in the pediatric age, the prevalence of asthma is estimated at 8% and atopic dermatitis of 8-20% of the population pediatrics. This chronic inflammatory diseases can affect significantly the quality of life of the patient and the family environment.

Objectives: Identify the prevalence, trends and risk factors for asthma, allergic rhinoconjunctivitis and atopic dermatitis in children and adolescents through a questionnaire validated and standardized with the method ISAAC.

Results: A prospective, cross-sectional, analytical and observational pilot study was conducted to know the prevalence of the most common allergic diseases through ISAAC, which is validated for this purpose. It was out in random manner, including schools belonging to the North of the Mexico city, it was subsequently selected participating individuals of how random those who are on the official lists of the institution.

ISAAC questionnaires were answered by the parents in the Group of school children of 6 and 7 years; the adolescents between 13 and 14 years old themselves answered the questionnaire.

In 9 schools were applied 302 questionnaires of adolescents and 285 schoolchildren. In the schoolchildren group 49.8% were men and 50.2% women, distributed by age 6 years 49.1% and 50.2% 7 years, in regard to the group of teenagers the 57.9% were men and 42.1% women.

In the schoolchildren group found a cumulative prevalence for symptoms rhinitis 68.1%, these affected the quality of life in 5.6%, asthma 9.1%, allergic conjunctivitis 35.1% and atopic dermatitis 9.1%.

In the group of teenagers found a cumulative prevalence for symptoms of rhinitis 66.2%, these affected the quality of life in 4.3%, asthma 10.6%, of these 0.7% referred affected the quality of life, allergic conjunctivitis 18% and atopic dermatitis 5.6%.

Conclusions: The allergic diseases in the north of Mexico City persist with a high prevalence, however with an apparent decrease in symptoms of allergic rhinitis and atopic dermatitis, unlike asthma symptoms have increased in both groups evaluated in comparison with the results of the 2002 ISAAC.

0638 | Rural area of the Natural Park Lonjsko Polje, Croatia—Prevalence of allergic disease symptoms in young adolescents

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Introduction: The study on prevalence of allergic diseases in The Natural Park Lonjsko Polje was started in the year 2015. Prevalence of symptoms of wheezing (Wh), allergic rhinitis (AR) and atopic dermatitis (AD) in a population of 100 children of 6–7-years-age group was 11% for Wh, 8% for AD and 14% for AR. The aim of this study was to explore the prevalence of allergic diseases among adolescents in the area of the Natural Park Lonjsko Polje, Croatia, a special ornithologic reserve and the largest swamp area in Europe

Objectives: Original ISAAC questionnaires, consisting of questions on child's demographic characteristics, core modules on wheezing, atopic dermatitis and allergic rhinitis and supplementary modules were completed by parents of 13–14 year-old (13 years 0 months–13 years 11 months) children from five elementary schools of the surrounding area of The Natural Park Lonjsko Polje. A total number of 160 questionnaires were returned and analyzed.

Results: 75 children (47%) were boys and 85 (53%) were girls. 62% of children live or have lived earlier in their lives in small villages and 26% in suburbs with a lot of green areas. 100% of participants eat mixed meat diet. Prevalence of wheezing in a 12-months period was 0.6%, of itchy rash on predilectic areas for atopic dermatitis was 4.3%, while 12-months prevalence of c of allergic rhinitis was 9.4%.

Conclusions: Results on 13–14-year-age group show lower prevalence of allergic disease symptoms in comparison with 6–7-years-age group. Compared with results in the coastal part of Croatia, in which in the seven years period there was observed a significant increase in the current prevalence of all symptoms related to asthma, AD and AR (in a school year 2008/2009 a 12-months prevalence of Wh was 14%, of AD 5.9% and of allergic rhinoconunctivitis 25%), our results show lower prevalence as well. These result might show protective role of the lifestyle in this area. For better comparison, larger number of participants will be needed.

[Correction added on 21 November 2017, after first online publication: Abstract 0638 has been added.]

0640 | Overview of allergic rhinitis incidence and treatment in Slovak Republic in 2015: results from nationwide prospective study

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Introduction: Allergic rhinitis (AR) represents a global health problem affecting 10-20% of the population. According to local publications, allergic rhinitis is the most common allergic diseases in Slovakia. Since AR is not considered as serious life-threatening disease its symptoms are very often underestimated and treatment is neglected.

Objectives: The objective of the study was to map on the sample of 7020 patients with confirmed allergic rhinitis in Slovakia in 2015 the type of allergic rhinitis, treatment with allergy immunotherapy, length of treatment, form of treatment, consumption of allergy pharmacotherapy and subjective presence of allergic rhinitis symptoms.

Results: Results showed that grass AR was the most frequent among patients (27.4%) followed by combination of grass and trees AR (16.9%), trees AR (15.0%) and house dust mites AR (14.1%). Allergy immunotherapy (AIT) received 46.6% patients, allergy pharmacotherapy 53.1% patients and 0.3% patients received combination of AIT and allergy pharmacotherapy. Length of treatment after 2 years was detected among 56.5%, with 16.5% patients receiving treatment for 5 and more years. Univariate analysis did not show any important significant difference between men and women. Comparison between children and adults showed several interesting results where adults received more frequently AIT compared to children (48.4% vs 44.2%; RR=0.9; $CI^{95\%}$ 0.84-0.96; $P = .0007$), subcutaneous AIT was most frequent in adults compared to children (7.5% vs 4.8%; RR=0.73; $CI^{95\%}$ 0.62-0.85; $P < .0001$), decrease in symptomatic treatment consumption was greater in adults compared to children (46.4% vs 42.7%; RR=0.93; $CI^{95\%}$ 0.86-0.97; $P < 0.003$).

Conclusions: Study had unique design for Slovak conditions and brings important epidemiological information about AR and AR treatment. AIT was used in more than half of screened patients and it is considered as highly effective treatment from the clinical perspective. We found additional room for improvement in earlier initiation of AIT in children.

0641 | Do pharmacy customers make good choices when they manage their allergic rhinitis?

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Introduction: Allergic rhinitis (AR) is frequently underestimated by both health care professionals(HCPs) and patients. Its management is often suboptimal as a result of delayed diagnosis, uninformed attempts by patients to self-manage with over-the-counter (OTC) medication or failure to engage a HCP.

Objectives: This study aimed to describe the demographic and clinical characteristics of adults who purchase medication(s) for the management of allergic rhinitis (AR) and evaluate the appropriateness of medication(s) purchased Methods: A cross-sectional observational study was conducted in a convenience sample of community pharmacies from the Sydney metropolitan area. Participants completed a researcher-administered structured questionnaire that included items covering demographics; symptoms; medication history and advice received from HCPs. An expert panel of clinical research pharmacists evaluated questionnaire responses and identified those that had AR and the appropriateness of medication(s) purchased according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines.

Results: Of the 296 participants that purchased medication(s) for nasal symptoms from 8 pharmacies, 201 were identified as having AR (44% intermittent and 56% persistent), 68% were female, 55% were aged $\geq$ 40 years and 66% had an AR diagnoses from a HCP. Almost 70% self-medicated with medications OTC and 30% had an interaction with the pharmacist. Overall, 88% purchased suboptimal treatment based on ARIA guidelines. The main reason reported by pharmacy customers to self-manage was experiencing persistent symptoms which were not having a major impact on their quality of life/well-being.

Conclusions: Most adults with AR self-select treatments from community pharmacy without seeking advice from a HCP. The high incidence of suboptimal selection of treatment provides tremendous opportunities for pharmacists to assess treatment choices and intervene appropriately to optimise the management of AR.

0642 | Patient perspectives with regards to how they measure allergic rhinitis severity and allergic rhinitis control

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Introduction: Despite the prevalence, chronicity and burden imposed on individuals and society, allergic rhinitis (AR) continues to be trivialized by some patients.

Objectives: This study sought to understand how people with AR gauge its severity as well as their perceptions of what constitutes disease control.

Methods: Explorative semi-structured qualitative interviews were conducted with adults with self reported allergic rhinitis. Participants were recruited via traditional print media, social media and invitations to a volunteers database. Interviews were transcribed and analysed thematically.

Results: Forty five people with AR participated in an interview. Several factors were identified with which people with AR use to gauge the severity of their condition. These included: their response to non-prescription medicines(i.e. it is not severe if can be treated with over the counter medicines); the frequency of medicines use required to reduce impact of AR on their quality of life (QOL)(i.e. the more frequent their use of medicines, the more sever the AR); the need to consult a health care professional to obtain a medicine to provide symptom relief(i.e. require a medicine that can only be prescribed to obtain symptom relief were thought to be more severe); the existence of comorbidities(i.e. where they also have asthma and recognized their AR can make their asthma worse) and their existing relationship with their general practitioner(i.e. those with existing relationships were more informed about how to gauge their AR control). AR control was perceived to be where symptoms were reduced to where they did not impact on QOL. There was an overall sentiment, that symptoms would never be completely resolved with the use of medicines and a reduction in severity was the most that could be expected.

Conclusions: People with AR that do not consult a health care professional use their personal experience with over the counter medicines with which to gauge their AR severity and control. Resources need to be developed for these people to more accurately self assess their condition and be able to identify when they need to consult with a health care professional about their AR.

0643 | Calcium preparations do not inhibit allergic reaction—A randomized controlled trial

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Introduction: Calcium preparations are commonly used in most of Central and Eastern Europe in many allergy-related skin reactions associated with severe itching, erythema and wheals, allergic rhinoconjunctivitis and as a remedy medication for insect bites. The mechanism of action is unknown. Well designed, controlled studies are lacking. The aim of this study is to assess the efficacy of calcium on allergic reactions of the first type.

Objectives: This is a randomized, double-blinded, placebo-controlled study. Forty adult volunteers suspected of having an pollen-induced allergic rhinitis, allergic rhinoconjunctivitis or asthma were included to the study. The subjects received oral calcium carbonate (1000 mg) or placebo (lactose) 3 times a day for 3 days. Skin-prick tests (SPT) were performed pretreatment, 4 hours after the intake of the first dose and 72 hours after the first performed SPT (after application of all doses of drugs). SPTs were performed with 11 common standard aeroallergen extracts, histamine as positive control and diluent as negative control. The size of wheal response to SPTs was measured. Skin reactivity was also estimated by using visual analog scale (VAS) to assess pruritus intensity. The percentage reduction of wheal responses and itching sensation vs baseline by test drugs was calculated.

Results: In the calcium and placebo group, differences between mean diameters of the wheal measured at 2 time points compared to baseline was not significant ($P > .05$). There were no significant differences between study drugs in mean standard error VAS scores for itching perception after SPTs inoculation.

Conclusions: Using a SPT model, we found that calcium preparation neither given in one dose nor in three-day treatment does not reduce the size of the wheal and symptoms of pruritus in comparison with placebo. Therefore, even when calcium supplement is administered for a long period, it doesn't need to be stopped prior to allergen skin testing.

		Mean % reduction in wheal area (vs baseline)		*P* (verum vs placebo)
	Time	Verum	Placebo	
histamine	4 h	−3.33%	−4.58%	.8581
	72 h	−4.79%	−2.08%	.6119
pollen allergens	4 h	1.48%	−0.54%	.8418
	72 h	−0.88%	4.99%	.4698

		Mean % reduction of itching (vs baseline)		*P* (verum vs placebo)
	Time	verum	placebo	
SPTs	4 h	−3.93%	4.08%	.3788
	72 h	13.79%	17.78%	.7191

0644 | Comparison of the prevalence of allergic diseases and risk factors of asthma development in urban and rural Pomeranian region

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Introduction: The research Epidemiology Allergic Diseases in Poland (ECAP) showed differences in the prevalence of allergic diseases depending on the place of residence indicating that citizens have a higher prevalence of asthma and allergic diseases. The research compared the major provincial cities and areas Zamojszczyzna. Observations of patients living in Pomeranian region suggest to the mixed character of the rural area of Tri-City agglomeration.

Objectives: The aim of research was to determine the prevalence of diseases (asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, urticaria, food allergies, allergy to insect venom and drugs) in the population of the province of Pomerania, among patients living in the city and countryside. The second objective was to evaluate the significance of the factors predisposing to the development of asthma and allergy (sex, smoking, having a bird or cat, housing conditions). The analysis was based on constructed for the research questionnaire containing questions used in epidemiological studies ISAC, ECHRS, ECAP. Statistical analysis of the collected results was made in the program Statistica v.12, Chi2 test.

Results: The research group consisted of 619 people - 457 women and 162 men, 180 residents of villages and 439 urban residents. A statistically significant difference and a higher incidence among residents of the city were found in patients with food allergies ($P = .0002$); urticaria ($P = .009$); atopic dermatitis ($P = .0025$); allergies to drugs ($P = .0001$). There were no differences in the prevalence, depending on the place of residence, of asthma, allergic rhinitis, allergic conjunctivitis, allergic reactions to insect venom. More frequent development of asthma was observed in patients treated for allergic rhinitis OR=4.29 (CI 1.02-18.03). Sex, smoking, having a bird or a cat, the living conditions were statistically insignificant.

Conclusions: The results of the work suggest the necessity of conducting education on healthy nutrition, reduce polypharmacy, and the diagnosis and treatment of allergic conjunctivitis in patients treated for allergic rhinitis. In spite of not finding the correlation between the habit of cigarette smoking and an increased risk of developing asthma in the study group, based on other works it is recommended to encourage smokers to treat addiction in order to reduce the risk of developing and dying from tobacco-related diseases.

SUNDAY, 18 JUNE 2017
TPS 05
DIAGNOSIS AND MANAGEMENT OF RHINITIS

0646 | A model proposal for allergic rhinitis studies: isolated sensitivity to juniper pollen

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Introduction: Considering that patients with allergic rhinitis spend their lives interacting with the environmental factors, we reckon that the studies conducted in the natural environment have much more precious, and we believe they could be used to support allergen challenge chambers (ACC) studies.

Objectives: The present study was planned to determine whether an efficient "natural environmental model" exists in order to ascertain and compare the validity of clinical and experimental studies that are conducted in ACC, which pose many disadvantages.

Results: Juniper pollination season was found to be between the 4th week of January to the 4th week of September. Peak juniper pollen level was observed in March. Total symptom scores of the patients showed significant correlation with the pollen levels ($P < .05$). Pollen levels showed a positive correlation with temperature ($P < .05$), and a negative correlation with humidity ($P < .05$). Pollen levels did not show significant correlation with wind speed or amount of precipitation.

Conclusions: Isolated sensitivity to juniper pollen constitutes a natural model for treatment and follow-up of allergic rhinitis as it demonstrates isolation regarding both the allergic season and the patients. In order to support ACC studies with natural environment studies, we believe that isolated juniper pollen sensitivity model would be an appropriate model.

0647 | Real life effectiveness of mp-azeflu®* in persistent allergic rhinitis, assessed by visual analogue scale and endoscopy: data from Ireland

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Introduction: Most allergic rhinitis (AR) patients attending clinic have moderate/severe persistent disease. Meda Pharma's AzeFlu* (MP-AzeFlu) comprises intranasal azelastine hydrochloride, fluticasone propionate and a novel formulation, in a single device. Its real-life effectiveness is established in AR during 14 days. But, its effectiveness in those with persistent AR (PER) over the longer term is unknown.

Objectives: To assess the effectiveness of MP-AzeFlu in routine clinical practice in PER patients, using the ARIA-endorsed language of AR control (i.e. visual analogue scale (VAS)). A VAS score cut-off of 50/100 mm is recommended to assess control and guide treatment. The study had a prospective, observational design and included 53 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to label. Patients assessed symptom severity using a VAS from 0 mm (not at all bothersome) to 100 mm (very bothersome) in the AM prior to MP-AzeFlu use, on Days 0, 1, 3, 7, 14, 21, 28, 35 and 42. An endoscopy was performed on Days 0 and 28 and symptoms of 'oedema', 'discharge' and 'redness' scored on a 3-point scale for both nostrils (max score=12).

Results: MP-AzeFlu (1 spray/nostril bd; daily doses: AZE=548 μg; FP=200 μg) patients experienced a rapid VAS score reduction from 73.4 mm (SD 20.3) at Day 0-31.5 mm (SD 25.0) at Day 28 ($P < .0001$) to 28.1 mm (SD 24.1) on Day 42 ($P < .0001$), a reduction of 45.3 mm. VAS score reduction was rapid, with statistical significance vs baseline noted from Day 1 ($P = .0106$), and was consistent irrespective of phenotype, patient age, and disease severity. On average patients achieved the ARIA-defined VAS score cut-off of 50 mm before Day 7. Total endoscopy score reduced from 7.5 (SD 3.1) at baseline to 3.5 (SD 2.5) at Day 28. The % of patients with severe oedema on endoscopy (weighted mean of both nostrils) reduced from 53.1% at baseline to 3.8% at Day 28. A similar reduction in the incidence of thick/mucusy discharge (28.3% to 4.8%) and severe redness (34.9% to 0%) was also observed.

Conclusions: MP-AzeFlu provides effective and rapid control of PER in a real-world setting assessed by VAS. Symptom improvement was noted from Day 1, sustained for 42 days and associated with improved mucosal appearance after just 28 days. These data support MP-AzeFlu's position as the drug of choice for AR.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies.

0648 | Review of the efficacy and safety of MP-AzeFlu®* in children with allergic rhinitis

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Introduction: Meda Pharma's AzeFlu (MP-AzeFlu) (a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP) in a single spray) is approved for use in the U.S. in patients aged ≥6 years with moderate/severe allergic rhinitis (AR).

Objectives: To review MP-AzeFlu's paediatric efficacy and safety data. Two studies were conducted. The first (MP4008), a randomized double-blind, 14-day parallel trial compared MP-AzeFlu and placebo in children (n = 348) with moderate/severe SAR. Efficacy was assessed by children or caregivers using reflective total nasal symptom score (rTNSS) and reflective total ocular symptom score (rTOSS). The second study (MP4007) was a randomized, open label, 3-month trial comparing MP-AzeFlu with FP. Efficacy was assessed by subject-reported allergy symptom severity, in a subset of patients (aged 6-12 years; MP-AzeFlu: n = 264; FP: n = 89), rated daily on a 4 point scale from 0 to 3. Safety was assessed by subject and/or caregiver-reported adverse events (AEs) and nasal examinations.

Results: As the extent of children's self-rating increased, so did the treatment difference between MP-AzeFlu and placebo; MP-AzeFlu provided significantly better relief than placebo for rTNSS ($P = .002$), rTOSS ($P = .009$) and each nasal and ocular symptom assessed (except rhinorrhoea; $P = .064$) when children mostly rated their own symptoms. When treated for 3 months, MP-AzeFlu-patients experienced significantly greater symptom relief than that afforded by FP (−0.68 vs −0.54 pt reduction; Diff: −0.14; 95% CI: −0.28, −0.01; $P = .04$), corresponding to a −5.44 change from baseline in AM + PM rTNSS. The % of subjects with AEs was comparable between treatment groups. The most frequently reported AEs with MP-AzeFlu and FP, respectively, were: epistaxis (10% and 9%), headache (7% and 3%), cough (4% and 3%) and diarrhoea (1% and 4%). Improvements in nasal examination findings were observed in both groups. There were no findings of nasal mucosal ulceration or septal perforation.

Conclusions: MP-AzeFlu provides significantly greater symptom relief than either placebo or FP in children (aged ≥6-12 years) with AR. Caregivers are less able to accurately assess response to treatment with available tools. MP-AzeFlu is well-tolerated when given continuously for 3 months, with no safety signal noted which would preclude its long-term use.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies.

0649 | The evaluation of life quality changes and the analysis of influencing factors before and after the treatment of adult allergic rhinitis patients

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Introduction: Allergic rhinitis (AR) is a global health problem. The effectiveness of currently available medications is limited and therefore investigation for more effective drugs is essential. Intranasal corticosteroid sprays (INCSs) are commonly used for therapy of AR. The most effective treatment is immunotherapy.

Objectives: To investigate the level of life quality and the influence factors and furnish basis for improving life quality and treatment compliance of patients with allergic rhinitis.

Results: Adopt the rhino-conjunctivitis quality of life questionnaire (RQLQ), visual analogue scales (VAS), curing to obey the sex grade point questionnaire, quality of life and patient's compliance on cross sectional study. From January to December of 2015, 298 patients enter the inquisition. According to received with medicine guide, divided into group A1 and B1, and according to received medicine supervision, divided into group A2 and B2. Medicine guide include: the guide of using nasal spray in the morning and at night. Medicine supervision include: analysis of therapeutic effect and adverse effect. Multiple databases were established based on the questionnaire survey. SPSS17.0 software was used for the statistical analysis. The coefficient correlation of patient's compliance, cognitive level, RQLQ score, VAS score has statistical significance with the various aspects of life quality ($P < .05$).

Conclusions: Treatment adherence, the length of the course of the disease and the degree of education will influence the level of quality of life. Enhance the patient's compliance can improve the life quality of AR patients.

0650 | To study the value of patient education in treatment of allergic rhinitis

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Introduction: Allergic rhinitis (AR) is a global health problem. In recent years, its incidence is rising. Treatment systems include environment control, medicine treatment, immunotherapy and patient education. At present, medicine treatment still is the main therapy method. However, patients with the cognition to the disease process, personality characteristics of the disease itself, patients' adherence to treatment and the adverse drug reactions of treatment have important influence on therapy effect.

Objectives: To evaluate the effect of patient education on patients with allergic rhinitis (AR).128 patients of allergic rhinitis were recruited from July 2014 to December 2016. The patients were randomly divided into experimental group or control group according to Stochastic tables law, 64 patients in control group accepted only medicine treatment, 64 patients in experimental group accepted both medicine treatment and patient education. The difference in compliance with treatment, treatment effect, incidence of adverse drug reactions and complications, average costs and times of treatment between two groups were evaluated by the rhino-conjunctivitis quality of life questionnaire (RQLQ) score. The independent sample T-test and Chi-squared test were used for statistical analysis of SPSS17.0 software.

Results: The patients of experimental group showed more positive attitude to treatment compared to the patients of control group ($P < .01$). The average scores of each classification and overall symptoms after treatment in experimental group were lower than those in control group ($P < .05$).The incidence of adverse drug reactions and complications in patients with AR in experimental group was lower than that in control group ($P < .05$). The average times of treatment and costs of diagnosis and treatment in experimental group were significantly lower than those in control group ($P < .05$). The total score for RQLQ and the scores of seven dimensions in experimental group were lower than those in control group ($P < .05$).

Conclusions: Patient education can help the patient with AR to cooperate actively with treatment, to reduce the incidence of adverse drug reactions and AR complications, and to save medical costs and improve the life quality of AR patients.

0651 | Adaptation and validation of the rhinitis control assessment test (RCAT) for children between six and eleven years of age (RCAT kids)

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Introduction: Allergic rhinitis is highly prevalent and has a great burden among children. According to recent recommendations, allergic rhinitis management should be guided by the disease level of control. However, there is a lack of validated instruments to measure allergic rhinitis control in children. The Rhinitis Control Assessment Test (RCAT) is a simple and self-applicable questionnaire developed to assess allergic rhinitis control in adults and adolescents.

Objectives: To adapt and to validate the RCAT for children between six and eleven years of age. Sequential interviews with groups of 10 children and their parents were performed to test the comprehension and reliability of the questionnaire and its adapted versions. The final version (RCAT kids) was applied to 97 children with allergic rhinitis and their parents in two visits (4 weeks apart). Nasal and extra nasal symptom score (NSS and ENSS), peak nasal inspiratory flow (PNIF) and medical opinion were recorded in both visits.

Results: In the final version, the same six original RCAT questions were maintained: three were addressed to the parents and three to the children, with the inclusion of a face scale. Correlations between RCAT kids score and NSS, ENSS and PNIF were, respectively: −0.78, −0.54, 0.39 ($P < .001$). RCAT kids score was significantly different according to the medical opinion. 23 points was the best cut-off to discriminate controlled from uncontrolled rhinitis: 79% of sensitivity, 86% of specificity and AUC of 0.82. Among children with stable clinical conditions in both visits (N = 78), RCAT kids showed agreement of 86% and Kappa of 0.63 ($P < .001$).

Conclusions: RCAT kids is a valid and reproducible questionnaire to evaluate allergic rhinitis control among children between 6 and 11 years of age.

0652 | Usefulness of electronic nose breath analyzer in patients with persistent rhinitis

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Introduction: Rhinitis is a heterogeneous inflammatory condition. The electronic nose (e-nose) is a new technology capable of distinguishing volatile organic compound (VOCs) breath-prints in exhaled breath among different inflammatory diseases. We hypothesized that e-nose can distinct patients with rhinitis from healthy subjects.

Objectives: The aim of the study was to investigate the capacity of e-nose breath-print analysis to discriminate patients with persistent rhinitis and healthy controls.

Results: Twenty-four consecutively enrolled patients with persistent moderate rhinitis and fifteen healthy subjects were included in a cross-sectional pilot study. Breath-prints were analyzed by discriminant analysis on principal component reduction, resulting in cross-validated accuracy values. These two groups had similar demographic, clinical and functional characteristics. Breath-prints from patients with rhinitis were not distinguishable from healthy subjects (accuracy 83%; $P = .28$) in oral out-breath samples. Likewise, in nasal out-breath samples, breath-prints did not show any difference either (accuracy 73%; $P = .36$).

Conclusions: The recognition of VOCs profiles in exhaled air by an e-nose device is not able to discriminate patients with persistent moderate rhinitis from healthy controls.

0653 | Mp-AzeFlu®* improves sleep quality in patients with persistent allergic rhinitis: data from Austria, Ireland and Sweden

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Introduction: Most allergic rhinitis (AR) patients attending clinic have moderate/severe persistent disease and frequently report reduced sleep quality. Meda Pharm's AzeFlu (MP-AzeFlu) comprises intranasal azelastine hydrochloride, fluticasone propionate and a novel formulation, in a single device. Its real-life effectiveness has been established in AR during 14 days. However, its impact on sleep quality is unknown.

Objectives: The aim of this abstract was to assess the impact of MP-AzeFlu on sleep quality when used in routine clinical practice by patients with persistent AR (PER). 428 patients (≥12 years old) with moderate-to-severe PER were recruited into 3, prospective, non-interventional studies carried out in Austria (n = 214), Ireland (n = 53) and Sweden (n = 161). MP-AzeFlu was prescribed according to its summary of product characteristics. Patients assessed their sleep quality (7-days reflective) on days 7, 14, 21, 28, 35 and 42 using a 5-point scale from 'very good' to 'very bad'.

Results: Many patients in each country reported sleep disturbance prior to MP-AzeFlu prescription: n = 112 (52.3%) in Austria; n = 41 (77.4%) in Ireland; n = 82 (50.9%) in Sweden. MP-AzeFlu* treatment (1 spray/nostril bd; daily doses: AZE=548 μg; FP=200 μg) was associated with improved sleep quality, evidenced by an increase in the proportion of patients reporting 'very good' or 'good' quality sleep in the first 28 days of treatment, and a corresponding reduction in the proportion of patients reporting 'bad' or 'very bad' sleep quality (Table). Sleep quality improved at each time point assessed (all p-values for Day 7, 14, 21 and 23 are <0.0001 compared to baseline). Improved sleep quality occurred irrespective of phenotype (when classified traditionally)—in those with perennial AR (PAR) only and in those with both PAR & seasonal AR.

Conclusions: MP-AzeFlu improves sleep quality in patients with moderate-to-severe PER in a real-world pan-European setting. These data support MP-AzeFlu's position of the drug of choice for AR.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies

	Austria† (n ≤ 214)		Ireland (n ≤ 53)		Sweden† (n ≤ 161)	
	Day 0	Day 28**	Day 0	Day 28**	Day 0	Day 28**
Very good	2.4%	35.3%	0.0%	24.5%	3.7%	15.7%
Good	25.1%	44.6%	24.5%	50.9%	28.6%	44.4%
Fair	36.5%	17.3%	32.1%	15.1%	34.2%	25.9%
Bad	28.0%	2.2%	32.1%	5.7%	27.3%	12.0%
Very bad	8.1%	0.7%	9.4%	0.0%	6.2%	1.9%

†% without missing values; **$P < .0001$ in non-parametric signed rank test

0654 | Real life effectives of MP-AzeFlu®* in persistent allergic rhinitis, assessed by visual analogue scale: data from Austria

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Introduction: Most allergic rhinitis (AR) patients attending clinic have moderate/severe persistent disease. Meda Pharma's AzeFlu*

(MP-AzeFlu) is an intranasal AR treatment comprising azelastine hydrochloride, fluticasone propionate and a novel formulation, delivered in a single device. Its real-life effectiveness has been established in patients with AR over 14 days. However, effectiveness in those with persistent AR (PER) over the longer term remains to be determined.

Objectives: This study aimed to assess the effectiveness of MP-AzeFlu in routine clinical practice in PER patients, using the VAS (visual analogue scale) to determine AR control. A VAS score of 50/100 mm is recommended by ARIA (Allergic Rhinitis and its Impact on Asthma) as the cut-off to assess control and guide treatment decisions. The study had a prospective, observational design and included 214 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to summary of product characteristics. Patients assessed symptom severity using a VAS from 0 mm (not at all bothersome) to 100 mm (very bothersome) in the AM prior to MP-AzeFlu use, on Days 0, 1, 3, 7, 14, 21, 28, 35 and 42.

Results: MP-AzeFlu treatment (1 spray/nostril bd; daily doses: AZE=548 μg; FP=200 μg) was associated with a significant reduction in VAS score from 53.5 mm (SD 26.3) at baseline to 25.3 mm (SD 21.0) on Day 28 ($P < .0001$) and to 19.6 mm (SD 17.4) on Day 42 ($P < .0001$), an overall reduction from baseline of 33.9 mm. The VAS score reduction was rapid, with a statistically significant ($P < .0001$) reduction from baseline noted at Day 1. On average patients achieved the ARIA-defined VAS score cut-off of 50 mm after only 1 day of treatment. Results were consistent irrespective of patient age (i.e. 12-17 years, 18-65 years, >65 years), gender, severity (i.e. more severe: baseline VAS score 50-74 mm; less severe: baseline VAS score 75-100 mm) or traditional AR phenotype (i.e. PAR only or SAR + PAR).

Conclusions: MP-AzeFlu provides effective and rapid control of PER in a real-world setting in Austria assessed by VAS. Symptom improvement was noted from Day 1 and was sustained for 42 days. These data support MP-AzeFlu's position as the drug of choice for AR.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies.

0655 | Real life effectiveness of MP-AzeFlu®* in persistent allergic rhinitis, assessed by visual analogue scale: data from Sweden

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Introduction: Most allergic rhinitis (AR) patients who see their doctor have moderate/severe persistent disease. Meda Pharma's AzeFlu (MP-AzeFlu) is an intranasal AR treatment comprising azelastine hydrochloride, fluticasone propionate and a novel formulation, delivered in a single device. Its real-life effectiveness has been established in those with seasonal and/or perennial AR over 14 days. However, effectiveness in those with persistent AR (PER) over the longer term remains to be determined.

Objectives: This study aimed to assess the effectiveness of MP-AzeFlu in routine clinical practice in PER patients, using the new language of AR control (i.e. visual analogue scale (VAS)). A VAS score of 50/100 mm is recommended by Allergic Rhinitis and its Impact on Asthma (ARIA) as the cut-off to assess control and guide treatment decisions. The study had a prospective, observational design and included 161 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to label. Patients assessed symptom severity using a VAS from 0 mm (not at all bothersome) to 100 mm (very bothersome) in the AM prior to MP-AzeFlu use, on Days 0, 1, 3, 7, 14, 21, 28, 35 and 42.

Results: MP-AzeFlu treatment (1 spray/nostril bd; daily doses: AZE=548 μg; FP=200 μg) was associated with a significant reduction in VAS score from 61.4 mm (SD 22.4) at baseline to 32.1 mm (SD 24.6) on Day 28 ($P < .0001$) and 26.1 mm (SD 24.3) on Day 42 ($P < .0001$), an overall reduction from baseline of 35.3 mm (SD 28.2). This VAS score reduction was rapid, and significantly reduced from baseline by Day 1 ($P = .0011$). On average patients achieved the ARIA-defined VAS score cut-off of 50 mm before Day 7. Results were consistent irrespective of age (i.e. 12-17 years, 18-65 years, >65 years), gender, baseline severity (i.e. more severe: baseline VAS score 50-74 mm; less severe: baseline VAS score 75-100 mm) or traditional AR phenotype classification (i.e. perennial AR only or seasonal & perennial AR).

Conclusions: MP-AzeFlu provides effective and rapid control of PER in a real-world setting in Sweden assessed by VAS. Symptom improvement was noted from Day 1, was sustained for 42 days. These data support MP-AzeFlu's position as the drug of choice for AR.

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0656 | Survey on the clinical characteristics of paediatric allergic rhinitis

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Introduction: To investigate the clinical symptom, precipitating factor, associated symptom, family history and life quality of pediatric patients with allergic rhinitis,analyze the clinical symptom characteristic

Objectives: A questionnaire survey on pediatric AR patients since June 2008 to June 2016, Five hundred and forty-six pediatric AR patients were divided into 2 groups, group A (n = 160) included children the six and under six years old, group B (n = 386) included children aged from seven to fifteen. The extent of clinical symptom was assessed by visual analogue scale

Results: The incidence rate of sneezing,runny nose,stuffy nose, itchy nose were 85.35%(466/546), 92.67%(506/546), 90.84%(496/546), 71.98%(393/546) respectively. The incidence rate of itchy eyes, red eyes, swollen eyes, runny eyes were 77.84%(425/546), 40.84%(223/546), 21.98%(120/546), 40.84%(223/546) respectively. The incidence rate of breathlessness, gasping, cough, thorax pressure sense were 11.90%(65/546), 5.31%(29/546), 45.97%(251/546), 4.76%(26/546) respectively. Preschool age children has more severe rhinocleisis, more severe cough and less rhinorrhea than school age children. ($P < .05$, $P < .05$, $P < .05$), according to the classification criteria of ARIA 2008,preschool children has more mild intermittent AR and less moderate-severe persistent AR than school age children. The precipitating factor of common cold, passive smoking, fitment, climate, environment factors were 21.98%(120/546), 1.83%(10/546), 4.58%(25/546), 15.02%(82/546), 3.48%(19/546), the others was 4.76%(26/546), no obviously precipitating factor was 41.94%(229/546). The rate of parent or parents who had allergic disease history was 16.12% (88/546) Quality of sleep that 65.93% (360/546) were upset and 58.97% (322/546) had no cathexis

Conclusions: Six and under six years old children have different clinical symptom characteristic from the seven to fifteen years old children, and we got some clinical data of paediatric AR patients, those were beneficial to the diagnose and therapy of paediatric AR.

0657 | Children acute rhinosinusitis and intermittent allergic rhinitis

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Introduction: Acute sinusitis appear to be misdiagnosed in children because of the lack of proper symptoms.

Objectives: The purpose of the study is to identify the correlation between exacerbation of nasal allergy and affected paranasal sinuses by Recurrent acute rhinosinusitis; this is defined as multiple episodes of acute rhinosinusitis in which the symptoms and signs of infection resolve completely between episodes.

Material and Method. We include in this study 84 patients aged between 6-12 years who was consulting in Municipal Hospital of Oradea presenting: nasal congestion, rhinorrhea, sneezing, itching associated with intermittent cough and postnasal drip.

We perform endocavitary examination of the nose and we noticed: turbinated hypertrophy, swollen nasal mucosa, pale bluish in coloration, purulent secretion at the level of middle meatus and who drain posteriorly at the level of choanal orifices. In selected case we perform imagistic evaluation to appreciate the alteration of sinus mucosa. All of this patients was treated previously for allergic rhinitis. Sixty-five patients (77%) were boys and fifty patients (59.5%) had family history of atopy. All patients was previously diagnosed with intermittent nasal allergy.

Results: Results. From the total number of patients 95.2% present nasal purulent discharge, 64.2% present more predominant nasal congestion, 42.8% present sneezing and 30.9% present postnasal drip more accentuated in the time of sleep. Correlated was more accentuated secretion in middle meatus bilateral in 20.2% cases. Sinusitis was unilateral in 72.6% and more affected sinus was maxillary .

Conclusions: Conclusion: In this study we conclude that exacerbation of intermittent allergic rhinitis can contribute to appear acute sinusitis in children. The accurate diagnosis of acute rhinosinusitis is challenging because of the overlap of symptoms with other common diseases and we must have a high index of suspicion in selected cases of allergic patients.

0658 | A herbal medicine might be effective for the chronic rhinitis patients

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Case Report: [Aim] Chronic rhinitis with the aging is relatively common in outpatient clinic. We usually use antihistamine, nasal spray containing steroid, and expectorant for these patients who have running nose and nasal obstruction. However, it is sometimes difficult to improve their symptoms. We report here that Hochuekkito (a herbal medicine) is effective for the chronic rhinitis patients for whom no medicine is curable.

Case: Case is 76-year-old male, who has running nose and increasing sputum. When he came to our outpatient clinic, the nasal mucosa performed mild redness and it was a dry tendency. We thought that he had a symptom with the chronic rhinitis and we gave him expectorant and antihistamine. Although he also bought a commercial nasal spray by a self-judgement, these symptoms were not improved for more than one year.

Two years later, he said he had cold of hands and feet in addition to his nasal symptoms. We gave him Hochuekkito in order to improve his cold of hands and feet. Two months later, his nasal symptoms were completely healed and his cold of hands and feet was also improved. He took this Hochuekkito for a year and stopped taking it afterwards.

Results: We prescribed antihistamine, nasal spray containing steroid, and expectorant for the aging-related chronic rhinitis patient. However, there was no improvement of these symptoms. After being the onset of systemic symptoms, we added Hochuekkito and their symptoms were dramatically improved. Hochuekkito is said to affect the immunological switching of Th1/Th2 and then improve allergic reactions. In this case, the immunological switching from Th2 to Th1 might be induced, and then the nasal symptoms were improved.

Conclusions: We report here the chronic rhinitis patients who treated with Hochuekkito. A herbal medicine is sometimes effective for these patients.

SUNDAY, 18 JUNE 2017
TPS 06
MANAGEMENT OF ASTHMA

0659 | Tiotropium add-on therapy improves lung function in children and adolescents with moderate and severe symptomatic asthma, independent of markers of allergic status

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Introduction: Tiotropium add-on therapy has demonstrated efficacy and safety in 6-17-year-old patients with moderate and severe symptomatic asthma despite inhaled corticosteroid (ICS) treatment ± other controllers.

Objectives: Since allergic asthma is the most common phenotype, we assessed whether the allergic status impacts lung function improvements with tiotropium add-on therapy in these patients.

Methods: Analyses involved four Phase III, randomised, double-blind, placebo-controlled, parallel-group trials in patients aged 6-11 years and 12-17 years. Two were 12-week trials (severe symptomatic asthma; NCT01634152/NCT01277523) and two were 48-week trials (moderate symptomatic asthma; NCT01634139/NCT01257230). Patients received once-daily tiotropium or placebo delivered as two puffs via the Respimat® inhaler (tiotropium 2 x 1.25 μg or 2 x 2.5 μg), as add-on to ICS ± other controllers. *Post hoc* modelling analyses included change from baseline (response) in peak forced expiratory volume in 1 second (FEV_1) within 3 hours post-dose ($FEV_{1(0\text{-}3\ h)}$; primary endpoint in each study), trough (pre-dose) FEV_1 response, FEV_1/forced vital capacity (FVC) ratio, forced expiratory flow ($FEF_{25\text{-}75\%}$) response and in-clinic trough (evening) peak expiratory flow (PEF) response in pooled datasets at the time of primary endpoint assessment (severe asthma: Week 12, moderate asthma: Week 24) across the full range of baseline blood eosinophil counts (0-2000 cells/μL) and total serum IgE levels (0-2000 μg/L)

Results: A total of 1590 patients were treated (n = 798 moderate and n = 792 severe asthma). Baseline demographics and disease characteristics were generally balanced between treatment groups. At the time of primary endpoint assessment, significant improvements were observed with tiotropium vs. placebo in peak $FEV_{1(0\text{-}3\ h)}$ response (moderate asthma, tiotropium 2.5 μg: 159 mL [95% CI: 98, 219 mL; $P < .0001$]; tiotropium 5 μg: 168 mL [95% CI: 109, 228 mL; $P < .0001$]; severe asthma, tiotropium 2.5 μg: 74 mL [95% CI: 8, 140 mL; $P = .0273$]; tiotropium 5 μg: 117 mL [95% CI: 51, 183 mL; $P = .0005$]), trough FEV_1 response, FEV_1/FVC ratio, $FEF_{25\text{-}75\%}$ response, and in-clinic trough (evening) PEF response. These improvements were independent of the magnitude of baseline IgE levels and blood eosinophil counts.

Conclusions: Once-daily tiotropium as an add-on to ICS maintenance therapy ± other controllers improves lung function in children and adolescents with moderate and severe symptomatic asthma, irrespective of IgE levels and blood eosinophil counts.

0660 | Efficacy of mepolizumab in patients with severe eosinophilic asthma who had previously received omalizumab treatment

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Introduction: Mepolizumab has been shown to improve health-related quality of life (HRQoL) and exacerbation rates in clinical studies of patients with severe eosinophilic asthma (SEA). A substantial proportion of patients in these studies were atopic and had been previously treated with omalizumab. Therefore, understanding the efficacy of mepolizumab in this subset of omalizumab-treated patients is of clinical interest.

Objectives: MUSCA was a Phase IIIb, placebo-controlled, randomised, double-blind, parallel-group, multicentre study. Patients with SEA and a history of ≥2 exacerbations in the previous year, despite regular high-dose inhaled corticosteroids plus other controller(s), received subcutaneous mepolizumab 100 mg or placebo, in addition to standard of care, every 4 weeks for 24 weeks. Efficacy endpoints included change from baseline in St George's Respiratory Questionnaire (SGRQ) score, Asthma Control Questionnaire (ACQ-5) score, forced expiratory volume in 1s (FEV_1) and exacerbation rate at Week 24 (4 weeks post last dose). A post hoc subgroup analysis was performed to determine the efficacy of mepolizumab on these endpoints in patients with/without prior omalizumab use.

Results: Of the 551 patients in MUSCA, 86 (16%; mepolizumab n = 40; placebo n = 46) had prior omalizumab use. In patients with/without prior omalizumab use, the geometric mean baseline blood eosinophil count was 350/320 cells/μL; mean (SD) baseline SGRQ and ACQ-5 scores were 52.7 (16.6)/45.8 (18.6) and 2.54 (1.01)/2.14 (1.14), respectively. Mean change from baseline in SGRQ score at Week 24 was greater with mepolizumab vs placebo, both in patients

with prior omalizumab use (difference: −13.1 [95% confidence interval [CI]:-19.8,-6.5] and without prior omalizumab use (difference: −6.6 [95% CI: −9.7, −3.5]). A similar pattern was seen with SGRQ domain scores. ACQ-5 scores also improved from baseline with mepolizumab vs placebo in patients who had/had not previously received omalizumab, with respective treatment differences of −0.91 (95% CI: −1.40, −0.43) and −0.31 (95% CI: −0.50, −0.11). FEV_1 improvements and exacerbation rate reductions were similar between patients with/without prior omalizumab use.

Conclusions: In patients with SEA, mepolizumab efficacy on HR-QoL, asthma control, lung function and exacerbation rates was shown regardless of prior omalizumab treatment, demonstrating consistent and meaningful clinical benefits in this patient population.

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0661 | Statin use is associated with decreased asthma-related emergency department visits and hospital admissions

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Introduction: Statins have pleiotropic anti-inflammatory and immunomodulatory effects, but the effect of statin use on asthma-related emergency department (ED) visits and hospital admissions has remained unclear, especially in Asian populations.

Objectives: The aim of our study was to examine the effect of statin therapy on asthma-related ED visits and hospital admissions using a large nationwide population-based cohort.

Results: There were 1946 asthma-related ED visits and hospital admissions in this study. The incidence rate of asthma-related ED visits and hospital admissions among statin users was 10.8 per 1000 person-years (95% confidence interval (CI): 11.4-11.3). Statin users were associated with a reduced risk of asthma-related ED visits or hospital admissions (adjusted hazard ratio [aHR]: 0.71; 95%CI: 0.62-0.92) compared to non-statin users. In addition, the risk of asthma-related ED visits and hospital admissions was decreased among those with a higher cumulative defined daily dose (DDD), greater average DDD and longer cumulative-day users than the counterparts.

Conclusions: Statin use is associated with decreased risk of asthma-related ED visits and/or hospital admissions in individuals with asthma. Further investigations on underlying regulatory mechanisms will be merited.

0662 | Tiotropium add-on therapy has a safety profile comparable with that of placebo in children and adolescents with symptomatic asthma

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Introduction: We assessed the safety and tolerability of once-daily tiotropium add-on therapy in a pooled analysis using data from >1600 patients aged 1-17 years with symptomatic asthma of different severities.

Objectives: The following randomised, double-blind, placebo-controlled, parallel-group trials were included: NCT01634113, NCT01634139, NCT01634152, NCT01277523 and NCT01257230. All were Phase III trials, except NCT01634113 (Phase II/III). NCT01634139 and NCT01257230 were of 48 weeks' duration, and the rest were of 12 weeks' duration. Patients had persistent asthmatic symptoms (NCT01634113) or persistent asthma of moderate (NCT01634139, NCT01257230) or severe (NCT01634152, NCT01277523) intensity. Once-daily tiotropium 5 μg or 2.5 μg (2 puffs of 2.5 μg or 1.25 μg) or placebo (2 puffs) was administered via the Respimat Soft Mist inhaler as add-on to inhaled corticosteroid maintenance treatment, with or without other background therapies. A spacer (valved holding chamber with facemask) was used to administer treatments in patients aged 1-5 years. Pooled safety analysis was based on treatment-emergent adverse events (AEs) occurring between first drug intake and until 30 days after the last dose of trial medication.

Results: Across all studies, 1696 patients were randomised and 1691 were treated: 1-5 years, n = 101; 6-11 years, n = 801; 12-17 years, n = 789. Baseline demographics and disease characteristics were comparable between treatment groups within each trial. Overall, 52% of patients (n = 879) experienced an AE (Table). The proportion of patients aged 6-17 years reporting any AEs was similar across the tiotropium and placebo arms. Among those aged 1-5 years, a lower proportion of any AEs was reported by patients in the tiotropium groups than those in the placebo group. The most common AEs reported in ≥5% of patients in the pooled dataset (in any treatment arm by preferred term) were asthma worsening/exacerbation, nasopharyngitis, decreased peak expiratory flow rate and viral respiratory tract infection. The majority of AEs were mild or moderate in intensity. The frequencies of reported drug-related AEs, AEs leading to discontinuation

Overall summary of AEs in patients aged 1-17 years

n (%)	Tiotropium 5 μg once daily	Tiotropium 2.5 μg once daily	Placebo once daily
Pooled: 1-17 years	n = 560	n = 559	n = 572
Patients with any AE	283 (50.5)	286 (51.2)	310 (54.2)
Patients with investigator-defined drug-related AEs	7 (1.3)	1 (0.2)	8 (1.4)
Patients with AEs leading to discontinuation	2 (0.4)	0	5 (0.9)
Patients with serious AEs	10 (1.8)	8 (1.4)	13 (2.3)
NCT01634113: 1-5 years	n = 31	n = 36	n = 34
Patients with any AE	18 (58.1)	20 (55.6)	25 (73.5)
Patients with investigator-defined drug-related AEs	2 (6.5)	0	2 (5.9)
Patients with AEs leading to discontinuation	0	0	0
Patients with serious AEs	0	0	3 (8.8)
NCT01634139/NCT01634152: 6-11 years	n = 265	n = 271	n = 265
Patients with any AE	138 (52.1)	145 (53.5)	155 (58.5)
Patients with investigator-defined drug-related AEs	1 (0.4)	0	4 (1.5)
Patients with AEs leading to discontinuation	2 (0.8)	0	2 (0.8)
Patients with serious AEs	5 (1.9)	5 (1.8)	8 (3.0)
NCT01277523/NCT01257230: 12-17 years	n = 264	n = 252	n = 273
Patients with any AE	127 (48.1)	121 (48.0)	130 (47.6)
Patients with investigator-defined drug-related AEs	4 (1.5)	1 (0.4)	2 (0.7)
Patients with AEs leading to discontinuation	0	0	3 (1.1)
Patients with serious AEs	5 (1.9)	3 (1.2)	2 (0.7)

Treated set. Percentages calculated using total number of patients per treatment as denominator (Medical Dictionary for Regulatory Activities version 18.1). Tiotropium or placebo administered as add-on to background therapy

and serious AEs were low and comparable across the treatment arms. No serious AEs were considered treatment-related or led to treatment discontinuation. No deaths were reported.

Conclusions: Tiotropium add-on therapy has a safety profile comparable with that of placebo in patients aged 1-17 years with symptomatic asthma.

0663 | Effect of omalizumab on asthma control, exacerbation rate and quality of life in Italian patients with severe allergic asthma: results from the longitudinal phase of the proxima study

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Introduction: Patients with severe allergic asthma (SAA) have poor disease control and increased exacerbation rate, which impacts their quality of life (QOL).

Objectives: The PROXIMA study, a 2-phase observational study with cross-sectional and longitudinal phases, assessed the prevalence

of perennial allergic asthma and the effect of omalizumab on disease control in patients with SAA in the Italian real-life setting (25 centres). Here, we present the results from the longitudinal phase, on the effect of omalizumab on asthma control, exacerbations and QOL.

Methods: Patients with SAA (GINA step 4) requiring a therapeutic step-up were enrolled in the cross-sectional phase and those who started treatment with omalizumab as per the clinician judgement at the baseline visit were included in the longitudinal prospective phase. The primary variable was the proportion of patients who achieved asthma control (Asthma Control Questionnaire [ACQ] score<4) with omalizumab after 6 months of treatment and maintained it at 12 months. Secondary variables included the incidence of asthma exacerbations during the study period and quality of life (assessed by the EuroQoL 5D-3L questionnaire) at 6 and 12 months.

Results: Of 365 patients enrolled in the PROXIMA main study, 123 contributed the longitudinal population. ACQ scores were evaluated in the per-protocol set, which included 99 patients. A high proportion of patients achieved asthma control with omalizumab after 6 months and maintained it at 12 months (95.96%; n = 95/99; 95% CI: 89.98-98.89%). In addition, ACQ score significantly improved ($P < .0001$) from baseline till 6 and 12 months. The mean±SD number of asthma episodes/patient occurred during the study was 0.6 ± 1.2 (N = 121) and the mean change in number of asthma episodes/patient with respect to 12-month before enrollment was −4.0 ± 4.2 (N = 117), with a reduction of 87% vs baseline. Omalizumab treatment resulted in an increase in the proportion of patients showing an improvement in QOL at 6 and 12 months from baseline (Table); a significant increase in the visual analogue scale score was observed from baseline to 6 and 12 months ($P < .0001$). No new safety signals were observed with omalizumab in this study.

Conclusions: In the Italian real-life setting, omalizumab treatment resulted in a high improvement in asthma control during the 12-month period. In addition, omalizumab was effective in reducing the rate of exacerbations and improving QOL in patients with SAA.

Parameter (%)	Baseline	6 months	12 months
No problems in walking	47.9	73.5	72.8
No problems in self-care	74.4	91.2	90.3
No problems in performing usual activities	36.7	58.4	65.0
No pain/discomfort	31.4	61.9	63.7
No anxiety/depression	34.7	57.5	57.3

	CONTROLLED ASTHMA (ACT ≥ 20)			NON-CONTROLLED ASTHMA (ACT < 20)			Inference		
	Mean (SD)	%	n	Mean (SD)	%	n	OR	95%CI	*P*
Sociodemographic data									
Age	45.94 (16.21)		417	47.5 (17.97)		304		−0.06 to 0.24	.222
Female sex		61.4%	417		68.5%	302	1.37	1.00-1.87	.049
Clinical characteristics of asthma									
Exacerbations (12 previous months)	—	31.2%	423	—	77.7%	310	7.70	5.49-10.79	<.0001
Patients with FEV_1 < 80%	—	25.5%	420	—	52.9%	308	3.29	2.40-4.50	<.0001
Incorrect inhalation technique	—	2.1%	420	—	16.6%	307	9.10	4.40-18.80	<.0001
Adherence TAI (Test of Adherence to Inhalers)									
•Total score	47.41 (3.83)		406	45.4 (5.95)		306		0.25-0.55	<.0001
•Poor adherence (TAI ≤ 46)		22.4%	406		35.9%	306	1.94	1.40-2.70	<.0001
•Sporadic non-adherence		53.6%	414		61.4%	308	1.37	1.02-1.85	.0404
•Intentional non-adherence		34.2%	415		46.9%	309	1.70	1.26-2.30	.0007
•Inadvertent non-adherence		4.6%	414		20.4%	304	5.33	3.11-9.12	<.0001
Morisky-Green questionnaire									
•Total score	3.17 (0.91)		422	2.82 (1.16)		309		0.19-0.49	<.0001
•Poor adherence		55.5%	422		63.4%	309	1.39	1.03-1.88	.0332
Satisfaction TSQM (general treatment)									
•Score	79.12 (14.51)		423	66.86 (15.8)		309		0.66-0.96	<.0001
•Low satisfaction		31.4%	423		65.4%	309	4.12	3.01-5.62	<.0001
FSI-10 (specific of inhaler)									
•Score	44.25 (6.36)		410	40.2 (7.51)		301		0.43-0.73	<.0001
•Low satisfaction		39.8%	410		65.4%	301	2.87	2.11-3.91	<.0001
Quality of life (MiniAQLQ)									
Total score	5.57 (0.56)		399	4.22 (0.96)		297		1.54-1.9	<.0001
Poor quality of life		23.3%	399		85.5%	297	19.44	13.06-28.93	<.0001

0664 | Control of asthma, adherence to inhaled therapy and usefulness of the test of adherence to inhalers (TAI). results of the ascona study

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Introduction: Although deficient adherence to therapy is related to poor asthma control, some studies have been unable to confirm this association, probably due to the low resolution capacity of the methods used to identify poor adherence. In this regard, the Test of Adherence to Inhalers (TAI) has recently been developed.

Objectives: 1. To validate the usefulness of TAI in the clinical practice setting for identifying deficient adherence to therapy associated to poor asthma control; 2. To identify other parameters of inhaled therapy as possible risk factors for poor control of the disease.

Methods: A cross-sectional, multicenter observational study was carried out involving patients with stable moderate to severe persistent asthma (GEMA score ≥ 3), referred from the outpatient clinics of Spanish Hospitals. The following was carried out in all cases, on occasion of a single visit: Asthma Control Test (ACT), Treatment Satisfaction Questionnaire for Medication (TSQM) and Feeling of Satisfaction with Inhaler (FSI-10); general adherence to therapy (Morisky-Green questionnaire) and specific adherence to inhalers (TAI); and quality of life (Mini-Asthma Quality of Life Questionnaire).

Results: A total of 778 patients with a mean age of 46.8 $\pm$ 17 years (489 females [64.4%]) were included in the study. In comparison with controlled asthma [ACT $\geq$ 20], the patients with non-controlled asthma [ACT < 20] were significantly older, suffered more exacerbations, had poorer lung function, presented poorer inhaler use, were less adherent to therapy, showed higher rates referred to type of non-adherence (sporadic, intentional, inadvertent), and reported poorer treatment satisfaction and quality of life (see Table). The logistic regression analysis found good asthma control to be independently correlated to: high specific inhaler satisfaction (FSI-10), OR: 1.627 (95%CI: 1.107-2.392); high general satisfaction (TSQM), OR: 2.906 (95%CI: 1.99-4.244); and high inhaler adherence (TAI), OR: 1.54 (95%CI: 1.034-2.293). Although the investigators estimated that 14.5% of their patients were non-adherent, the TAI (<50) and the Morisky-Green green questionnaire yielded non-adherence rates of 60.5% and 58.4%, respectively.

Conclusions: The TAI is useful for identifying deficient adherence as a possible cause of poor asthma control. Since physicians overestimate adherence among their asthmatic patients, the use of other more reliable methods is advisable.

Study sponsored by Orion Pharma, S.A.

0665 | Omalizumab in severe asthmatic patients: discontinuation effects

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Introduction: Severe asthma represents a major public health issue. Long-term treatment with omalizumab might have disease-modifying activity but data on the consequences of discontinuing treatment after a positive response are limited.

Objectives: The purpose of this study was to investigate, in real-life prescribing conditions, what happens when omalizumab is discontinued in patients who have responded well to anti-IgE treatment. Secondarily, we've studied if there were any differences between long-course (>36 months) and a briefer-course (<36 months) of treatment with omalizumab.

Results: Cross-sectional retrospective study, including patients with severe allergic asthma treated with omalizumab for at least 12 months and that discontinued this treatment. Medical records were reviewed for data on pre-treatment allergen sensitization, total IgE and eosinophils (absolute); data on %FEV1 and control, assessed with CARAT questionnaire (CARAT total score, CARAT(T); upper airways score, CARAT(U); lower airways, CARAT(L)), was retrieved prior treatment initiation and after discontinuation.

Ten patients were included, 7 females with a median (interquartile range, IQR) age of 53.5 (24.3) years. All patients were sensitized to dust mites and 6 were polisensitized. The average duration of omalizumab treatment was 50.2 $\pm$ 27.5 months (median: 48.5; range 18-95 months) and, after discontinuation, the mean follow up duration was 9.2 $\pm$ 7.3 months.

Median(IQR) eosinophils, CARAT(U) and CARAT (L) score improved significantly in the evaluation after discontinuation when compared to basal scores prior to omalizumab treatment (180(190) vs. 275 (179), $P = .024$; 7(6.5) vs 5(5.8), $P = .011$; 8.5(5.5) vs 5(8), $P = .09$; respectively), while neither total IgE ($P = .445$) nor FEV1 ($P = .086$) presented significant differences.

In relation to treatment duration, significant and improving changes in FEV1, CARAT(U) and CARAT (L) scores were observed in patients with long-course treatment (n = 5; $P = .043$; $P = .029$; $P = .027$, respectively). No significant changes were observed in patients with a briefer-course of anti-IgE treatment (n = 5; $P > .1$).

Conclusions: In this sample, there was a significant improvement in blood eosinophils, upper and lower airways CARAT scores after discontinuation of omalizumab treatment.

In these patients with severe allergic asthma, a longer course of anti-IgE treatment demonstrated a significant clinical and lung function improvement, however a study with a larger sample is needed to confirm these preliminary results.

0666 | Wellbeing of older adults with asthma

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Introduction: Asthma, despite the significant advances made, is a substantial life burden across the ages, with, in particular, a limited knowledge of how older adults over the age of 60 years live and manage their illness.

Objectives: To measure the quality of life and the perception of symptoms of older asthmatic patients in order to better understand their daily wellbeing and coping with asthma.

Results: Thirty asthmatic patients aged 60 and over, of both sexes, 21 of whom attended a public hospital and 9 a private practice, both in Cordoba, Argentina, have completed a reduced version of the Elizabeth Juniper Mini Asthma Quality of Life Questionnaire (AQLQ), version validated in Spanish and divided into four domains for analysis, namely: Symptoms, Activity Limitations, Emotional Function and Environmental Stimuli, with scores ranging from 1 (severe impairment) to 7 (none), and 4 (intermediate). In addition, to assess patient's emotional perception of the symptoms of asthma, two Visual Analogue Scales (VAS) with 10 point Likert scales were used, with 10 being most intense/negative. Additionally, a Spanish version was divided into the categories of Mild, Moderate, Intense, whilst the English version asked patients to rate their symptoms from no distress to unbearable. To gain a better insight into the patient's experiences of the daily living with asthma, short qualitative questions were addressed covering the topics such as asthma symptoms, treatment, daily lifestyles. The Mini AQLQ was able to detect changes within individual asthmatic patients, however on the total sample of 18 females and 12 males, the mean of Symptoms domain was 4.55, Activity Limitations—5.28, Emotional Function—4.51, and Environmental Stimuli—3.38. Whilst, the Spanish version of the VAS scored the average of 4.23 covering the category of the moderate affect on patients asthma symptoms, the English version scored 2.76 indicating limited distress.

Conclusions: Based on the Mini AQLQ, it was found that the domain of activities was least affected indicating a normal quality of life, especially when compared with both VAS that proved patients have experienced little emotional affect regarding their asthma symptoms. However, the qualitative phase has uncovered more fluctuating tendencies indicating the troublesome experiences with asthma, thus prompting that more investigative work has to be done in the attempt of understanding daily living of older asthmatics.

0667 | Response to omalizumab in urticaria & asthma: "a life-time together?"

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Introduction: Omalizumab is a recombinant human-monoclonal-antibody that blocks the IgE receptor. Omalizumab is indicated in severe-asthma (SA) and chronic-idiopathic-urticaria (CIU) .The aim of this study was to demonstrate that omalizumab used in SA and CIU may differ.

Objectives: Follow-up data of 26 patients who were treated with omalizumab between march 2014-june 2016 in our clinic, were retrospectively evaluated. In SA, omalizumab were given according to total IgE/wt, whereas in CIU 300 mg/month. In group SA, omalizumab was administered for prophylaxis of immunotherapy reactions in one-moderate-asthmatic patient.

Results: Omalizumab appears to be more effective in CIU, while as it increases tolerance to immunotherapy, as well as disease control in severe asthmatic patients.

Conclusions: Three quarters of patients (n: 20) had CIU and 23.1% (n: 6) had SA (53.8%F, mean age 42.53 $\pm$ 14.76 years). Durations of omalizumab treatment were 15.33 $\pm$ 13.29 months in SA, and 7.55 $\pm$ 5.15 months in CIU, while as 54.2% of the patients were still on that treatment. Partial response was observed in 50% of CIU, and 66.7% of SA group. Complete remission was observed only in CIU patients (n: 10), who were older, more likely to have drug allergy, and, dermatographism, and those with partial response were predisposed to thyroid dysfunction. However treatment failure was seen only two asthmatic patients, with nasal polyps and with higher total IgE levels, and one with ABPA. Treatment nonadherence was 30% in CIU and 16.7% in SA (*P*:.51). Two patients with SA experienced an asthma attack, four patients showed improvement in asthma control test, and all had improvement in pulmonary function tests. In addition to omalizumab treatment, antihistamine and montelukast were administered in CIU and SA (80% and 50%; 65% and 83.3%, respectively). The recurrence rate following discontinuation of omalizumab was 43.8% in CIU and 83.3% in SA (*P*:.16).

0668 | Ease of use of inhalers and its impact on treatment adherence and control of asthma. an observational study

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Introduction: We aimed to assess the impact of the ease of use of inhalers on adherence to treatment and on the control of asthma symptoms.

Objectives: Three different inhaler devices were compared in a observational, cross-sectional, multicentre study conducted from April until July 2015 in patients with asthma receiving any kind of asthma medication with the same inhaler at least 3 months before the study. Patients with disabling comorbidities and/or cognitive dysfunction were excluded. We collected data about the severity of asthma according to Spanish Guideline on the Management of Asthma (GEMA), its control (Asthma Control Test), patient's satisfaction with the inhaler (FSI-10/TSQM), adherence (Test of the Adherence to Inhalers (TAI)/Morisky-Green) and quality of life (QoL) (Mini-AQLQ). The sample was stratified into three groups according to the type of maintenance inhaler used: Easyhaler (n = 541), Turbuhaler (n = 124) and Accuhaler (n = 74).

Results: The study included 739 patients, 62.7% were women and the mean (SD) age was 45.72 (16.9) years. Only 14.0% of patients were classified as having intermittent or mild persistent asthma. FSI-10 questionnaire showed a favourable trend towards Easyhaler, especially in the items referring to the ease and comfort in use ($P < .05$). The TSQM questionnaire showed the same tendency, highlighting the results in the items that assess the ability of the treatment to prevent or treat asthma and convenience ($P < .05$ vs Turbuhaler). There were no significant differences between groups in any of the adherence questionnaires. According to ACT, the percentage of patients with controlled asthma (ACT≥20) was significantly higher in the Easyhaler group (65.3%) vs. Turbuhaler (52.1%) and Accuhaler (53.5%) ($P < .05$ in both comparisons). Those results were reflected in the QoL, where patients with Easyhaler slightly surpassed the other devices studied in the global mini-AQLQ score. Specifically, Easyhaler was superior to Turbuhaler in the domain of environmental stimuli ($P < .05$) and to Accuhaler in activity limitation ($P < .05$).

Conclusions: The comparison between three different inhaler devices shows a general trend favouring Easyhaler in patient's satisfaction, control of asthma and higher QoL. The outcomes achieved with this device are likely related with a greater ease of use, once excluded differences between inhalers in patient adherence.

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0669 | Impact of asthmatic patient satisfaction with the inhaler upon adherence, disease control and quality of life. Results of the ascona study

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Introduction: In general, the opinion about the drug inhaler among patients with chronic respiratory disease does not generate the required interest among clinicians. Nevertheless, the clinical practice guides on asthma recommend taking patient inhaler preference into account in decision making at the time of drug prescription. Few studies have evaluated the clinical relevance of patient satisfaction with the inhaler

Objectives: To determine the impact of patient satisfaction with the regular inhaler upon adherence to therapy, disease control and quality of life.

Methods: A non-postmarketing, cross-sectional, multicenter observational study was carried out involving patients with stable moderate to severe persistent asthma (GEMA score ≥ 3). The following was carried out in all cases, on occasion of a single visit: collection of asthma morbidity and clinical data; level of control (Asthma Control Test [ACT]); general satisfaction with treatment (Treatment Satisfaction Questionnaire for Medication [TSQM) and specific

		Type of dpi							
		Easyhaler		Turbuhaler		Accuhaler		Total	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
FSI-10 questionnaire		$43.46_{a,b}$	6.64	41.49	7.08	40.64	8.46	42.85	6.98
TSQM—Comfort		79.04_{a}	14.15	73.32	16.05	77.18	17.44	77.89	14.98
Mini-AQLQ	Environmental stimuli	4.71_{a}	1.13	4.40	1.28	4.48	1.26	4.64	4.64
	Activity limitation	5.78_{b}	1.18	5.65	1.38	5.24	1.61	5.70	1.28
		n	%	n	%	n	%	n	%
Asthma under control (ACT ≥20)		$333_{a,b}$	65.3%	62	52.1%	38	53.5%	433	61.9%

	HIGH SATISFACTION (FSI-10 score ≥ median) n = 389			LOW SATISFACTION (FSI-10 score < median) n = 389			Inference		
	Mean (SD)	%	n	Mean (SD)	%	n	OR	95%CI	*P*
Sociodemographic data									
Age	43.63 (16.12)		364	49.99 (17.36)		368		0.23-0.53	<.0001
Female sex		59.1%	362		69.3%	368	1.56	1.15-2.12	.0043
Clinical characteristic of asthma									
Exacerbations (12 previous months)		41.6%	368		60.5%	377	2.15	1.60-2.88	<.0001
Patients with FEV_1 < 80%		28.4%	366		44.8%	375	2.04	1.51-2.77	<.0001
ACT—Total score	20.79 (4.06)		351	18.03 (4.53)		360		0.49-0.79	<.0001
Poorly controlled asthma (ACT)		29.6%	351		54.7%	360	2.87	2.11-3.91	<.0001
Incorrect inhalation technique		2.2%	365		14.2%	374	7.37	3.45-15.73	<.0001
Adherence									
TAI—Total score	47.30 (4.21)		356	45.83 (5.37)		368		0.15-0.45	.0001
Poor adherence (according to TAI)		22.2%	356		34.8%	368	1.87	1.34-2.60	<.0001
Morisky-Green—Total score	3.13 (.98)		367	2.93 (1.09)		375		0.05-0.33	.0077
Poor adherence (according to Morisky-Green)		54.2%	367		62.4%	375	1.40	1.05-1.88	.0256
General satisfaction (TSQM)									
General satisfaction	80.27 (14.80)		367	67.72 (15.25)		377		0.69-0.99	<.0001
Low satisfaction		24.8%	367		65.0%	377	5.63	4.10-7.73	<.0001
Quality of life (MiniAQLQ)									
Total score	5.28 (.90)		348	4.70 (1.05)		359		0.44-0.74	<.0001
Poor quality of life		37.9%	348		61.3%	359	2.59	1.91-3.51	<.0001

satisfaction with the regular inhaler (Feeling of Satisfaction with Inhaler [FSI-10]); general adherence to therapy (Morisky-Green questionnaire) and specific adherence to inhalers (Test of Adherence to Inhalers [TAI]); and quality of life (Mini-Asthma Quality of Life Questionnaire [MiniAQLQ]).

Results: A total of 778 patients with a mean age of 46.8 ± 17 years (489 females [64.4%]) were included in the study. On redistributing the sample into two groups—high specific satisfaction (HSS) and low specific satisfaction (LSS) —according to the total FSI-10 score (HSS: FSI-10 score ≥ median; and LSS: FSI-10 score < median), the bivariate analysis showed that in comparison with the LSS patients, the HSS individuals were significantly younger, females, with fewer exacerbations, better lung function, improved disease control, better use of the inhaler, more adherent to therapy, and with greater general treatment satisfaction and superior quality of life (see Table). The logistic regression analysis found HSS to be independently correlated to: younger age, female status, with asthma control, good adherence, the presence of moderate asthma, and a correct inhalation technique

Conclusions: High patient satisfaction with the inhaler device results in greater adherence to therapy, and therefore to better disease control. Patient preference should be very much taken into account when deciding which inhaler device to prescribe.

Study sponsored by Orion Pharma, S.A.

0671 | Budesonide easyhaler®: dose consistency under simulated real-life conditions and low inspiratory flow rates

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Introduction: Robustness of inhaler performance and constant function with different inspiratory flow rates (IFR) is a requisite for successful asthma and COPD management. The aim was to determine the delivered dose (DD) uniformity of the multi-dose dry powder inhaler Budesonide Easyhaler® (EH) in various simulated real-world conditions as well as with different IFR.

Objectives: The in vitro DD uniformity of Budesonide EH (100, 200 and 400 μ/dose inhalation powder) was measured during in-use periods of 4-6 months, after exposure to 30°C / RH60% storage conditions, and in dropping and vibration tests. In addition the influence of IFR (30-60 l/min) was measured on the DD, which was analysed using Ph.Eur. methods.

Results: DD remained constant at all measured in-use periods and after exposure to 30°C/RH60% storage conditions up to 6 months.

Dropping and vibration did not affect DD. No device breakages were detected and functionality remained unaffected after dropping. DD was constant across the different IFRs (Table 1).

Table 1. Results of delivered dose measured using 2, 4 and 6 kPa flow rates. Values are means of 30 doses.

	Delivered doses (μg), mean (SD)		
Strength (μg/dose)	2 kPa (31 L/min)	4 kPa (43 L/min)	6 kPa (54 L/min)
100	97 (8.2)	99 (8.8)	100 (7.3)
200	191 (11.9)	193 (13.0)	200 (13.5)
400	366 (34.0)	362 (17.8)	373 (26.8)

Conclusions: These results indicate that Budesonide EH delivers consistently accurate doses with different IFRs, as well as after exposure to high temperature and humidity and after dropping and vibration tests.

0672 | Under-utilization of spirometry and mis-diagnosis of lower airway obstructive diseases (asthma and COPD) in primary setting

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Introduction: Spirometry is an easy, rapid, cheap and widely diffused diagnostic tool for assessing lung function and it is mandatory to make a correct diagnosis of lower airway obstructive diseases such as asthma and COPD. Scientific literature data shows that spirometry is under-utilized even in patients with suspect lower airway obstructive diseases.

Objectives: This is the report of data collected through a no-profit organization ("Ricerca & Respiro ONLUS") the purpose of which is to facilitate the access to spirometry for symptomatic patients. Therefore, this can be considered a "real-life" study.

The aims of the study are: (i) to analyze demographic, clinical and functional data of enrolled patients, putting this data in relation with the number and the frequency of spirometric measures done in the past; (ii) to check the knowledge the patients have about their respiratory diseases and comparing it with a functional diagnosis made through the spirometric measures.

All consecutive patients attending the spirometry lab of "Ricerca & Respiro ONLUS" in a 4 months period were enrolled into the study, were enquired by their demographic data and clinical history (in particular, data about the diagnosis received by their general practitioner, the type and frequency of symptoms, and the frequency of spirometric measures were recorded) and underwent to a spirometry plus a bronchodilator test with salbutamol 400 mcg.

Results: 78/115 enrolled patients (67.8%) had a doctor-diagnosis of at least one lower airway obstructive diseases: 66 (57.4%) asthma, 32 (27.8%) COPD, and 2 (1.7%) bronchiectasis.

Spirometry was previously done in 54 (47%) patients (on average 11.25 + /- 0.75 months before), 14.8% of whom received the advice to regularly assess spirometry.

Patients with a doctor-diagnosed asthma have done at least one spirometry in the past in 61.2% of cases (significantly higher than in doctor-diagnosed COPD: 46.9%, $P = .008$).

12/49 (24.5%) and 4/32 (12.5%) patients respectively with doctor-diagnosed asthma and COPD had typical pre- and post-bronchodilator spirometric patterns of the doctor-diagnosed disease.

Conclusions: Spirometry is still under-utilized in primary care. Relying only on clinical presentation without assessing lung function lead to a great proportion of mis-diagnosis of asthma and COPD.

0673 | Two components of patient adherence in the treatment of asthma: regular use and correct inhaler technique

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Introduction: The adherence of patients to medications and good inhaler technique play a crucial role in the good outcomes of asthma. In this study we aimed to assess the adherence rates and inhaler technique of the patients and the factors influencing adherence to asthma treatment.

Objectives: In this cross-sectional study, the patients who have been followed for at least 1 year with a diagnosis of asthma and prescribed at least one controller were included. Demographic features, as well as disease characteristics, medications, attitudes for regular doctor visits, knowledge about their medications and inhaler device techniques were recorded. Adherence to therapy was evaluated according to pharmacy records (objective assessment, OA) and statement of the patients (subjective assessment, SA). If the estimated number of boxes the patients should be consumed in one year period was in accordance with pharmacy records the patient was considered to be compliant according to OA. Subjective assessment was based on reports of the patients about frequency and the dosage of prescribed drug usage and categorized as compliant and uncompliant.

Results: A total of 102 patients (87F/15M) with a mean age of 51.7 ± 10.9 were enrolled to the study. Two thirds (n = 65) of the patients were followed in the outpatient clinic for at least five years and 73% of the patients had regular visits. Fifty seven percent of the patients were on step-4 asthma treatment and in 82% inhaler

devices were not changed in the previous year. In terms of adherence, there was a significant discordance between OA and SA of compliance (48% vs 67%, respectively) ($P = .01$). Rate of compliance was higher in patients who had regular doctor visits ($P = .01$), multiple systemic comorbidities ($P = .006$) and who had basic information about the effect of controller medication ($P = .06$). Although 80% of the patients were trained previously on inhaler technique, 47% of them still used their inhaler incorrectly. Type of inhaler device had no effect on this incorrect usage.

Conclusions: This study showed that patients' statement for evaluation of compliance is not a reliable tool for assessment of asthma adherence. Regular doctor visits and repeated education for correct use of inhalers as well as rationale for medication use should be encouraged in order to increase asthma adherence.

0675 | Does oil supplementation with omega—3 -fatty acids protect for exercise induced asthma? A placebo controlled trial

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Introduction: Many patients suffering from exercise-induced bronchoconstriction (EIB) have normal lung function at rest and show symptoms and a decline in FEV1 when they do sports or during exercise-challenge. It has been described that omega-3 polyunsaturated fatty acids could exert a protective effect on EIB.

Objectives: In this study the protective effect of oil supplementation with polyunsaturated fatty acids (total 1.19 g/ day) were investigated in an EIB cold air provocation model. Primary outcome measure: Decrease in FEV1 after exercise challenge in cold air as measured by spirometry (FEV1, percent predicted) -before and after oil supplementation vs placebo.

Results: 99 patients with exercise-induced symptoms aged from 10 to 45 were screened by a standardized exercise challenge in a cold air chamber at 4°C. Before and 5, 10, 15 and 30 minutes after exercise the spirometry was done. 73 of 99 patients aged 19.3 ± 6.0 years fulfilled the inclusion criteria of a FEV1 fall >15%. Then 73 patients were treated placebo-controlled for weeks either by oil supplementation or placebo. 32 patients in each group completed the study.

Mean FEV1 fall after cold air exercise challenge was unchanged before and after oil supplementation (before treatment placebo 31.68% vs. verum 31.06% and after 4 weeks treatment (placebo 26.36% vs. verum 26.99%, n.s).

Conclusions: Oil supplementation with polyunsaturated fatty acids at a dose of 1.19 g/ day did not have any protective effect on EIB.

0676 | Effectiveness and safety of bronchial thermoplasty for severe asthma in daily clinical practice

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Introduction: Bronchial thermoplasty (BT) is a minimally invasive procedure consisting of the application of thermic energy to the airways with the aim of producing the ablation of the hypertrophic smooth muscle. It is approved for use in moderate-severe asthma in Spain since 2010.

Objectives: The aims of the present study are to analyze the effectiveness and the safety of the BT in clinical practice.

Methods: This is a cohorts study. Participants had a confirmed diagnosis of severe asthma and poor control without therapeutic alternative. Effectiveness was measured by comparing exacerbations and admissions rates, asthma control, changes in medication and spirometry prior and one year after the BT was completed. All complications occurred after treatment and along the first year were collected.

Results: Patients had a mean age of 51(SD 8) and were predominantly women (15/21). Previous to BT the equivalent dose of inhaled corticosteroids (ICS) was 1621 (1015) μg of budesonide and 15 patients were on oral corticosteroids (OCS) with a mean equivalent dose of 19 (17) mg of prednisone. All the participants had at least three asthma controller medications.

The average number of activations per patient was 147. After BT the asthma control test improved 7.1 (3.7) points ($P = .018$). The number of ER visits-year was reduced by 75% ($P < .001$). A 38% reduction in admissions-year was also observed ($P = .03$), that in spite of a reduction of 420 (720) μg of budesonide and 6.6(17) mg of prednisone ($P = .058$). Furthermore in 5 patients the third controller could be withdrawn. There were no changes in FEV1.

Complications were related mostly to exacerbation of asthma in the days following the procedures. In 9 out of the 65 treatments (14%) the patient had to stay at the hospital, but only in 1 case (1.5%) for more than 5 days. This latter needed of non-invasive mechanical ventilation. After 6 of the procedures (9.2%) patients reported mild chest pain. One patient (1.5%) (with asymptomatic isolated bronchiectasis and on clopidogrel treatment) had an episode of hemoptysis 23 days after a procedure.

Conclusions: Bronchial thermoplasty is effective and safe for severe uncontrolled bronchial asthma.

SUNDAY, 18 JUNE 2017
TPS 07
PEDIATRIC RESPIRATORY ALLERGY

0677 | Risk factors of overweight and obesity in children with allergy

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Introduction: There is groving evidence that obesity increases the risk of asthma and morbidity from asthma. Also, obesity worsens asthma severity of control—via multiple mechanisms. Asthma in obese children is a complex, multifactorial phenotype. Obesity and its complications must be managed as part of the treatment of asthma in obese children.

Objectives: The aim of the study was the identifying risk factors for obesity in children with allergy.

Results: The study was performed in 106 children with allergy (mean age 12.1 ± 3.4; M 60, F 46;,) from Department of Allergology. 43 (40.5%) of children presented ANN and 63 (59.4%) asthma. Clinical data, detail interview about the risk factors of allergies, assessment of nutritional status, allergy skin test (*Allergopharma*) and spirometry (*Jaeger*) were evaluated. Diet was assessed by 24-hour dietary recall. The statistical analysis was done using program Statistica v 10.0. In study group mean centile of BMI was 49.45. 25.4% of children were underweight, 55.66% with normal BMI and 18.8% presented overweight or obesity. Multiple regression analysis showed significant (Adjusted R-squared: 0.97; $P < .05$) association between high BMI and snacking between meals, high intake of sweets an low physical activity. No association between severity of diseases and BMI or body composition was observed.

Conclusions: The independent risk factors of overweight and obesity in children with allergy are snacking between meals, high intake of sweets an low physical activity. Among children at risk for asthma important is the implementation of prevention habits to prevent overweight and obesity.

0678 | Cost of asthma treatment in children in Poland

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Introduction: Asthma is a disease that mainly affects young people and constitutes a significant economic burden to the society as well as the family of the patient. Asthma is connected not only to the cost of drugs, visits at the specialist, the emergency department or hospitalisations, but also the costs of informal care or reduced effectiveness at work.

Objectives: The purpose of the conducted pharmacoeconomic analysis was to estimate the costs of childhood asthma treatment in Poland.

Results: The cost of childhood asthma treatment was evaluated on the basis of data obtained in a randomised, double-blind study. The retrospective analysis covered 6 months prior to the inclusion in the study, and the prospective covered 9 months of observation. The costs were calculated from the social perspective, with regard to both the direct and indirect costs. The study utilised the conversion data, i.a. of the National Health Fund, the financial section of hospitals and clinics, as well as the market data on the prices of drugs in the years 2014-2015.

The cost-of-illness analysis was conducted in the years 2014-2015 on a group of 120 children with chronic asthma aged 6-17 treated in the Lublin Province. The total direct cost of asthma treatment was estimated at the level of EUR 564.83 /person/ year, including direct medical—EUR 459.43 /person/year and non-medical- EUR 105.4 /person/year. The direct cost was mainly generated by expenses related to visits to the clinics and hospitalisations, which comprised 51% of these costs. The indirect costs were calculated at the level of EUR 1044.53 /person/year and they constituted up to 65% of the total expenses incurred in relation to this disease. The indirect costs included the costs of lost productivity—EUR 239.91 / person/year, costs of reduced effectiveness at work—EUR 500.32 / person/year, costs of informal care- EUR 251.21 /person/year and the costs of unpaid work and lost free time—EUR 53.09 /person/ year. The total cost of asthma treatment in children amounted to—EUR 1609.36 /person/year.

Conclusions: 1. This study is the first pharmacoeconomic analysis of the costs of asthma treatment in children in Poland.

2. The economic burden of asthma in Poland is high, comparable to the other highly developed countries of Europe.
3. Unplanned visits to specialists and hospitalisations generate the highest direct costs of asthma treatment.
4. The indirect costs of treatment are among the highest in Europe.

0679 | Serum vitamin d and IL-31 levels in children with allergic or nonallergic rhinitis

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Introduction: Vitamin D and interleukin-31 (IL-31) are known to be related to atopic dermatitis, but its relationship to other allergic conditions such as allergic rhinitis is unclear.

Objectives: The purpose of this study was to investigate whether serum IL-31 and vitamin D were related to allergic(AR) and nonallergic(NAR) rhinitis, and the relationship between IL-31 and vitamin D. We recruited 59 children with AR only and 36 controls without any allergic diseases. Serum IL-31 and 25(OH)D levels were assayed using enzyme-linked immunosorbent assay and high-performance liquid chromatography, respectively. Atopic sensitization to common allergens was determined using immunoCAP assay and defined positive when level of specific IgE was greater than 0.35 IU/mL.

Results: In children with AR, twenty two children were non-atopy (NAR) and 37 children were atopy(AR). Serum 25(OH)D level was significantly lower in AR and NAR group compared to control group, while there was no significant difference between AR and NAR group. Serum IL-31 levels increased significantly in AR and NAR group compared to control group, whereas there was no difference by atopic sensitization. Serum 25(OH)D levels were inversely correlated with serum IL-31 levels and blood eosinophil counts, but not with serum total IgE levels.

Conclusions: Serum vitamin D and IL-31 are related to AR and NAR, but not to atopic sensitization or IgE.

0680 | Between the questionnaire and cotinine level for studying exposure to tobacco smoke among allergy and healthy children

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Introduction: Several International Study of Asthma and Allergies in Childhood (ISAAC) studies have showed that environmental tobacco smoke (ETS) was strong risk factor for allergic diseases. The underreporting of ETS exposure by parents of study children may depend on the instrument used. We evaluated exposure to ETS by questionnaires and urinary cotinine level to validate the questionnaire.

Objectives: The study population was composed of 340 children ages 4-6 years. Parent-reported questionnaires provided information on household smoking. Urine cotinine was measured using enzyme immunoassay. The questionnaires were three categories, during pregnancy, first year of birth, and previous 12 months.

Results: The urinary cotinine concentrations were higher in children living with smoking parents (22.1 $\pm$ 4.3 ng/mL) compared with children not exposed to parental smoke (5.6 $\pm$ 3.2 ng/mL; P = .017). In passive smoker group, Urine cotinine levels were significantly higher in asthma compared to healthy child (P = .005).

Conclusions: Cotinine levels were higher in passive smokers compared to non-passive smokers. Besides, cotinine was predictive risk factor for asthma. In addition, cotinine levels could be useful in assessing the degree of exposure smoke.

0682 | Hygiene hypothesis in childhood asthma

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Introduction: A protective effect of early childhood infections and an aggravating effect of antibiotics use on allergic diseases through redirecting of dominant Th2 to balanced Th1/Th2 immune response have been suggested. The aim of the study was to examine the impact of family size, overall space in home, daycare attendance and antibiotics use on asthma in childhood in The Republic of Macedonia as a developing country with a low prevalence of asthma, common childhood infections as well high antibiotics use.

Objectives: Data from 2310 children aged 5-15 years from Skopje, the capital of R. Macedonia, which was obtained through a parental-completed standardized questionnaire on respiratory health in 2015/2016 was used for the analysis. Number of siblings (≥3 vs <3), number of rooms at home (≥3 vs <3), daycare attendance, and antibiotics use, adjusted for confounding factors were correlated to wheeze (W) and diagnosed asthma ever, current W, current sleep-disturbing W, current exercise-induced W, and current night dry cough apart from a chest infection. Odds ratios (OR, 95% CI) in binary multiple logistic regression were performed for statistical analysis of data.

Results: It was determined that the antibiotics use significantly increased the risk of W ever (OR 2.32, 1.91-2.82; P = .000), current W (OR 6.50, 3.96-10.67; P = .000), sleep-disturbing W (OR 6.79, 3.46-13.31; P = .000), exercise-induced wheeze (OR 3.51, 1.64-7.50; P = .001), night dry cough (OR 2.40, 1.81-3.19; P = .000) and ever-

diagnosed asthma (OR 3.37, 1.70-6.69; $P = .001$). Rooms at home ≥3 increased the risk of asthma (OR 2.25, 1.12-4.52; $P = .023$). An association between the other investigated factors and asthma was not established.

Conclusions: The results suggest an increased risk of asthma and asthma symptoms by antibiotics use, and an increased risk of asthma by higher living space, which support the hygiene hypothesis in asthma.

0683 | Residential greenness and allergic respiratory disease in children and adolescents: a systematic review and meta-analysis

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Introduction: The aetiology of allergic respiratory diseases in children is not yet fully understood. Environmental factors play a part. The amount of green vegetation surrounding the home (residential greenness) has been recently identified as a potentially important exposure.

Objectives: Our goal was to conduct a systematic review and meta-analysis of the evidence regarding the relationship between residential greenness and allergic respiratory diseases in children.

Peer-reviewed literature published prior to October 2016 was systematically searched for studies relating residential greenness to allergic disease. We used nine electronic databases (Medline, EMBASE, CINAHL, AMED, Scopus, Informit Health, Web of Science, ProQuest central and Google Scholar) and included all human studies, published in English with a study population of children less than 18 years old. Study eligibility and risk of bias (GRADE guidelines) assessments were conducted. Random effects meta-analyses were used to pool data where possible.

Results: We included 12 articles across three broad outcomes of: asthma, allergic rhinitis and atopic sensitisation. Our ability to conduct meta-analyses was limited. The pooled odds ratios for asthma (OR: 1.01 95%CI: 0.93-1.09) and allergic rhinitis (OR: 0.99 95%CI: 0.87-1.12) were not significant. The estimates reported across the studies were highly heterogeneous ($I^2 = 68.1\%$ and $I^2 = 72.9\%$ respectively), indicating a high degree of inconsistency. Studies were conducted with varying methodologies, definition of outcomes and measures of exposure to define residential greenness.

Conclusions: Inconsistencies between the studies were too large to accurately assess the association between residential greenness and allergic disease. A standardised global measure of greenness which accounts for seasonal variation at a specific relevant and standardised buffer size is needed to create a more cohesive body of evidence and for future examination of the effect of residential greenness on allergic respiratory diseases.

0684 | Bronchial hyperresponsiveness phenotypes can be modified by atopy, air pollution, overweight and early-life respiratory infections

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Introduction: Bronchial hyperresponsiveness (BHR) is an elemental factor to diagnose asthma. Unsupervised statistical methods to classify asthma phenotypes have been used in severe asthma or preschool wheeze, but none in BHR itself.

Objectives: We analyzed the risk factors for BHR, classified the phenotypes of BHR, and defined the characteristics of the phenotypes.

Results: A total of 488 subjects with BHR, defined as $PC_{20} \leq 8$ mg/mL in methacholine provocation tests, were included from a 4-year prospective follow-up study. Comprehensive questionnaire, blood tests for total IgE and eosinophils, skin prick tests for common allergens, and spirometry were conducted. Exposure to air pollution including NO_2 and PM_{10} was evaluated by the monitoring system from the birth. The risk factors for BHR were analyzed by using chi square test, student t-test, and logistic regression. The latent class analysis (LCA) was used to classify the BHR phenotypes.

The risk factors for BHR were younger age, a use of antibiotics in infancy, higher exposure to early life PM_{10} and recent NO_2, atopy, high serum IgE and the fraction of blood eosinophil, and lower lung functions. From the LCA, four phenotypes were classified—Class 1 (non-atopic, non-symptomatic: 28.7%), Class 2 (low-atopic, air pollution related: 30.3%), Class 3 (high-atopic, air pollution related: 29.3%), and Class 4 (high-atopic asthma: 11.7%). Symptoms of allergic diseases within the recent 12 months were prominent in Class 4. Class 2 and 3 phenotypes were associated with early life and recent

exposure of air pollutants. The remission rate of BHR in Class 3 and 4 was lower than that of Class 1 and 2. The overweighted subjects in Class 3 were more likely to have asthma symptoms compared with the non-overweighted children. The use of antibiotic in infancy and the history of bronchiolitis in the first 2 years were higher in Class 4 compared with Class 3.

Conclusions: Atopy, exposure to air pollution, overweight and early-life respiratory infections are the crucial variables to classify BHR phenotypes. Controlling exposure to air pollution in early childhood and life-style modification may help to prevent the development of BHR and subsequent asthma.

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0685 | Associations of urine phthalate level with small airway dysfunction and bronchial hyperresponsiveness in 6 year-old children

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Introduction: Phthalates are a family of chemicals and widely used in many consumer products, including building materials, clothing, children's toy, and so on to make plastics flexible. They are known as endocrine disruptors and associated with adverse neurobehavioral and reproductive effects in children. Moreover, significant associations with asthma, rhinitis, airflow obstruction, and airway inflammation were reported. We investigated the clinical implications of urine phthalate levels in lung function, especially focusing on small airway.

Objectives: A population-based cross-sectional study was conducted in the Seongnam Atopy Project in the year of 2016 (SAP 2016). Demographic data, such as age, sex, height, and weight were collected and questionnaires were completed by their parents. Questionnaires included symptom histories of wheezing, nasal symptoms, eczema, cough more than 1 month, and urticaria and past history of asthma, rhinitis, atopic dermatitis, and allergy to food, drug, and insect bite. Skin prick test to common inhalant and food allergen was conducted and spirometry and impulse oscillation system (IOS) was performed. Three metabolite of phthalate, mono-(iso-butyl) phthalate (MiBP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) were measured using liquid chromatography with triple quadrupole tandem mass spectrometry method in urine samples of children.

Results: A total of 131 children, first graders at an elementary school, were included in the study. Mean age was 7.1 years old and male consisted 59.5%. Mean BMI was 16.6 kg/m^2 and BMI scores were transformed into z-score. Mean urine MiBP, MEOHP, and MEHHP levels were 114.9 μg/L, 9.4 μg/L, and 25.4 μg/L, respectively. Thirty (22.9%) children experienced wheezing previously and 13 (9.9%) were diagnosed as asthma.

Urine MiBP level was correlated with resistance at 5 Hz (Rrs5) and reactance at 5 Hz (Xrs5) ($r = 0.197$, $P = .028$; $r = -0.352$, $P < .001$) and higher in children with ever wheeze than those without it (204.9 ± 421.3 μg/L vs 88.1 ± 94.7 μg/L, $P = .013$). MEOHP and MEHHP were also correlated with Rrs5 ($r = 0.158$, $P = .078$; $r = 0.200$, $P = .025$) and Xrs5 ($r = -0.178$, $P = .047$; $r = -0.233$, $P = .009$) and urine MEOPH level was higher in children with ever wheeze (11.0 ± 10.1 μg/L vs 8.9 ± 8.5 μg/L, $P = .046$).

Conclusions: Urine phthalate metabolites were correlated with IOS parameters, which reflecting small airway dysfunction, and significantly higher in children with ever wheeze.

0312A | Atopic status in asthmatic children—comparison between two atopy multi-screening tests

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Introduction: Atopy and allergy have long been associated with asthma. According the literature data ImmunoCAP Phadiatop/fx5 is the "gold standard" for atopy detection from all the laboratory tests.

Objectives: A cross-sectional study evaluating atopy status in 48 asthmatic children aged from 6 to 17 years old (mean 10.65 ys. ± 4.14). For all patients detailed asthma history, treatment regimen, clinical indices, pulmonary function tests (PFT), bronchodilator response, eosinophil count in nasal smear, asthma control level and ACQ were performed. We drew blood for IgE against inhalation and food allergies antibodies detection. IgE were detected with the predesigned kit EurolinePediatric (Euroline Allergy Profile Pediatrics, Enzyme Allergo Sorbent Test (EAST) of Euroimmune ® (Medizinische Labordiagnostica, AG, 2014, Germany) and with ImmunoCap, Phadia (Thermo Fischer Scientific Inc, Manufacturer Phadia AB, Uppsala, Sweden—Phadiatop/fx5). Results of both test were compared.

Results: The results of our study showed very good correlation between the two methods in terms of sensitivity and specificity. The methodology of EUROIMMUN (Pediatric) showed even an advantage in detecting children with atopy (41 vs. 35 out of 48). When using correlation, regression and factor analysis found that the predictive index ImmunoCAP Phadiatop / fx5 gives 19% error compared to EUROIMMUN (Pediatric). This error is less when EUROIMMUN is compared with Phadiatop Fx, probably due to the wider range of aero-allergen embedded in strips of EUROIMMUN.

Conclusions: Both tests are reliable, correlate well and have a high sensitivity and specificity for identifying atopy in children. ImmunoCAP Phadiatop and fx5 does not define the precise IgE specificity, while as an advantage EUROIMMUN Pediatric gives titers of specific positive IgE. Additionally EUROIMMUN does not require specialized equipment and is easily applicable in everyday clinical and laboratory practice. Acknowledgements: This work was supported by a grant from the Medical University of Sofia (Council of Medical Science, project no. 23-D/2013, grant no. 35-D/2013)

0687 | Evaluation of reversibility with impulse oscillometry in pre-school children with recurrent upper and lower respiratory symptoms

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Introduction: Impulse oscillometry is a respiratory function test, used to measure impedance (X) and resistance (R) in lower airways. It is easier to carry out than spirometry, especially in lower age groups with known cooperation difficulties.

Objectives: In this study, we aimed to determine the diagnostic value of IOS to show reversibility in children with asthma and allergic rhinitis less than 6 years of age.

Methods: Recurrent cough, wheezing and dyspnea with clinical response to bronchodilators, inhaled corticosteroids or LTRA therapies were defined as asthma. Atopy, asthma treatments and IOS results were analyzed in 54 subjects with symptoms of asthma and allergic rhinitis. Skin prick tests with food and aero allergens were performed and all children made IOS test. With IOS method, a 30% decrease in R5 or 29% decrease in AX at the 20th minute after bronchodilator usage was defined as reversibility.

Results: Mean age of group was 5.1 $\pm$ 0.5 years, 33% of them were female. 61.5% of the subjects were atopic, mostly to mites (87.5%), grass pollen (22%), cat (10%). In the study group 46% of the subjects experienced asthma symptoms and 15% had allergic rhinitis symptoms whereas 39% had both. While performing IOS test 50% of subjects were at the stable status for asthma. Reversibility measured with IOS was observed in 68% of subjects with asthma, 81% with both asthma and allergic rhinitis and 75% with allergic rhinitis (P = .606). Positive reversibility response to bronchodilator shown by IOS was similar in atopic children (72%) and non-atopic ones (80%) (P = .510).

Conclusions: Our results demonstrated that IOS is a non-invasive, feasible method and may be used, especially for pre-school children experiencing difficulties in forced inspirium and expirium maneuvers, to show increased airway resistance. Long time follow-up is needed to evaluate the diagnostic value and usage of IOS defined reversibility in preschool children with allergic rhinitis for possible asthma development in the future.

0688 | Elevated exhaled nitric oxide levels in adolescents are related to new-onset allergic symptoms to cat within four years

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Introduction: Fraction of exhaled nitric oxide (FeNO) is an established marker of airway inflammation and FeNO is elevated in asthma and rhinitis, and in non-symptomatic subjects with allergic sensitisation but without respiratory symptoms. Previous studies suggest that elevated FeNO in adolescents relate to higher likelihood of subsequently developing wheeze and rhinitis. However, little has been studied regarding the development of allergic symptoms in relation to FeNO.

Objectives: To examine if elevated FeNO predicts the onset of allergic symptoms within four years in a population-based cohort of adolescents.

Results: At baseline, 959 randomly selected adolescents, aged 12-15 years, answered an adapted questionnaire from the ISAAC study including items on respiratory and allergic symptoms and performed lung function and FeNO measurements. A total of 921 (96%) subjects completed a shorter version of the baseline questionnaire four years later.

The subjects with incident allergic symptoms to cat (n = 50) had at baseline higher FeNO (P < .001) and $FEV_{1\%}$ predicted (P = .01) values as well as reported current asthma (P = .001) and rhinitis symptoms (P < .001) to a larger extent than subjects without allergic symptoms to cat at both timepoints (n = 776). Adolescents with incident allergic symptoms to pollen (n = 85) did not differ in baseline FeNO levels (P = .08), but were more commonly reporting having current asthma, rhinitis symptoms and having siblings with rhinitis at baseline (all P < .05).

In a logistic regression model, the risk for incident allergic symptoms to cat was 4.4 (2.3, 8.1) [OR (95% CI)] times higher for FeNO >75th percentile at baseline and 8.1 (3.0, 21.4) [OR (95% CI)] times higher

when subjects with reported current asthma and rhinitis symptoms at baseline were excluded. These analyses were done after adjustments for $FEV_{1\%}$ predicted, height, current asthma and rhinitis symptoms.

Conclusions: Elevated FeNO is associated with an increased risk of developing allergic symptoms to a perennial allergen (cat), but not to seasonal allergens (pollen), within four years. This supports the view that FeNO signals for subclinical allergic airway inflammation that, if perennial, may turn symptomatic within a few years.

0689 | Nasal cellulose powder in children with allergic rhinitis, a randomized, double-blind, placebo-controlled trial

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Introduction: Nasal cellulose powder (NCP), which can prevent assessment of allergen to nasal mucosa, may reduce rhinitis symptoms in dust mite-sensitized children.

Objectives: This study was to assess the efficacy of cellulose powder in improving the clinical symptoms, nasal airflow limitation and nasal inflammatory cells response.

Methods: Children with dust mite-sensitized AR aged 6-18 years were recruited. After 4-week run-in period, NCP or placebo was administered 1 puff per nostril 3 times daily for 4 weeks. Nasal provocation tests (NPT) with *Der p* were performed before and after treatment. Daily nasal symptom score (DSS), daily medication score (DMS), peak nasal inspiratory flow (PNIF), nasal airway resistance (NAR), maximum tolerated dose of NPT and eosinophil count in nasal scraping were evaluated.

Results: Sixty children (30 NCP, 30 placebo) were enrolled. Before treatment, there were no significant differences in age, dust mite control measures, DSS, DMS, PNIF, NAR, maximum tolerated dose of NPT, and nasal eosinophil score between children receiving NCP or placebo. After treatment, there were no significant differences between NCP and placebo group in median (range) of outcomes measured; DSS: 2.06 (0.18-3.77) *vs* 1.79 (0.08-7.79), $P = .756$), DMS: 1.6 (0-5.13) *vs* 0.56 (0- 4.84), $P = .239$), PNIF: 110 (60-160) *vs* 100 (50-180) lpm, $P = .870$), NAR: 0.4 (0.2- 0.97) *vs* 0.39 (0.24-1.32) $Pa/cm^3/s$, $P = .690$), the maximum tolerated dose of NPT, and nasal eosinophil score: 1 (0- 4) *vs* 1 (0- 4), $p= 0.861$).

Conclusions: Treatment with NCP may not effective than placebo in dust mite-sensitized AR children.

SUNDAY, 18 JUNE 2017
TPS 08
ADVANCES IN MOLECULAR ALLERGY

0690 | IgE response to Der p 1 and Der p 2 in Portuguese house dust mite allergic patients

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Introduction: Der p 1 and Der p 2 have been considered the most relevant allergens in house dust mite allergy. However their relative importance and associations seem to change for different geographic regions.

Objectives: Our aim was to assess the role of Der p 1 and Der p 2 in house dust mite allergy, as well as to identify associated factors, in a Portuguese population. A group of 366 patients with allergic respiratory disease and skin prick tests positive for *Dermatophagoides pteronyssinus* was studied. Specific IgE to nDer p 1 and rDer p 2 were assessed in every case and results were analysed considering sex, age and disease phenotype.

Results: Patients were 215 male and 151 female, mean age 18.9 ± 14.2 years, 213 having asthma and/or rhinitis and 153 only rhinitis. Most of them (69.4%) had positive IgE to Der p 1 and Der p 2, 12.3% only to Der p2 and 7.9% only to Der p 1. In 10.4% IgE to both molecular were negative. Logistic regression for Der p 1 positivity showed significant odds ratio of 1.81 for male sex, 2.85 for having asthma and 0.96 for age considered in years. For Der p 2 positivity the odds ratio was 1.98 for male sex and 0.98 for age. Comparing IgE values mean IgE to Der p 1 was higher in men (39.9 kUA/L vs 26.9 kUA/L, T Student test, $P < .05$), and both IgE to Der p 1 and to Der p 2 were higher in patients with asthma vs patients with only rhinitis (respectively 42.5 kUA/L /22.7 kUA/L and 45.8 kUA/L /23.2, kUA/L, T Student test, $P < .001$).

Conclusions: Most of *Dermatophagoides pteronyssinus* allergic patients had IgE to Der p 1 and Der p 2, being the latter more frequent. Male are twice positive for Der p 1 and Der p 2 and have higher Der p 1 values. Asthmatic patients show higher levels of IgE to Der p1 and Der p 2 and IgE to both molecular decrease with increasing age.

0691 | Specific IgE to Der p 1 and Der p 2, do they explain IgE response to dermatophagoides pteronyssinus?

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Introduction: Most house dust mite allergic patients have specific IgE to Der p 1 and/or Der p 2. However, specific IgE to other molecular allergens were identified, reported by some authors to be frequent and possibly relevant for respiratory allergy.

Objectives: The aim of this study was to evaluate IgE response to Der p1 and Der p2 and its relation to IgE response to total *Dermatophagoides pteronyssinus* extract. To achieve it we analysed IgE to nDer p 1 and rDer p2 of 290 serum samples with measured IgE to total *Dermatophagoides pteronyssinus* superior to 2 kUA/L. Those belonged to 180 male (62%) and 110 female (38%), mean age 16.9 ± 13.6 years.

Results: Mean IgE to total extract was 87.6 kUA/L ± 119.8, to Der p 1 41.5 kUA/L ± 63.0 and to Der p 2 44.1 kUA/L ± 66.2. Neither Der p1, nor Der p2 were recognized by 7 patients (2.4%). Mean difference between IgE to total extract and the sum of IgE to Der p 1 and Der p 2 was 2.3, ranging from −313.0 to +212 kUA/L. Expressed in percentage of IgE to total extract, mean difference was 2.7%, minimum −217.7% and maximum +99.8%. Most of the patients, 158 (54.5%) showed a positive difference, which was 25% to 50% in 42 (14.5%) and superior to 50% in 34 patients (11.7%).

Conclusions: Most allergic to *Dermatophagoides pteronyssinus* people exhibit IgE response to Der p 1, Der p 2 or both. Nevertheless, in more than a half sera the amount of IgE to total *Dermatophagoides pteronyssinus* exceeds the sum of Der p1 and Der p 2 IgE sum, being this difference higher than 25% in 26.2% of patients. Data suggest that in at least one fourth of cases allergy to other allergens than Der p1 and Der p2 may be expected and looking for those may be important.

0692 | Elevated level of IgE specific to can f 2 is related to dyspnea in patients with pet allergies

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Introduction: Nowadays an important issue is to connect the sensitization to specific allergen components with clinical manifestations. Assessing the relevance of using component resolved diagnosis (CRD) in clinical practice is also crucial.

Objectives: The aim of this research was to connect the sensitization to specific allergen components with clinical manifestations

Results: 70 patients (42F, 28M, 18-65, 35.5 on average) with a positive feline or canine allergy diagnosis and 30 healthy controls

went through an allergological interview and a physical examination. Skin prick tests with common inhalatory allergens were conducted. The total IgE (tIgE) concentration of all patients as well as their allergen-specific IgE (asIgE) against feline and canine allergens and canine (Can f 1, Can f 2, Can f 3, Can f 5) and feline (Fel d 1, Fel d 2, Fel d 4) allergen components were measured (ImmunoCap). No statistically important relationship between the clinical image of an allergic disease and the concentration of IgE specific to a given allergen component of cat or dog was found. Heightened levels (>= 0.35kU/L) of specific IgE against the dog allergen component extract and Can f 2 was connected to a more frequent occurrence of dyspnea symptoms.

Within the research group the levels of asIgE were not related to owning a cat or a dog. The most frequent clinical symptom after exposure to a sensitizing animal was allergic rhinitis.

Conclusions: Correct interpretation of results and the assessment of indications for component resolved diagnosis is a crucial issue. Further study is necessary, and as more research is conducted, the list of indicators for CRD will continue growing.

0693 | Increased diagnostic accuracy by using allergen component tests in hazelnut allergy: a systematic literature review and meta-analysis

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Introduction: Hazelnut allergy (HA) diagnosis is supported by positive sIgE test results. In vitro tests for sIgE to hazelnut storage proteins are now available, and several studies using these have been published.

Objectives: Our aim was to systematically investigate the clinical sensitivity and specificity of hazelnut allergen components for diagnosing hazelnut allergy in children.

A systematic literature review was conducted to identify studies providing information on the performance of hazelnut allergen components in the diagnosis of HA suspected children. Oral food challenge was used as reference standard, allowing for exceptions only in cases of recent anaphylaxis. A random effects meta-regression was performed, and pooled estimates for each index test were calculated (sensitivity, specificity, positive/negative likelihood ratios LR+ and LR-) and reported with 95% confidence intervals (CI); the meta-regression analysis was performed using 0.10 kU/L or 0.35 kU/L as cut-off thresholds for Cor a 9, Cor a 14 and hazelnut sIgE.

Results: Six studies met the inclusion criteria; five of these were included in the meta-regression analysis, all characterized by a single-gate design, which is representative of the scenario in which the tests would be used in clinical practice. The included studies presented data on young children with a suspicion of HA from four European countries, and one from the USA. Only one study reported data on Cor a 1, so no calculations could be made for this test. Comparative data of hazelnut extract IgE results was collected only from the included studies.

Using 0.35 kU/L as the cut-off threshold, results show that the hazelnut extract sIgE test had a significantly higher diagnostic sensitivity (95%; CI [84-99%]) than Cor a 14 (78%; CI [71-84%]). The sensitivity of Cor a 9 was 83% (CI [71-91%]). The diagnostic specificity of both Cor a 9 (73%; CI [57-86%]) and Cor a 14 (81%; CI [76-86%]) were significantly higher than the hazelnut extract sIgE test (20%; CI [13-30%]). Results show that Cor a 14 had a significantly better LR+ than the hazelnut sIgE test.

Results using 0.1 kUA/L as cut-off threshold will be presented.

Conclusions: Both Cor a 9 and Cor a 14 storage protein tests of hazelnut had higher specificity and lower sensitivity for diagnosing HA than the hazelnut extract-based sIgE test. These results suggest that a combination of the two types of tests would improve the level of accuracy in identifying HA children.

0695 | The molecular allergen pattern to asthma and rhinitis in a cross sectional study among adolescents in southern Sweden

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Introduction: ABISS is a multi-center population based cohort, started 2012/2013, among adolescents aged 13-14 years in the south of Sweden. The study is designed to assess the prevalence of allergic diseases. The relationship between IgE sensitization and atopic disease is well known. However, there are only few data of IgE reactivity ≥0.3 kUA/L and development of eczema, asthma, rhinitis and allergic multi-morbidity in adolescence. Even though there is a strong and consistent association between IgE sensitization and these diseases, they also exist in non-sensitized humans, as well as sensitization is also found among individuals without allergy-related diseases. So it is of importance to make further population based studies to plan and evaluate strategies to use in the clinic part, to prevent and stop severity of the allergic diseases.

Objectives: The aim of this study was to analyse the sensitization profile in a representative sample from the population and to relate patterns of allergens and allergen components to allergic diseases and symptoms reported.

Results: Sensitization to airborne allergens was significantly more common than to food allergens, 43% *vs*. 14% respectively. The level of IgE was significantly higher to airborne allergens in both the children reporting rhinitis ($P < .001$) and in eczema ($P < .01$). Out of 53 children with allergic disease, 40% were not sensitized. The highest frequency of individuals with no IgE response was found in the current asthma group 56% followed by 38% and 18% of individuals in the current eczema and rhinitis groups respectively. The allergen components best associated with current asthma was allergens to cat (Fel d4), mite (Der f2) and dog (Can f5). IgE to timothy grass (Phl p 1) was best associated with current rhinitis. No child had IgE to the peanut storage proteins (Ara h 1,2,3 & 6).

Conclusions: We find that grass sensitization is associated with rhinitis and cat-, mite- and dog sensitization to asthma. A substantial number of children reporting current asthma were not sensitized to any allergen component. No genuine peanut sensitization was found. Microarray IgE testing is useful when examining the molecular allergen pattern in a general population of adolescents.

0696 | Combination of allergen component microarray and urea buffer allows the discrimination between specific IgE of high or low functional affinities

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Introduction: As shown by in vitro models, affinity of IgE for allergens is crucial for the activation of effector cells. However, IgE's functional affinity is not explored by currently available biological tests. Chaotropic agents such as urea or thiocyanate are commonly used to measure the avidity of IgG directed against infectious agents with the aim to estimate the time elapsed since primary infection.

Objectives: We incubated sera from 12 patients presenting severe allergic symptoms in presence of a tris-urea buffer. Comparison of IgE binding to the 112 components on a biochip with or without urea allowed us to estimate the affinity of specific IgE from these patients (as the % of ISU-E that remained in presence of urea).

Results: While anti-PR-10 specific IgE were present in higher concentrations compared to anti-LTPs IgE ($P < .0001$), specific IgE directed against LTP display higher functional affinities (50% with urea) than anti-PR-10 IgE (4.5% with urea; $P < .0001$). This suggests that the mild symptoms associated with the presence of anti-PR-10 IgE could be due to their intrinsic low affinity rather than to the thermolability of PR-10 proteins. Moreover, we found that affinities of IgE specific for LTP components from food allergens (Pru p3, Jug r3, Ara h9, Cor a8, Tri a14) were higher than those of IgE directed against pollen LTP components (Art v3, Ole e7, Par j2, Pla a3; $P = .0006$). The same discrepancy exists for anti-PR-10 IgE, where anti-Mal d 1 and anti-Cor a 1.0401 IgE possess higher affinities compared to IgE directed against other PR-10 components, including birch pollen's Bet v 1. Thus, we estimate that the primary sensitization of the patients studied here does not originate from pollens containing PR-10 proteins (such as birch), but comes from exposure to food PR-10 components.

As for non-cross-reactive components, we found a good agreement between the presence of high affinity IgE and the allergy symptoms presented by the patients. High-affinity IgE were frequent for peanut and nuts SSP, egg (Gal d1), cow milk (Bos d5/d8), soy (Gly m5), parvalbumin, animal danders, mites (Der p1/ f1), weeds (Pla l1), trees (Ole e1), molds (Alt a1) and polcalcins.

Conclusions: Despite more patients are required for definite conclusions, we propose that the estimation of IgE affinity by means of chaotropic compounds allows a new and potentially helpful interpretation of sensitization profiles, especially for patients with complex and severe allergies.

0697 | High fidelity of an allergen microarray for first line screening of type i allergy: results from a clinical study

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Introduction: Classical allergy diagnostic workup "from symptoms to molecules" comprises 1) clinical investigation, 2) extract-based skin prick- and IgE- testing, and recently, 3) molecular allergy testing. We examined whether the approach "from molecules to clinic" could achieve similar diagnostic fidelity, using an allergen microarray.

Objectives: 202 patients with clinically suspected allergic sensitizations were enrolled in 2 study centers. Cohort "ISAC-first" at an allergy clinic was subjected to allergen microarray testing followed by selected skin prick tests (SPT), while cohort "SPT-first" at a dermatology clinic started with SPT followed by microarray testing.

Results: Considering patient's history, SPT-first patients had significantly more allergic skin symptoms, but their IgE profile to major allergen sources did not differ from ISAC-first patients. A significantly lower number of SPTs was needed for confirmation of allergy diagnosis in the ISAC-first cohort (median 4 vs. 14). In 19% of patients of the ISAC-first group and in 34% of the SPT-first group

additional respiratory allergens could be detected in SPT which were not positive in the ISAC microarray; whereas in 18% of ISAC-first and 32% of SPT-first patients additional sensitizations were found in the ISAC microarray compared to SPT. For food allergens, 13% and 12% additional sensitizations were detected by the microarray not detected by SPT in the two groups. No additional food allergen was found by SPT in the ISAC-first group, while in 6% of the cases in the SPT-first group sensitizations were not positive in the microarray. Most respiratory allergens were detected by the microarray with high specificity and sensitivity.

Conclusions: For the diagnostic verification of clinically suspected allergy, the novel concept "from molecules to clinic" offers a reliable diagnostic workup in shorter time. Due to lower skin test numbers it is especially applicable for young children and seniors, in atopic patients, and whenever skin tests get difficult or unreliable.

0698 | The first allergen components profile of five main food allergens in 492 atopic children: an important absence of major allergen components

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Introduction: Molecular allergology give the possibilities to build allergen components profile for every allergen source. The picture of major and minor allergens in atopic children is extremely important for diagnosis, prophylaxis and treatment. In this cross-sectional, prospective study, allergen components profile in atopic children using component resolved diagnostics (CRD) was analyzed.

Objectives: Serum specific IgE to 112 allergen components were measured by using multiplex microarray in 492 atopic children (age: 0-18 years). Sensitization to five main food allergens (hazelnut, peanut, soy, walnut, wheat) and allergen components profile for every allergen source was analyzed.

Results: IgE reactivity to hazelnut was found in 229 (46%) children and the profile from the most frequent to the most rare component was as follows: Cor a 1.04 (71%), Cor a 9 (27%) and Cor a 8 (10%) whereof in 73% of children the major hazelnut allergen Cor a 9 was absent. IgE sensitization to peanut components was found in 222 (45%) children and the profile was as follows: Ara h 8/2/1/6/9 and Ara h 3 (63, 36, 30, 29, 15 and 14% respectively), whereof in 49% of children the major peanut allergens Ara h 1/2/3 and Ara h 6 were absent. IgE sensitization to soy components was found in 152 (31%) children and the profile was as follows: Gly m 4 (70%), Gly m 6 (39%) and Gly m 5 (21%) whereof in 54% of children the major soy allergens Gly m 5 and Gly m 6 were absent. IgE reactivity to walnut components was found in 131 (27%) children and the profile was as follows: Jug r 2 (51%), Jug r 1 (39%) and Jug r 3 (37%) whereof in 21% of children the major walnut allergens Jug r 1 and Jug r 2 were absent. IgE sensitization to wheat allergens was found in 47 (6%) children and the profile was as follows: Tri a aA_TI (68%), Tri a 14 (57%) and Tri a 19 (36%).

Conclusions: CRD is critical in recognition of the reactivity to major allergens of allergen source in atopic children. A sizable part of children have no sensitization to major allergen components. This fact has an important impact on diagnosis, prophylaxis and treatment.

0699 | Component resolved diagnosis for phleum pratense in a multinational multicenter clinical trial of a depigmented polymerized phleum pratense extract

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Introduction: In the recent years, the use of component resolved diagnosis (CRD) in pollen allergy has helped to correctly identify suitable candidates for immunotherapy, as well as cross-reactivity reactions with food allergens among others. To better understand the sensitization profile of pollen allergic patients, a CRD to *Phleum pratense* components was carried out within the context of a multinational multicenter clinical trial with a depigmented polymerized *P. pratense* extract.

Objectives: To describe the sensitization profile to *P. pratense* components of the patients from a multinational multicenter clinical trial with a depigmented polymerized *P. pratense* extract and compare it by country.

Material and Methods: The clinical trial was conducted in Germany, Poland and Spain (EuDRA-CT No.: 2014-004732-19). Subjects were selected on the basis of a consistent clinical history of allergic rhinitis and/or conjunctivitis, with or without intermittent asthma due to a sensitization against grass pollen, confirmed by a positive specific IgE to *P. pratense* ≥0.7 kU/L.

After inclusion in the study, a baseline assessment of specific IgE to *P. pratense* components (Phl p 1, Phl p 2, Phl p 4, Phl p 5b, Phl p 6, Phl p 7, Phl p 11 and Phl p 12) was done. Values ≥0.35 kU/L were considered positive. Major and minor allergens from *P. pratense* were identified. Country-based assessment was also carried out to evaluate possible regional differences.

Results: A total of 189 patients were evaluated, 94 from Germany, 56 from Poland and 39 from Spain. Regarding *P. pratense* components, more than 50% of total included population were sensitized to Phl p 1, Phl p 2, Phl p 4, Phl p 5 and Phl p 6, highlighting Phl p 1 and Phl p 4 with respective 98% and 99% of patients. Phl p 7 was the lowest in prevalence, with a 6.3%.

The analysis per country showed similar frequencies of sensitization between countries, except for Phl p 7 which was absent in Spain, and Phl p 12 which was higher in Poland (26.8%) compared to Germany and Spain (12.8% and 15.4% respectively).

Conclusions: We have identified 5 *P. pratense* allergens behaving as major allergens in the population studied, with almost all patients sensitized to Phl p 1 and Phl p 4. Similar frequency of sensitization to components was identified in the country-based analysis, except for small differences in some minor allergens.

SUNDAY, 18 JUNE 2017

TPS 09

ADVANCES IN SKIN TESTING AND CHARACTERISATION OF NOVEL ALLERGENS

0701 | Effects of acute stress on the reliability of skin prick testing and mediator release: clinical study in healthy and allergic volunteers using the Trier social stress test

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Introduction: Skin prick testing (SPT), besides IgE determination and clinical history, belongs to the cornerstones of allergy diagnosis and is tightly regulated by guidelines. Some factors from the patient side, such as left or right arm testing, stress and arousal just before the visit, were so far not considered, but might affect the fidelity of the allergy diagnosis by SPT.

Objectives: We aimed in this clinical study to investigate whether (i) SPT in the same person varies between the left and right arm, and (ii) whether acute stress in the standardized Trier social stress test (TSST) would impact the wheal and flare reaction in SPT in the skin of healthy volunteers vs allergic patients. Furthermore, we attempted to determine released candidate mediators in the blood with a potential influence on the neuroendocrine-immune axis.

Methods: (i) 14 grass pollen allergic patients (4 female, 10 males) were pricked with allergen extract, histamine and negative control by the same operator on the left, compared to the right arm. (ii) 15 healthy and 25 allergic patients were first subjected to SPT with grass and birch pollen, and house dust mite extract, histamine and negative control, followed by TSST, and then again SPT on the contralateral forearm. Before and after this procedure also saliva and blood samples were collected and mediators analysed by commercial ELISAs.: serotonin, cortisol, platelet activating factor (PAF), Prostaglandin$_2$ (PGD_2), Oxytocin, Adrenocorticotropic hormone (ACTH) and substance P (SP).

Results: (i) No significant differences left-right were seen in the wheal areas. Therefore, any difference between SPT size in volunteers subjected to the TSST should give valid information. (ii) The TSST was controlled by saliva cortisol measurements. No significant differences were recorded regarding the sizes (areas and diameters) of the wheal or flare reactions to any of the three tested allergens, neither in the perception of itch of allergic or healthy volunteers, before and after the stress test. In accordance, no significant differences between before and after the stress were seen in the tested mediators.

Conclusions: A comparison of SPT between the right and the left hand of the same person is a reliable tool in clinical studies. Furthermore, acute stress seems to have no influence on the extent and quality of skin prick tests, which confirms them as reliable and valuable tool for assessing allergies.

0703 | The role of microneedle patch test in the diagnosis of atopic dermatitis

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Introduction: Atopic dermatitis (AD) is a disease well-known to be associated with sensitization to housedust mite, and atopy patch test has been used evaluate the elicitation of atopic skin reactions. Microneedle patches allow the increased penetration of allergens with constant and controlled depth and amount.

Objectives: To evaluate the efficacy of the microneedle patch test in the diagnosis of sensitization to housedust mite in AD by comparing *Dermatophagoides farinae(D. farinae)*-loaded microneedle patch with Finn chamber patch test among patients with AD, allergic rhinitis (AR) and normal subjects.

Results: Patients with AD and AR had significantly increased total IgE levels and *D. farinae*-specific IgE levels, but no differences were observed between the two groups. The positivity rate of microneedle patch was comparable to that of Finn chamber patch in patients with AD. Patients with AR had a significantly lower positivity rate than that of patients with AD. No serious complications occurred.

Conclusions: Microneedle patch may be a useful tool for atopy patch test confirming the elicitation of skin reactions after the exposure to housedust mite in AD. The amount of *D. farinae* required in microneedle patch is less than the amount used in Finn chamber, in which microneedle patch can be suggested as more efficient method for atopy patch test.

0704 | Comparison of commercial skin prick test reagents using in vivo and in vitro methods

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Introduction: Precise detection of culprit allergen through skin prick test (SPT) is critical for management of allergic patients. However, each manufacturer utilizes its own potency units and quality control programs. And they use different raw materials to make their own products. These make clinicians in confusion when they compare the potency of SPT reagents. This study aims to compare the allergen potency of commercially available SPT reagents.

Objectives: Allergenicity of 7 important inhalant allergens (Dermatophagoides farinae, Dermatophagoides pteronyssinus, Oak, Ragweed, Mugwort, Cat dander, Dog dander) provided from 3 manufacturers were compared. For comparison of in vitro properties, Bradford assay, sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), 2-site enzyme-linked immunosorbent assay (ELISA), inhibition assay and Western-blot were used. For in vivo comparison, 94 allergic patients were enrolled for SPT. Analysis of SPT positivity and concordance rates results were compared.

Results: Positive rate and concordance rate with results of inhibition were varies significantly among SPT reagents in each allergen. In concordance rate of allergens to inhibition results, kappa showed variable results of 0.209 to 0.849. Most of SPT reagents showed fair to moderate concordance rates. Significant differences in the concentration of major allergen of house dust mite, pet animals were found among the 3 different products. The results of 50% inhibition concentration, which directly reflects allergenicity of SPT reagents, were also showed significant differences.

Conclusions: Allergen potencies vary among commercial SPT reagents. These differences are critical for precise diagnosis of allergic diseases so that clinicians should consider properties of each SPT reagents when they prescribe SPT.

0705 | The optimal conditions for the long-term storage of the extracts of sawtooth oak, Japanese hop, ragweed and mugwort pollens

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Introduction: Sawtooth oak, Japanese hop, ragweed, and mugwort pollens are important causes of seasonal allergic rhinitis in Korea. Precise diagnosis and effective treatment by pollen extracts are greatly dependent on the stability of the extract.

Objectives: In this study, we tried to find out the optimal storage conditions of four pollen allergen extracts from sawtooth oak (*Quercus acutissima*), Japanese hop (*Humulus japonicus*), ragweed (*Ambrosia artemisifolia*), and mugwort (*Artemisia vulgaris*).

Results: The lyophilized allergen extracts were reconstituted in various buffer (normal saline, 0.3% phenol saline, and 50% glycerol with saline) and stored at room temperature (RT, 18-26°C) or refrigerated (4°C). Subsequently, protein concentration and allergen content in the extracts were examined over one year. At least 62.6% of the original protein concentration in all four extracts examined was detected when 50% glycerol was added and refrigerated, whereas 16.2 to 37.7% remained in the extracts at RT over one year. Without 50% glycerol, 23.6 to 86.2% of protein was detected in the refrigerated extracts whereas 3.7 to 33.0% remained at RT. Japanese hop (97.2% of protein left over one year) and mugwort (72.6%) were found to be stable when reconstituted in 0.3% phenol and 50% glycerol, and 50% glycerol for oak (65.9%) was shown to be the best constituent for a long term storage. Amb a 1, a major allergen of ragweed, was almost completely degraded in 9th week at RT when reconstituted in a buffer without 50% glycerol. However, more than 50% of Amb a 1 was detected after one year of incubation at RT when 50% glycerol was added. No loss of Amb a 1 was observed when refrigerated.

Conclusions: Addition of 50% glycerol as well as refrigeration was found to be the important to increase the shelf-life of allergen extracts from pollens of allergenic importance.

The optimal conditions for the long term storage of the extracts of sawtooth oak, Japanese hop, ragweed and mugwort pollens

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Conclusions: Addition of 50% glycerol as well as refrigeration was found to be the important to increase the shelf-life of allergen extracts from pollens of allergenic importance.

0706 | Specific IgE to propolis extracts among pollen allergic patients

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Introduction: Propolis (bee glue) is the resinous substance that bees collect from living plants for the construction, protection and disinfection of their nests. Although propolis is widely marketed as a natural health supplement, it may cause allergic reactions among patients with a history of pollen allergy.

Objectives: The objective of this study was to investigate the presence of specific IgE reactivity to propolis among pollen polysensitized patients. For this purpose, propolis samples were collected from two geographically distinct areas; a humid sub-tropical forest (HF) on the edge of the Caspian Sea and a semi-arid area (SA) in the southern side of Alborz Mountains (Markazi, Iran). Sera from ten pollen polysensitized patients were first screened against propolis water extracts using a dot blot assay. For Western blot experiments, propolis proteins were extracted in phosphate-buffered saline and subsequently separated by 10% SDS-PAGE. The separated proteins were then transferred to PVDF for IgE immunoblotting using a pool of representative positive sera.

Results: All tested sera showed positive reactions to at least one of the two dot-blotted propolis samples. SDS-PAGE protein profiles revealed that two Iranian propolis contained quite similar protein bands ranging from 15 to180 kDa. Considering the low protein content of both propolis extracts (about 50 μg per ml), silver staining was performed to visualize all separated protein bands. Specific IgE-binding patterns to HF and SA propolis samples were also very similar and included three major IgE-binding proteins with relative molecular masses of about 15, 53 and 60 kDa.

Conclusions: The two propolis samples exhibit similar protein and sIgE binding patterns, despite their different geographical origins. This could be due to the dominant share of the *Apis mellifera* proteome in both extracts or the preponderance of the poplar-type resin in Iranian propolis samples, as confirmed by our previous phytochemical analyses (HPLC-DAD). In-depth proteomic experiments are planned to determine the nature of these newly-identified propolis putative allergens and to evaluate the risks of IgE cross-reactivity with other allergenic sources.

0707 | Mono-sensitization to only one allergen component is rare in canine and feline allergic patients

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Introduction: A highly relevant issue for most patients is the co-occurrence of sensitizations to a selection of allergen components, not only cross-reactive but also originating in different protein families. The aim of this study was to establish the frequency of polysensitization in pet allergic patients.

Objectives: Establishing the frequency of sensitization to canine and feline allergen components in pet allergic patients.

Results: 70 patients with a positive feline or canine allergy diagnosis and 30 healthy controls went through an allergological interview and a physical examination. Skin prick tests with common inhalatory allergens were conducted. The canine (Can f 1, Can f 2, Can f 3, Can f 5) and feline (Fel d 1, Fel d 2, Fel d 4) allergen components were measured. Heightened levels (≥0.35 kU/L) of specific IgE to at least one of the allergen components of felines were found in 65 patients, and against at least 1 allergic component of canines in 42 patients. Out of the research group, 3 patients did not have heightened levels of specific IgE to any canine and feline components, and for 21 (30%) of patients a monosensitization to only 1 canine or feline component was noted. The majority of patients were sensitized to feline allergen component Fel d 1 - 87.1% of the study group and canine allergen component Can f 1 - 40% of the study group. No patients were mono-sensitized to Fel d 2.

Methods: In patients sensitized to canine and feline there is a high risk of sensitization to multiple allergen components, both intra- and inter-specie.

0708 | Ragweed pollen allergy - patterns and cross-reactivity

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Introduction: Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated disease that affects approximately 25% of the population of Europe. Repeated exposure to allergen may induce facilitated antigen presentation, and eventually lead to polysensitization. Weed, cereal and grass pollens are the most frequent outdoor allergens that cause AR in the Western part of Romania, and out of these, ragweed pollen is the most important allergen.

Objectives: Our study aims to establish the connection between ragweed pollen allergy and other outdoor allergens, and to correlate the clinical aspects with the skin prick test (SPT) and with specific serum IgEs.

Results: Mean patient age was 31.2 ± 8.9 years, with a mean allergic disease age of 3.62 ± 3.15 years. 40% of the patients were men, and 60% women. Based on ARIA guidelines, most of the patients (73%) had moderate-severe intermittent allergic rhinoconjunctivitis. Increased specific serum IgE (sIgE) to the major ragweed allergen Amb a 1 was found in 90% of the 84 patients with positive SPT to ragweed pollen extract (5% class 1, 35% class 2, and 45% class 3 sIgE levels). Using SPT as gold standard, the sensitivity and specificity of ImmunoCAP ISAC microarray (determining the sIgE to Amb a 1 in vitro) vs. SPT (determining the reactivity to RP extract in vivo) were 85.88% (95% CI: 76.63% 92.48%), and 90.91% (95% CI: 58.67% to 98.49%), respectively. A significant cross-reactivity between Amb a 1 and Cry j 1 ($P < .05$) in the ImmunoCAP ISAC microarray results was demonstrated, but no such cross-reactivity existed between Amb a 1 and Cup a 1 ($P < .05$).

Conclusions: There is a small fraction of patients that are allergic to minor ragweed pollen allergens and they are not identified by standard in vitro diagnostic procedures. There is cross-reactivity between ragweed pollen allergens and other allergens. Component-based diagnosis using microarrays is needed for the selection of the appropriate allergen source for specific immunotherapy.

0709 | Study of results of modified skin prick test [MSPT] with 140 allergens performed in single sitting in cases of severe persistent allergic rhinitis [SPAR] in Central India

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Introduction: In country like India where number of allergens are too many and allergen detection is not possible by patient himself or only history correlation doesn't suffices, there comes role of allergy testing in a single sitting for common 140 allergens by gold standard diagnostic test modified skin prick test [MSPT].

Objectives: Material & Method: 910 patients of severe persistent allergic rhinitis[SPAR] in the age group of 07 to 63 years of either sex from year 2006 to year 2016 were taken for study of allergen pattern by modified skin prick test[MSPT] for 140 common allergens in a single sitting. Allergens included were Mite[1] Pollens[50],Fungi[9], Insects[6],Dusts[9],Danders[6],Fabrics[3]Food [54] Miscellaneous[2].
After detailed history. Patient were off the antihistaminic for minimum of seven days. allergy test by modified skin prick test [MSPT] was performed on both upper limbs on volar aspect of forearms. Glycerinated histamine acid phosphate as positive control and glycerinated buffer saline as negative control were used. each patient was tested for same 140 allergens in the single sitting, mean distance between two allergens were 1.2 to 1.5 cms only wheal [induration] palpated and recorded in mms.

Results: Out of 910 patients only 10 patients showed overlapping of wheal response for maximum of three allergens. At the same sitting those three allergens with overlapping response were tested 2 cm above cubital fossa area skin to make final reading of MSPT.

Conclusions: The above study gave us a crystal clear overview regarding testing large number of allergens to be tested for severe persistent allergic rhinitis [SPAR] where number of allergens are too many and allergen detection is not possible by patient himself or history correlation alone. This way i could make the allergy diagnosis precise, save time, energy and money.
This may be of some help in deciding future guidelines for allergy testing.

0710 | Manufacturing of guideline-conform human sera pools for assessment of IgE reactivity

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Introduction: Regarding analytics and control of carbohydrate structures, the Guideline on Allergen Products (GUIDELINE ON ALLERGEN PRODUCTS: PRODUCTION AND QUALITY ISSUES (EMEA/CHMP/BWP/304831/2007)) demands,

For an IHRP: Data should be provided on protein and, whenever possible, carbohydrate composition. The relevance of glycoproteins for the IgE-binding should be considered.

For a sera pool: Sera recognizing carbohydrate epitopes . . . should not be included in the pool.

Objectives: We wanted to elucidate, whether the demand of the Guideline - that inclusion of sera recognizing carbohydrate epitopes into sera pools should be avoided - can be fulfilled for different allergen sources.

Results: Sera pools specifically detecting major allergens of either Phleum pratense, Dermatophagoides pteronyssinus or Olea europaea were manufactured. Sera pools were analyzed regarding recognition of CCDs (Cross-reactive carbohydrate determinants) by IgE testing and by Western blot analyses using allergen extracts of the respective allergen source. To investigate the effect of carbohydrate modifications of allergens on binding of IgE antibodies, allergen extracts were deglycosylated. As control protein bromelain from pineapple stem was processed in parallel to the allergen extracts. Sera of individuals recognizing CCDs served as positive control sera. In sera pools specific for Phleum pratense and Dermatophagoides pteronyssinus no carbohydrate-dependent binding of IgE antibodies was observed. In the sera pool specific for Olea europaea, antibodies binding to CCDs could be detected by Western blot analysis, although the measurement with ImmunoCAP showed no CCD-specific IgE antibodies.

Although the sera pool specific for Olea europaea contained IgE antibodies binding to carbohydrate moieties, they retained binding to major allergens after deglycosylation of the allergen extract.

Finally, individual sera were screened by IgE testing in order to qualify sera for a sera pool specifically detecting Plantago lanceolata allergens. Almost all of the sera contained IgE antibodies binding to CCDs.

Conclusions: Based on our observation we suggest to redefine the inclusion criteria for individual sera into a sera pool in the following manner:

An individual serum can be included into a sera pool, if binding of specific IgE antibodies to the major allergen(s) of a given allergen source is still preserved after deglycosylation of the proteins of the allergen source.

SUNDAY, 18 JUNE 2017
TPS 10
ATOPIC DERMATITIS

0711 | Staphylococcus spp. susceptibility to antimicrobial agents in atopic dermatitis: current prevalence of methicillin-resistant staphylococcus aureus and methicillin-resistant staphylococcus epidermidis

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Introduction: Various topical and systemic antimicrobial agents are included in treatment of atopic dermatitis (AD). The prevalence of methicillin-resistant *S. aureus* (MRSA) as well as methicillin-resistant *S. epidermidis* (MRSE) has been increasing. Resistant strains can be the reason of difficult-to-treat AD. At the same time MRSA and MRSE carriers can be a source of severe community-associated infections that is of particular importance in immunocompromised individuals.

Objectives: To analyze antimicrobial susceptibility patterns in AD skin lesions and to determine the prevalence of MRSA and MRSE.

Results: A total of 146 children aged 2 months to 17 years with clinical signs of AD were included in an observational cross-sectional study. Written informed consent for participation in the research and publication of the results were obtained from children's parents. From 146 children 93 isolates of S. aureus, 54 isolates of *S. epidermidis* isolates were obtained. All isolates of *S. aureus* were susceptible to gentamicin, vancomycin, levofloxacin, ciprofloxacin, linezolid and rifampicin. The isolates exhibited less susceptibility to oxacillin, cefepime, tetracycline, macrolides, clindamycin, chloramphenicol and trimethoprim/sulfamethoxazole and no susceptibility to benzylpenicillin and ampicillin. *S. epidermidis* strains showed the highest resistance rate to chloramphenicol and macrolides followed by β-lactam antibiotics, gentamicin, tetracycline, clindamycin, rifampicin, levofloxacin and trimethoprim/sulfamethoxazole. All *S. epidermidis* were susceptible to vancomycin, ciprofloxacin, linezolid and resistant to benzylpenicillin and ampicillin. Multidrug resistance was found in 19% of the colonizing *S. aureus* strains and 92.5% *S. epidermidis* strains. MRSA was detected only in one patient (1%). The prevalence of MRSE was 25.9% (14/54). No correlation was found between the rate of resistance of *S. aureus* strains and patients' age, severity of the disease and clinical types of lesions. That was also true for *S. epidermidis* strains.

Conclusions: *S. aureus* strains remained susceptible to most antimicrobial agents, including Gentamicin, which is important as this antimicrobial agent is widely used for topical treatment of AD lesions. All isolates of *S. aureus* and *S. epidermidis* were resistant to benzylpenicillin and ampicillin. In this study the prevalence of MRSA and multiple drug resistance in AD children was low. *S. epidermidis* strains were in general more resistant.

	Antimicrobial susceptibility				
Drug	*S. aureus*		*S. epidermidis*		*P*-value
Benzylpenicillin	0		0		
Ampicillin	0		0		
Amoxicillin/ clavulanic acid	91/92	98.9%	41/54	75.9%	$P < .05$
Oxacillin	92/93	98.9%	40/54	74.0%	$P < .05$
Cefazolin	91/92	98.9%	41/54	75.9%	$P < .05$
Cefepime	86/87	98.8%	40/51	78.4%	$P < .05$
Imipenem	90/92	97.8%	40/54	74.0%	$P < .05$
Gentamicin	93/93	100%	48/54	88.9%	$P < .05$
Tetracycline	79/87	90.8%	36/54	66.6%	$P < .05$
Erythromycin	84/93	90.3%	25/53	47.1%	$P < .05$
Clarithromycin	41/45	91.1%	19/35	54.2%	$P < .05$
Azithromycin	72/82	87.8%	24/53	45.2%	$P < .05$
Chloramphenicol	79/90	87.7%	11/54	20.3%	$P < .05$
Vancomycin	93/93	100%	54/54	100%	$P > .05$
Clindamycin	84/93	90.3%	44/54	81.4%	$P > .05$
Levofloxacin	93/93	100%	52/54	96.2%	$P > .05$
Ciprofloxacin	51/51	100%	24/24	100%	$P > .05$
Linezolid	64/64	100%	41/41	100%	$P > .05$
Rifampicin	93/93	100%	53/54	98.1%	$P > .05$
Trimethoprim/ sulfamethoxazole	91/93	97.8%	42/54	77.7%	$P < .05$

0712 | Assessment of IL-31 level and disease severity in children with atopic dermatitis

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Introduction: Atopic dermatitis is chronic, relapsing, highly pruritic, inflammatory skin disease with increasing prevalence of 10% to 20% in children. Pruritus is the main complaint, inducing and aggravating inflammation, altering quality of life of affected patients. Current H1 receptor antagonist therapies are ineffective in treatment of pruritus suggesting the role of different mediators other than histamine. One of these mediators is IL-31 secreted by CD4 + T cells, causing pruritus by binding its receptors on keratinocytes and epithelium cells.

Objectives: We aimed to assess the correlation between IL-31 level and the severity of the disease in patients with atopic dermatitis through Severity SCORing of Atopic Dermatitis (SCORAD) index

and the degree of itching assessed subjectively. We included patients with AD who were followed at Istanbul University Istanbul Medical Faculty Pediatric Allergy and Immunology outpatient clinic between January and June, 2013.

Results: 135 children were enrolled in the study in total, 70 children with atopic dermatitis diagnosis (29 female, 41 male) and 65 children in control group without any allergic or skin disease. Data on demographic features (age, gender, family history of atopy) and lab values of serum eosinophil, total IgE, IgM, IgA, IgG levels and skin prick test results were collected through patient files. We assessed the severity of the disease by SCORAD index and used subjective itch intensity score in SCORAD index. We studied plasma IL-31 levels of the patients. Demographic features and lab values of the patients demonstrated in Table 1.We found significant difference in IL-31 levels of AD patients and control group (*P*:.0001). There wasn't significant difference between IL-31 levels and SCORAD index/subjective itch intensity.

Conclusions: IL-31 level is higher in AD patients.

There is not any correlation between IL-31 level and severity of the disease and itch intensity.

Further research on larger population is needed.

	Mean ±Standard deviation	Lowest-Highest
Age	5.99 ± 3.48 months	1-17 months
Follow-up period	10.92 ± 17.77 months	1-120 months
Serum Eosinophil level	493.74 ± 328.844 /mm³	47-1880/ mm³
Total serum IgE level	420.20 ± 581.977 ku/L	2-2000 ku/L
SCORAD	39.14 ± 16.07	4-86.1

0713 | Prick to prick skin test improved clinical outcome of atopic dermatitis in infants

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Introduction: Atopic dermatitis in infants is closely related to food allergy. However, most food allergens are instable and easily degradable, only few commercial food allergen extracts are available for allergen diagnosis. Prick to prick test with fresh food allergens has been applied in clinical practice for years.

Objectives: To evaluate the clinical value of fresh food prick to prick test in the diagnosis and management of atopic dermatitis (AD) in infants.

Results: Infants diagnosed with AD between 0 to 6 years old were enrolled from January, 2010 to December, 2015. All the patients were performed skin prick tests with 19 inhalant allergens and 10 commercial food allergens. Serum specific IgE were measured with ImmunoCAP. Prick to prick test with specified food allergens were performed additionally if clinical history indicated suspected foods. SCORAD was used to evaluate the severity of symptoms.

A total of 137 infants were enrolled in our study. 113(82.5%) of them showed positive results in skin prick test, the most common allergens were dust mite, animal dander, egg and milk. 109(79.6%) showed positive results in specific IgE test. 71(51.8%) of 137 patients showed positive results in prick to prick test, and we found nuts, mixed rice flour, meat, formula milk powder, fruit were the most common allergens. Food excluded and re-introduce from food diary were consistent with the positive results of food prick to prick test. 57(80.3%) infants had symptomatic relief after avoidance of the food allergens confirmed by prick to prick test. Compared with that before the prick to prick test (21 cases, 29.6%) ($P < .05$).

Conclusions: Prick to prick test with fresh food provide additional information in the allergen diagnosis of AD and helps to improve the outcome of AD in infants.

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0714 | The role of staphylococcus spp. in clinical course of atopic dermatitis

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Introduction: *S. aureus* skin infection at least partly drives the pathogenesis of atopic dermatitis (AD). It was proposed that exacerbations of AD are characterized by the growth of *S. aureus* skin colonization and the reduction of microbial diversity. *S. epidermidis* may play a compensatory role also increasing in attempt to restrict the growth of *S. aureus*. The diversity was shown to be restored by the same strains of microorganisms.

Objectives: To estimate the role of *Staphylococcus spp*. in the course of AD in children and to assess antimicrobial susceptibility of *Staphylococcus spp*. in dynamics.

Results: Forty patients aged 2 months to 17 years with clinical signs of AD were enrolled in an observational cross-sectional study. Swabs were taken from skin lesions twice: during the exacerbation and 10-14 days later during the period of clinical improvement of AD. Moderate and potent topical steroids, along with appropriate skin care and moistening agents were used for treatment of skin lesions. The severity of eczema was determined with the SCORAD index. The mean SCORAD score during exacerbation and clinical improvement of AD was 60 (SD=23.3) and 40 (SD=24.1), respectively ($P < .05$). The prevalence of *S. aureus* skin colonization was 79% at the beginning decreasing to 35.5% after the second assessment. The density of *S. aureus* culture correlated with the severity of AD ($P < .05$). Conversely, the prevalence of *S. epidermidis* in AD skin lesions increased from 18.6 to 35.5%. The prevalence of other coagulase-negative species and the percentage of patients with sterile

swabs were also higher during clinical improvement of AD. In 20 patients drug resistance of *S. aureus* was assessed in dynamics and revealed no significant differences in susceptibility to 20 main antimicrobial agents. The fact of showing susceptibility after resistance proves the possibility of colonization by new strains, not only reactivation of previously existing strains.

	Exacerbation of AD		Clinical improvement of AD	
No growth	5	(11.63%)	11	(35.48%)
S. aureus	34	(79.07%)	11	(35.48%)
S. epidermidis	8	(18.60%)	11	(35.48%)
S. haemolyticus	3	(6.98%)	4	(12.90%)
S. warneri	1	(2.33%)	2	(6.45%)
S. cohnii	0	0.00	1	(3.23%)
All coagulase-negative species	12	(27.91%)	17	(54.84%)
Coagulase-negative species without S. epidermidis	4	(9.30%)	6	(19.35%)

	Antimicrobial susceptibility of *S. aureus* in dynamics				
Drug	Exacerbation of AD		Clinical improvement of AD		*P*-value
Benzylpenicillin	0		0		
Ampicillin	0		0		
Amoxicillin/clavulanic acid	34/34	100%	11/11	100%	$P > .05$
Oxacillin	34/34	100%	11/11	100%	$P > .05$
Cefazolin	34/34	100%	11/11	100%	$P > .05$
Cefepime	34/34	100%	11/11	100%	$P > .05$
Imipenem	34/34	100%	11/11	100%	$P > .05$
Gentamicin	34/34	100%	11/11	100%	$P > .05$
Tetracycline	29/33	87.8%	10/11	90.9%	$P > .05$
Erythromycin	29/34	85.3%	10/11	90.9%	$P > .05$
Clarithromycin	18/21	85.7%	11/11	100%	$P > .05$
Azithromycin	27/33	81.8%	11/11	100%	$P > .05$
Chloramphenicol	27/34	79.4%	11/11	100%	$P > .05$
Vancomycin	34/34	100%	11/11	100%	$P > .05$
Clindamycin	31/34	91.2%	10/11	90.9%	$P > .05$
Levofloxacin	34/34	100%	11/11	100%	$P > .05$
Ciprofloxacin	15/15	100%	11/11	100%	$P > .05$
Linezolid	24/24	100%	11/11	100%	$P > .05$
Rifampicin	34/34	100%	11/11	100%	$P > .05$
Trimethoprim/sulfamethoxazole	33/34	97.0%	11/11	100%	$P > .05$

	Antimicrobial susceptibility of *S. epidermidis* in dynamics				
Drug	Exacerbation of AD		Clinical improvement of AD		*P*-value
Benzylpenicillin	0		0		
Ampicillin	0		0		
Amoxicillin/clavulanic acid	6/8	75.0%	8/11	72.7%	$P > .05$
Oxacillin	6/8	75.0%	8/11	72.7%	$P > .05$
Cefazolin	6/8	75.0%	8/11	72.7%	$P > .05$
Cefepime	6/8	75.0%	8/11	72.7%	$P > .05$
Imipenem	6/8	75.0%	8/11	72.7%	$P > .05$
Gentamicin	7/8	87.5%	10/11	90.9%	$P > .05$
Tetracycline	4/8	50.0%	8/11	72.7%	$P > .05$
Erythromycin	4/7	57.1%	4/11	36.3%	$P > .05$
Clarithromycin	4/7	57.1%	3/7	42.8%	$P > .05$
Azithromycin	5/8	62.5%	4/11	36.3%	$P > .05$
Chloramphenicol	2/8	25.0%	2/11	18.2%	$P > .05$
Vancomycin	8/8	100%	11/11	100%	$P > .05$
Clindamycin	7/8	87.5%	10/11	90.9%	$P > .05$
Levofloxacin	8/8	100%	11/11	100%	$P > .05$
Ciprofloxacin	3/3	100%	4/4	100%	$P > .05$
Linezolid	8/8	100%	11/11	100%	$P > .05$
Rifampicin	8/8	100%	11/11	100%	$P > .05$
Trimethoprim/sulfamethoxazole	6/8	75.0%	8/11	72.7%	$P > .05$

Conclusions: Exacerbations of AD are accompanied by *S. aureus* skin colonization. There is positive correlation between the density of *S. aureus* culture and the severity of AD (SCORAD) ($P < .05$). In period of clinical improvement activation of *S. epidermidis* growth and reduction in *S. aureus* growth are detected, demonstrating protective role of *S. epidermidis* by displacing more pathogenic bacteria such as *S. aureus*. During the course of the disease *S. epidermidis* strains showed susceptibility to different antimicrobial agents.

0715 | Mold exposure during fetal periods is associated with the development of atopic dermatitis in infants through allergic inflammation

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Introduction: Mold exposure in early life has been known to be associated with the development of atopic dermatitis (AD) with inconclusive results. Also, studies on its underlying mechanisms are lacking.

Objectives: To investigate the underlying mechanisms of the association between mold exposure, especially during the critical period, and the development of AD. To elucidate the relationship between mycobiome in environment at 36 weeks of gestation and biomarkers including cord blood immunoglobulin E (IgE) and total serum IgE levels at age 1.

Results: Prenatal mold exposure was significantly associated with AD (adjusted odds ratio, 1.36, 95% confidence intervals, 1.02-1.81), but not postnatal mold exposure. The relative abundance of uncultured Ascomycota was higher in infants with AD compared with healthy infants, although there was no statistical significance. The relative abundance of uncultured Ascomycota in environment at 36 weeks of gestation correlated with IgE levels in cord blood ($r = 0.941$, $P < .001$) and total serum IgE levels at age 1 ($r = 0.613$, $P < .001$).

Conclusions: Indoor mold exposure during fetal periods is associated with the development of AD through allergic inflammation.

0716 | Water-soluble fullerene C60 stimulates filaggrin expression

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Introduction: Fullerene C_{60} is a molecular carbon form possessed a strong antioxidant activity with low toxicity and lack of immunogenicity. The main purpose of our research was to assess the WSF effect on the filaggrin expression in the experimental model of atopic dermatitis (AD).

Objectives: The WSF was prepared as previously described [1]. AD experimental model was induced by the epicutaneous ovalbumin sensitization of BALB/c mice. WSF was administrated epicutaneously (EC) (1 mg/kg) and subcutaneously (SC) (0.1 mg/kg). Skin specimens were removed for histological examination and evaluation of filaggrin expression level by a quantitative real time PCR.

Results: The experiments clearly showed that only the EC treatment by WSF leads to significant increase in expression of filaggrin. The expression levels were twice as much as levels in group of untreated mice. Histological examination of skin samples indicated pronounced reduction of the eosinophil and leukocyte infiltration after WSF treatment. Moreover, the epidermal necrosis, destructive hemorrhage in dermis and hyperkeratosis either were absent or were mild compared to non-treated of mice. We also evaluated the histologic pictures in semi-quantitative histological index (score) comparing WSF-treated and non-treated groups with each other based on the microscopic features. This analysis showed that the WSF therapy improved histological picture reducing an allergic inflammation by approximately 42% and 25%, respectively for epicutaneous and subcutaneous applications compared with the untreated mice.

Conclusions: These data point out the potential of the WSF as a stimulator of the filaggrin expression. Potential utility of such therapy is indicated by known published facts that a modest 20% increase in filaggrin copy number leads to the 40% reduction in AD susceptibility. Now we do not know why EC application is more effective then SC one. Perhaps, WSF EC application increases the fullerene availability to the immune system in the skin with AD.

Reference:

[1] Andreev S., Purgina D., Bashkatova E., Garshev A., Maerle A., Andreev I., Osipova N., Shershakova N., Khaitov M. Study of fullerene aqueous dispersion prepared by novel dialysis method: simple way to fullerene aqueous solution. Fuller. Nanotub. Carbon Nanostruct. 2015; 23(9):792-800.

0718 | Atopic dermatitis and probiotics: a real life experience

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Introduction: Atopic dermatitis is a disease with a lot of clinical interest because it is the point of attachment between allergic diseases and autoimmune diseases. Specific probiotics and symbiotics favour the expression of anti-inflammatory Th1 cytokines which produces therapeutic benefits in patients with atopic dermatitis as revealed by recent meta-analysis.

Objectives: Six patients (3 women and 3 men) suffering from moderate atopic dermatitis aged between 16 and 28 years were treated with *Bifidobacterium lactis* BS01, *Lactobacillus rhamnosus* LR05 and prebiotic fructo oligosaccharides (2 x 10^9 CFU) once daily in a period of four months added to their previously scheduled topical treatment. SCORAD index and atopic dermatitis quality of life test (QoLIAD) prior to treatment and four months after treatment were analysed.

Results: After 4 months of treatment clinical improvement was shown by a reduction in the SCORAD index (average of 6 points) and an improvement in QoLIAD test results in 5 of the 6 patients. Previously scheduled medical treatment remained unchanged and no side effect was observed in any of the patients treated.

Conclusions: Most of our patients treated obtained clinical improvement in quality of life without adverse effects. This supports the results of recent studies that conclude that the use of probiotics in daily clinical practice showed no signs of side effects, and may be effective in the treatment of atopic dermatitis.

0719 | Patients with atopic dermatitis and allergic rhinitis treated with slit for house dust mite

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Introduction: Allergen immunotherapy (AIT) is immune modifying and casual treatment for allergic rhinitis (AR) and allergic asthma (AA), but effectiveness for atopic dermatitis (AD) is still under discussion

Objectives: Patients with AD and AR treated with sublingual immunotherapy (SLIT) for house dust mite filled questionnaires after at least one year of therapy. Additional to general data we got information about symptoms for AR and AD before and at least one year after SLIT therapy. For evaluation of SLIT we used symptom medication score (SMS) for AR and additional questionnaire for skin symptoms was used for AD. T test was used to compare improvement of symptoms.

Results: We included five patients, 4 men and 1 women, average 30 years old. All of them had SLIT for house dust mite, one had additional SLIT for birch. SMS before SLIT was 1.5 and after at least one year of SLIT 0.9 ($P < .01$). Questionnaire for skin symptoms before SLIT was 1 and after at least one year of SLIT was 0.6 ($P < .01$).

Conclusions: Our patients with AD and AR treated with SLIT for house dust mite at least for one year reported some improvements for nasal and skin symptoms.

0720 | Is it possible to predict the development of infectious complications in specific immunotherapy in children with atopic dermatitis?

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Introduction: The purpose of the study is to develop criteria for the prognosis of infectious complications (IC) in children (Ch) with moderate to severe atopic dermatitis (M-SAD).

Objectives: Ninety-four Ch aged 5 to 17 with M-SAD and disease duration of 1-15 years in the remission stage were comprehensively examined, using biochemical, clinical, immunoallergological (with house dust mite allergens – HDM) methods, aimed at the detection of clinical and laboratory signs of allergen-induced inflammation. A control group included 30 practically healthy Ch. Clinical examination was directed to collect allergic anamnesis and the estimation of severity of clinical symptoms by SCORAD scale. Clinically the AD had multiple and extensive inflammation with exudation or infiltration, lichenification, excoriation and severe itching, which led to the accession of secondary infection.

Results: The examination allowed us to divide patients into two main different immunopathogenetic phenotypes (IPGF) groups: the 1^{st} group with IgE-mediated and the 2^{nd} group with non-IgE-mediated forms of AD. Ch in the 2^{nd} group had no IgE-sensitization to HDM and observed a decline in macrophage-phagocytic immunity (MPI). The IgE-mediated phenotype of AD includes 3 forms of AD: allergic, mixed (with allergic rhinitis, asthma), and a combined immunocompromised form (CICF). The allergic and mixed forms have a proven sensitivity to HDM, which provoke the development of symptoms in AD. The CICF has shown a decline in the MPI (phagocytic number-PhN, phagocytic index-PhI, phagocytic activity of neutrophils-PhAN). In Ch with IgE-mediated AD were identified immune imbalances: reductions of PhAN, PhI and PhN; IL-4 and IL-13 in serum, local and systemic specific IgE were increased and IFN-γ decreased with worsening of the clinical course of the disease. The SCORAD index before treatment of M-SAD was 42.57 ± 3.41 - 48.2 ± 5.7 points. The inclusion of allergen-specific immunotherapy (AIT) in the comprehensive treatment (CT) of immunocompromised Ch with AD and impaired function of the PhAN, led to the development of IC in 78% of the cases. There were no complications or worsening of the clinical course of AD in the group of Ch with AD in plans that included AIT and an immunomodulator that activates PhAN.

Conclusions: Thus, monitoring of the blood levels of PhI and PhN in IgE-mediated AD predicts the development of IC in Ch with AD.

0721 | Skin-tropic immune responses of house dust mite allergens in atopic dermatitis and allergic march

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Introduction: Although there are several studies and hypothesis to explain the patho-mechanisms of atopic dermatitis (AD) and allergic march (AM), there are only a few studies to elucidate sensitized allergen fraction differences between AD and AM.

Objectives: In this study, we evaluated immune responses of allergen fractions of *Dermatophagoides farinae* (*Der f*) including *Der f 1*, *Der f 2*, *Der f 6*, *Der f 11 and Der f 14*, as *D. farinae* is one of well-known major allergens in AD and AM.

Results: First, 2D-Western blot was done to identify allergen fraction proteins in serum of AD and AM patients.

Next, we co-cultured monocyte-derived dendritic cells (DCs) with CD4 + T cells from peripheral blood mononuclear cells (PBMCs) of AD and AM patients, and treated with *Der f* fractions including *Der f 1*, *Der f 2*, *Der f 6*, *Der f 11 and Der f 14* for 48 hours and analyzed the level of Th2 cytokines. We also evaluated immune responses of *Der f* fractions using skin and lung single cell suspensions from normal and AD mouse models. By using 2D-Western blot, we identified and *Der f 14*, *Der p 14* and *Der f 11* from serum AD group and *Der f 1* from serum AM group. We treated whole *Der f*, *Der f* 1, *Der f 2*, *Der f 6*, *Der f* 11 and *Der f* 14 on co-cultured cells with DC+ CD4 + T cells and IL-4 was significantly increased when treated with *Der f* 14 in AD patients. In AM patients, both *Der f 1* and *Der f 14* treatment produced significant IL-4 level elevation. While other allergen fractions mostly increased IL-4 level in AM group, *Der f 14* noticeably increased IL-4 in AD group. We performed a further study by using normal and AD mouse skin and lung cells to display skin–tropic immune response. Among those allergen fractions, *Der f 14* showed strong Th2 response only in skin cells but not in lung cells, exhibiting skin-tropic reactions.

Conclusions: It would be important to discover skin-specific immune reaction from various allergen proteins of house dust mite and further study is required to validate these proteins.

0722 | Polymorphism of tTLR2 and TLR4 cell receptors and cytokine levels in patients with atopic dermatitis

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Introduction: Research participation of various polymorphism of genes that control the innate and adaptive immune responses in the pathogenesis of atopic dermatitis (AD) appear relevant. Polymorphism rs5743708 TLR2 leads to disruption of cell activation through TLR2-signaling pathway. We had an interesting to explore relationship gene polymorphism tlr2 and tlr4, encoding the TLR2 and TLR4, with the level of cytokines in patients with AD.

Objectives: The study included 50 people with AD and 100 persons without atopy. Polymorphism of genes TLR2 (p.Arg753Gln) and TLR4 (Asp299Gly) were determined by PCR, genomic DNA was isolated from blood leukocytes and buccal epithelial cells (DNAExpress, Liteh Russia).The level of IL1, 2, 4, 6, 8, 10, IFNγ was determined by ELISA(Vector-Best, Russia).Genotype distribution by criterion $\chi 2$, the significance of differences of quantitative traits were assessed using t -test for unequal variance.

Results: Genotypes by gene polymorphisms TLR2 and TLR4 were distributed as follows: 91.6% homozygotes, heterozygotes 8.4%, homozygous for the mutant allele of 0%. In the groups studied distribution of frequencies of alleles and genotypes consistent with the Hardy-Weinberg-Kastla, and was in equilibrium. Among patients with AD incidence homozygous genotype G/G was 1.2 times lower and heterozygous genotype G/A* 3.3 times higher as compared with control. INFγ levels in the serum of AD patients was 1.5 times, and the level of IL1,2 2 times lower in heterozygous patients, the IL4, 8 were above 1.4 and 1.8 times. The frequency of allele rs4986790 TLR4 in patients was 92.4%, in the control 94.0%, while the allele G* patients 3.5%, in the control 4.5%(p-value $\chi 2 > 0.05$). In patients with AD serum INFγ level was below 1.6 times, IL1 and 2 1.7 times in the heterozygotes compared with homozygotes. Levels of IL4, 6 heterozygotes serum were increased by 1.3 and 1.6 times compared with homozygotes.

Conclusions: Therefore, set the importance of genetic polymorphisms (p.Arg753Gln, rs5743708) gene TLR 2 and (Asp299Gly, tlr4, rs4986790) TLR 4 in the pathogenesis of dysregulation of cytokine production by cells, the body's expression of TLR4 and TLR2, implementing regulation of the balance of TH -subpopulations lymphocytes involved in the immune responses in AD.

SUNDAY, 18 JUNE 2017
TPS 11
ALLERGY AND IMMUNE-RELATED DISORDERS

0723 | Altered mast cell reactivity in patients with mastocytosis

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Introduction: Patients with systemic mastocytosis (SM) have clinical signs of mast cell (MC) activation and increased levels of mediators. It is unclear whether their MCs have a hyperactive phenotype, i.e., are more easily triggered.

Objectives: We sought to determine the reactivity of MCs to clinically relevant secretagogues in subjects with SM.

Mast cells were derived in vitro from enriched peripheral blood CD34-positive cells from patients with indolent SM (n = 14) and healthy controls (HC, n = 11). In vitro derived MCs were activated by using anti-IgE, morphine and mannitol and the reactivity of the MCs were determined by measuring the release of histamine and prostaglandin (PG)D_2 in supernatants. Moreover, the levels of IL-31, IL-33 and SCF in plasma were explored by ELISA. Also using multiplex proximity extension assay, plasma levels of 157 inflammatory biomarkers were analyzed.

Results: No difference were observed between the groups in the growth of MCs; however, we detected an increased expression of FcR1 ($P < .05$) on the MCs derived from SM patients. There were no differences between the groups regarding release of histamine and PGD_2 in response to anti-IgE or morphine. Nevertheless, MCs derived from SM patients released significantly higher levels of PGD_2 in response to mannitol stimuli ($P < .05$). Although plasma levels of cytokines did not differ between the groups, we identified increased levels of three novel protein biomarkers associated with SM, in particular SM patients with anaphylaxis.

Conclusions: The reactivity of MCs in patients with SM appears to be complex and dependent on different stimuli. Our study reveals a unique response profile with increased secretion of lipid mediator PGD_2 and some newly identified potential biomarkers that could be sign of a hyperreactive MC phenotype in patients with SM. This might even improve the prediction of anaphylaxis in SM patients; however, these results need validation.

0724 | Aeroallergen sensitization and irritable bowel syndrome

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Introduction: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder characterized by recurring abdominal pain or discomfort associated with diarrhea or constipation. The pathogenesis of irritable bowel syndrome is not completely elucidated and recent studies have looked into the potential role of allergic sensitization, as well as the possible involvement of mast cells in this disorder.

Objectives: We aimed to investigate whether patients with irritable bowel syndrome have higher rates of allergic sensitization and whether abdominal symptoms in those who are sensitized could be alleviated by treatment with antihistamines or mast cell stabilizers.

Results: The study included 64 adult patients diagnosed with irritable bowel syndrome and a control group consisting of 30 healthy adults. At the first visit, all subjects underwent skin prick testing with panel of aeroallergens, total IgE counts were measured, and visual analogue scale questionnaires regarding the severity of abdominal symptoms were administered to the patients in the study group. Subsequently, IBS patients who were found to have at least one allergen sensitization were randomly divided into three groups that received an oral non-sedating antihistamine (levocetirizine), a mast cell stabilizer (ketotifen) and no treatment, respectively, for three months; concomitantly all patients received diet recommendations and IBS guideline directed treatment. Patients were reassessed at three months and questionnaires were re-administered.

Twenty eight IBS patients (43%) were found to have at least one allergen sensitization, compared to 23% of the patients in the control group. Mean value of total IgE was found to be higher in IBS patients compared to the control group, and the difference was found to be statistically significant. Assessment of therapeutic intervention revealed no difference between questionnaire scores of patients who received levocetirizine compared to those who received no additional treatment. An improvement of questionnaire scores of patients who received ketotifen was observed, but this difference was not found to be statistically significant.

Conclusions: We found high rates of allergic sensitization to aeroallergens, particularly house dust mites in patients with IBS. However, therapeutic intervention with antihistamines did not provide symptomatic relief; mast cell stabilizer treatment resulted in slight improvement of abdominal symptoms, possibly due to its sedative effect.

0725 | Can plane tree be considered a marker of polisensitization to pollens?

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Introduction: Plane tree pollen is an important cause of pollinosis in Europe.

Objectives: To determine the frequency of sensitization to plane pollen (*Platanus acerifolia)* in a group of atopic patients followed in the outpatient clinic and establish other sensitizations eventually associated.

Methods: Retrospective review of the 832 skin-prick tests (SPT) results from patients observed for the first time in our outpatient clinic, during 2015. All patients were submitted to SPT using a hospital standard panel including *P. acerifolia*, other pollen and panallergens extracts (Pho d 2, Pru p 3). A positive result is defined as a wheal diameter ≥3 mm. In the subset of patients with plane sensitization, demographic and clinical data was also collected. Data analysis using SPSS 21.

Results: From the 832, 613 (73.6%) patients with SPT positive to at least one allergen were included. Within these, 374(61%) had sensitization to pollens. Plane sensitization was stablished in 104 (28%) patients, being this the third most frequent pollinic sensitization, preceded by grass (73%) and olive (61%). Patients with plane tree sensitization (54% female, median age (±SD) of 39.5 (±16.7) years, 10% with <18 years, a median wheal (±SD) diameter of 7 ± 4 mm) 97% had rhinitis (28% with asthma), 36% conjunctivitis, 18% food allergy (rosacea and nuts the most frequent), 13% had LTP sensitization and 26% to profilin (table 1). No mono-sensitization to plane tree was found. When considering just the pollinic sensitization, 4(1%) patients had sensitization only to plane tree but all of them had sensitization to house dust mites. Different frequencies of other associated sensitizations were found between the groups of patients with or without SPT positive to plane as the frequency of sensitization to olive ($P = .001$), parietaria, mugwort and profilin ($P < .001$) was higher in the first. No differences regarding grass or LTP sensitization between groups. Patients with plane sensitization had more frequently sensitization to ≥ 3 pollens (62.4%) than those without plane sensitization (14.7%). In the later, the majority had monosensitization to pollens (45%).

Conclusions: Plane tree was the third most frequent pollinic sensitization, appearing only in polysensitized patients. The broad spectrum of pollinic sensitization and the high frequency of sensitization to profilin within the patients with plane sensitization, suggest that plane can be a marker of polysensitization.

0726 | AllergoOncology: the canine IgE antibody 'can225IgE-?' triggers strong and specific effector-cell mediated cytotoxicity against EGFR+ tumor cells

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Introduction: Preclinical studies with recombinant tumor antigen specific immunoglobulins of the IgE class provided evidence of a

	n	% Rhinitis	% Asthma	% Rhinitis + Asthma	% Conjunctivitis	% LTP Sens.	% Profilin Sens.	% FA
Plane tree sensitization	104	70	1	28	36	13	26	18
Pla$^+$	4	75	0	28	50	25	25	0
Pla$^+$ and Grass$^+$	9	78	0	22	22	22	0	11
Pla$^+$ and Olea$^+$	2	0	0	100	0	0	0	0
Pla$^+$ and Pariet$^+$	3	67	33	0	33	0	0	0
Pla$^+$ and Artem$^+$	3	67	0	33	0	33	0	33
Pla$^+$ and other 2 pollinic sensitizations	18	72	0	22	28	11	0	11
Pla$^+$ and ≥3 other pollinic sensitizations	65	74	0	26	40	15	40	25

Abbreviations: FA – food allergy; Artem$^+$ - Artemisia vulgaris sensitization; Grass$^+$ - grasses sensitization; Olea$^+$ - Olea europeae sensitization; Pla$^+$ - Plane tree sensitization; Pariet$^+$ - Parietaria judaica sensitization; Sens. – sensitization.

superior function of IgE against cancer. Current xenograft mouse models lack some of key features necessary for the conduction of studies fulfilling at the same time allergy and oncology requirements. On the contrary, dogs (*Canis lupus familiaris*) spontaneously may suffer from both cancer and allergies and are immunologically much more similar to humans, specifically in the IgE receptor distribution.

Objectives: We aimed to develop a recombinant canine IgE antibody, can225IgE-λ, against the EGFR (epidermal growth factor receptor) tumor antigen, which is highly homologous among human, and dog. can225IgE-λ was transiently expressed in a shaker culture of Expi293F cells using the pVitro1-hygro plasmid and then purified using a custom anti-dog IgE resin by an automated FPLC system. Purified can225IgE-λ was tested for purity, integrity, specificity and binding to FcεR expressing cells by PAGE, western blots and flow cytometry. The functionality of the antibody was then evaluated in a flow-cytometric ADCC and ADCP assay using the human U937 and the canine DH82 monocyte-like cell lines against the EGFR-overexpressing tumor cell line A431.

Results: The yield of the recombinant can225IgE-λ was 5.5 μg/mL and it was correctly assembled with an apparent molecular weight of 235 kDa. Specific binding of can225IgE-λ to recombinant human EGFR could be demonstrated in immunoblots. Specific binding to EGFR-expressing human and canine cancer cell lines, as well as dose-dependent Fc-mediated binding to human and canine effector cells, was confirmed by flow cytometry, can225IgE-λ triggered a significant tumor killing response by both human and canine monocyte-like cell lines, which significantly exceeded the effects by its IgG counterpart, 'can225IgG'.

Conclusions: In conclusion, can225IgE-λ as the first of its kind, is a fully functional recombinant canine IgE utilizing FcεR-bearing immune cells for highly effective tumor killing. We anticipate that can225IgE-λ will be i) an important tool to investigate the in vivo safety and efficacy of an anti-cancer IgE antibody in a biologically relevant organism, and ii) that it may represent a future therapeutic in canine cancer patients.

0727 | Chronic eosinophilic pneumonia and bronchiolocentric interstitial pneumonia associated with angioimmunoblastic T-cell lymphoma

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Case report: Angioimmunoblastic T-cell lymphoma is a rare type of non-Hodgkin lymphoma with systemic manifestations, including fever, lymphadenopathy, rash, and rarely eosinophilic pneumonia. We report the case of a patient who presented with chronic eosinophilic pneumonia and bronchiolocentric interstitial pneumonia. A 56-year-old woman was admitted because of dyspnea with bilateral central consolidation and effusion on chest CT images. The pathologic report of video thoracoscopic lung biopsy was "chronic eosinophilic pneumonia in a background of bronchiolocentric pneumonia with granulomas". At initial diagnosis, the patient had multiple lymphadenopathy, but that was not prominent. The result of bone marrow biopsy showed only increased eosinophilic hyperplasia and no evidence of lymphoma. Although her symptoms and pulmonary infiltration improved with systemic steroid, they recurred 3 months later by tapering of steroid. At the time of recurrence 1 month later, the patient visited our clinic because of palpable mass on right axilla for several days. Angioimmunoblastic T-cell lymphoma was diagnosed with axillary lymph node biopsy. After chemotherapy, consolidation on chest CT was improved, but not complete remission.

0728 | Low molecular-weight heparins could be useful in selected cases of chronic urticaria

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Case report: Chronic urticaria is a frequent cause of life quality disturbance and medical presentation. It is a clinical statement recognized on its own or in more complex medical situation. Because in clinical practice urticaria, especially chronic type, remains very often without a certain etiology several attempts are made to identify any causality. Coagulation factors, in particular tissue factor and thrombin, might participate in the disease pathophysiology.

Material and Method: We identified 2 patients with preexisting chronic urticaria resistant to anti H1 treatment, they has been examined in 2015 and 2016 in our service due to deep venous thrombosis (clinically, Doppler examination, elevated D dimers).

Both of them has been treated with enoxaparin 150 UI anti-Xa/kg for 5 days and dicoumarol added from day 3 with discontinuation of anti H1 drugs. During the heparin treatment, urticarial lesions decreased, remittance observed at follow up exam 3 weeks later. Meanwhile D dimers level decreased in one month.

Conclusion: We show that in certain cutaneous inflammatory condition as chronic urticaria the vascular endothelial damage may be associated,therapy with low -weight molecular heparin could adjust clinically course of the skin lesions.

0729 | Bird fancier's lung: the importance of an early suspicion and a detailed medical interview

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Case report: Background: Extrinsic allergic alveolitis, also called hypersensitivity pneumonitis, is a syndrome characterized by the pulmonary response to repeated inhalation of a variety of organic powders or fungi, causing an immune response. The bird fancier's or pigeon-breeder's lung (BFL) is the most common type of hypersensitivity pneumonitis. It is caused by the exposure to avian proteins present in the dry dust of the droppings and sometimes in the feathers of a variety of birds.

Case report: A 36-year old man with no history of atopy was referred for study because he had presented a sudden onset that began with persistent non-productive cough of nocturnal predominance, chest discomfort, breathlessness, wheezing, chills and fever. Antitussive syrups, antipyretics and antibiotics were prescribed without improvement. Eight months later, he was admitted due to fever and weight loss, diagnosed with respiratory tract infection with bronchial hyperreactivity, that improved with intravenous corticosteroids, antipyretics, antibiotics and aerosol therapy. Nine months later he is sent to our unit for persistence of the symptoms, cough, crackling sound while breathing and malaise. The patient used to work at the construction and raised pigeons and other exotic birds for several years.

Results: Skin prick test with inhalant allergens proved negative for mites, epithelia, fungi and pollens. Pulmonary function testing showed a restrictive pattern and decreased carbon monoxide diffusion (DLCO) capacity, exhaled nitric oxide test was normal. Laboratory data revealed positive precipitins against pigeons' droppings and feathers and high levels of angiotensing –converting enzyme. Radiological findings (high resolution CT scan) showed a hypersensitivity pneumonitis pattern. The patient presented clinical improvement after inhaled and steroid treatment in addition to the removal of the birds from their environment and activity.

Conclusions: We report a case of bird fancier's lung. The accurate diagnosis of BFL depends on an early suspicion and a detailed medical interview. Avoiding the exposure and thus removing the antigen remains the most important facet in the treatment of BFL.

0730 | Unusual cause of throat swelling in the allergy clinic

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Case report: Throat angioedema with upper airway involvement can be a life-threatening symptom, often reported by patients referred to the allergy clinic. It can be a feature of systemic allergic reaction and rarely, a manifestation in immunological diseases such as hereditary and acquired angioedema. Anatomical abnormalities of the pharynx remain a differential.

A 75-year-old lady with a history of mild stable asthma and hay fever was referred to the allergy clinic following two episodes of throat swelling, associated with dysphonia, spaced 11 months apart. The first episode occurred approximately 1 hour after taking Co-codamol tablets, previously tolerated. The second episode occurred sometime after eating fresh pineapple, also tolerated in the past. Both episodes required A&E admissions and were managed as "allergic reactions" including adrenaline.

Investigations in the allergy clinic did not confirm food or drug allergy. SPT and sIgE to pineapple were negative. Acquired angioedema was excluded with normal C3, C4 and C1 esterase inhibitor protein level and function. Detailed anamnesis evidenced a 3-years history of worsening dysphagia and epigastric pain, hence a barium swallow through was requested. This confirmed a Killian-Jamieson diverticulum ("pharyngeal pouch") with associated cricopharyngeal muscle spasm. ENT review established the link between the symptoms and the diverticulum and the patient was referred for endoscopic stapling procedure.

In summary, pharyngeal diverticuli, although very rare, should be kept in mind as a differential diagnosis for throat symptoms, especially if triggered by swallowing and associated with dysphonia, in the absence of allergy or complement deficiency.

0731 | Is mastocytosis really rare disease? Three case experience

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Case report: Mastocytosis is a rare disease group that is characterized by accumulation of mast cells in one or more organs. We here report three different types of mastocytosis.

Case 1: 36 year-old male have been suffering from attacks of flushing, hot flushes, shortness of breath, change in voice, palpitations, abdominal pain, confusion and change in memory for 3-4 years. In the beginning, attacks have occurred 5-6 times a month but then, they have turned once a week in frequency. The attacks have been triggered with hot weather, spicy foods, tomatoes, seafood, red meat, tea, smoking, coffee and emotional changes. He was on antihistamine, steroid and omalizumab therapy during the diagnosis of chronic urticaria when he referred to our department. He was diagnosed as having Indolent Systemic Mastocytosis.

Case 2: 56 year-old male complained about fever, redness, diarrhea and loss of consciousness 30 minutes after subcutaneous bemiparin-sodium injection 2.5 years ago. Secondly, numbness and redness occurred after 8th dose of amoxicillin-clavulanic acid treatment 1.5 years ago. Two months ago, right eyelid of the patient swollen so much following 12 hours of bee sting on forehead of the patient

ISM: Indolent Systemic Mastocytosis, CM: Cutaneous Mastocytosis, SM-AHNMD: Systemic Mastocytosis associated with clonal hematologic non-mast cell lineage disease NHL: Non-Hodgkin's Lymphoma, AVR: Aortic Valve Replacement

	Case 1	Case 2	Case 3
Physical Examination	Hepatomegaly Cervical lymphadenopathy	Urticarial papules on the back	Liver is 3 cm palpable under the costa
Tryptase level (N: <10 μg/L)	80 and 52.8	29.2 and 31.7	35.6 and 22.1
Total IgE (kU/L)	202	224	11.8
Abdomen and cervical ultrasound	Hepatic Steatosis, Pancreatic SteatosisSubmandibular, Cervical Lymphadenopathy	Normal	Hepatomegaly
Other Diagnostic Tests	Cranial diffusion MRI: Normal ECHO: Normal Colonoscopy: Hyperplastic polyp in sigmoid colon	Skin prick test: Apis mellifera (100Ü) 6x6 mm Vespula vulgaris (300Ü) 4x4 mm Apis mellifera spIgE:18.9 kU/L, Vespula vulgaris spIgE: 4.7 kU/L	Skin prick test: Apis mellifera and Vespula vulgaris 100Ü and 300Ü: negative Apis mellifera and Vespula spIgE: negative Intradermal test: Vespula 6x6 mm
Bone marrow Flow Cytometry	1% mast cells	No significant mast cell infiltration was detected	0.05% mast cells
Bone marrow Karyotype Analysis	Normal	Normal	Normal
C- kit Mutation (A2468T/D816V)	Not detected	Not detected	Not detected
Bone Marrow Histopathology	10% Atypical spindle mast cell infiltration	Normocellular bone marrow showing mild mast cell increase	Focal nodal B lymphoid cell proliferation associated with atypical mast cell proliferation
Bone marrow Immunohistochemistry	Needle cells in small communities; CD117, tryptase and CD25: strongly positiveCD30 and CD2: pale positivity	CD117: mildly elevated mast cells; Tryptase staining: positive	Spindle cells strong stained with CD117, CD25 and tryptase Increased B lymphoid cells in lymphoid foci stained with CD20 Scattered positive staining in T lymphocytes with CD5 Staining with CD3: Around the foci defined before and within the T cells
Skin Biopsy	Not performed	Superficial perivascular dermatitis and mild mast cell infiltration. Microscopic appearance is compatible with urticaria pigmentosa	Not performed
Diagnosis	ISM	CM	SM-AHNMD (SM-NHL)
Treatment	Avoidance from triggers H1 and H2 blockers PPI Xolair: 300 mg/month Epipen auto-injector	Epipen auto-injector Avoidance from triggers AR: H1 blockers, LTRA, nasal steroid CM: H1 blockers and dbUVB AVR: β blocker was stopped. Penicillin allergy: azithromycin as needed	Epipen auto-injector Protection from triggers Venom immunotherapy with Vespula vulgaris Wait and watch for Lymphoma

and the symptoms resolved in 2 days. After hot shower, edema of lips and cheeks and hoarseness of the voice developed. He was diagnosed as having Cutaneous Mastocytosis.

Case 3: 37 year-old female had a history of vespula sting on her head 20 years ago. 5 to10 minutes later, pruritus, redness, swellings of the whole body and nausea had developed. Again, a vespula sting had occurred 15 years ago and then, inability to walk, palpitations, shortness of breath had developed after 15 minutes. Six years ago, following a vespula stung on leg of the patient; she had experienced nausea, vomitting, palpitations, shortness of breath, incontinence and loss of consciousness after 5 minutes. She was diagnosed as having Systemic Mastocytosis associated with clonal hematologic non-mast cell lineage disease.

Diagnostic details of cases are summarized in the Table.

Conclusion: Physicians dealing with allergic diseases should be kept in mind suspicion of mastocytosis and patients who had a history of anaphylaxis should be evaluated with basal tryptase levels.

0732 | Acquired angioedema – a link to immunologic dysregulation

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Case Report: Background: Acquired deficiency of C1-inhibitor (AAE) is a rare disorder clinically similar to hereditary angioedema (AE). AAE has a higher prevalence in older patients, and most have associated concomitant diseases. It's often associated with autoimmune or lymphoproliferative disorders.

Case Report: The authors report the case of a 51 year old female patient, referred to our outpatient department with complaints of sudden onset swelling of lips, tongue and face associated with oropharyngeal tightening and abdominal cramps. She had not experienced other symptoms, namely urticaria, dyspnea, cough, vomiting or diarrhea. There were no identifiable precipitating factors attributing to angioedema. She denied any personal or family history of atopy or allergy. Already under therapy with loratadine and cetirizine, without improvement. Background: followed in Rheumatology for Hypocomplementemic urticarial vasculitis. Serologic studies showed low levels of C4, C1q and C1-INH and the electrophoretic proteinogram showed IgM kappa monoclonal peak. A diagnosis of AAE in a patient with MGUS was made, and she started prophylactic treatment with tranexamic acid 500 mg 3 times a day. On follow-up consults she reported some episodes of minor cervical AE, with no oropharyngeal tightening and without need of observation in the emergency department.

Conclusion: This case of AAE as a first manifestation of MGUS highlights the importance of having a high degree of suspicion to exclude occult malignancies or underlying disease in patients with adult onset angioedema. About half of AAE patients carry an underlying haematological disorder including monoclonal gammopathy of uncertain significance (MGUS).

0733 | C1 inhibitor concentrate - Impact of consumption

Lourenço T[1]; Fernandes M[2]; Lopes A[1]; Santos AS[1]; Cosme J[1]; Marcelino J[1]; Ferreira R[1]; Aguiar R[1]; Pestana L[2]; Almeida P[1]; Caiado J[1]; Duarte F[1]; Neto M[1]; Costa AC[1]; Alonso E[1]; Ferreira MB[3]; Pedro E[1]; Barbosa MP[3]

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Introduction: Hereditary angioedema (HAE) is characterized by a quantitative and/or functional deficiency of C1-inhibitor (C1-INH), which can lead to angioedema attacks.C1–INH is used in the treatment of angioedema attacks and also in the short and long-term prophylaxis.

Objectives: Characterize the C1-INH consumption by the patients (pts) followed in the Immunoallergology (IA) outpatient department with the HAE diagnosis and compare it with the national consumption.

Methods: Retrospective analysis of the registry of pts our IA department with HAE who did C1-INH therapy from January 2011

			2011	2012	2013	2014	2015	2016
Use of C1 Inhibitor (500 U = 1)	National/NHS (Infarmed)		210	313	275	176	319	202
	Centro Hospitalar Lisboa Norte (CHLN)	Crisis	32	29	47	103	119	24
		Short-term prophylaxis	12	20	29	16	24	14
		Long-term prophylaxis	25	118	15	12	80	58
		Total	69	167	91	131	223	93
	% total of CHLN in relation to NHS (Infarmed)		32.9	53.4	33.1	74.4	69.9	47.5

to June 2016. Pts were characterized with regard to demographics, HAE type and therapeutic modality - crisis, short and long-term prophylaxis. Based on data available from Infarmed, the consumption of C1-INH was compared to its use in the national health system (NHS).

Results: The 114 pts (45.5% M, 54.5% F, mean 43.1 years, SD ± 18.9 years-min3, max85) with HAE diagnosis (HAE1-43.8%, HAE2-52.7%, HAE with normal C1-INH-3.5%). 64 pts went to emergency or daycare hospital in result of a crisis (263 crisis), 162 of the crisis were treated with C1-INH. 6% had to repeat therapy and 15% needed hospitalization. The mean of crisis/pt in this group was 4 in 5 years (min1, max23). 35% of pts underwent for short-term prophylaxis, with an average of 1.5 times in 5 years (min −1, max4). The most frequent reason was tooth extraction (68.6%), followed by surgery (24%) and complementary diagnostic tests (7.4%). 31.4% of pts were submitted to more than one procedure. Long-term prophylaxis was done in 4 pts. In this group the mean realization/pt was 1.3 times in 5 years, resulting in a mean of 21 administrations. The most frequent reason was pregnancy (60%), followed by poor control of the disease (40%). The C1-INH consumption of our Immunoallergology department are characterized in the attached table according to the modality of therapy performed and compared with the national consumption.

Conclusions: This IA department acts as a reference center for the HAE, representing about 50% of the national consumption of C1-INH. Focusing on the reality of this hospital, it was verified that it is in crisis that the consumption of C1-INH is higher, with a progressive and significant increase in the last 3 years, namely in 2015. It is also observed that, despite the reduced number of pts doing long-term prophylaxis, the number of administrations was high due to the specificity of this treatment.

0734 | Off-label subcutaneous use of 1500 ie c1-inh – A new approach for prophylaxis in hae?

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Case Report: Background: Hereditary angioedema (HAE) is a rare autosomal dominant disorder affecting approximately 1/50000 people. Patients suffering from HAE show recurrent swellings of subcutaneous and submucosal structures in various regions of the body. Bradykinin-induced increased vascular permeability leads to edema formation. Current therapy consists of C1-esterase-inhibitor (C1-INH), B2 bradykinin receptor antagonists or the kallikrein inhibitor ecallantide. In most cases an on-demand therapy of acute attacks is sufficient, in severe cases, however, a prophylactic therapy is needed. Therefore C1-INH intravenously (IV) was shown to be safe and efficient.

Methods: We present the case of a patient with HAE-I who was under prophylactic therapy with C1-INH IV due to a high number of attacks during on-demand therapy. An implanted port guaranteed a periodical and safe apply of the medication until the device had to explanted due to an infection. Because of a bad vein status repeated IV application failed. After stopping the prophylactic therapy he suffered from recurrent and partially severe attacks again. Therefore we tried a subcutaneously off-label use of 1500 IE C1-INH as prophylaxis over 12 months.

Results: After a brief training session the self-application was easily managed by the patient. Under the prophylaxis the number of attacks was reduced from 4.33 to 1/month. No severe attack and none of the upper airway was noticed over 12 months. The quality of life measured by the AE-QoI could be improved. The results were similar to those under the approved IV therapy.

Discussion: Subcutaneous use of 1500 IE C1-INH seems to be easy and safe. In our case it showed similar effectiveness compared to the IV therapy. No adverse events could be noticed. The quality of life measured by the AE-QoI could be approved. By learning a self-application the patient gained independence. The results of this case seem promising, however bigger studies are needed to underline our findings.

0735 | Gender influence on hereditary angioedema with C1-inhibitor deficiency

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Introduction: Hereditary Angioedema (HAE) is a severe, heterogeneous, underdiagnosed and inadequately treated disease. We assess the influence of gender on the phenotype of HAE with C1-inhibitor deficiency.

Objectives: Cross-sectional study characterizing patients with HAE with C1-inhibitor deficiency according to gender in a reference center.

Results: Ninety-four patients with HAE were included, 94% type I and 6% type II; 66% being female and 34% male. Family history was observed in 66% of women and 81% of men. The average-ages of symptoms were 12 years in both sexes. The average-ages of diagnosis were 19 years for males and 28 years for females ($P < .01$). The average duration of attacks was not statistically different, being 72 hours in men and 84 hours in women. Hospitalization was reported in 49% of patients, 24% were admitted in ICU and 14% undergone OTI, without significant differences between genders. Laparotomy was done in 17% of patients, 22% of women and 6% of men. As triggering factors, 71% reported spontaneous attacks; 60% stress, trauma or pressure; 22% dental procedures; 17% surgery; 11% temperature variation; and 9% infection. Among women, 25%

reported worsening with menstrual cycles, 20% with exogenous estrogen intake and 46% with pregnancy. Long-term prophylaxis was prescribed for 72% of patients, 65% with Danazol, 36% with tranexamic acid and 10% with both. Among women, 16% were taking progesterone, 6% progesterone and danazol, and 3% progesterone and tranexamic acid. The average doses of Danazol and tranexamic acid were 177 mg and 833 mg, respectively, and were not different between genders.

Conclusions: The study showed a higher prevalence and a longer delay in the diagnosis of HAE in women. Disease severity was similar in both genders. We observed clinical worsening during pregnancy and with exogenous estrogen intake.

0736 | Icatibant: only in the treatment of hereditary angioedema attacks?

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Introduction: Icatibant is indicated for treatment of severe attacks of hereditary angioedema (HAE) in adults. Recent studies have demonstrated its efficacy in the treatment of angioedema-induced by angiotensin-converting enzyme inhibitors (AECI) with asphyxiation.

Objectives: Quantify the administration of icatibant and characterize the clinical profile of the population submitted to this treatment in Centro Hospitalar Lisboa Norte (CHLN) also evaluating the impact of the consumption of icatibant compared to its total consumption in Portugal.

Methods: Retrospective analysis of clinical history of icatibant-treated patients through hospital pharmacy drug consumption records between Jan 2011-Jun 2016.The impact of drug consumption per units/year (1 unit of icatibant=30 mg/3 mL) compared to the respective National Health System/Infarmed data was also calculated during this period.

Results: A total of 52 patients were treated with icatibant. 42 with HAE diagnosis (mean age 44 ± 13.9 years min 19;75, ♀54.8%) out of a total population of 114 patients (mean age 43 ± 19.04 years) with HAE (HAE I 43.8% HAE II 52.7% HAE with normal C1-INN 3.5%). Of the remaining patients 9 were treated in the emergency department due to ACEI-Induced AE and 1 with suspicion of AEH but without confirmation. In HAE patients treated with icatibant the most frequent attacks manifestation was oro-laryngeal (26.1%) followed by abdominal pain (16.6%). Of these 21.4% (7.8% of the total) had icatibant for self-administration with 28 units of drug being consumed under these conditions. In the ACEI-induced group (mean age 59 ± 16.1 years min 40; 90, ♀78%) the attacks involved the lips and/or tongue but none had required orotracheal intubation. The distribution of the use of icatibant per year according to the CHLN data as well as its national consumption and the proportion of his use in CHLN vs national are described in the table 1.

Conclusions: There is a growing increase in icatibant consumption over the years in this hospital which corresponds to about 50% of the NHS consumption. It should be noted that from 2014 icatibant has been used in the treatment of severe angioedema due to ACEI which demonstrates that professionals are aware of this reality. However the criterion for eventual indications of icatibant in patient with AE due to ACEI still needs to be systematized.

Table 1: Icatibant consumption between 2011-2016

		Icatibant use (dose 30 mg/3 mL)				
		HAE	ACE Inhibitor-Induced Angioedema	Total consumption in CHLN	Nacional/ NHS (Infarmed*)	% annual consumption in CHLN compared to National/ NHS
Years	2011	11	0	11	31	35.5
	2012	32	0	32	51	62.7
	2013	25	0	25	39	64.1
	2014	25	1	26	49	53.1
	2015	32	4	36	74	48.6
	2016	11	5	16	23	69.5
Total		136	10	146	267	

*Infarmed data.

0737 | Is isolated angioedema in the perioperative setting a symptom of allergy? – a retrospective single-centre study

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Introduction: In the perioperative setting angioedema is a potentially life-threatening condition. Causes of angioedema are numerous and the pathophysiology not fully understood. Angioedema presenting with urticaria or other allergy symptoms may be IgE mediated, but the role of allergy in angioedema presenting as the only symptom is unknown. The Danish Anaesthesia Allergy Centre (DAAC) is the national reference centre for investigation of perioperative allergy. Patients are investigated for all drugs and substances they

were exposed to prior to the reaction using skin tests, specific IgE tests and provocation tests. A relevant clinical allergy is confirmed by a positive provocation test or two other positive test results.
The aim of this study was to examine whether allergy could be identified in patients referred to DAAC with angioedema as the only symptom of suspected perioperative allergy.

Objectives: A retrospective review of the DAAC database included 421 patients (median age 56, 58% women) investigated for suspected perioperative allergy in the period 2004-2015. Other skin symptoms than angioedema, respiratory and circulatory symptoms were correlated to the result of allergy investigation in patients presenting with angioedema.

Results: In total 132 of 421 (31%) reacted with angioedema (70% women). Of these 115 (87%) had one or more additional symptoms suggestive of allergy e.g. skin (urticaria/unclassified rash/flushing), respiratory or circulatory symptoms. In this group allergy was confirmed in 44 (38%) and this was comparable to the proportion of confirmed allergy in the total cohort 158 of 421 (38%). The remaining 17 (13%) patients presented with isolated angioedema with no other allergy symptoms or additional itch only. Of these, only two had allergy confirmed on investigation: one had elevated tryptase at the time of reaction and the other was on antidepressants, which potentially inhibit allergic skin symptoms due to an antihistamine effect. In four of the 17 patients (24%) concomitant ACE inhibitor treatment could explain the angioedema and none of these had allergy confirmed on investigation with exposures from the perioperative setting.

Conclusions: Angioedema presenting as the only symptom in the perioperative setting, with normal serum tryptase at the time of reaction in patients not on medication that inhibits skin symptoms, is unlikely to be due to allergy. ACE inhibitors can cause non-allergic angioedema, also in the perioperative setting.

0738 | Uvular edema in the emergency department

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Introduction: Isolated Edema of the Uvula (IEU) is an unusual form of presentation of upper airway disorders, sometimes misdiagnosed as an angioedema. It can be caused by many different clinical conditions. The aim of this study was to determine the incidence and characteristics of IEU at the Emergency Department (ED) and the study at the Allergy Service of a third-level Hospital in Madrid.

Objectives: A retrospective-descriptive study including all patients older than 15y/o diagnosed with IEU at the Emergency Department (ED) from Jan-2013 to Dec-2015.

Results: 455 937 patients were attended at the ED in 3 years, out of which 97 had IUE (incidence 0.02%). Mean age 48y±18.6, median: 46, 69.1% males. 36.5% suffered breathing difficulties, 51.04% swallowing difficulties and 15.46% dysphonia. 34% were diagnosed with Hypertension, 7.2% of diabetes and 12.4% of snoring The suspected etiology at the ED was unknown in 53.6%, drugs: 24.7% (NSAID: 6.2%, ACE inhibitor-AE 7.2%, others 11.34%), food:13.4%, infection:.1%, *Anisakis simplex:* 2.1% and other allergies: 2.1%. None of them required neither Orotracheal intubation nor hospitalization. 45/97 patients (46.4%), were attended at the Allergy Department for further studies after which the main diagnosis was inflammatory edema 48.9% (24.4% irritative, 15.6% infection, 8.9% gastroesophageal reflux), ACE inhibitor-AE: 17.8%, idiopathic histaminergic AE: 15.6%, food: 6.7% and *Anisakis simplex:* 6.7%. There was a discrepancy in 73.3% of the diagnosis between the suspected etiology at the ED and the final diagnosis.

Conclusions: The incidence of Isolated Edema of the Uvula at the ED was low. It is more common in middle-aged men, and the initial suspected etiology is in many cases inaccurate. The most frequent symptom is swallowing disturbances. Only one third of the patients had non-life-threatening breathing difficulties. In almost half of the patients, there is an irritant cause of the edema.

SUNDAY, 18 JUNE 2017
TPS 12
DRUG ALLERGY: CLINICAL ASPECTS

0740 | Exanthematic reaction to methocarbamol

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Case Report: Introduction: Methocarbamol is a drug belonging to carbamate group used as a skeletal muscle relaxant,. Although its pharmacological mechanism of action is unknown, it is supposed to exert a sedative effect due to depression of CNS.
Some described adverse effects of methocarbamol are flushing, bradycardia, hypotension, syncope, drowsiness, vertigo, headache or insomnia. Hypersensitivity reactions are exceptional.

Objectives: We present a thirty-one year-old female that received Robaxisal compuesto® [methocarbamol (380 mg) plus paracetamol (300 mg)], and naproxen (550 mg) due to cervical pain. Ninety minutes after the first administration, the patient developed erythematous itchy lesions on trunk and extremities, without other systemic symptoms. She received treatment with a single dose of intramuscular (im) dexchlorpheniramine with improvement of lesions in less than 24 hours.
The patient denied having received methocarbamol previously and she had tolerated paracetamol after this episode.

Results: After obtaining a written informed consent, patch test with methocarbamol (10% pet) were performed with negative results at 48 and 96 hours.. Intradermal tests could not be performed because parenteral methocarbamol is not available. Single-blind placebo-controlled drug provocation tests with AAS and naproxen were negative. A Single-blind placebo-controlled drug provocation test with increasing doses of methocarbamol up to 500 mg was performed. Two hours after the last dose the patient developed an itchy skin rash in chest and neck. She was treated with oral cetirizine and im methylprednisolone (1 mg/kg) with resolution of the episode in few hours.

Conclusion: We present an exantemathic reaction due to methocarbamol confirmed with a positive drug provocation test. Although the pathophysiological mechanism is unknown, it could be a hypersensitivity reaction. We only found a previous case of vasculitis due to methocarbamol reported in literature but no any other case of immediate or delayed hypersensitivity reactions.

0741 | Stevens-Johnson syndrome without mucosal lesions: report of a rare entity

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Case Report: Background: Stevens-Johnson syndrome (SJS) is a potentially life-threatening, delayed hypersensitivity reaction affecting predominately the skin with oral, nasal, conjunctival and genital mucosa involvement. Most cases of SJS are associated with drugs such as sulfonamides, aromatic anticonvulsants, β-lactam antibiotics, abacavir, nevirapine, nonsteroidal anti-inflammatory drugs, allopurinol, lamotrigine, tetracyclines and quinolones. SJS without skin involvement has been previously described as Fuchs' syndrome. We report an atypical case of SJS without mucosal involvement.

Methods: A 47-year-old male presented confluent dusky erythematous maculopapular rash and vesiculobullous lesions located predominantly on the dorsal side of his trunk, upper and lower extremities, five days after his admission to the intensive care unit for hemorrhagic stroke and myocardial infarction. Nikolsky sign was present indicating epidermal necrosis. A diagnosis of SJS was made and skin biopsies were obtained. Piperacillin-tazobactam was considered to be the culprit drug and was promptly withdrawn. The patient presented additional skin lesions on the ventral side during the following 5 days, without mucosal involvement. He was treated with methylprednisolone that was discontinued approximately 1 month later without further recurrence.

Results: Histological examination including direct immunofluorescence analysis of the skin biopsies was performed in order to rule out differential diagnoses such as erythema multiforme major, pemphigus vulgaris, bullous pemphigoid, generalized bullous fixed drug eruption and staphylococcal scalded skin syndrome. The results of the skin biopsies revealed apoptotic keratinocytes, full-thickness epidermal necrosis, subepidermal blistering and perivascular lymphocytic infiltrate within the dermis, thus confirming the clinical diagnosis of SJS syndrome.

Conclusions: We present an unusual case of isolated skin lesions without mucosal involvement, suggesting incomplete SJS. The diagnosis of SJS was confirmed by histopathologic analysis of lesional tissue.

0742 | Clinical characteristics and predictors of non-steroidal anti-inflammatory drug (NSAID) hypersensitivity in Thailand

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Introduction: Non Steroidal Anti-inflammatory Drug (NSAID) is the most common drug use and hypersensitivity. This the first study of NSAID allergy in Thailand.

Objectives: The aim of this study was to evaluate clinical characteristics and the factors that predict NSAID hypersensitivity

Methods: A retrospective study of patients suspecting NSAID hypersensitivity consulted to Allergy Immunology and Rheumatology (AIR) unit from Jan 2012 to Dec 2016 was conducted. This included patients visiting allergy clinic and those admitted to the hospital. Drug hypersensitivity questionnaire according to European Network for Drug allergy and drug provocation test (DPT) results were reviewed. Definite NSAID hypersensitivity were either cutaneous reaction from ≥ 3 NSAIDs or positive DPT. We evaluated predictors of NSAID hypersensitivity by comparison between definite group and negative DPT group.

Results: Of 85 patients enrolled, 5 patients with delayed cutaneous reaction were excluded. Majority were female (88.8%). Common underlying diseases were allergic rhinitis and atopy, 82.5 and 77.5%, respectively. Common history was reaction to multiple NSAIDs (57.6%), most common culprit was Ibuprofen (43.8%) and most common cutaneous reaction was isolated angioedema (50%), while urticaria and anaphylaxis were presented in 40% and 10% respectively. Of 80 patients included, 48 patients were classified as definite NSAID hypersensitivity, 19 patients without NSAID hypersensitivity (negative DPT) and 13 with incomplete testing. Univariate analysis revealed predictors of NSAID hypersensitivity that were history of multiple NSAIDs (OR=78.00, 95% CI = 9.18-663.04, P = .0001), paracetamol intolerance (OR=9.72, 95% CI = 2.48-38.18, P = .001), atopy (OR=6.50, 95% CI = 1.95-21.73, P = .002), angioedema (OR=5.60, 95% CI = 1.58-19.80, P = .008), positive skin testing for aeroallergens (OR=5.18, 95% CI = 1.35-19.85, P = .016), allergic rhinitis (OR=5.01, 95% CI = 1.35-18.67, P = .016), first episode of urticaria (OR=3.95, 95% CI = 1.27-12.28, P = .018), onset of reaction <1 hour (OR=3.42, 95% CI = 1.09-10.68, P = .034) and never had similar symptom (OR=3.34, 95% CI = 1.11-10.06, P = .032). Multivariate analysis confirmed multiple NSAIDs as a strong predictor of NSAID hypersensitivity

Conclusions: Isolated angioedema is the most common cutaneous reaction of NSAID hypersensitivity. Reaction to multiple NSAID is the best predictor of NSAID hypersensitivity. Carefully using NSAID in this group is essentials.

0743 | Individuals monosensitized to acetaminophen

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Introduction: Increased consumption of NSAIDs in recent years is increasing sensitivity to these drugs. Acetaminophen, an NSAID of the para-aminophenols group, is one of the most widely used antipyretics and analgesics. We report the cases of patients with reaction exclusively to acetaminophen and not other NSAIDs.

Objectives: Nine patients were referred for reaction with the use of acetaminophen. All of them underwent complete medical history taking emphasizing previous tolerance of anti-inflammatory drugs. Depending on symptoms, controlled challenge test (CCT) was conducted with acetaminophen and/or aspirin (ASA).

We report the cases of patients with reaction exclusively to acetaminophen and not other NSAIDs.

Results: We studied nine patients, five women and four men, with a mean age of 39 years (16-75). Together they reported a total of 13 episodes of reactions following the use of acetaminophen. It always occurred after the first dose and all reactions occurred within one hour. On three occasions the symptom was angioedema with urticaria, one patient had nonspecific symptoms, seven had urticarial rash, one had urticaria with dyspnoea and another experienced anaphylactic shock within 30 minutes of taking acetaminophen 1 g. Six patients reported having subsequently tolerated ibuprofen, two metamizol and one diclofenac. Five underwent CCT with acetaminophen, remaining positive throughout, and seven underwent CCT with ASA (1 g), all being negative.

Conclusions: Although hypersensitivity to acetaminophen is very rare in the general population, we should not underestimate its diagnosis to make precise recommendations. The definitive diagnosis of a selective or multiple pattern is reached based on tolerance or not to aspirin or other NSAIDs.

0745 | Anaphylactic reaction induced by diclofenac

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Introduction: Non-steroidal anti-inflammatory drugs (NSAID) might produce hypersensitivity reactions mediated by immunological or non-immunological mechanisms; on top of other adverse reactions. Hypersensitivity manifestations might include rhinoconjunctivitis, bronchospasm, urticaria, angioedema and anaphylaxis.

Diclofenac sodium is a NSAID member of the Arylacetics family. There have been few cases of IgE-hypersensitivity mediated to this drug. Next, we report on a case of IgE-mediated Diclofenac hypersensitivity.

Objectives: A 44 year-old woman without previous history of pathology, after 30 minutes of taking Diclofenac sodium (75 mg) developed pruritus on hands and soles which subsequently spread followed by a erythematous macular papular rash, facial edema, and dyspnea. She attended the emergency room where she was treated with epinephrine, antihistamines and corticosteroids which eased her condition.

Subsequently, she has tolerated paracetamol.

Skin prick tests with ibuprofen (20 mg/mL) where carried out as well as intradermal tests with lysine-acetylsalicylate (90 mg/mL), metamizole magnesium (400 mg/mL), diclofenac sodium 25 mg/mL, diluted at 1/100 and 1/10. Oral challenge tests with ibuprofen 600 mg and etoricoxib 30 mg were also perform.

Results:

Intradermal tests with diclofenac sodium diluted at 1/10: tested positive.

Intradermal and akin prick tests with lysine-acetylsalicylate, metamizole and ibuprofen: tested negative.

Oral challenge tests with ibuprofen and etoricoxib: tested negative.

Conclusions: Skin tests results as well as medical history confirm anaphylaxis diagnosis (IgE mediated) by diclofenac. The fact that the patient tolerated other non-steroidal anti-inflammatory drugs supports this diagnosis because during non-immunological hypersensitivity reactions, the mechanics of the reaction is given by the strength which the drug inhibits the cyclooxygenase (COX). Thus, in such cases intolerance is usual not selective.

It was suggested to the patient to avoid diclofenac in all its forms, and as a preventive measure all other non-steroidal anti-inflammatory drugs members of the arylacetics family due to the similarities in chemical structure amongst them.

0746 | Iodide mumps: report of two cases

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Introduction: Iodide mumps (IM) is an uncommon condition induced by iodinated contrast media (ICMs), characterized by bilateral painless and enlargement of salivary gland, possibly due to the deposition of iodine in ductal systems of salivary glands.

Objectives: We present two cases of patients with IM after administration of ICM.

Case 1: A 66-years-old man presented swollen neck twice, 12 hours after an abdominal computed tomography (CT) scan, with unknown ICM, for follow-up of liver transplantation. The patient improved in 2-3 days without treatment.

Case 2: A 66-years-old woman, with nephrolithiasis, developed upper inflammation of the neck 6 hours after an abdominal CT scan without other symptoms. Three months later, presented a similar reaction 4 hours after coronary CT scan for angina of effort, The ICM was unknown twice and she improved in 2-3 days with anti-inflammatory treatment.

Patch tests with readings at 48 and 96 hours were performed with different undiluted ICM. Skin prick test undiluted and intradermal skin test with 10-fold dilutions (with immediate and delayed readings) were performed in both patients with the same ICMs. After the results of skin tests, both received ICM again.

Results: Patch and prick test with Iohexol, Iopromide, Ioversol and Iodixanol were negative in both cases.

Case 1: Intradermal test with Iohexol, Iopromide, Ioversol and Iodixanol: negative. We recommended premedication with antihistamines and corticoids if the use of ICM were indispensable. Later, the patient received Iohexol with correct pre-treatment in an abdominal CT scan and presented swollen neck again.

Case 2: Intradermal tests with Iohexol, Ioversol and Iodixanol were negative and positive with Iopromide. Intravenous controlled exposure test with iohexol was performed, and 6 hours after the test, the patient presented neck swelling without other symptoms.

Neck Ultrasounds showed enlarged bilateral submandibular glands in both cases.

Both patients improved with corticosteroids and ICMs were forbidden.

Conclusions: Iodide mumps should be considered in the differential diagnosis in patients with neck swelling after administration of ICM.

0747 | New syndrome caused by angiotensin inhibitors

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Introduction: Angiotensin inhibitors (AI) group, composed by Angiotensin Converting enzyme (ACE) inhibitors, Angiotensin Receptors Blockers (ARB) and aliskiren a Direct Inhibitor of Renin (DIR), are being used with increasing frequency for treatment of hypertension and congestive heart failure. Although AI are usually well tolerated, a considerable number of patients experience Adverse Drug Reaction (ADR) like cough, angioedema, urticaria, rhinitis, asthma, conjunctivitis, foreign body in pharynx, itching, purpura, lichen, aphonia, anaphylaxis, hiccup or dyspnea. These are included in the Summary of Product characteristics (SPC).

The number of symptoms associated to these ADRs might allow us to consider them as a “new syndrome”. The allergist should consider

that a patient has this syndrome when two or more of these symptoms are present.

Objectives: Design: A case series of 300 patients with ADR associated with AI.

Scope: Allergy service, Hospital Central de la Defensa, Madrid.

Period: March 2009 to December 2015. Main variables assessed: demographic, clinical, treatment, evolution and causal relationship between drugs and ADR according to modified Karch Lasagna algorithm used by Spanish Postmarketing Surveillance System.

Patients have given written informed consent for the publication research.

Results: Three hundred cases, age average 68 + /-11.46 years old (22-91); 204 females. Clinical characteristics of ADR: Syndrome 102 cases; cough 63; angioedema 48; itching 22; rhinitis 21; skin reactions 14; anaphylaxis 11; foreign body in pharynx 10;lung and digestive symptoms 6; conjunctivitis 3. Drug involved: ACE 199; ARB 100; DIR 1. Re-exposure to drug n = 224. Treatment was drug withdrawal, achieving complete remission in all cases. The causal relationship between drugs and ADR were defined in 224/300 and probable in 76/300.

Conclusions: "New syndrome" is the most frequent ADR found. Dysregulation of the renin-angiotensin-aldosterone system would play a significant role in the development of this syndrome.

High level of re-exposure shows that, in most cases this "new syndrome" is underdiagnosed, unappreciated and unreported, mainly due to the variability in which it is developed and the number of different specialists involved. An adequate knowledge of these ADR should obviate the need for unnecessary and expensive diagnostic evaluation, leaving aside the important effect of saving patients a number of visits to the specialists.

0748 | Kounis syndrome caused by amoxicillin

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Introduction: Kounis syndrome is a special type of allergic vasospasm of coronary arteries with acute coronary syndrome associated . This syndrome is at present emergent in clinical practice, but recognition is difficult .On the other hand consideration of this syndrome it's crucial to prevent coronary acute syndromes or cardiac arrest.

Objectives: We present a clinical case of amoxicillin induced kounis syndrome Female 62 year old. Associated pathologies:rheumatoid arthritis and diabetes not insulin dependent.

The patient was recovered in other Internal medicine department and in the course of amoxicillin and clavulanic acid infusion undergoes anaphylactic symptoms of pruritus, urticaria, dyspnea,low blood pressure.

Associated Symptom:angina: after this clinical evolution the patient was transferred in Intensive coronary unit .In this unit the patient undergoes to coronary angiography,with demonstration of normal coronary circulation.

After this study we received the patient in our Internal medicine unit.

Results: The RAST for beta-lactam antibiotics showed: Penicilloyl G 6.97 U, Penicilloyl V 26.4 U, Ampicillin 4.74 U, Amoxicillin 10.70 U. Total IgE level 52 U

Normal levels of tryptase excluded a mastocytosis.

At the time to the patient was forbidden the use of any beta-lactam drug.

However it has been programmed skin test for beta-lactam drugs to test the future tolerability of cephalosporins and carbapenems

Conclusions: The coronary involvement in hypersensitivity reactions is probably a side effect of the increase in circulating inflammatory mediators, mainly histamine, proteases such as tryptase and kinase or products of arachidonic acid metabolism. The mast cell, which is also found in the vessel wall, plays a central role in this mechanism. Degranulation of mast cell and anaphylaxis or anaphylactoid reactions may in fact occur after exposure to medication

recognition of Kounis syndrome by the cardiologist, with the help of the allergy specialist, helps the prevention of severe anaphylactic recurrences.

0749 | Potential adverse and allergic reaction from topical complementary and alternative medicine (CAM)

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Introduction: Complementary and alternative medicine (CAM) are usually considered to be without side effect.

Objectives: Visits were made to pharmacies and market places in Kuala Lumpa, Malaysia, Changsha, China and Hong Kong, China.

Some topical CAM were found to contain ingredients with potential adverse and allergic reaction.

Results: Three topical CAM, one from Kuala Lumpa, Malaysia (1), one from Changsha, China (2), and one from Hong Kong, China (3) were found to contain Chinese herbal medicine and antiseptic agent with potential adverse and allergic reaction.

(1) Minyak Ubat Urut (Oil)
Formula
Myrrha, Methyl Salicylate, Turbutine Oil, Cassia Oil, Camphor, Resina Draaconis. Cortex Erythrina variegata
Indications
Insect bites, Stomache, headache and lumbar pain
Potential reaction
Myrrha—allergic contact dermatitis

(2) Shexiang Dieda Fengshi Gao (Ointment)
Composition

Several Chinese herbs including nonprocessed Cao Wu and nonprocessed Chuan Wu
Indications
Rheumatism, arthritis, muscle strain/sprain, painful swelling
Potential Reaction
Cao Wu (wild Aconite)
Chuan wu (Sichuan Aconite)
endangered, toxic and illegal in United States

(3) Oronine Ointment
Composition
30% Chlorhexidine Gluconate Solution 1%
Hydrophilic Ointment base 99%
Indications
Acne, Eruptions, Minor burns, Chapped skin, Chilblains.
Minor cuts, Dry athlete's foot, Ringworm
Potential Reaction
Chlorhexidine gluconate—Anaphylaxis

Conclusions: Some topical CAM are found to contain Chinese herbal medicine and antiseptic agent with potential serious adverse and allergic reaction.

Reactions include allergic contact dermatitis, toxic reaction and anaphylaxis.

Careful examination of the ingredients of CAM should be carried out.

These topical CAM with adverse and allergic reaction should not be purchased or used.

0750 | DRESS syndrome induced by methotrexate

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Case Report: Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe delayed type IV hypersensitivity reaction which is T-cell mediated and is commonly characterised by a maculopapular rash, fever, eosinophilia, lymphadenopathy, organ involvement and haematological abnormalities. It often occurs 2-8 weeks after drug exposure. Implicated drugs typically include antiepileptics, anti-inflammatory agents, sulphonamides and antimicrobials. Here we report a rare case of DRESS syndrome induced by methotrexate.

Case Report: A 73 year old male underwent treatment with amoxicillin/clavulanic acid, piperacillin/tazobactam, meropenem and gentamicin for severe biliary sepsis. He was also on methotrexate during the admission for known rheumatoid arthritis but this was discontinued. Three weeks later he developed a profound maculopapular exanthema across his entire body with mild mucosal and genital involvement. He had an eosinophilia of $13x10^9$/L with deranged liver function. Skin biopsy was consistent with a drug eruption. He was diagnosed with DRESS syndrome as per RegiSCAR inclusion criteria and treated with Prednisolone 30 mg daily reducing regimen for four weeks until the drug eruption resolved. Four months after resolution of the reaction, skin prick and intradermal testing with amoxicillin/clavulanic acid, amoxicillin, piperacillin/tazobactam, meropenem and gentamicin were all negative on immediate and delayed reading. Lymphocyte transformation tests were then performed on all implicated drugs which revealed weak positive lymphocyte proliferation and induction of interferon-gamma cytokine release with methotrexate. All the four antibiotics tested (amoxicillin/clavulanic acid, piperacillin/tazobactam, meropenem and gentamicin) failed to demonstrate any evidence of drug induced lymphocyte proliferation or cytokine release. Methotrexate was deemed to be the most likely cause of the DRESS syndrome and he was advised to completely avoid it. To broaden his antibiotic options he later underwent an oral challenge to amoxicillin/clavulanic acid using a delayed protocol, which was negative.

Conclusion: To our knowledge this is the first reported case of methotrexate-induced DRESS syndrome. Lymphocyte transformation tests are useful in cases of severe drug eruption where multiple drugs are implicated and where progressing straight to a challenge would be unsafe.

0751 | Recurrent drug eruption and recurrent fever in a pediatric case

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Case Report: Background: Fixed drug eruption (FDE); is the type of cutaneous drug reaction that occurs with the involvement of the skin or mucous membranes, occurring in the same body region after each use of the responsible drug. The most common cause of periodic fever in childhood is periodic fevers with aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome. The most commonly used drugs are ibuprofen and paracetamol as antipyretic during the fever periods.

Case: A 3-year-old girl presented with fever and multiple skin lesions. Since 1 year, she has presented episodes of fever up to 39.5°C that recur with a regular periodicity average every 4 weeks and lasting 4-5 days. The fever is accompanied by continuous sore throat with inflamed cervical lymph nodes in each episodes and exudative tonsillitis in some episodes. Her family stated that she has skin lesions in certain areas of the trunk and limbs after each use of ibuprofen, and recently also in new areas. She has no complaints during the feverless periods. Personal and family history was

unremarkable. Physical examination revealed that fever (39.5°C) and, oval / round shaped erythematous plaques, located on both lower extremities, trunk, back, neck, jaw and face with the size of 5x6 cm in the largest one. Oropharynx was hyperemic, there were submandibular, and the bilateral cervical lymphadenopathies. Other systematic findings were normal. Laboratory tests were normal. PFAPA syndrome is thought for the etiology of recurrent fever episodes according the history and clinical findings and the fever was dramatically resolved after single dose of 1 mg / kg methylprednisolone. Biopsy revealed histopathological findings that supported FDE in the form of CD8 + T lymphocyte infiltration with diffuse single cell necrosis in epidermis. After 4 weeks from the treatment, patch test with ibuprofen was detected negative in lesional and nonlesional sites. Oral provocation test was not done due to the risk of dissemination of the reaction. It has been suggested to use paracetamol, which has been successfully tolerated instead of ibuprofen, in fever periods. We report here multiple FDE lesions induced by ibuprofen in a children with PFAPA syndrome. In addition to being interesting, to the best of our knowledge, this is the first case reported of FDE and PFAPA syndrome in the same patient. We want to emphasize that it is important to use safe alternative drug in fever periods in a such patient.

0752 | Anaphylaxis and severe immune haemolytic anaemia developed in the course of desensitization with a carboplatin: a case report

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Case Report: Rationale: Carboplatin-induced immediate hypersensitivity reactions are relatively common among patients with ovarian cancer, and the desensitization as a single intervention strategy in these patients.

Drug-induced antibodies to carboplatin are rare but can cause severe, even fatal, haemolysis.

Aim: We describe a case of autoimmune haemolytic anaemia with thrombocytopenia in a woman with ovarian cancer who had received previously multiple desensitization protocol with carboplatin

Case Report: The patient was 66-years-old woman, with ovarian cancer who had received several lines treatment with chemotherapeutic *agents and however* she develops a hypersensitivity reaction (flushing of the face and body, breathlessness and oxygen saturation plummeted), treated with adrenaline. Skin testing with intradermal test with carboplatin was positive, therefore, it was decided to start desensitization protocol with carboplatin. The initial desensitization was well-tolerated during 5 years and in the last cycle, after completing the total dose she had an episode of generalized malaise, intense pain in the bac, lumbar zone and epigastrium, faintness, cold in extremities without any sign of anaphylaxis. Sequential peripheral blood samples were obtained: haemoglobin: of 5.9 g/dL, Leukocytes:1.7x103 mcL-^{1,} platelets decreased to 4x10^{4}mcL^{1,} with an increase in LDH, and total bilirubin with normal conjugated fraction. The final diagnosis was a haemolytic anaemia and thrombocytopenia in previously diagnosed of anaphylaxis to carboplatin induced by the same drug.

Conclusions: We report a case of anaphylactic episodes and anaemia haemolytic with thrombocytopenia in the same patient. Caution must be taken in those cases who suffer similar episodes in the course of desensitization to carboplatin. To our knowledge this is the first case reported in the literature.

0754 | Profile of a population of 69 patients allergic to NSAIDs

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed for the treatment of inflammatory diseases, and its generalized use causes allergic reactions. NSAID hypersensitivity is seen in up to 11% of patients with asthma, and in up to a 35% of patients diagnosed of chronic urticaria. NSAIDS have been reported as responsible for at least 25% of all Adverse Drug Reactions.

Objectives: We aimed to assess the profile of the patients who have been diagnosed of NSAID hypersensitivity in our Allergy Department during the last 7 years.

Results: A total of 69 patients were diagnosed of hypersensitivity to NSAIDS (49 women,20 men; mean age:46 years old), out of 234 patients of any kind of drug allergy diagnosed in our hospital (Total NSAIDs′ allergy: 29.49%). 41 patients suffered an urticarial reaction (59.42%); 28 showed angioedema with/without urticaria (40.59%). Of note, 18 patients showed urticaria and angioedema (26.09%). 15 patients had suffered anaphylaxis (21.74%). Only 2 patients had a confirmed diagnosis of nasal polyps (2.90%), and 9 patients bronchial asthma (13.04%). 18 patients showed aeroallergen sensitization (26.09%). Out of 69 patients, 41 were diagnosed by challenge test (59.42%), 16 patients showed positive IDR (23.19%), 13 patients had positive SPT (18.84%). 33 patients showed positivity to pyrazolones (47.83%), 27 patients to Acetyl Salicylic Acid (ASA) (39.13%), 8 patients showed positivity to aril-propionics (11.59%) and 2 patients to aril-acetics (2.90%). Out of the 69 patients: 31 tolerated Celecoxib (44.93%); 30 patients showed good tolerance to other groups′ NSAIDs (43.48%); 4 patients tolerated Meloxicam and 48 patients

were also Paracetamol tolerant (65.57%). 6 patients have not fulfilled an alternative anti-inflammatory challenge yet (8.69%)

Conclusions: Hypersensitivity to NSAIDs poses to a third of the total hypersensitivity reactions diagnosed in our Department in the past 7 years. Women are more likely to be diagnosed with this disorder. Pyrazolones allergy entails about half of the NSAID allergy episodes. In order of frequency, the clinical picture observed in our patients was: 1) Urticaria; 2) Exclusive Angioedema; 3) Urticaria and Angioedema; 4) Anaphylaxis and 5) Respiratory symptoms. The oral provocation test constitutes the best diagnostic procedure, entailing the avoidance of unnecessary medication restrictions to our patients.

0755 | Delayed hypersensitivity reaction to epoetin beta: a case report

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Case Report: Epoetin beta is a synthetic, recombinant form of erythropoietin which stimulates erythropoiesis. It is used to treat anemia, commonly associated with chronic renal failure and cancer chemotherapy. Up to now, only a few cases of hypersensitivity reactions with the involvement of anti-erythropoietin antibodies have been reported.

We present a 61-year-old woman with a history of pre-dialysis stage of chronic kidney disease, rheumatoid arthritis, psoriatic arthritis and a not documented penicillin allergy.

She started on epoetin beta 2000 UI/week for the treatment of renal anemia. She received this dose twice, presenting several hours later the administration bad general condition, cutaneous itching and generalized arthralgia of 48-72 h of duration. Due to a mild effect, the dosage was increased to 3000 UI/week presenting the same reaction together with not measured fever, cervical lymphadenopathy with odynophagia and hoarseness, and a generalized macular exanthema with residual purple skin pigmentation and desquamation of 4 weeks of duration after drug disruption. No eosinophilia was observed. No other hematological or biochemical data is available. The patient continued with her regular medication (pantoprazole, calcium supplements, lepicortinolo, enoxaparin, vitamins B12/B1/B6/B2/C and nicotinamide complex, allopurinol and furosemide) without any other episode.

Regular systemic steroids treatment prevents us from to carry out epicutaneous patch test. Drug challenge was contraindicated due to the severity of the reaction. The time relationship and the improvement after drug disruption lead us to the diagnosis.

To our knowledge, this is the first report of a presumed delayed hypersensitivity reaction to epoetin beta.

0756 | A patient worsening with acute COPD exacerbation treatment

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Case Report: Ranitidine is a well tolerated H2 receptor antagonist commonly used in peptic ulcer treatment and stress ulcer prophylaxis. Anaphylaxis is rarely observed with ranitidine. We report a 57 year-old male patient that developed anaphylaxis after intravenous injection of ranitidine due to acute COPD exacerbation treatment. Since his anxiety and fear that treatment may worsen his condition, he had increased relieving short acting beta-agonist therapy to 7-8 times a day and refused to admit to any hospital after this time. After identifying causative drug and safe alternatives, he was reported to be able to get his exacerbation treatment without any problem. This article underlines the importance of awareness that in COPD acute exacerbation treatment, ranitidine, which is usually administered besides methylprednisolone, also have anaphylaxis potential other than antibiotics.

SUNDAY, 18 JUNE 2017
TPS 13
ANAPHYLAXIS FROM CHILDHOOD TO ADULTHOOD

0757 | Prevalence of anaphylaxis among children 3 to 18 years of age in Kuwait

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Introduction: Anaphylaxis is an acute and potentially life-threatening multisystem allergic reaction characterized by a rapid inception and progression following exposure to an allergen. Even though anaphylaxis has been on the rise for the past decade with reported rates of 350% increase among food induced and 230% increase among nonfood induced reactions, there is still paucity of data on the prevalence and outcome of anaphylaxis in various populations. A descriptive cross-sectional study with a multistage stratified cluster sampling of children aged three to eighteen was conducted in Kuwait. 2828 registered students in the selected schools were sequentially recruited in the school years 2014-2015 and 2015-2016 over a period of 9 months to participate in the study.

Objectives: This study aims to; (i) assess the lifetime prevalence of anaphylaxis among the school age paediatric population (3-18 years old), (ii) identify the most at risk age, and (iii) evaluate the main trigger for the condition.

Results: The overall prevalence of anaphylaxis in the study population was 4.24 per 1000 with a 95% confidence interval of 1.85-6.64 per 1000 population. A total of 12 (0.42%) participants fulfilled all the criteria for diagnosing probable anaphylaxis, out of which 66.7% were diagnosed during the incidence by a medical physician. Food was the major trigger in 9 (75.0%) children, of which nuts was the most common in 4 (33.3%), followed by milk and egg, both in 2 (16.7%) and another 2 (16.7%) for other types of unspecified food. Medicine was the trigger in 2 (16.7%) of them and one was not sure of the trigger.

Conclusions: Anaphylaxis during childhood is relatively common with food being the main trigger. Anaphylaxis in children is an important but challenging subject requiring further targeted large studies, to assess the prevalence of this disease, and improve the management of this serious condition.

0758 | Anaphylaxis in children- our experience

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Introduction: Anaphylaxis is a severe, life-threatening systemic hypersensitivity reaction characterized by rapid onset. Symptoms and signs usually occur within 2 hours of exposure to the allergen or even faster with parenteral medication or insect sting. Although a common clinical emergency, epidemiological studies on anaphylaxis are rare, especially in children. The aim of the study was to explore clinical features, causes and treatment strategy in children treated of anaphylaxis in Children's Hospital Zagreb from January 2012- January 2017.

Objectives: We included all children aged 0-18 years who fulfilled clinical criteria for anaphylaxis and were treated in Children's Hospital Zagreb, Croatia from January 2012- January 2017

Results: 28 children were included. 18 were boys and 10 were girls. The middle age of patients was 4 years. In 23 patients (28%) anaphylaxis was caused by food allergens, and the most frequent causes were cow's milk allergens, peanut, fish, hazelnut and egg. Medications caused anaphylaxis in 2 cases and bee sting also in 2 children. 27 (96%) of children had acute urticaria, 16 children (57%) had angioedema, 17 of them (60%) had respiratory symptoms, 5 of them (18%) developed hypotension and 7 (25%) patients had gastrointestinal symptoms. In 9 children (32%) adrenaline was applied

Conclusions: Our results showed that food allergens were the most common cause of anaphylaxis, as previously described in the literature. Clinical symptoms most commonly involved skin. The middle age of children was 4 years, while recent epidemiological study on anaphylaxis in USA showed an increasing prevalence of anaphylaxis in teenagers. Although adrenaline is strongly recommended as a first line therapy in the management of anaphylaxis, it is still rarely applied. Further research on epidemiology of anaphylaxis should include larger sample of children.

0759 | Cold-induced anaphylaxis in pediatric age: an imminent fatal risk

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Introduction: Cold urticaria (CU), an inducible chronic urticaria, can be responsible for severe anaphylactic reactions, potentially life threatening, namely during aquatic activities due to the risk of drowning.

Objectives: Retrospective characterization of 10 pediatric patients with cold-induced anaphylaxis followed at our Immunoallergy Department, including clinical presentation, aetiology, ice cube challenge test (ICCT) result, atopy and control/remission.

Results: The mean age of onset was 10.6 ± 3.3 years old [2;14], without gender predominance. Most patients were atopic (80%).

One case had family history of CU. Eight patients presented a type III pattern of CU with mucocutaneous symptoms associated with hypotension after cold exposure, and two patients a type II pattern of CU, one with angioedema, abdominal pain and dyspnoea and another with generalized urticaria and bronchospasm. Symptoms occurred few minutes after exposure to cold (median of 4.5 minutes; ranging from immediate reactions to 15 minutes later); 50% had at least 6 previous episodes of CU. All cases were classified as idiopathic. Aquatic activities (swimming, sea bathing) and cold air exposure were the main triggers. Some children developed reactions when handling cold objects (2), with cold beverages intake (1) and intraoperative (1). ICCT were positive in all children: ≤3 minutes of stimulation in 4 patients, 5 minutes in 1, 10 minutes in 3 and 20 minutes in 2 of them. All patients had they CU successfully controlled with prophylactic antihistamines and avoidance measures. Adrenaline auto-injector was prescribed in all children. Five patients overcame the symptoms in less than 5 years (mean: 3.4 years).

Conclusions: Cold-induced anaphylaxis is a rare and severe form of inducible urticaria in paediatric age, being mainly idiopathic. ICCT is an important tool in the diagnostic approach and follow-up of these patients. In order to prevent severe reactions, it is important to recognize and avoid the triggers, related in most children with aquatic activities. Timely recognition of anaphylactic episodes and prompt administration of adrenaline are crucial to prevent symptom progression.

0760 | Anaphylaxis by PR10 at pediatric age

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Case Report: Background: Hazelnut and apple are common causes of food allergy in Europe. In northern Europe, symptoms are usually mild and associated with cross-reactivity to the birch pollen allergen, Bet v 1. PR10s are among the so-called low allergenic proteins, but with high potential for sensitization through cross-reactions with Bet v 1-like proteins. PR 10 is found in many fruits (rosacea: apple, pears, peaches), vegetables (celery, soya),but also hazelnut and peanuts. Clinical reactions after ingestion of the raw food are generally limited to an oral syndrome in contrast to LTP. This study presented 4 patients with anaphylactic reactions to hazelnut, peach, soybean, kiwi.

Methods: Four patients fulfilling the criteria for anaphylaxis, previously with only mild symptoms (oral allergy) to hazelnut and/or peach, apple, soy were recruited. Allergy to birch has evolved for more than 4 years. Specific immunoglobulin E to birch pollen, apple, hazelnut and PR10-proteins (rBet v 1, rPru p 1, rMal d 1, rCor a 1, rGlym4), recombinant LTP or storage proteins(rPru p 3 and rCor a 8,rCora9,rCora14,rGlym5,rGlym6) was measured by ImmunoCAP.

Results: All the patients were sensitized to PR10-proteins, and none was sensitized to LTP. In these 4 cases we find severe allergic reactions in relation to hazelnut, kiwi and soya following sensitization to PR10. The evolution for more than 4 years of birch allergy as well as the association of cofactors such as stress, infection, consumption of anti-inflammatory drugs—were certainly amplifiers of severity. At the same time ingestion in large quantities of liquids like juice, Smoothie—are also risk factors—since the patient does not develop the usual oral syndrome.

Conclusion: These clinical cases at the pediatric age warn to the severity of PR10- sensitization and question on the light to moderate character of this cross reaction. We have been able to identify a severe phenotype of a cross-vegetal-food reaction and so improve the advice to be provided: encouraging consumption according to tolerance, good knowledge of risk factors, avoiding rapid consumption of large quantities—especially in liquid juice, smoothies.

0761 | Mite anaphylaxis, flour and drug hypersensitivity, a distinctive clinical phenotype in teenagers

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Introduction: Oral mite anaphylaxis (OMA) in teenagers is rare and a few cases have been reported*.

Objectives: The goal of this study is to describe OMA in a selected group of teenagers in a subtropical area.

Results: Teenager-patients with respiratory allergy due to sensitization to dust mites and some episode of OMA. Study consisted in a positive anamnesis of respiratory symptoms and/or drug allergy. Skin test, specific IgE to mites and single-blinded placebo-controlled oral challenge (SBPCOC) were also performed.

Patients (n = 16; 10-17 years-old) who present documented anaphylaxis immediately after ingestion of homemade food with flour. They had history of rhinoconjunctivitis and/or asthma with no food allergy associated.

Skin prick test (SPT) to common inhalant were positive to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Blomia tropicalis* and negative to the remaining inhalants and the different food implicated.

SPT also were positive to *Thyreophagus entomophagus* in all cases.

Serum total IgE had a range between 72.1 and 2155 UI/L. Serum specific IgE against *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* were positive with a range [1.5- >100 KUA/L] and [4.75- >100 KUA/L] respectively.

SBPCOC with flour was negative in all patients.

Furthermore, 9 of 16 patients (56%) had a convincing history of non-steroidal anti-inflammatory drugs (NSAID) hypersensitivity.

Conclusions: We report 16 cases of OMA in teenagers with no food allergies along. Interestingly, the prevalence of NSAID hypersensitivity is much higher in this distinctive phenotype compared to general population.

To our knowledge, this is the largest reported OMA series involving teenagers.

0762 | Anaphylaxis from ingestion of mites: oral mite anaphylaxis

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Case Report: Anaphylaxis from ingestion of mites (oral mite anaphylaxis, OMA), also known as "the pancake syndrome" is a new recognized clinical syndrome occurring in patients sensitized to mites, after consumption of mite contaminated foods. Foods prepared with wheat and corn flour are most commonly involved in this clinical entity. Domestic mites, as well as storage mites are responsible for the OMA. Here, we describe an interesting case of a boy with OMA after eating cereals contaminated with mites.

We encountered a 14-year-old boy presented with diffuse erythema, wheals, angioedema of the eyelids and shortness of breath, nearly thirty minutes after ingestion of cereals with milk. He was treated at the Emergency Department with intravenous dimethindene, methylprednisolone and inhaled salbutamol with complete resolution of his symptoms within 1 hour.

He reported symptoms of perennial allergic rhinitis, mainly nasal congestion and sneezing during morning hours. Also, he described episodes with dyspnea after consumption of shrimps, as well as after inhaling shellfish vapors. He consumed wheat containing products without any problem.

In the context of the allergological workup, skin prick testing (SPT) with commercial extracts to food and inhalant allergens, as well as prick to prick to fresh foods were performed. Also, specific IgE antibodies in serum to culprit foods were assessed by the ImmunoCap system.

SPTs revealed sensitization to house dust mites and storage mites. Regarding foods, skin testing was positive for shrimp and octopus, whilst wheat and gliadin were negative. In vitro evaluation showed sensitizations to domestic and storage mites (Acarus siro, Lepidoglyphus destructor, Glycyphagus domesticus), as well as to shrimp and octopus. Component resolved diagnosis confirmed sensitization to tropomyosin (Der p10), whilst specific IgEs to ω5 gliadin (Tri a19) and lipid-transfer protein in wheat (Tri a14) were negative.

Based on the clinical presentation and the results of the allergy testing, anaphylaxis from mite ingestion seems to be the most possible diagnosis in this clinical scenario. OMA may potentially be a severe condition, that in many cases remains unrecognized and untreated. Physicians should be aware of this clinical syndrome and suspect it when they deal with patients who experience anaphylactic reactions temporally associated with consumption of flour containing meals.

0763 | Immunologic evaluation of perilla seed-induced allergic reactions

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Introduction: Incidence of the food allergy or food-related allergic reactions in adults has been recently increased in Korea, and several specific foods accounts for the majority of the cause of food allergy. Although perilla seeds are frequently consumed in many food products as seasonings and seed oil in Asia including Korea, perilla seed-induced allergic diseases has been rarely reported.

Objectives: This study was performed for immunologic evaluation of the perilla seeds-induced allergic diseases.

Three patients with perilla seed allergy were enrolled. Two patients had developed anaphylactic symptoms after eating perilla seed contacting foods, and one patient had a several experiences of oral allergy syndrome after contact perilla seeds. Skin prick tests, specific IgE measurement, IgE inhibition tests and IgE immunoblotting were performed.

Results: The skin prick test with perilla seed extracts showed positive reactions, and serum specific IgE antibodies to perilla seeds were detected by ELISA. ELISA inhibition tests showed significant inhibitions of specific IgE responses with additions of perilla seed extracts in dose-dependent manners, however, sesame seeds showed no inhibition of the IgE binding to perilla seeds. Immunoblot assay identified several IgE binding components with molecular weights of around 22, 25.5, 27, 32, and 34 KDa.

Conclusions: We demonstrated the presence of specific IgE to perilla seeds in patients with allergic reaction to these foods, and also identified specific IgE binding component. These results suggest that perilla seed can induce IgE-mediated allergic reactions in sensitized patients, and it should be taken into consideration as a cause of food allergy.

0764 | Anaphylaxis to pumpkin seed

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Introduction: Food allergy to pumpkin seed is an extremely rare allergy. Here we report a pediatric case of food anaphylaxis to pumpkin seed.

Objectives: An eight-year-old boy, with a history of allergic asthma, outgrown IgE-mediated food allergies to cow milk and cashew nut and persistent goat and sheep milk allergy, declared a grade 3 anaphylaxis with deep faintness, vomiting, facial and pharyngeal edema, almost immediately after consuming a multigrain bread bun containing sunflower and pumpkin seeds.

The child consumes without any problems the different cucurbits (different pumpkin and squash varieties, zucchini, cucumber and melon varieties including cantaloupe, canary melon and watermelon), peanuts and all kinds of nuts

Results: Skin prick-to-prick tests were positive with different kinds of pumpkin seeds but negative with pumpkin pulp and pumpkin seed oil. Prick-to-prick tests were slightly positive with other kinds of edible seeds and negative with linseed oil, sesame oil, peanut, all kinds of nuts, zucchini, melon, cucumber, watermelon and different kinds of flours.

Specific IgE to pumpkin seed were positive at 3.75 KU/L while they remained negative to pumpkin pulp as well as to the other edible seeds.

An oral challenge test with a seed mix (sunflower, flax, sesame and poppy seed) was proposed on account of the cutaneous sensitization to these seeds and remained negative at significant doses.

Conclusions: Having been traditionally used since antiquity, pumpkin seeds have been incorporated in the modern diet with the advent of diets rich in omega-3 and omega-6 polyunsaturated fatty acids.

Besides profilin and proteins of molecular weight of 13, 36, 48, 69, 77, and 87 kDA found in pumpkin seeds, potential allergens may correspond to storage proteins such as 7S globulins, 11S globulins and 2S albumins. Their compact structure, their important size and abundance in the seeds, as well as their resistance to heat denaturation and to hydrolysis by digestive proteases are thought to be responsible for their important allergenic properties.

Because of their potential therapeutic effects in the prevention of cardiovascular disease, cancer and aging process, seeds like pumpkin seeds are increasingly included in many foods, in alternative or natural medicines and in cosmetics. Pumpkin seed food allergy may therefore be expected to increase in the future. It should be assessed by carefully taking the patient's medical history and by including common edible seeds in food allergy testing panels.

0765 | Beer: un uncommon cause of anaphylaxis

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Case Report: Background: Beer is one of the most popular beverages in the world. Its basic ingredient is malt, which derives from germinated barley. IgE-mediated reactions following beer ingestion are uncommon.

Case Report: A 32-year-old male patient presented with dyspnea, thoracic oppression, wheezing, oropharyngeal edema, hoarseness, urticaria and angioedema, a few minutes after drinking beer. The patient repeated the ingestion with other beer brands, always with a similar pattern of symptoms. He ingested cooked beer in meals, as well as other alcoholic beverages without symptoms.

He reported a very similar episode after the ingestion of a type of bread, and 2 episodes after the ingestion of almond and hazelnut, in which he developed hoarseness, oral pruritus and thoracic oppression.

Recently, this patient avoids every type of beer, hazelnuts and almonds. There was no previous personal allergic history, no daily medication nor family history of allergy.

Prick-to-prick tests with multiple brands of beers were performed, all with positive results (4-5 mm). Prick test with almond commercial extract was negative, and positive with extracts from peach, hazelnut, wheat, corn and barley. Oral provocation test was not performed due to the severe previous reactions.

We searched for the presence of serum-IgE that recognized proteins present in various beer brands (white and black beers) and in cereal (wheat, barley and corn). SDS-PAGE immunoblotting with 2-mercaptoethanol, showed IgE-binding bands of 15 kDa and 9 kDa in barley and corn extracts, a band of 15-16 kDa in wheat extract, and bands of 40 kDa, 28 kDa, 18 kDa y 9 kDa in Franziskaner® beer extract. Immunoblotting-inhibition assay showed that extracts from wheat, barley and corn, and purified Pru p 3 were able to produce a total IgE-binding inhibition to beer extract.

According to these results, it seemed very likely that the 9 kDa-IgE-reactive band appeared in beer extract was the LTP derived from cereals used in beer production.

Conclusions: In this patient, the allergic reaction was caused by the ingestion of beer, probably due to the cereal LTP.

0766 | Fdeia—which allergen to blame?

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Case Report: Background: Food-Dependent Exercise Induced Anaphylaxis (FDEIA) can be a fatal disease. Gliadins (namely Ω-5-gliadin) and N*on-specific Lipid Transfer Proteins* (nsLTPs) are the most frequent allergens involved in these reactions.

Case Report: The authors describe two cases of anaphylaxis induced by exercise.

Case 1: Male patient, 37 years old, referred to our Allergy and Clinical Immunology Department, after several episodes of facial edema, dyspnea, wheezing and generalized rash during exercise. In all episodes he had a light meal (usually a sandwich) 2 hours before physical activity. No personal history of allergy, nor usual medication.

We proceeded to skin prick tests (SPT) and blood analysis. Those of clinical importance were: SPT (mm) to commercial extracts of alder 3, olive tree 3, mugwort 5, *Dermatophagoides farinae* 8, *Lepidoglyphus destructor* 6, *Chenopodium* 4, oats 15 x 3, raspberry 6; peanut 7; specific IgE (kU/L) to mugwort 0.53, *Dermatophagoides pteronyssinus* 8.34, *Dermatophagoides farinae* 3.93, *Lepidoglyphus destructor* 1.67, wheat 5.56, rye 4.16, barley 5.34, oats 38.20, peanut 1.0, almond 0.51, chestnut 2.61, malt 5.09, raspberry 1.94, rTri a 14 1.33, Ara h 9 4.51.

Case 2: Female patient 23 years old, sent to our consultation after an episode of dyspnea and generalized rash after 30 mins of physical exercise. One hour before that episode, she had ingested fish, potatoes, bread and apple. Previous medical history of allergic rhinitis. No usual medication. We proceeded to SPT and blood analysis. Those of clinical importance were: SPT (mm) to commercial extracts of grass pollen 4, apple 4, pepper 3, parsley 4, curry 3, soy 3, corn 4. Negative prick tests to all fishes. sIgE to: *Dactylis glomerata* 1.43, *Phleum pratense* 1.16, *Olea europea* 7.05, Apple 3.6; rPru p 3 2.71.

In Case 1, we recommended avoiding cereals, raspberry, nuts and peanut 1 h before and 2 h after physical exercise. In Case 2, *rosacea* fruits were restricted before and after exercise. On follow-up visits, both patients were asymptomatic.

Conclusion: In these two cases, we observed that nsLTP were the culprit allergens, a sensitization which is known to be quite frequent in the Mediterranean area. LTP sensitization is associated with serious systemic reactions. Therefore, it is very important to identify which allergens are involved in each patient, and perform the recommended restriction diet according to the patient's physical activity.

0767 | Fish anaphylaxis and anisakis simplex: a reason you don't have to forget

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Case Report: Introduction: Every year food allergies are most frequent in Allergy departments, being more typical to fruits, eggs, milk and fish. *Anisakis simplex* sensitization is very common at Mediterranean blue fishes, producing symptoms from digestive ones to anaphylaxis. Our aim is to show a patient with fish anaphylaxis, and the in vivo and in vitro studies we performed, and the obligation of performing a Food Provocation Test (FPT) with the culprit fish.

Patient and Methods: A 35 years-old patient came to our clinic referring arms urticaria with facial angioedema and dyspnea without hypotension 15 minutes after eating smoked salmon, needing adrenaline treatment. Good tolerance before this episode. We performed skin prick test with the main aeroallergens and panallergens, typical fishes and anisakis, and we studied basal tryptase, total IgE and specific IgE, and ISAC® to evaluate a molecular diagnose.

Results: Skin prick test was negative to aeroallergens and fishes, and very positive to A*nisakis simplex*. Total IgE was 80 KU/L, being the basal tryptase 3.5. Specific IgE to *Anisakis* was 10.2, and negative to tuna and salmon, with a positive result using ISAC® to Ani s3 and in an immunoblotting to Ani s3, Ani s5, Ani s7, Ani s11 and Ani s13. With these results, we performed a FPT with frozen salmon, being negative during 2 hours of observation as an inpatient and during 48 hours at home

Conclusions: We present a patient with moderate anaphylaxis after eating salmon, being the *Anisakis simplex* parasitization the main reason of it.

A good clinical report and in vivo/in vitro studies are very important to demonstrate the etiology.

A FPT is a very good tool to improve our diagnosis and to avoid mistakes.

0770 | Anaphylaxis secondary to progesterone hypersensitivity successfully treated with omalizumab

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Case Report: In women, one of the most frequent trigger/enhancing co-factor for anaphylaxis (often classified as "idiopathic") are

menses, rarely associated with IgE-mediated allergy to endogenous progesterone or other hypersensitivity mechanisms. The therapeutic options, apart from i.m. epinephrine for the acute treatment of each episode, include high-dose systemic steroids, hormone-targeted therapies, progesterone desensitization or surgical salpingo-oophorectomy.

A 12 y.o. girl (menarche at 11 years and 3 months of age) without any allergic signs or symptoms in her previous clinical history, presented at our Allergy Outpatients' Clinic for recent recurrent anaphylaxis (urticaria, labial and eyelid angioedema, dyspnea with chest tightness and wheezing, abdominal pain, nausea, diarrhea and hypotension) occurring 2 days before the onset of each menses. No drugs have been taken before each episode of anaphylaxis. No consistent history of any other common triggers of anaphylaxis (i.e. foods, hymenoptera stings. . .) or co-factors (NSAIDs, exercise, etc. . .) were found.

Skin prick tests for a panel of common airborne and food allergens were performed and resulted negative, and progesterone 50 mg/mL was tested: intracutaneous injection of 1/100 diluted progesterone induced a wheal of 6 mm (histamine wheal: 7 mm; negative control: 0 mm); the same skin test protocol was applied to a control group consisting of 5 healthy and reproductive females without any positive results. Masquerading conditions (i.e. carcinoid syndrome, pheochromocytoma, and systemic mastocytosis) were ruled out. We therefore concluded for recurrent/cyclic anaphylaxis due to progesterone hypersensitivity.

The patient was treated with omalizumab 300 mg s.c. monthly for 6 months: just after the first administration she stopped experiencing any allergic symptom before menses. Nowadays the patient ended the expected 6 months treatment period about five months ago, without relapses of allergic symptoms after the end of the treatment. After six months of treatment with omalizumab, the patient was tested again for prick and intracutaneous test with progesterone with negative results.

This is the first reported experience of progesterone-induced anaphylaxis successfully treated with omalizumab, possibly expanding its indication to selected complicated cases of recurrent anaphylaxis.

0771 | Anaphylactic shock to bilastine

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Introduction: Antihistamines are drugs that antagonize the activity of histamine receptors. H1-Antihistamines are first-line treatment for chronic urticaria and are used to treat allergic reactions. Anaphylactic reactions to antihistamines are very unusual.

Objectives: We describe the case of a 53-year-old woman with history of chronic urticaria experiencing urticaria, angioedema and syncope to multiple H1-antihistamines (hydroxyzine, cetirizine and fexofenadine). In order to proof tolerance with an alternative H1-antihistamine a double-blind provocation test with bilastine vs placebo was performed.

Results: After a cumulative dose of 37 mg bilastine (90 minutes), the patient developed generalized urticaria. Prednisolone 100 mg per os was given immediately. After 360 minutes, the patient felt dizziness with drop of blood pressure (84/54 mmHg) and tachycardia (107/min). The patient recovered after intramuscular injection of 0.3 mg adrenaline. One hour after the reaction, blood sample showed an elevated tryptase (36.7 μg/L) which normalized several days later, consistent with a mast cell-activation in IgE-mediated reaction. Finally, the urticaria was treated with monthly injection of 300 mg omalizumab with good tolerance without recurrence of urticaria (follow-up 5 months).

Discussion: Hypersensitivity reactions to H1-antihistamines are very rare and only twelve cases have been reported in literature. Above all, cetirizine has been implicated in these reactions. The exact mechanisms are speculative, but the piperazine ring has been implicated in some cases of cetirizine hypersensitivity. However, this hypothesis remains controversial as prochlorperazine, an antiemetic drug containing a piperazine ring, was well tolerated in another case after cetirizine anaphylaxis. Other groups suspected a hypersensitivity to side chains of cetirizine. Interestingly, an intolerance reaction to cetirizine has also been reported.

Conclusions: This is the first report of an anaphylactic reaction to bilastine. Patients may react to one single or multiple H1-antihistamines, which is challenging in the treatment of chronic urticaria. Prediction of crossreactivity is difficult because the epitope has not been identified. Careful assessment of the risk/benefit ratio is necessary to avoid potentially harmful provocation tests. Omalizumab should be considered as first choice treatment in patients with chronic urticaria and H1-antihistamines hypersensitivity.

0772 | Anaphylaxis caused by a "natural" microenema

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Case Report: Introduction: During the last years, it is increasing the consumption of "natural" medicines as they are popularly considered as harmless or with less side effects. We report a 46 year-old men who developed 10 minutes after applying a Melilax microenema® urticaria, angioedema and tearing and within 10 minutes pharyngeal itching occurred. He went to a hospital but he was improving and no alarm symptoms were found so they do not give any medicines and just adjust the treatment for the constipation. He

had no personal history of reaction with bee sting, food or drugs allergy.

Material and Methods: Skin prick test to common inhalants and a wide variety of food were tested. Prick-to-prick test with the Melilax microenema®, two types of honey which it includes (honeydew honey and honey mix) and two kind of multi-flowers honey (from Jaen and Valencia) were performed. Proteins from Melilax microenema® and the components from its formula were tested separately by means of SDS PAGE and analyzed by Western blot with the serum of the patient.

Results: Skin prick test were positive to Artemisia, Plantago, Parietaria, Olea and Profilin but negative to food. Prick-to-prick test with the Melilax microenema ® and the two types of honey which it includes (honeydew honey and honey mix) were positive. Prick-to-prick test with two kind of multi-flowers honey (from Jaen and Valencia) were also positive. Specific IgE test for honey was 0.20 kU/L The patient's serum recognized an allergen of 55 kDa from Melilax microenema®, honey mix and honeydew honey and another one of 28 kDa from honeydew honey

Conclusion: To the best of our knowledge this is the first case of anaphylaxis due to honey absorbed by the rectal mucosa after using a microenema. Our patient had a systemic reaction to honey and also had sensitivity to pollens according to what has been reported in the literature. Currently, the allergenic part of the honey is not well defined. With the increasing consumption of honey for "natural" skin care, healthy food or as a natural medicine, case reports of anaphylactic reactions due to honey are becoming more frequent.

SUNDAY, 18 JUNE 2017
TPS 14
FOOD ALLERGY AND MOLECULAR DIAGNOSIS

0774 | Study of a LTP syndrome in a Mediterranean area using microarray

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Introduction: Plant food allergies associated with lipid transfer protein (LTP) have been widely described in the Mediterranean Area.

Objectives: The aim of this study was to describe the clinical profile and pollen sensitization of a patients with LTP syndrome and to determine a clinical pattern of severity.

Patients with clear IgE-mediated symptoms associated with plant foods and a positive skin prick test to Pru p 3 and a control group were included in the study. The clinical evaluation comprised an exhaustive medical history, skin prick test with food and inhalant battery and specific IgE components by ISAC microarray.

Results: A total of 84 patients (IQR 3-62 y.o) were included: 44% anaphylaxis, 42.9% restricted reactions to skin and/or oropharyngeal tract and 13.1% asymptomatic sensitization to LTPs. Of this total, 47.6% suffered from respiratory allergy.

The three groups have a similar sex distribution but a statistically lower mean age and a lower mean value of Pru p 3 was observed among the asymptomatic ones. ($P < .05$).

We did not detect statistically significant differences between groups with clinical food allergy in terms of time of evolution, mean age of food allergy debut neither in food responsible for the first reaction. *Rosaceae* fruits (48.8%) were the most frequent food implicated. Cofactor enhanced food allergy in 35.7% of patients being more frequent in the group of patients with anaphylaxis ($P < .05$).

50% were sensitized to mugwort (64.3% showing IgE to Art v3) and 35.7% to plane tree pollen (82.1% with IgE to Pla a 3).

We observed an increase of the number of LTPs recognization in the food allergic patients with no matter to the severity of the allergic symptoms ($P < .05$).

Conclusions: The LTP syndrome in our area is related to atopic young patients, with multiple sensitizations to plant foods and pollens such as plane tree and mugwort. Rosaceae fruits are the main culprit food involved.

The patients with plant food allergy compared to asymptomatic LTP sensitized patients were older, have higher values of Pru p 3, recognized an increased number of LTPs (preferably Pla a 3 and Art v 3) regardless of the severity.

The presence of cofactors is the only variable associated to severity. Therefore, we recommend the prescription of adrenaline autoinjector to every patient sensitized to LTPs with cofactor enhanced food allergy regardless to the severity of the allergic symptoms.

0775 | How immunoblotting and mass spectrometry can help to diagnose kiwi fruit allergy

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Case Report: Introduction: Allergy to kiwi fruit is often associated with severe reactions in addition with oral allergy syndrome. Kiwi fruit matrix is very complex as it contains many allergenic proteins. We describe a clinical case of allergy to kiwi fruit (*Actinidia deliciosa*) in a woman presenting birch pollen allergy and recurrent urticaria.

Objectives: The diagnosis of kiwi fruit allergy is based on anamnesis, skin prick test (SPT) and specific IgE (sIgE) measurement to total kiwi fruit extract. Actually, the in vitro diagnostic tools cannot help the physician to define the precise kiwi allergen involved in the allergic reaction. Indeed, only one molecular allergen component is commercially available: Act d 8 (PR-10 protein, Birch Bet v 1-homologous). We aimed to adapt a 2D Western blot (WB) to get the molecular allergen sensitization profile of the patient. Afterwards, we used mass spectrometry (LC-MS/MS) to identify precisely the allergens.

Methods: We analyzed the serum of a 23 y.o. woman presenting a positive SPT to kiwi extract, low sIgE for kiwi extract (0.11kUA/L) and positive sIgE for Act d 8 (6.66 KUA/L). We extracted total *Actinidia deliciosa* proteins. Then, we separated proteins on the basis of their isoelectric point and molecular weight. The patient serum was analyzed by 2D WB in order to evaluate its sIgE reactivity against the different protein spots. Finally, the protein spots recognized by the patient sIgE were identified by LC-MS/MS.

Results: The patient sIgE sensitization profile showed 5 specific protein spots. Amongst them, we selected 2 spots and identified them by LC-MS/MS. The first spot situated around 25 kDa/pH5-6 was pointed out as Act d 1 (cystein protease). The second spot around 10 kDa/pH10 was identified as Act d 10 (LTP family). The result of sIgE against Act d 8 correlated perfectly with a third spot of 18 kDa/pH6-7.

Conclusion: We studied a birch pollen allergic woman presenting recurrent urticaria with low sIgE to kiwi extract but a positive SPT to kiwi. The 2D WB provided a sIgE profile showing multiple kiwi allergens. Amongst them, we confirmed Act d 8 which is associated with OAS in birch pollen allergic patients and identified Act d 1 and Act d 10, both frequently associated with severe reactions to food. We pointed out a potential role of Act d 1 and Act d 10 in the clinical symptoms of urticaria in this patient. Furthermore, we demonstrated superiority of 2D WB over the traditional diagnostic methods, unable to reach the same precision.

0776 | Identification of the IgE-binding protein pommaclein, Pun g 7, in pomegranate fruit

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Introduction: Pomegranate, Punica granatum L., is a temperate climate species, mainly cultivated in the Mediterranean area, Southern Asia, and in several countries of North and South America. The consumption of pomegranate is increasing as it is considered a health-promoting food. Nevertheless, it can trigger allergic reactions, sometimes severe. The LTP, Pun g 1, is the only pomegranate allergen reported so far.

Objectives: Aim of this study is the detection of still unknown allergens in Pomegranate fruit.

Results: Pommaclein, was isolated from the fruit juice, identified by direct protein sequencing and characterized as IgE-binding protein by immunoblotting, dot blotting and FABER test. Nineteen patients with a reliable clinical history of allergic reactions to pomegranate fruit and/or sensitization to Pru p 3 and Pru p 7 were selected for this study. Pommaclein is a 7 kDa protein, registered in the UniprotKB under the accession number C0HKC0. It displays high structural similarities with the peach allergen Peamaclein, Pru p 7. Among the nine patients tested with Pru p 7 by SPT, four resulted IgE positive to Pru p 7 and Pommaclein and one to Pommaclein only. Two patients out of 19 were monosensitized to Pommaclein, whereas four patients were positive to both pomegranate and peach homologous proteins. When IgE were detected in parallel for Pru p 7 and Pommaclein by FABER nanotech test, 16 sera out of 1751 were found positive for the former and 6 for the latter.

Conclusions: A new allergenic protein, Pommaclein, Pun g 7, was identified. It is a homolog of the peach allergen Pru p 7, but the immunological properties of the pomegranate allergen are not completely shared with those of the peach allergen. Pun g 7 can contribute to improve the allergy diagnosis to plant-derived foods and profiling the allergic patient IgE reactivity using panel of homologous molecules as already done for other allergen groups.

0777 | Diagnosis of peanut, tree nuts and sesame seed allergies: utility of skin prick tests and component resolved diagnosis

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Introduction: Diagnosis of peanut or tree nut allergy is difficult and usually leads to recommendation for the avoidance of all nuts and often also sesame. Improving the diagnostic efficacy of in vitro tests might reduce the need for oral food challenges, which is time consuming, costly and associated with risk of severe reactions.

Objectives: We included children aged from 0 to 16 years with at least one confirmed nut or seed allergy. Based on sequential challenges to 11 nuts/seeds used as a gold standard, we aimed to determine the real diagnostic value of skin tests as well as component resolved diagnosis in predicting clinical reactivity to different types of nuts in those children.

Results: A total of 93 children who underwent over 800 challenges have been prospectively recruited. Sixty one percent of patients were allergic to up to one nut. Skin prick tests had the larger ROC area under the curve (AUC) than specific IgE test to all nuts tested. SPT had equivalent AUC for component allergen tests for peanut, cashew, pistachio and Brazil nut but better for hazelnut and fresh walnut. Regarding hazelnut, peanut, cashew/pistachio, walnut and brazil nut, specific IgE to Cor a 14, Ara h 2, Ana o 3, Jug r 1 and Ber e 1, respectively, were the better discriminating in vitro tests with the largest AUC (90%, 83%, 91%, 85% and 90%, respectively), compared to specific IgE to whole extract. The AUC of the combination of specific IgE to Cor a 14 and Cor a 9 was similar to the one of specific IgE to Cor a 14 (84% and 83%, respectively). Similarly, we found the same AUC for specific IgE to Ara h 2 alone and the combination of specific IgE to Ara h 1, Ara h 2 and Ara h 3 (90% for both).

Conclusions: For most nuts, our data showed that SPT and/or specific IgE to recombinant allergens had a high diagnostic value to discriminate between allergic vs tolerant patients. SPT had higher sensitivity for predictive challenge proven nut allergy but component allergen testing had higher specificity.

0778 | Peanut allergen protein extraction from foods for immunoassay quantification

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Introduction: Management of allergens in food manufacturing and research into food allergy requires the accurate and precise quantification of food allergens. The most commonly used technique for quantification of food allergens is immunoassays—typically ELISA. Accurate quantification of allergens from food using immunoassays requires the optimisation of procedures used to extract allergen.

Objectives: Our aim was to examine the variability between extraction procedures for quantification of major peanut allergens. Allergens were extracted from various food types including flours, incurred matrices and real foods. A variety of extraction procedures were tested including variations to concentrations of salt in buffers, temperature during extraction, length of extraction time, and addition of agents such as fish gelatin. The variability of the extraction procedures was compared between users and on different days. Peanut allergen content in the extracted samples was measured using allergen specific immunoassays for Ara h 1, Ara h 2 and Ara h 6.

Results: When following the same protocol, the consistency of allergen extraction from user to user and on different days was very consistent. Variations in the allergen extraction procedure influenced the amount of allergen that was quantified. The extent of variation was greater with certain allergens and is likely due to the properties of the specific proteins. The variation was also altered with certain matrices or sample types.

Conclusions: These results highlight the complexity of allergen extraction efficiency. They suggest that each allergen protein is influenced differently by various extraction procedures. Sample type or matrix can also influence the extraction efficiency. A universal allergen extraction protocol that is optimal for all samples types and for all allergens may be difficult to achieve.

0779 | Quantification of peanut allergen absorption using autologous serum in a human model of passive cutaneous anaphylaxis

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Introduction: Anaphylaxis is the result of a complex series of events; however, the anaphylactic reaction is rapid in onset and usually occurs within one hour of food intake. Despite extensive research in the allergy field, there are still significant gaps in our understanding of the chain of events in the anaphylactic reaction. The gastrointestinal uptake and absorption time of allergens is one example. This study had two purposes: 1) to measure the absorption time of peanut allergens and 2) to determine the absorption peak for peanut allergens.

Objectives: In this study, the model of passive cutaneous anaphylaxis (Prausnitz-Küstner test) was used. In the first (preparation) part of the study, we collected blood samples at fixed time points (T = 0, ½, 1, 2, 3, 4, 8, 24, 48) from healthy volunteers (recipients, n = 8) after they had ingested 100 g of dry-roasted peanuts or peanut flour. In the second part of the study, we intradermally injected aliquots (100 mL) of serum from a human donor with severe peanut allergy into the volar surface of the forearms of the recipients. After 24 hours, we injected autologous aliquots (50 or 100 mL) of the serum collected during the first part of the study into the donor-sensitized skin sites. We recorded the positive skin reactions and measured wheal diameters.

Results: In the majority of recipients, there was a positive wheal-and-flare reaction (calculated mean wheal diameter [(D+d)/2] of ≥ 3 mm) in the skin sites injected with autologous serum sampled within 30 min after ingestion of peanut. Likewise, the largest reaction, i.e. wheal, generally developed with one of the autologous sera sampled within the first two hours of ingestion of peanut. Interestingly, we found positive reactions with autologous sera sampled as late as 24 hours after the ingestion of peanut.

Conclusions: Our findings support the notion that the absorption of peanut allergens generally is fast (≤ 30 min). Our results also indicate that the absorption of peanut allergens reaches a peak within two hours of peanut intake. Future research should determine whether these results have implications for the time interval between dose steps in food challenges in patients.

0780 | Patients allergic to fish: Clinical and immunological characterization of sensitization profile in the last decade

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Introduction: Fish consumption has been increasing, and with it, the frequency of reported cases of fish allergy, which prevalence in general population ranges from 0.2% to 2.29% and it goes up to 8% in people related to the fish industry.

Objectives: Clinical and laboratorial characterization of patients diagnosed with fish allergy by evaluation of sensitization profile to different fishes.

Methods: Observational retrospective study of patients(pts) diagnosed with fish allergy followed in our Immunoallergology department, from July 1st of 2005 to December 31st of 2016. We performed tests to evaluate serum specific IgE (sIgE) to several fishes and recombinant parvalbumin Gad c 1 (rGad c 1)(Unicap®, Thermo-Fisher). The population was characterized according to demographic data, fishes associated to reaction, symptoms, skin prick tests (SPT) and sIgE to selected fishes.

Results: 81 patients (68% male, 32% female, average age 14 ± 9 years, 24% melanodermic), 55 (68%) are atopics(78% rhinitis, 67% eczema, 43% asthma). Pollock (51%), mackerel (30%) and codfish (26%) were the most common species associated with allergic reactions. Pts presented symptoms with the ingestion of fish (96%), cutaneous contact (27%) and inhalation of cooking fish vapors (20%). 28% of pts had anaphylaxis and the most frequent manifestations were urticaria/angioedema (71%), gastrointestinal symptoms (35%) and Eczema (34%). Average age of 1st contact with fish was 9 months, 1st allergy manifestation age(excluding 4 pts who developed symptoms only in adulthood) was 22 months and 50% of pts presented symptoms during the 1st ingestion. 69 patients (85%) had positive SPT for at least one fish species (pollock 84%, codfish 77%, salmon 66%, halibut 56%). The sIgE (kUA/L) were, at first evaluation: codfish(32.2), sardine (22.9), pollock (17.5), salmon (13.9), halibut (9.0), tuna (4.52) and rGad c 1 (22.87). In the last consult about 63% was tolerating tuna, 25% codfish, 25% salmon and 22% whitefish. The average tolerance acquisition age for at least one species was 10.5 years.

Conclusions: Pts with fish allergy often don't tolerate any type of fish, although, in this study the complaints were most frequently associated to pollock due to its valuable presence in Mediterranean diet and it's one of the most consumed fish in Portugal. Half of the pts had symptoms at the first contact with fish, which lead to the possible assumption of an in-uterus sensitization. Overall, tuna was the most and the first tolerated fish.

0781 | Contribution of recombinant parvalbumin Gad c 1 in diagnosis and prognosis of fish allergy

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Introduction: Parvalbumin is a major allergen in fish and there's a high degree of cross-reactivity between parvalbumin from different fish species. Gad c 1 is a parvalbumin and a major codfish (*Gadus callarias*) allergen and a valuable tool for diagnosis and follow-up in patients with fish allergy.

Objectives: Analyze the contribution in diagnosis and prognosis of serum specific IgE (sIgE) values of recombinant fish parvalbumin Gad c 1 (rGad c 1) and the *prick-prick* test in the fish tolerance acquisition in allergic patients.

Methods: Observational retrospective study of patients diagnosed with fish allergy followed in our Immunoallergology department, from July 1st of 2005 to December 31st of 2016. We performed tests to evaluate serum specific IgE (sIgE) to recombinant parvalbumin Gad c 1 (Unicap®, Thermo-Fisher). The population was characterized according to demographic data, rGad c 1 serum levels and wheal diameter from *prick-prick* test to selected fishes before and after the acquisition of tolerance to at least one fish species. Statistical analysis: Wilcoxon test; SPSS v23.

Results: 81 patients (68% male, 32% female, average age 14 ± 9 years, 24% melanodermic), 55 (68%) are atopics (78% rhinitis, 67% eczema, 43% asthma). Pollock (51%), mackerel (30%) and codfish (26%) were the most common species associated with allergic reactions. 48 (60%) patients acquired tolerance to at least one fish species (60% tuna, 24% codfish, 22% salmon, 20% Pollock). For patients that already acquired tolerance, for at least one species of fish, the average serum value of rGad c 1 before tolerance acquisition was 16.9kUA/L and after tolerance was significantly lower 5.1kUA/L (P = .001). The average wheal diameter(mm) in *prick-prick* test was superior before Versus (Vs) after tolerance acquisition: codfish (9.3 Vs 3.4), sardine (9.0 Vs 2.5) and salmon (7.8 Vs 2.8). Statistically significant values were found only in pollock (P = .002) and salmon (P = .026). The average tolerance acquisition age was 10.5 years, 26% of patients keeps intolerance to all species and 6% acquired complete tolerance to fish, confirmed by food oral challenge.

Conclusions: In patients with fish allergy the decreasing of sIgE serum levels of rGad c 1 and the reduction of wheal diameter in *prick-prick* test with pollock and salmon, can be used as a marker of prognosis in the acquisition of tolerance to fish.

0782 | Prevalence of salmon roe allergy patients who also show allergic symptoms due to ingestion of other fish roe

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Introduction: Fish roe (salmon roe, cod roe, capelin roe and so on) is common food in Japan. Recently, children who show immediate allergic symptom by ingestion of salmon roe are increasing, but it is not examined clinically if they also show allergic symptoms due to ingestion of other fish roe.

Objectives: We investigated whether salmon roe allergy patients have allergic symptoms to cod roe or capelin roe from electronic medical record retrospectively. Among patients whose salmon roe specific IgE values are more than 0.70 KU/L, those who have allergic histories of salmon roe or diagnosed with oral food challenge (OFC) of salmon roe were included.

Results: 26 patients were included. 15 and 14 of them have ever eaten cod roe or capelin roe, respectively. And 5 (33%) and 2 (14%) of them have ever experienced allergy symptoms by ingestion of cod roe or capelin, respectively.

Conclusions: From our examination, most of patients with salmon fish roe allergy have not experienced allergy symptoms by ingestion of other fish roe. We will report the results including the result of immunoblotting performed with serum from salmon roe allergy patients. To confirm whether the patient with salmon roe allergy can eat other fish roe, it is recommended to perform OFC of concerned fish roe.

0783 | Analysis of IgA levels in patients with a diagnosis of cow's milk protein allergy

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Introduction: Immunoglobulin (Ig) A plays an important role in mucosal immunity. A decreased efficiency in mucosal immunity is known to play a role in the etiology of food allergy. However, the differences regarding IgA levels in IgE, non- IgE and mixed type food allergies are not known.

Objectives: We aimed to investigate the IgA levels in different types of food allergy based on immune mechanism. The patients who were given report for amino-acid based formula with a diagnosis of with cow's milk protein allergy in our hospital between May 2013 and August also 2016 and who were checked for IgA level for various reasons were included in the study. The patients were grouped in three as IgE mediated, non-IgE and mixed food allergy. The patients who had low IgA levels according to their age were accepted as IgA deficiency.

Results: Of the 347 patients who got report for amino-acid based formula, we excluded the patients whose IgA levels were not checked and those who got a report for metabolic disease or malabsorption, thus, the remaining 172 patients were examined retrospectively. 42 (24.4%) of the patients had IgE mediated, 93 (54%) had mixed and 37 (21.6%) had non IgE cow's milk protein allergy. Of the 172 patients, 58 (33.7%) had IgA deficiency. When IgA deficiency was compared between the groups, no statistically significant difference was found ($P > .05$). However, while non-IgE group had the highest frequency with 45%, this frequency was 26% for IgE mediated group and 32% for the mixed group.

Conclusions: In our study, IgA deficiency in patients with cow's milk protein allergy was found to be higher when compared with the normal population. Although no statistically significant difference was found between the groups, the difference between non-IgE and IgE food allergy groups was remarkable. Studies with large numbers of patients are required to understand the role of IgA better in cow's milk protein allergy.

0784 | What makes an allergen an allergen? the sensitization capacity to the paradigmatic lipocalin allergen bos d 5 critically depends on its ligand loading state in BALB/c mice

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Introduction: The mechanisms of allergic sensitization are still elusive. In previous studies we were able to demonstrate that the unloaded apo-form of the lipocalin allergen Bos d 5 promoted Th2 cells and inflammation, whereas the holo-form appeared to be immunosuppressive in vitro.

Objectives: We tested whether the loading state of the major allergen Bos d 5 as a model allergen for lipocalins had also an in vivo relevance using a nasal sensitization model in BALB/c mice.

Methods: An unloaded apo-form of Bos d 5 was generated by dialysis against deferoxamine and distilled water. A holo-form was generated by incubation of the apo-form with quercetin-iron complex (FeQ2) in the molar ratio Bos d 5:quercetin:iron of 1:2:1. BALB/c mice were nasally sensitized 6 times in biweekly intervals with apo-Bos d 5 or holo-Bos d 5. Control groups were sham-treated with water or with the iron-quercetin complex alone. An intraperitoneal challenge with apo-Bos d 5 led to an immediate and significant drop of body temperature as a sign of a systemic allergic reaction. Specific antibodies as well as cytokines of Bos d 5-stimulated splenocytes were analyzed by ELISA.

Results: Nasal allergic sensitization of mice to Bos d 5 was prevented when Bos d 5 was applied in its holo-form. Mice treated with

the apo-form had significantly elevated Bos d 5—specific antibodies (IgG1, IgG2a, IgA and IgE) and cytokine response (IL5, IL13 and IL10), compared to the group exposed to holo-Bos d 5 or controls. Sensitization with apo-, but not holo-Bos d 5 resulted in clinical reactivity leading to a significant body temperature drop upon specific allergen challenge.

Conclusions: The loading state of the lipocalin allergen Bos d 5 is decisive not only in vitro, but also for shaping the subsequent immune response in vivo. While the unloaded apo-form turned Bos d 5 to an allergen, the holo-form prevented allergy. This study therefore adds to our current understanding of allergenicity *per se*: the lack of lipocalin ligands belong to the critical parameters turning a harmless antigen into an allergen able to induce a Th2 response.

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0785 | Sensitization to alpha gal and to hymenoptera venom: the possible role of excessive alcohol consumption

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Introduction: IgE antibody response to mammalian oligosaccharide galactose alpha-1,3-galactose (α-gal) has been discovered only recently. Here we report a family case of sensitization to α-gal associated with chronic alcoholism.

Objectives: A hunter on ACE inhibitor therapy presented recurrent episodes of isolated tongue and neck edema, 3 to 5 hours after intake of mammalian meat or homemade innards, which had been ascribed to a sensitization to α-gal (IgE anti-α-gal = 43.2 KU/L). A new episode occurs despite red meat avoidance, resisting to epinephrine treatment. An ACE inhibitor-induced angioedema is diagnosed.

His sister presents severe anaphylaxis during the 1st infusion of cetuximab given to treat a head and neck squamous cell carcinoma. She does not have red meat allergy despite IgE α-gal antibodies at 33.1 KU/L.

The two patients are chronic alcoholics and adopted the family tradition of regularly preparing and eating game, homemade meat and innards. Both relate asymptomatic hymenoptera stings and the man also tick bites.

Results: Both patients have high serum total IgE levels and biologic sensitization to hymenoptera venoms.

Conclusions: A-gal is an oligosaccharide that is common in mammals but not in humans. It is responsible for delayed anaphylaxis to red meat and anaphylactic reactions during the 1st infusion of cetuximab, a chimeric mouse-human antibody.

Sensitization to alpha-gal is related to tick bites and in some cases to prior hymenoptera stings in the absence of tick bites.

Alcohol is a powerful immunomodulatory drug and is shown to induce a type 2 helper T cell deviation of the immune response, thus increasing serum total IgE, which in turn enhances the development of specific IgE antibodies in case of exposure to a given allergen. Sensitization to food allergens is moreover favored by alcohol-induced increased intestinal permeability or decreased protein digestion.

Interestingly, anaphylaxis to cetuximab is mostly seen in patients treated for head and neck squamous cell carcinoma, compared to patients treated for other types of cancers. Chronic alcoholism and elevated serum total IgE are reported to be risk factors for this type of cancer.

Family life style, exposition to tick bites and/or hymenoptera stings, associated with chronic alcoholism might explain the sensitization to α-gal and hymenoptera venom in this family case. We suggest a causal link between alcoholism, sensitization to α-gal and hymenoptera venom that should be assessed in further studies.

0786 | Prevalence of red meat allergy in rural mountainous area of Japan: Shimane CoHRE study

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Introduction: Red meat allergy is known to occur following to the tick bite. It was originally reported by *Commins*, that the geographic distribution of serum IgE antibodies to oligosaccharide galactose-α-1,3-galactose in the United States overlapped the region where the tick *Amblyomma americanum* is common and the region where the frequent area of rocky mountain spotted fever, suggesting that tick bites might be relevant to red meat allergy. Japan spotted fever (JSF) are common in west part of Japan including Shimane Prefecture. Vector for this disease are reportedly Haemaphysalis longicornis, which is also reported to be a possible cause of red meat allergy. To date, no previous study revealed the prevalence of red meat allergy in Japan.

Objectives: We sought to survey the prevalence of red meat allergy on the base of Shimane CoHRE Study, an epidemiological study project for the rural mountainous area in Shimane prefecture.

Results: This study was a part of the Shimane CoHRE Study, which was designed to examine the determinants of diseases, including food allergy. The Shimane CoHRE study was conducted by Shimane University, Japan, in collaboration with a health examination program that involved 2 areas (i.e. Unnan city, near the JSF-infested area and Ohnan-cho, far from the JSF-infested area). History of red meat allergy was assessed by face-to-face interviews conducted by trained

staff. Subjects were asked the following question: "Have you ever experienced allergic symptoms after the ingestion of beef?". Data were collected from a cross-sectional studies conducted on 2016. We analyzed data from total of 1148 participants in Unnan city and 732 participants in Ohnan-cho. As a result, the prevalence of red meat allergy was 1.0% (12/1148) in Unnan city and 0.4% (3/732 individual) in Ohnan-cho. Although the prevalence of red meat allergy were not significantly different among these areas ($P = .184$, Fisher's exact test), relatively higher prevalence of red meat allergy were observed in near the JSF-infested area (i.e. Unnan city).

Conclusions: Here we report the prevalence of red meat allergy in Japan for the first time and it was possibly higher in near the JSF-infested area. These novel findings are in concordance with the previous studies. Further detailed studies are essential to understand the specific mechanism behind these associations.

0787 | Galactose alpha-galactose allergy

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Introduction: Galactose alpha-galactose, commonly known as alpha-gal, is a cell membrane oligosaccharide present in non-primate mammals. It has been linked to a type of delayed anaphylaxis which takes place between three and four hours after eating food derivatives of these animals. We present a case of a 67 year old male, patient of our allergy division. He had urticaria and dyspnea 4 hours after eating sheep meat. The symptoms were preceded by vomiting and diarrhea. Subsequently, similar symptom were described after eating goat and beef meat. He works as a cattleman and frequently suffer from tick bites.

Objectives: Different in vivo test were performed: Skin prick test to food (beef, goat meat, sheep meat, pork, sheep's milk, goat's milk), latex and different aeroallergens (D. pteronyssinus, Blomia Tropicalis, Lolium, Artemis, Olivo, LTP, Dog, Cat, Cockroach). In vitro test: Total IgE, tryptase, specific IgE against Cow's epithelium, goat's epithelium, pig's epithelium, BSA, cow's milk, goat's milk, Sheep's milk, pork, beef, mutton and rabbit, and Gal-Alpha 1,3GG bovine TG.

Results: The patient presents positive prick test for beef, pork and goat's milk (negative serum and control histamine 5 mm) and serum tryptase 4.4 ug / L, BSA 0.19 kU / L, Cow's epithelium 0.50 kU / L, Goat's epithelium 0.60 kU / L, pig's epithelium 0.32 kU / L, IgE food specific: pork 5.81 kU / L, beef 6.19 kU / L, mutton 2.13 kU / L, rabbit 1.05 kU / L, Cow's milk 0.47 kU / L, Sheep's milk 0.88 kU / L, Gal-Alpha specific IgE 1.3 Gt bovine TG 14.6 KU / L.

Conclusions: he Alpha-gal is an oligosaccharide related to delayed anaphylaxis after intake of non-primate mammalian products. It has been established relationship with the tick bite of a few months before the beginning of these manifestations, the mechanism is not completely clear. The late onset of symptoms would be explained by the need to transport this molecule bound to lipids, so a diet rich in fats would increase the severity of the symptoms. With the diagnostic tests performed we can certainty diagnose about patient as allergy to meat by hypersensitivity to alpha-gal. The medium-term forecast is a decline in IgE levels to alpha-gal and tolerance to non-primate mammalian products in the future as long as contact with ticks-bite is avoided.

0788 | Adult red meat allergy: our clinical experience

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Introduction: Although meat consumption is high in developed countries, red meat allergy is rarely seen in adults. Information on red meat allergy is mainly derived from studies involving children with atopic dermatitis. In this study, diagnostic approach in adult red meat allergy was discussed.

Objectives: A retrospective review of the files of adult patients diagnosed with red meat allergy between January 2013 and September 2015 was conducted at the division Immunology and Allergic diseases.

Results: Nine male patients aged 19 to 25 years who had complaints of itching, redness, urticaria, angioedema, shortness of breath and fainting within 1-2 hours after eating sheep and beef were evaluated. While all patients had skin symptoms, 2 patients had anaphylactic symptoms. As a result of skin tests conducted, none of the patients had any sensitivity to inhaled allergens. Sheep and beef specific IgE values were measured, both cooked and raw red meat prick to prick skin tests and oral provocation tests were performed as diagnostic procedures for red meat allergy. Sheep and beef specific IgE measurements of the patients resulted as negative. Positive results were obtained with both sheep and beef prick to prick skin tests. A single blind placebo-controlled oral provocation was administered to 7 other patients, except 2 patients with anaphylactic symptoms, similar to doses previously administered to children. All seven patients received positive responses in the form of urticaria, hyperemia and itching.

Conclusions: The fact that low meat-specific IgE levels are not sufficient to exclude the diagnosis of red meat allergy. If the patient's story is compatible with red meat allergy, skin tests and oral provocation tests should be applied respectively.

0789 | Evaluation of a hypoallergenic wheat line 1BS-18 lacking omega-5 gliadin

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Introduction: Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a distinct form of wheat allergy typically induced by exercise after the ingestion of wheat products. Prevalence of wheat allergy is estimated to be 0.1-3.9% among Europeans in a meta-analysis, and, is 0.21% among Japanese adults in a cross-sectional study of rural mountainous area in Japan (Shimane CoHRE Study). There is no established treatment for WDEIA, patients are forced to limit their intake of wheat products. As wheat is one of the dietary staple, patient's quality of life is significantly lowered by this limitation. Among wheat allergens, ω-5 gliadin is one of the dominant allergens affecting WDEIA patients. Possible explanation for the higher allergenicity of ω-5 gliadin, the intestinal translocation capabilities via transcellular route is suggested in Caco-2 cell model (Bodinier et al., 2007). The use of ω-5 gliadin-free wheat flour in the regular diet is considered to be one of the prophylactic approaches against the sensitization to ω-5 gliadin.

Objectives: We sought to evaluate hypoallergenic bread wheat that lacked the genes encoding ω-5 gliadin.

Results: The deletion lines of bread wheat 1BS-18 were selected among deletion line of Chinese Spring, a well-established cultivar in wheat research field. Sensitization ability of gluten from deletion line 1BS-18 was much less than that of gluten from commercially available wheat. However, the practical feasibility of deletion line 1BS-18 was low from the point of cost-effectiveness. In addition, bread making property of 1BS-18 whole-grain was low because of less expansion when compared with the one of commercially available whole-grain (8 cm vs. 12 cm of height, respectively).

Conclusions: The use of the wheat products of the deletion line 1BS-18 in daily life have possibility to provide a feasible solution for the onset of wheat allergy. Further study is needed to confirm this hypoallergenic ability of 1BS-18. The bread making property of 1BS-18 Chinese spring is low, repeated backcrossing of the 1BS-18 line to elite commercial cultivars is desirable for better quality and practical feasibility.

0790 | Allergens involved in wheat food allergy with sensitization through different routes: cutaneous or digestive

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Introduction: Wheat allergy has been identified as responsible for the wheat-dependent exercise-induced anaphylaxis (WDEIA) syndrome. An increased incidence of a WDEIA subtype caused by sensitization through cutaneous route by exposure to hydrolysed wheat protein (HWP) present in cosmetics has been reported.

Objectives: To analyse the allergens involved in the clinical reactions experienced by two patients with WDEIA who were sensitized through different routes: cutaneous and digestive.

Results: A 27-year-old atopic Japanese woman had used for seven years a facial soap (Cha no Shizuku, Yuka) containing a type of HWP called Glupearl 19S, and two years later began to notice naso-ocular itching, facial papillomatous lesions, erythema and conjunctival injection, eyelid edema, rhinorrhea and sneezing. She stopped using the soap but began to experience episodes: generalized urticaria and bronchospasm, or asthma, urticarial and facial edema, or anaphylaxis, after eating wheat containing foods and performing exercise. Skin prick tests (SPTs) and specific IgE by ImmunoCAP were positive to wheat, rye, oats, buckwheat and lupine flours, and negative for gluten and allergens Tri a 14 and rTri a 19 (omega-5 gliadin).

A 26-year-old woman reported that at 7 years of age, when she ate foods containing cereals, 15-20 minutes later she suffered from malaise, itchy skin, hives and vomiting. The last episodes had occurred 5 years ago and last month. She noticed that reactions were more intense and faster when doing exercise. SPTs and ImmunoCAP were positive to wheat, rye and oats flours, gluten and rTri a 19.

The study was performed by SDS-PAGE/IgE-Immunoblotting with extracts prepared from wheat, rye and oats flours. Both patients recognized high molecular weight allergens from wheat flour extract and detected in several extracts an allergen around 27 kDa, compatible with Tri a 27 (thiol-reductase homologue). The main difference between two patients was the detection by the patient sensitized by digestive route of two allergens around 60-65 kDa in the oats flour extract, which could correspond with Tri a 19.

Conclusions: Omega-5 gliadin marks the difference between the two sensitization routes. The IgE-Immunoblotting offers a representation of each sensitization profile, providing additional information on the allergens involved.

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TPS 15
IMMUNE RESPONSES IN ALLERGY AND ASTHMA

0791 | The immunomodulatory effects of farm dust and urban air particulate matter: a pilot study

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Introduction: Exposure to particulate matter (PM) has been linked with increased cardiovascular morbidity and mortality worldwide, and it is also a potential risk factor for the development of asthma. In contrast, the risk of developing asthma is significantly reduced in children exposed to farm environment. The key immune mechanisms and the underlying exposures are still under investigation. Asthma-protection has been linked with the exposure to microbe-rich farm dust and induction of immune regulatory pathways. PM or its specific constituents may instead disrupt human immunoregulatory mechanisms and thus predispose to asthma. Dendritic cells (DCs) and monocytes are among first cells to react to airway exposures, and they have a critical role in the determination of subsequent immune responses.

Objectives: To investigate the effect of urban air PM ("high risk environment") and farm dust ("protective environment") on human immune responses. We stimulated peripheral blood mononuclear cells (PBMC) of five adults with increasing doses of farm dust extract (farm stable in Northern Savonia, Finland) and PM samples ($PM_{2.5\text{-}1}$, or $PM_{1\text{-}0.2}$ from Nanjing, China). Expressions of CD80 and ILT4 in myeloid DCs (mDCs), plasmacytoid DCs (pDCs) and monocytes were analyzed by flow cytometry.

Results: The percentages of mDCs and pDCs positive for immunogenic CD80 decreased in a dose-dependent manner after PM stimulations, whereas farm dust stimulation increased the percentage of CD80 + mDCs. Farm dust did not affect the percentage of CD80 + pDCs. A small decrease was seen in the percentage of CD80 + monocytes after PM stimulation, while farm dust also increased the percentage of these cells. The percentages of DCs and monocytes positive for tolerogenic ILT4 decreased after stimulation with PM. Farm dust stimulation did not affect the percentage of ILT4 + mDCs but decreased the percentage of monocytes and pDCs positive for this marker. Although PM samples induced parallel immune reactions, the strength of the effects was determined by the PM size-fraction.

Conclusions: Studied environmental samples were able to shape the immunogenicity and tolerogenicity of human peripheral blood immune cells. Interestingly, samples from "high risk" and "protective" environment had partly differing effects.

0792 | Circulating erythrocytes decrease and neutrophils increase upon airway allergen challenge in house dust mite allergic rhinitis subjects independent of sublingual immunotherapy

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Introduction: Specific allergen challenge is an established diagnostic procedure in allergic airway disease research for increasing our understanding of underlying pathophysiological mechanisms. We recently reported that circulating red blood cell counts decrease in grass-pollen sensitized allergic rhinitis subjects after airway allergen challenge.

Objectives: In this hypothesis-based study we aimed to 1) evaluate whether the decrease in circulating red blood cells can also be observed in house dust mite (HDM) allergy after allergen challenge and to 2) assess whether preceding immunotherapy modulates the observed effect. Blood sampling was performed before and after 6 hours of HDM allergen challenge.

Results: Seventy-seven (n = 77; age 26.8 ± 7.3 years; 54.5% female) otherwise healthy subjects with HDM associated allergic rhinitis, who were previously enrolled in a randomized, double-blind, monocentric trial for specific sublingual immunotherapy (SLIT) at the Vienna Challenge Chamber, were included. The subjects were divided into 3 groups according to preceding treatment: placebo (group 1, n = 22), low dose HDM (group 2, n = 29) or high dose HDM specific sublingual immunotherapy (group 3, n = 26).
Overall, a significant decrease in circulating erythrocytes and hematocrit ($P < .001$), as well as elevation of leukocytes ($P < .001$), particularly segmented neutrophils ($P < .001$), was observed after HDM allergen challenge. A slight decrease in eosinophil counts after allergen challenge was observed in the placebo group ($P < .05$) only. Significantly higher erythrocyte and hemoglobin levels were found at baseline in the placebo group compared to the high dose SLIT ($P < .05$, respectively) in male subjects. Gender had no significant effect on the observed changes in circulating blood cells after allergen challenge.

Conclusions: We report here that the decrease in circulating erythrocytes and increase of neutrophils after airway allergen challenge is not limited to grass-pollen, but can also be found in HDM associated allergic rhinitis subjects. This effect was found independent of preceding immunotherapy. Overall, our findings imply a trapping of

circulating erythrocytes and a rapid systemic mobilization of neutrophils within an immediate type hypersensitivity immune response upon allergen challenge.

0793 | immunomodulatory effects of autologous total IgG in patients with atopic dermatitis

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Introduction: Idiotype network theory proposes that antigen-binding portion (idiotype) of the autologous immunoglobulin is immunogenic enough to induce active immune response to itself. We hypothesized that intramuscular administrations of autologous total IgG could produce immunomodulatory effects in patients with allergic diseases.

Objectives: This study aimed to evaluate the immunomodulatory effects of intramuscular administration of autologous total IgG on hypersensitivity reaction in patients with atopic dermatitis (AD). Sixteen adult patients with AD received intramuscular injections of 50 mg autologous total IgG twice a week for 4 weeks (from 0 to 4 weeks). The serum concentrations of interleukin (IL)-4, IL-10, IL-12, and interferon gamma (IFN-γ) were measured using enzyme-linked immunosorbent assay at -4, 0 (baseline), 4, 8, and 12 weeks.

Results: The serum concentrations of IL-10 and IFN-γ significantly increased at 4, 8, and 12 weeks compared to baseline ($P < .05$). There were no significant changes in serum concentrations of IL-4 and IL-12 at 4, 8, and 12 weeks compared to baseline ($P > .05$). There were no significant changes in serum concentrations of IL-4, IL-10, IL-12, and IFN-γ between -4 week and baseline ($P > .05$).

Conclusions: Intramuscular administrations of autologous total IgG significantly increased the serum concentrations of IL-10 and INF-γ in patients with AD. Further studies are required to investigate the clinical significance and detailed mechanism of these immunomodulatory effects.

0794 | Aqueous fullerene C60 dispersion reduces the risk of lethal anaphylactic hypersensitivity in mice

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Introduction: Anaphylactic hypersensitivity (AH) is the most serious clinical concern facing allergists. However, for the majority of anaphylactic hypersensitivities, avoidance is the only therapeutic option available presently. Fullerene C_{60} has the unique electronic properties making it an attractive candidate for therapeutic application.

Objectives: The main purpose of our research was to assess the fullerene C_{60} therapeutic effect in a mouse model of AH.

Results: New efficient method for producing a water-soluble fullerene C_{60} (WSF) has been developed. Survival level of mice was evaluated. To assess the WSF effects on systemic anaphylaxis, AH experimental model was induced by the intraperitoneal sensitization of BALB/c mice with ovalbumin (OVA) using 2-fold injections. Two weeks after the last injection, the allergen was administrated intravenously. The WSF was also administrated intravenously in sensitized mice. Concentrations of OVA-specific antibodies in sera and cytokines produced by splenocytes upon OVA in vitro stimulation were detected by ELISA. Experiments showed that after final OVA administration in group AH the survival rate was zero. While the percentage of surviving animals at similar conditions but treated with the WSF fullerene was 60%. It should be noted that the IL-5 concentration was decreased in groups treated with WSF, while the IL-12 and IFN-γ concentrations were conversely raised. The ratio of OVA-specific IgG1/IgG2a was significantly decreased in groups treated with WSF.

Conclusions: Taken together, these results demonstrate that the water-soluble fullerene C_{60} significantly increases survival level in the mouse model of anaphylactic shock and shifts immune response from Th1 to Th2. Thus, fullerene C_{60} possesses a high therapeutic potential.

0795 | Olfactory epithelium-derived mesenchymal stem cells impact antigen-presenting cells when co-cultured ex vivo

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Introduction: Mesenchymal stem cells (MSC) derived from various tissues possess immunomodulatory activity including MSC derived from olfactory epithelium (OE) which impact T-cells ex vivo. This study assesses the impact of MSC OE on the immunophenotypic profile of human antigen-presenting cells (APCs): macrophages (Mf); B-cells; and dendritic cells (DC).

Objectives: MSC-OE (CD90 + CD105 + CD73 + /CD31-CD45-) were obtained from 11 patients with non-inflammatory nasal diseases. Blood monocytes adherent to plastic were used as a source for Mf and DC. DC were obtained from monocytes using a 6-day (GM-CSF/IL-4) protocol. MSC-OE were co-cultured for 72 h with

DC, monocytes and B-cells, providing direct cell-to-cell contact. DC, b-cells and Mf were also cultured with LPS (positive control, M1-control for Mf) and with MSC-OE conditioned media (CM). Mf were also cultured with M-CSF as M2-stimuli. After 72 h DC were assayed for immunogenic (CD80, CD86, HLA-DR) and tolerogenic markers (CD85k, CD273) as well as activation molecules (CD32 and CD83). Mf were assayed for expression of M1 and M2 markers (CD16, CD64, CD68, CD80, CD85k, CD86, CD206, CD273, CD274, CD284 and HLA-DR).

Results: DC cultured with MSC-OE CM maintained immature phenotype. DC co-cultured with MSC-OE had significantly increased expression of both immunogenic (CD80, CD32) and tolerogenic markers: CD85k (iDC—50.2 (21.3-70.5)%; MSC-DC—75.5 (31.2-86.4)%; $P = .03$) and CD273 (iDC—29.9 (24.3-37.0)%; MSC-DC—40.6 (35.1-54.0)%; $P = .02$). MSC-OE-induced Mf had similar expression of CD273 and CD206 comparable with M2-Mf, while the expression of M1-markers (HLA-DR, CD16, CD64 and CD284) was decreased. While MSC-OE stimulated the expression of CD80, the expression of CD86 was significantly lower compared with M1-Mf. B-cells were also characterized by decreased expression of CD86 and HLA-DR, but the expression of CD80 was comparable to the control.

Conclusions: Direct cell-to-cell contact of MSC-OE and mdDC led to the induction of a tolerogenic profile of the DC. MSC-OE induced an anti-inflammatory, tolerogenic immunophenotype in Mf co-cultured ex vivo, resembling M2-polarized cells. The effects of MSC OE on monocyte-derived DC, Mf and B-cells were similar, indicative of comparable influence of MSC on all myeloid- and lymphoid derived antigen-presenting cells.

0796 | Cow's milk and rice fermented with L. paracasei CBA L74 modulate gut microbiota in children

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Introduction: Cow's milk and rice fermented with *Lactobacillus paracasei* CBA L74 prevent infectious diseases in young schooled children. The mechanisms of this effect is still not completely defined.

Objectives: We speculated that these dietary strategies could shape gut microbiota composition. Stool samples (3 gr) were collected from healthy children (aged 12-48 months) before (t0) and after 3 months (t3) of dietary treatment with cow's milk (FM, group A) or rice (FR, group B) fermented with *L. paracasei* CBA L74, or placebo (PL, group C). Changes in gut microbiota composition was investigated by 16S rRNA gene amplicon sequencing (V3-V4 region) and innate (α- and β-defensins and cathelicidin LL-37) and acquired immunity biomarkers (secretory IgA) by ELISA.

Results: 30 children (19 males, 63.3%) with a mean (SD) age of 34.3 (9.7) months were randomly assigned to each group (n = 10/group). A significant increase of all biomarkers of innate and acquired immunity was observed only in groups A and B but not in group C. Both the treatments (in particular, the rice matrix) led to an increase in *Lactobacillus*, while PL showed higher levels of *Bacteroides* after 3 months. Different microbial signatures were detected according to the specific fermented matrix consumed: *Oscillospira* and *Faecalibacterium* abundance increased with fermented milk (FM) treatment, while *Blautia* and *Coprococcus* were boosted by fermented rice (FR). These genera were also positively associated to the increase in α-defensin, particularly evident in FM treated children. Sub-genus diversity of *Blautia*, *Roseburia* and *Faecalibacterium* was also evaluated. Individual *Blautia*, *Roseburia* and *Faecalibacterium* oligotypes were associated to FM or FR treatments and revealed the presence of sub-genus specific links with the immunity biomarkers. Finally, PICRUSt predicted metagenomes showed an increase in key genes involved in butyrate production pathway (acetate coA/acetoacetate coA-transferase—K01034, K01035; butyrate kinase—K00929) following FM treatment.

Conclusions: Dietary supplementation with cow's milk or rice fermented with *L. paracasei* CBA L74 modulates innate and acquired immunity biomarker and these effects are associated with specific signatures in gut microbiota.

0797 | IgE and IgG production to innocuous and live allergens

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Introduction: Mechanisms of IgE formation are not well understood but local B-cell switch to IgE production in nasal or bronchial mucosa is a very likely scenario.

Objectives: Earlier we have shown that in children, allergic to house dust mites (HDM), IgE response was not associated with the formation of other classes of immunoglobulins. Titers of Der f 2 specific IgM, IgG, and IgA were comparable in sera of HDM patients and healthy age-matched controls. At the same time immune response to *A. alternata* (Alt) fungus was characterized by both IgG and IgE formation to Alt a1. Analysis of IgG production by Alt patients and controls demonstrated a comparable age-dependent increase in IgG titers. We have hypothesized that this can be a result of fungal conidia ability to germinate in the site of their accumulation in the mucosa. Expression of TLR ligands by germinating conidia

could lead to macrophage activation which subsequently deliver the allergen to the lymph nodes (LN) where IgG is produced.

Results: To verify this hypothesis we have analyzed IgG and IgE responses to another innocuous allergen cat dander (Fel) and *A. fumigatus* (Asp f) fungus in sera of patients with allergy (n = 20 and n = 36 accordingly) and healthy donors (n = 38). Bacterial recombinant allergens Fel d 1 and Asp f 2/Asp f 3 were used to analyze IgE and IgG by ELISA. It was shown that IgE and IgG to Fel d 1 correlated significantly (r = 0.484, $P = .05$) and were higher in allergic patients in comparison with controls. At the same time IgG and IgE titers did not depend on a patient age. An age-dependent change in Asp f specific IgG was found both in allergic patients and healthy controls (r = 0.435 and −0.410 accordingly, $P < .05$). Moreover, there was no difference in Asp f specific IgG titers between allergic patients and controls in the same way as it was found for Alt a 1 antigen.

Conclusions: These results show that a long-time exposure to live and innocuous allergens induce different IgG responses. Live allergens such as fungi *A. alternata* and *A. fumigatus* induce IgG production which depends on the patient's age i.e. on the time of allergen exposure. IgE production correlated neither with age, nor with IgG titers showing IgE and IgG independent formation. IgE and IgG responses to innocuous allergens such as HDM or Fel have not depended on the age of patients and were likely to manifest local immune response formation.

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0800 | Dose dependent anti-proliferative effect of an organophosphate pesticide on proliferation in an in vitro Th2-induced model

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Introduction: Over the past years, the rates of food allergy have increased especially among young children who are particularly vulnerable because of the immaturity of their immune system. One hypothesis is the contribution of external factors such as food contaminants. Indeed, pesticide residues from vegetables are found in "homemade food" of infants. The role of these contaminants on the development of allergies is not well understood.

Objectives: In this context, the purpose of this study is to determine if the chlorpyrifos (CPF), a widely used organophosphate pesticide present in the diet of infants, can alter the CD4 + T helper cells (Th) differentiation in vitro. Human naive CD4 + CD45RA+ T cells isolated from PBMC were activated during 5 days in the presence of anti-CD3/CD28 beads and interleukin-4 (IL-4) in the absence (controls) or presence of 3-10 or 30 μmol/L of CPF. The analysis of Th2 phenotype was performed by flow cytometry using specific markers (CD4 + CD25 + IL4 +) and by RT-qPCR with the measure of specific Th cells transcription factors expression. The viability and proliferation were assayed by flow cytometry through specific dyes.

Results: The highest dose of CPF has cytotoxic effect on Th cells which is associated with 90% cell mortality. The intermediate dose of CPF inhibits by 7 times (vs 1.5 times for the lowest dose) the proliferation of activated Th cells without causing mortality compared to the control conditions. The lowest dose of CPF increases the production of IL-4 by activated Th cells but no differences were noted for the expression of the transcription factors.

Conclusions: These results show that food contaminants such as CPF may inhibit proliferation and disrupt the differentiation of activated Th cells resulting in a possible impact on the development of food allergies.

0801 | A new combination of probiotics and prebiotics attenuates symptoms in a mouse food allergy model

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Introduction: Food allergy is an IgE-mediated disease whose incidence has increased during the last decade. Exposure to food allergens could induce reactions from mild local symptoms up to anaphylactic reactions (e.g. eczema, diarrhea, edema, anaphylactic shock). Currently, the only efficient solution offered to patients to prevent allergic reactions is food allergens avoidance. Different studies reported that food allergies are often linked to microbiota dysbiosis. Probiotics and prebiotics are known to promote health benefits such as restoration of microbiota equilibrium and/or stimulation of the immune system.

Objectives: This work was aimed at studying the effect of a new combination of probiotics and prebiotics on a mouse-model of food allergy. The symbiotic was prepared from a combination of probiotics and prebiotics selected for their efficiency on the microbiota and the immune system. Three-week-old male mice were sensitized twice every 7 days with ovalbumin (OVA) adsorbed on aluminium hydroxide (n = 10 per group). Oral daily symbiotic treatment (OST) began 10 days after the last sensitization until the end of the experiment. The allergen exposition started 5 days after OST and mice have been challenged every 3 days for 18 days. Anaphylactic score

was determined by using a scoring system based on observations of scratching, ruffled hair, activity and abnormal breathing. Concerning diarrhea, stools were evaluated by the following scoring: normal stools, wet stools, wet stools with perianal staining, watery stools and watery stools containing flecks of mucus. Mice were observed during 1 hour after each challenge.

Results: Non-treated allergic (NTA) mice displayed allergic symptoms from the first challenge reflected by an increased anaphylactic score (puffy eyes, scratching, decrease activity and ruffled hair). Furthermore, diarrhea scores from NTA mice were increased compared to control mice. At the last challenge, NTA produced watery stool containing flecks of mucus. In contrast, symbiotic-treated allergic (STA) mice presented significant lower symptoms (i.e. lower anaphylactic score and lower diarrhea score) than NTA mice.

Conclusions: The prepared symbiotic proved its efficiency in lowering and delaying the allergic clinical signs. More investigation shall be undertaken to further understand its positive effect on the immune system and the gut microbiota.

0802 | Effects of titanium dioxide nanoparticles on food allergy development

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Introduction: Growing interest regarding the influence of titanium dioxide (TiO_2), which is a widespread white food pigment and often added to pharmaceutical products and cosmetics, on the immune response is based on its huge amount continuously entering the human body via different routes of exposure as well as on its nano-sized particles (NPs) structure.

Objectives: In this study, we aimed to evaluate the intestinal and systemic effect of TiO_2-NPs on the immune response in naïve organisms and to analyze the influence on a later development of food allergy. Female BALB/c mice were fed TiO_2-NPs with or without pre-absorption to Bovine serum albumin (BSA) for 14 days intragastrically. Thereafter, mice were either sacrificed to evaluate the immune response after oral TiO_2-NPs gavages or sensitized to the egg allergen Ovalbumin (OVA) with concomitant acid-suppression.

Results: After 14 days of oral feeding we observed slight elevations of total IgA levels in the intestinal lavages of animals fed with TiO_2-NPs-adsorbed to BSA and fed with pure TiO_2-NPs compared to naive animals, however without reaching statistical significance. After the subsequent sensitization of oral OVA feeding under concomitant acid-suppression, systemic allergen challenges induced a significant drop of body temperature and higher levels of mMCP1 in serum of sensitized animals pretreated with TiO_2-NPs or with BSA compared to naïve mice ($P < .05$), but not in animals pretreated with TiO_2-NPs-adsorbed to BSA. In intestinal lavages higher levels of OVA specific IgE and IgA antibodies were found in OVA-sensitized animals receiving pretreatment with pure TiO_2-NPs or with BSA alone compared to animals pretreated with TiO_2-NPs-adsorbed to BSA and naïve mice.

Conclusions: These data indicates that binding of TiO_2-NPs to proteins can change the immunogenic characteristics of TiO_2. Thus, we are fully convinced that our work represents an important contribution to current research efforts evaluating the safety of TiO_2-NPs ingestion.

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IMMUNE RESPONSES IN INFLAMMATION

0803 | Changes in subpopulations of peripheral blood monocytes in patients with acute vs chronic oral lichen planus

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Introduction: Monocytes are not a homogeneous cell population, containing a subpopulation of monocytes with phenotype CD14+ CD16 seen in immature dendritic cells (DC), and a subpopulation of cells with phenotype CD14+ CD16+, with a high level of expression of the molecules CD86 and HLA-DR which are able to induce a Th1 immune response.

Objectives: 97 patients aged 18 to 60 years were studied including 35 with erosive oral lichen planus, 32 with non-erosive oral lichen planus and 30 healthy control subjects of similar age. Lymphocyte subsets and CD14 + monocytic cell population were assessed using monoclonal antibodies to CD14, CD16, FcgRII/CD23, FcgRI antigens by direct immunofluorescence with flow cytometry analysis performed on a FACScan (Becton Dickinson, USA).

Results: In the blood of patients with erosive oral lichen planus in the acute stage, the number of CD14 + CD16 + monocytes was increased (20.3 ± 1.1%; control 8.1 ± 1.3%) while the number of monocytes CD14 + CD16- were decreased (53.2 ± 2.2%; controls 75.1 ± 1.3%; $P < .05$). Patients with non-erosive oral lichen planus had no significant variations in percentage of cells with the phenotype CD14 + CD16 + (11.2 ± 3.2%) and CD14 + CD16- cells (67.1 ± 1.3%). In the acute stage of erosive oral lichen planus there was an increase in the number of cells expressing the high affinity receptor for IgG FcgRI (7.3 ± 1.2%) also seen in acute relapse of the non-erosive form (3.2 ± 2.4%; control 2.2 ± 1.2%). CD14 + monocytes expressing the low affinity receptor FcgRII/CD23 were similar in patients with the erosive form of lichen planus (1.6 ± 3.2%), with the non-erosive form (1.5 ± 1.3%) and in controls (1.3 ± 2.1%).

Conclusions: CD14 + CD16- monocytes expressing the high affinity receptor for IgG FcgRI appear in peripheral blood during acute relapses of erosive lichen planus, resulting in increased inflammation in the affected mucosa. Changes in the balance of the subpopulations of CD14 + CD16 + and CD14 + CD16- monocytes occurs in the transition from acute to chronic forms of oral lichen planus.

0804 | Interrelations of depression, cytokines in semen and chronic pain syndrome in patients with chronic abacterial prostatitis

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Introduction: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a common chronic pelvic pain condition largely unresponsive to medical interventions. Comorbid depression and chronic pain are highly prevalent in individuals suffering with chronic abacterial prostatitis perhaps due to direct or indirect effects of cytokines. Cytokines interact with the neuronal environment, and thus modulation of the duration of inflammation may alleviate the depressive and pain symptoms that result.

Objectives: The interrelation of depression, CP/CPPS symptoms and cytokines in patients with chronic prostatitis/chronic pelvic pain syndrome was studied using the National Institutes of Health (NIH)—Chronic Prostatitis Symptom Index (CPSI) for severity of CP/CPPS. Patient Health Questionnaire-9 (PHQ-9) was used to assess depression. The levels of cytokines in semen were assessed by ELISA. 64 patients who were enrolled received basic treatment with rectal electrostimulation every other day for 10 sessions lasting 15 minutes. Patients in Group 1 (n = 32) additionally received oral Sertraline with an initial dose of 50 mg gradually increased to 200 mg treated for 1 month. Patients in Group 2 (n = 32) were the control group. Distribution of patients was random.

Results: Indicators of cytokines in the ejaculate and results of the survey of patients of the main and control group after treatment differed. In patients with CP/CPPS after using rectal electrical stimulation (Group 2) there was a significant positive correlation between NIH-CPSI total scores and PHQ-9 and with IL-1β, TNF-α and IL-8 ($P < .05$). In patients of Group I after using rectal electrical stimulation and Sertraline was a negative correlation between levels of IL-10, TGF- β and NIH-CPSI total scores and PHQ-9 ($P < .05$). Clinical efficacy of combined treatment of patients with CP/CPPS was 84% in Group 1 and 63% in Group 2 compared to the symptoms of prostatitis, and 63% in Group 1 and 34% in Group 2 compared to symptoms of depressive disorders.

Conclusions: There was an interrelation of depression, cytokines in semen and chronic pain syndrome in patients with chronic abacterial prostatitis and effectiveness of a combination of physical therapy and an antidepressant (sertraline) in patients with CP/CPPS.

0806 | Immune status and the susceptibility to alcohol hangover

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Introduction: The day after heavy alcohol consumption, levels of pro-inflammatory cytokines are significantly increased. This finding suggests a role of the immune system in the pathogenesis of the alcohol hangover.

Objectives: Purpose of the current study was to examine the relationship between perceived immune functioning and having an alcohol hangover after a heavy drinking session.

Dutch students were invited to complete an online survey. Past month alcohol consumption was recorded. To assess perceived immune functioning, the Immune Function Questionnaire (IFQ) was completed. The IFQ consists of 19 items (sore throat, headaches, flu, runny nose, coughing, cold sores, boils, mild fever, warts, pneumonia, bronchitis, sinusitis, sudden high fever, ear infection, diarrhoea, meningitis, eye infection, sepsis, and long healing injuries) which are rated on a 5-point Likert-type scale. Perceived immune functioning of those with a hangover was compared to those reporting not to have a hangover, using a nonparametric independent samples Mann-Whitney U Test. To be included in the analyses, they had to reach an estimated blood alcohol concentration (eBAC) of at least 0.18% on their heaviest drinking occasion.

Results: N = 460 healthy Dutch students (79.2% female, mean [SD] age 21.1 [1.9] years old) were included in the analysis. N = 380 reported a hangover and N = 80 (17.4%) reported no hangover on their heaviest past month drinking occasion. Relative those with no hangover, those who reported a hangover had a significant higher mean ± SD IFQ score (10.5 ± 3.6 vs 13.1 ± 4.9, $P = .0001$), indicating a poorer immune status. Significantly higher scores were reported on the IFQ-items diarrhoea (1.1 ± 0.9 vs 1.4 ± 1.0, $P = .008$), sinusitis (0.1 ± 0.3 vs 0.3 ± 0.6, $P = .008$), coughing (1.6 ± 0.9 vs 2.0 ± 1.0, $P = .002$), headache (1.7 ± 0.9 vs 2.1 ± 0.9, $P = .008$) and sore throat (1.3 ± 0.8 vs 1.7 ± 0.9, $P = .0001$).

Conclusions: Those who reported having a hangover after heavy drinking had significant poorer scores on perceived immune functioning, including more severe ratings on signs of weakened immune system functioning such as diarrhoea, sinusitis, coughing headache and sore throat.

0807 | Changes over time in saliva cytokine concentrations the day following heavy alcohol consumption

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Introduction: The immune system responds to toxic substances such as alcohol. Cytokines are important mediators of this immune response. It has been shown that blood cytokine concentrations are elevated the day after heavy alcohol consumption.

Objectives: The purpose of the current study was to assess saliva cytokine levels the day following heavy drinking, and examine if they fluctuate throughout the day.

Students of Utrecht University, the Netherlands, participated in a naturalistic study. The day after an evening of alcohol consumption, and after an alcohol-free control day, saliva samples were collected hourly from 9am to 4 pm, and cytokine concentrations (GM-CSF, IFN-γ, TNF-α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8 and IL-10) were determined. For each assessment, for each cytokine the relative change (percentage, %) in concentration between the hangover and control day was computed. Data from these assessments were allocated to subsequent time points, relative to the drinker's stop time of alcohol consumption. Subsequently, for each time point, the average % change was computed for pro-inflammatory cytokines (GM-CSF, IFN-γ, TNF-α, IL-1β, IL-2, IL-6, and IL-8) and for anti-inflammatory cytokines (IL-4, IL-5, and IL-10). For each timepoint after stopping drinking, the overall pro- and anti-inflammatory immune response was tested for significance, using paired sample T-tests.

Results: N = 16 healthy subjects completed the study (56.3% men). Their mean (SD) age was 21.8 (2.0) years old. Significant increases in pro-inflammatory cytokine concentrations were observed 6-12 hours after stopping drinking. The biggest effect was seen 6-9 hours after drinking. No significant increases in cytokine concentrations were seen for anti-inflammatory cytokines.

Conclusions: A significant increase in the concentration of pro-inflammatory cytokines was seen the morning following an evening of alcohol consumption. These effects were not seen for anti-inflammatory cytokines.

SUNDAY, 18 JUNE 2017
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IMMUNOTHERAPY—IMPROVING THE EVIDENCE BASE

0808 | A cost-effectiveness study on the grass pollen tablets for seasonal rhinitis

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Introduction: The allergic respiratory disease is a significant health problem with high pharmacoeconomic impact.

Objectives: This study seeks to estimate the cost-effectiveness of two sublingual treatments and to pharmacologic therapies administered to the patients to control the allergic symptoms.

Results: The analysis uses a Markov model built on the natural history of the disease, populated with efficacy data from the scientific literature and cost data extrapolated from investigations realized in the Italian setting. The model results are expressed in terms of "Incremental CostEffectiveness Ratio" (ICER). To verify the robustness of the model to changes in parameters, both a deterministic and a probabilistic sensitivity analysis were performed.

As to the adult population, the first sublingual treatment was associated to costs for 1290.97/patient and to 7.19 Quality Adjusted Life Years (QALYs), while the second has a cost of 1864.43 on the time-horizon considered (9 years) and the same impact as the former in terms of effectiveness. The symptomatic therapy costs 366.55 and allows a gain of 7.12 QALYs. The ICER of the second sublingual treatment vs symptomatic therapy amounts to 21611.98; the ICER of the first treatment vs symptomatic therapy is 13337.90. As to the children cohort, both sublingual treatments have a total cost of 1585.14 and 2158.95, respectively. The symptomatic therapy costs 773.81: sublingual IT settle on the same level of QALYs gained (7.18); the symptomatic therapy allows to achieve 7.07 QALYs. The differential in terms of resources consumption of sublingual IT vs the symptomatic therapy amounts to 1385.14 and 811.33, respectively. sublingual IT allow to obtain 0.11 QALYs more than those achievable by symptomatic therapy. The ICER of treatment 1 vs symptomatic therapy is equal to 7675.90; the ICER arising from the comparison of treatment 2 and the symptomatic therapy amounts to 13104.71. By directly comparing sublingual IT a differential of resources employed in favor of first treatment of 573.81: this reduction determines a dominant ICER

Conclusions: For an ex-factory price of 60.15/pack, the treatment based on sublingual treatment 1 for the management of the symptoms due to seasonal allergic rhinitis appears to be dominant or cost-effective in comparison respectively with sublingual treatment 2 and symptomatic treatment.

0809 | Nasal provocation test with house dust mite allergens as the final step of allergic rhinitis child evaluation before allergen-specific immunotherapy

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Introduction: Precise evaluation of the causative allergen is critical for successful allergen-specific immunotherapy (ASIT). In our climate zone, most of pollen allergy causes could be revealed from medical history. Unlike seasonal, persistent respiratory allergy symptoms often need an inquiry.

House dust mite (HDM) allergy is quite typical for children with perennial allergic rhinitis (AR) and asthma in St. Petersburg. Meanwhile many children have persistent symptoms due to cat or mold allergy, without HDM sensitization. Moreover, in children with clinically proven HDM allergy, skin prick tests (SPT) sometimes demonstrate only weak positive or doubtful results. Diagnostic tools differ in sensitivity and specificity and tissue challenge tests demonstrate the best.

Objectives: 48 children (31 boys, 17 girls) 5-17 years old were included. All patients were regarded as candidates for HDM ASIT based on typical persistent symptoms of AR or AR+asthma with prominent worsening at home, in bed or during room cleaning. We performed precise medical history collected by experienced allergist, SPT with HDM extracts and 5-step nasal provocational test (NPT) with standardized HDM (50% *D. pteronyssinus*, 50% *D. farinae*) extract (Stallergenes Greer, France). The sample size well represents mean amount of patients investigated for HDM ASIT possibility in an ordinary allergist office per year. The main goal was to introduce HDM NPT as useful and valuable tool in routine allergist practice for ASIT candidate evaluation.

Results: 32 children (20 boys, 12 girls) had positive or doubtful SPT with HDM and proceeded to the NPT.

Among them, 19 (59.4%) had typical symptoms, positive SPT and positive NPT with HDM. We have confirmed the diagnosis and recommended ASIT commencement.

In 6 (18.7%) cases we revealed typical symptoms, doubtful SPT and positive NPT with HDM. Positive NPT was crucial for diagnosis confirmation and ASIT commencement.

Of most interest were 7 (21.9%) cases with typical symptoms, doubtful or even positive SPT and negative NPT. We insist that negative NPT is the exclusion criteria for an ASIT candidate. One can speculate that symptoms were due to other causative allergens. The SPT result may reflect non clinically significant sensitization.

Conclusions: In case of HDM allergy we propose NPT as the final evaluation step for a child with AR before ASIT start. Negative NPT could exclude the erroneous treatment start.

0810 | Assessment of cat subcutaneous immunotherapy in allergy unit of hospital Universitario Fundacion Alcorcon (Madrid, Spain)

Gonzalez-Moreno A; Vargas Porras W; Perez Fernandez E; Macias Iglesias J; Perez Codesido S; Privitera Torres M; Rosado Ingelmo A

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Introduction: Cats are a frequent cause of allergic rhinoconjunctivitis (RC) and / or asthma. The prevalence of cat sensitization ranges up to 15% in some areas of northern Europe and in many cases requires a multimodal therapeutic approach.

Objectives: To evaluate the evolution of patients with cat subcutaneous immunotherapy (IT). A retrospective review was conducted among patients with rhinoconjuctivitis with or without asthma receiving cat subcutaneous IT between 2010-2015. The data that we collected were: treatment, FEV1, specific IgE, number of exacerbations, ACT (asthma control test), allergen exposure and patient satisfaction with the treatment at 6-12 months after of the first dose of cat IT.

Results: During our review period, 19 patients were received cat subcutaneous IT, 16 females, mean age 33 years (19.9-47.3). 57.9% had RC and asthma, 31.6% asthma and 10.5% RC. The history of known respiratory symptoms when were in contact with cats before IT was 4.8 years (0.4-18), 10.5% were smokers. The mean cat IgE was 33.42 (0.57-101), and cluster IT (3 weeks) was used in the 100% of the patients; then, all of them received a monthly dose.

Pre IT: 10.5% needed antihistamines and β2. 63.2% inhaled corticosteroid (IC) + and long-acting β2-agonist (LABA) and antihistamines. 42.1% had ≥1 exacerbation per year and 36.8% used β2 > 2 times per day.

After IT: 73.7% continued using IC + LABA ($P > .05$). 5.3% still had ≥ 1 exacerbation ($P < .05$) and 21.1% still needed β2 > 2 times a day ($P < .05$). 100% reported improvement but with persistent respiratory symptoms.

There were no differences between FEV1 pre-IT and post-IT (94% vs 92%) and FeNO pre-IT and post-IT (71PPB vs 57PPB). There were differences in ACT ($P < .05$, 18 vs 23). 94.7% of the patients had ≥1 cats; and the 89.5% didn't remove the animal from home.

Conclusions: There was improvement in the number of exacerbations, use of β2 and in the ACT score. No differences were seen between the initial treatment and the treatment after 6-12 months of IT. 89.5% do not remove the animal, when it is the first-line therapeutic measure in cat allergic patients.

0811 | Assessment of dog subcutaneous immunotherapy, in allergy unit of hospital Universitario Fundación Alcorcón (Madrid, Spain)

Vargas Porras W; Gonzalez Moreno A; Perez Fernandez E; Macías Iglesias J; Privitera Torres M; Perez Codesido S; Rosado Ingelmo A

Hospital Universitario Fundación Alcorcón, Madrid, Spain

Introduction: Animal dander is a frequent cause of rhinoconjunctivitis (RC) and allergic asthma. The treatment of these diseases includes, avoidance of the exposure to the animal, pharmacological treatment and specific immunotherapy (IT).

Objectives: To evaluate the patients evolution with dog subcutaneous immunotherapy.

Methods: This is a retrospective review, that was conducted among patients with RC and asthma who received dog subcutaneous IT, between 2010-2016. We measured initial treatment, spirometry, specific IgE, ACT score (asthma control test), number of exacerbations, animal exposure and patient`s satisfaction, previously and one year after starting of IT. We performed a database for statistical analysis.

Results: We collected 12 patients, all with RC and allergic asthma, mean age was 32 years (24-40).The symptom evolution time before IT was 7 years (3-11). 58% were men, 25% were smokers. The mean dog IgE levels was 37.9 mg/dL (5-69).75% received initial cluster IT (3 weeks) and all of them received a monthly dose. Pre IT, 41.7% of the patients received antihistamines, nasal corticoids and inhaled corticosteroids (IC) + long acting β_2 agonist (LABA). In addition, 25% used β_2 ≥2 times/day and 50% once/weekly. 67% had ≥1 exacerbations in the previous year. After one year of IT,16% of the patients were yet treated with antihistamines, nasal corticoids and IC+LABA ($P > .05$). 91.7% required $\beta_2 \leq 1$ time per month ($P < .05$). 91% hadn't exacerbations in previous year ($P < .05$). The 91.5% patients were satisfied with the treatment. There were differences in average ACT score pre/post 17(14-20) vs 22 (20-24) and FENO pre/post IT (68 vs 31 ppb) ($P < .05$). But there were no differences in FEV_1 pre/post IT (88% vs 96%). 50% didn`t remove the animal from the home.

Conclusions: We obtained an improvement in the use of β_2, ACT score, FENO, number of exacerbations and in the subjective assessment of the patients. There was no improvement in baseline treatment and FEV_1, which could be evidenced after a longer follow-up period.

0812 | Early efficacy onset, already prior to the start of the birch pollen season, after sublingual immunotherapy with a liquid birch pollen extract

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Introduction: Allergic rhinitis/rhinoconjunctivitis (ARC) is an important problem worldwide and may significantly impair quality of life. Previously, a phase III study was conducted to establish the clinical efficacy and safety of pre- and co-seasonal sublingual immunotherapy (SLIT) for the treatment of birch pollen induced ARC. The primary analysis of this study showed a statistically significant and clinical relevant improvement on the primary efficacy endpoint: Combined Symptoms Medication Score (CSMS) during the birch pollen season after SLIT compared to placebo (Pfaar et al. Allergy (2016); 71 (suppl.102): 45 (abstract 87)). Considering allergen cross-reactivity and structural homology within the birch homologous tree group, the present post-hoc analysis aimed to evaluate whether the primary CSMS endpoint would reach statistical significance prior to measurement of the first positive birch pollen count.

Objectives: The study was a randomized, double-blind, placebo-controlled, parallel-group study, with treatment with a liquid Birch pollen extract (40 000 AUN/mL) starting at least 12 weeks before the birch pollen season and continuing during the birch pollen season (ClinicalTrials.gov NCT02231307), performed in 40 clinical study centers in 5 European countries. Study population consisted of 406 patients, 18-65 years of age, suffering from moderate to severe birch pollen induced ARC with or without mild to moderate, controlled asthma. CSMS was evaluated during the period 1 March 2015 until measurement of first positive birch pollen count.

Results: After treatment with birch SLIT, a clinically relevant and statistically significant 30.1% improvement in CSMS was observed compared to placebo ($P = .0021$), as measured in birch allergic patients prior to the appearance of the first birch pollen count.

Conclusions: The results of this post-hoc analysis support a beneficial effect of SLIT with a liquid birch pollen extract on allergic symptoms and medication, already visible prior to measurement of the first birch pollen count in birch allergic patients. These findings suggest an early onset of efficacy of this liquid SLIT birch pollen extract related to concomitant allergies for other early spring trees due to cross-reactivity and/or structural homology within the birch homologous tree group.

0813 | Sublingual immunotherapy with a liquid birch pollen extract is similarly effective in birch pollen allergic patients with high sensitization profile compared to patients with low sensitization profile

Pfaar O[1]; Bachert C[2]; Kuna P[3]; Panzner P[4]; Džupinová M[5]; Yu D[6]; Mantikou E[6]; Moed H[6]; Klimek L[7]; De Kam PJ[6]

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Introduction: Allergic rhinitis/rhinoconjunctivitis (ARC) is an important health problem worldwide and may significantly impair quality of life. Previously, a phase III study was conducted to establish the clinical efficacy and safety of pre- and co-seasonal sublingual immunotherapy (SLIT) with a liquid birch pollen extract for the treatment of birch pollen induced ARC. This study showed a statistically significant and clinical relevant improvement on the primary efficacy endpoint: Combined Symptoms Medication Score (CSMS) during the birch pollen season compared to placebo (Pfaar et al. Allergy (2016); 71 (suppl.102): 45 (abstract 87)). The objective of this post-hoc analysis was to evaluate if birch pollen SLIT is similarly effective in patients with a high sensitization profile compared to patients with a low sensitization status.

Objectives: The study was a randomized, double-blind, placebo-controlled, parallel-group study, with treatment with 40 000 AUN/mL birch SLIT (ClinicalTrials.gov NCT02231307), performed in 40 clinical study centers in 5 European countries. In total, 406 patients, 18-65 years of age, suffering from moderate to severe birch pollen induced ARC were randomized.

The effect of SLIT was assessed in a subgroup of patients with high sensitization profile; defined as either birch specific SPT, NPT or IgE results in the upper 75% quartile compared to patients with a low sensitization profile (below the upper 75% quartile of all three diagnostic tests). The clinical efficacy of this liquid birch pollen extract (40 000 AUN/mL) for both sub-groups was assessed by the difference in the primary CSMS endpoint during the birch pollen season between the active vs placebo treatment group using the Intent-to-Treat population.

Results: A clinically relevant and statistically significant CSMS reduction was reached for both the high and low birch sensitization subgroups compared to placebo ($P = .0008$ and $P = .0048$, respectively). Moreover, in absolute terms the CSMS improvement was comparable in both subgroups and exceeded the pre-defined clinical relevant CSMS effect of 23% (relative difference of 34% and 29%, respectively).

Conclusions: Results of this post-hoc subgroup-analysis support the hypothesis that SLIT with a liquid birch pollen extract is similarly effective in high and low birch pollen sensitized patients, indicating that patients with high and low sensitization status can benefit from this immune therapy to a similar extent.

0814 | Effectiveness and tolerability of sublingual allergen immunotherapy (ait) with or without titration in routine medical practice in house dust mites allergic patients

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Introduction: The aim of this non-interventional study was to document the tolerability and the effectiveness of chemically modified allergen extracts (monomeric allergoid) of HDM tablets (300 UA/tablet, 1000 UA/tablet) under special emphasis on selected titration scheme in everyday practice.

Objectives: This non-interventional, open, prospective, non-controlled, multicenter study across Germany was conducted for the period between December 2015 and January 2017, with the goal to recruit 300- 400 patients. Patients were treated according to the SmPC of the product.

Rhinoconjunctivitis symptoms will be analyzed as combined scores of severity (scale: 0 [none]—3 [severe]) and frequency (scale: 0 [none]—4 [very often]). In the combined RC score, the severity of rhinitis and conjunctivitis will be pooled. Furthermore, allergic symptoms (10 items, on a 4-point scale: 0 [none]—3 [severe]) will be analyzed as well.

Results: 97 specialized outpatient allergy centres recruited up to 5 (10) patients each. The percentage of patients requiring symptomatic medication will be analyzed as well. All adverse reactions will be documented and analyzed.

Conclusions: In a large population of patients treated pre-seasonally with 4 days titration or without titration in routine medical practice we evaluate the effectiveness and tolerability of sublingual allergen Immunotherapy (AIT) in patients suffering from house dust mite-induced allergic rhinoconjunctivitis.

0816 | Safety and tolerability of a subcutaneous vaccine (SCIT) with native extract of parietaria judaica

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Introduction: This is a Phase I clinical trial of a SCIT with native extract of *Parietaria judaica* pollen in an aluminum depot preparation, administered following a five increasing doses build-up scheme. Preliminary results on safety as well as on cutaneous reactivity changes are shown.

Objectives: It is an open, multicenter clinical trial, in patients aged between 18 and 60 years with rhinoconjunctivitis with or without concomitant mild asthma sensitized to *Parietaria judaica* allergen extract. The aim of the study is to evaluate the safety and tolerability of the vaccine. Secondary endpoint includes surrogate efficacy parameters evaluation: changes in immunoglobulin levels (specific IgE, IgG and IgG4) and changes in cutaneous reactivity. Patients were under study treatment for 17 weeks: five for the induction phase (weekly injections) and 12 for the maintenance phase (monthly injections).

Results: 51 patients were included in 4 Spanish sites from May 2015 to March 2016. No patient was withdrawn from the study. 43 patients (84.3%) were diagnosed of persistent moderate/severe rhinitis according to ARIA guidelines and 17.6% had concomitant mild asthma. Previous immunotherapy with *Parietaria judaica* was reported by 9.8% of patients, in all cases ended at least 5 years before starting the present trial. The sensitivity profile was varied, with specific IgE levels to *Parietaria judaica*, of class 3 in 39.2% of cases, class 4 in 27.5%, class 5 in 19.6% and class 2 in 13.7%. Adverse reactions occurred in 36 patients and were mostly mild reactions in severity. From a total of 470 administered doses, 27.7% elicited adverse reactions: 22.9% local reactions and 4.7% systemic reactions. Among local reactions most of them (17.7%) were no clinically relevant late local reactions. A total of 22 systemic reactions were registered: 2.3% were nonspecific reactions and the other 2.3% were Grade I systemic reactions, being the most reported ones rhinitis and urticaria. Concerning the efficacy parameters evaluation, cutaneous reactivity at the final visit vs baseline was significantly decreased with all tested vials.

Conclusions: Preliminary results of *Parietaria judaica* SCIT in depot vaccine in an abbreviated updosing scheme showed an adequate safety and tolerability profile and induced in vivo changes.

0817 | Preliminary results of a tolerability study of SCIT with native depot Olea europaea pollen extract

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Introduction: Grass pollens are the most commonly allergens responsible for rhinoconjunctivitis in Spain. However, olive pollen can be considered the main cause in certain areas of Andalusia, such as Jaén and Córdoba, where pollen counts in the air can reach peaks higher than 15 000 grains / m^3 during the pollination period.

Objectives: The aim of this phase I, multicenter, open clinical trial was to evaluate the safety and tolerability of subcutaneous immunotherapy (SCIT) in depot presentation. Patients with rhinoconjunctivitis sensitized to *Olea europaea* received an abbreviated schedule consisting of: five weeks of initiation with six injections and a maintenance period of three months with a monthly administration. The primary outcome was the number, percentage, and severity of adverse reactions with this regimen. Secondary endpoint included evaluation of the subrogate efficacy parameters: changes in immunoglobulin titers (specific IgE, IgG and IgG4) and changes in cutaneous reactivity.

Results: Currently, there are 42 patients ongoing treatment, in five hospitals. Following ARIA 2010 guidelines, 95.2% of patients were diagnosed of persistent moderate/severe rhinitis. The mean age is 37.5 $\pm$ 11.6 years, being 57.1% female. Moreover, 57.1% of the patients had concomitant mild/moderated asthma. The mean in years from the diagnosis of rhino-conjunctivitis to the informed consent signing is 10.2 $\pm$ 7.7 years. At baseline, patients showed the following sensitivity profile for IgE in KUa/L, for *Olea europaea*: class 2; 19.0%, class 3; 14.3%, class 4; 28.6%, class 5; 19.0% and class 6; 19.0%.

According to International 2010 Guidelines, six systemic reactions were registered, representing 2% of the administered doses: five reactions grade 0, (described as nonspecific ocular pruritus, nasal herpes, general discomfort, localized non-specific pruritus plus nausea and non-specific pruritus in throat) and a grade II reaction, (generalized urticaria). All reactions were classified as mild or moderate intensity and only two required symptomatic treatment. There was only one clinically significant late local reaction, which was higher than 10 cm and involved modifications in next dose.

Conclusions: These preliminary results of an abbreviated schedule with *Olea europaea* SCIT in depot vaccine, provides evidence of its adequate safety and tolerability profile.

0818 | A prospective open multi-centre non-interventional study to assess the tolerability, the safety profile and the adherence of different up-dosing schemes for a sublingual immunotherapy treatment

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Introduction: Since a relatively long or complicated up-dosing scheme of specific immunotherapy is sensitive to disruption an optimized up-dosing period is desirable for better patient compliance. The primary aim of this study was to compare the tolerability of a new (summer 2016), optimized up-dosing scheme with two pre-existing up-dosing schemes of a sublingual immunotherapy (SLIT), to be documented in a patient population under the usual application conditions in therapeutic practice.

Objectives: In October 2016, an ongoing prospective open multicentre non-interventional study was initiated to document the up-dosing period of children and adults with allergic rhinoconjunctivitis and/or allergic asthma treated with a SLIT containing purified, aqueous extracts of birch, alder, and hazel pollen. The following up-dosing schemes were freely selectable: scheme A consists of an up-dosing period of 12 days at the patient's home using the standardized pollen extract in three different solution strengths to reach the maximum dose; scheme B performed only with the highest solution strength at the physician's office within 2 hours; and the new scheme C which is a regimen for initiation at the physician`s office and continuation at the patient`s home also exclusively using the highest solution strength and takes 4 days. Data were documented by physicians and in patients' diaries. The study was approved in Germany and Austria by the local ethic committees and all parents and/or patients gave informed consent.

Results: Data for the up-dosing period was collected from 67 patients aged 6-73 years for an interim analysis. Conventional up-dosing scheme A was applied by 35 patients, 12 patients decided on the ultra-rush regimen B, and 20 patients on the new scheme C, respectively. In total, three adverse events (AE) have been documented during the up-dosing period. One patient on scheme B reported mild ear pruritus after the first application of the maximum allergen dose. Another patient on scheme B reported unspecific laryngopharyngeal discomfort after application of the second dose of the allergen extract. Additionally, one patient on scheme A documented mild enoral irritation, mild pruritus and irritation of the lips and red spots around the mouth.

Conclusions: We concluded from this interim analysis that all three up-titration schemes were well tolerated with no apparent differences in safety or tolerability between the groups.

0819 | Allergenicity and immunogenicity of chemically modified ragweed pollen extract

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Introduction: Allergenicity and immunogenicity of chemically modified allergen extracts vs non-modified allergenic extracts should markedly differ due to the modification process. A ragweed extract was assessed pre- and post- modification.

Objectives: Ragweed pollen was collected from the Krasnodar area of the Kuban Region in southern Russia. Pollen was assessed for contamination with other pollens, fungus spores and mites. Common ragweed pollen extract (W1) was prepared by extraction with ammonium bicarbonate buffer. Protein composition was assessed by SDS-PAGE electrophoresis and gel filtration. W1 extract was chemically modified with succinylation (sW1) using modification of ε-groups of lysine residues. Comparative study of allergenicity of sW1 was performed using inhibition of IgE-binding activity in pooled sera from ragweed sensitized patients (positive history, skin tests and allergen specific IgE; Pharmacia UniCap 100 system). To detect immunogenicity of W1 or sW1 BALB/c mice were immunized four times in two week intervals with 50 μg/mouse (protein equivalent) W1 or sW1. Serum anti-W1 IgE, IgG1 and IgG2a antibodies after the 3rd and 4th immunizations were detected by ELISA.

Results: Ragweed pollen collected in Krasnodar area was *Ambrosia* not contaminated with other pollens, mold spores and mites. Extract W1 had a protein content 17.2% (range 14-116 kDa). Succinylated extract sW1 (99.7% of modification) possessed low activity to bind specific IgE vs non-modified extract W1. Immunization of mice with sW1 led to decrease of anti-W1 IgE antibody formation vs immunization with non-modified W1. Anti-W1 IgG1 responses after immunization with sW1 decreased while anti-W1 IgG2a response was substantially increased after the 4th immunization.

Conclusions: Chemical modification of ragweed extract by succinylation may be useful for creation of a novel Ambrosia vaccine with reduced allergenicity and preserved immunogenicity.

0820 | Oral immunotherapy in severe milk allergy in adults—results

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Introduction: There is evidence of efficacy of oral immunotherapy in severe cow milk allergy in children but less information on adults. In comparison with pollen immunotherapy, oral food immunotherapy is more often associated with adverse reactions.

ObjectivesMaterial and methods

Thirteen adult patients were selected for the trial, 11 women and 2 men (mean 39 years, range 21-66 years). The diagnosis of cow milk allergy was verified with positive symptom history, skin prick test and allergen specific IgE antibodies. In addition, milk allergy was verified with an open food challenge. Patients were not excluded due to multiple food allergies or asthma.

Results: Eight patients (62%) have continued oral milk immunotherapy from 4-96 months with a mean of 24 months. Five (38%) patients in total have discontinued the desensitization due to allergic reactions (4) or pregnancy (1). The dose range of oral immunotherapy at the current time point is from 3-130 mL. Maximum dose has been 200 ml. Six patients have reached the maintenance dose while two are still on the initiation phase. Overall milk and casein IgE levels have decreased in patients receiving the maintenance dose, indicating a possible decease in immunologic reactions against the allergen.

Conclusions: Oral immunotherapy is a promising treatment instead of total avoidance in some patients but careful and optimal patient selection is needed.

0822 | Control of allergic rhinitis after one year of sublingual immunotherapy with 5 grasses/4 cereals extract

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Introduction: The long-term goal of management of patients with respiratory disease, such as allergic rhinitis (AR), is to achieve control. Effectiveness of sublingual immunotherapy (SLIT) in reducing symptoms of AR is well documented, especially in adults. However, studies on control are insufficient.

Objectives: The aim of the study was to investigate the control of allergic rhinitis on the first year after completion of a three-year treatment with 5grasses/4cereals sublingual immunotherapy.

Results: A total number of 59 patients: range 12-48 years [46 adults (77.97%) and adolescence—13 (22.03%)] who completed a three-year course of SLIT with 5 grass/4 cereals extract were followed up Control of AR was assessed during the first pollen season (May and June) after SLIT completion by Rhinitis Control Assessment Test (RCAT), validated in Bulgaria.

When assessed on the first season after completion, AR symptoms were well-controlled in 47 (79.66%) of patients: in 10 (76.92%) of the adolescence—5 boys (50%) and 5 girls (50%) and in 37 of the adults (80.43%)—22 men (59.46%) and 15 (40.54%) women. No significant difference in control between adults and adolescence was established ($P > 0.1$).

Conclusions: The results from our study demonstrated sustained control of AR after one year of 5 grasses/4 cereals SLIT completion —in adults and as well as in adolescence.

0823 | Allergen specific IgE-modulating effect of sublingual immunotherapy in mono- and poly-sensitized patients

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Introduction: Levels of specific IgE may be impacted by use of sublingual allergen immunotherapy (SLIT).

Objectives: 60 patients with allergic rhinoconjunctivitis with or without asthma (19-46 years old) received SLIT for 2 years (allergen extract drops). Group 1 had 30 patients with allergic rhinitis with asthma (6) or without asthma (24), receiving monotherapy with grasses or Artemisia. Group 2 had 30 patients with allergic rhinitis with asthma (9) patients or without asthma (21), receiving combination SLIT with grasses or Artemisia and dust mites or indoor molds. Inclusion criteria were history of allergic rhinitis plus positive skin prick tests and allergen specific IgE (class 3) detected by Allergy Panel Testing for Quantitative Analysis of specific IgE).

Results: In Group 1 before SLIT specific IgE level to grass pollens (Gx) in 17 patients was 9.20 (6.28-16.22) IU/mL; Specific IgE level to Artemisia (W6) in 13 patients was 15.85 (7.44-100.0) IU/mL. In Group 2 before SLIT specific IgE to Gx in 17 patients was 11.76 (6.59-31.62) IU/mL; Specific IgE level to W6 in 13 patients was 11.06 (4.42-100.0) IU/mL; Specific IgE to Penicillium notatum (M1) in 15 patients was 6.41 (5.05-13.21) IU/mL; Specific IgE to Aspergillus fumigatus (M3) was 4.95 (4.44-10.27) IU/mL; Specific IgE to Dermatophagoides pteronyssinus (D1) in 15 patients was 16.60 (8.08-36.72) IU/mL and to Dermatophagoides farinae (D2) was 10.07 (4.39-43.92) IU/mL. After 2 years of SLIT specific IgE to grass ($P = .002$) and to Artemisia ($P = .008$) was significantly decreased in Group 1. Specific IgE to grass ($P = .0003$), to dust mites ($P = .0006$) and indoor molds ($P = .0006$) was significantly decreased in Group 2. SLIT was effective reducing overall symptom scores and rescue drug intake, with highly significant reductions in Group 1 and in Group 2 ($P < .0001$).

Conclusions: SLIT reduces the level of specific IgE to the treated inhalant allergens in conjunction with symptoms and medication score reduction in both mono- sensitized and poly-sensitized patients.

0824 | Study of efficacy of sublingual immunotherapy (SLIT) in cases severe persistent allergic rhinitis

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Introduction: Sublingual immunotherapy is now a well established modern treatment modality in treatment of respiratory allergies.

Objectives: To asses efficacy of sublingual immunotherapy in cases of severe persistent allergic rhinitis in patients age between 7 and 63 years of either sex.320 patients of severe persistent allergic rhinitis were included to asses efficacy of sublingual immunotherapy. These patients were regular in treatment for more than 36 months. Symptom score were recorded on regular intervals. All patients follow up done about 4-5 times during immunotherapy. Rescue medications need also taken in to account. Number of Aeroallergens included ranges from average of 2-3 allergens. Glycerinated aqueous allergenic extract from various allergens were taken as per their sensitivity pattern. Different Allergen extracts suspended in extracting fluid [coca solution] containing 50% glycerine i.p. according to w/v ratio. Usual concentrations were Initiation 1:500, build up 1:250, 1:100, 1:50, 1:20, maintanance 1:10

Results: In above study results were encouraging. In symptom score scale of 0-3. [0 no symptoms, 1 mild, 2 moderate, 3 severe] All patients were having severe symptoms before starting of sublingual immunotherapy. At the completion of 36 months of sublingual immunotherapy. Out of 320 patients 225 patients were on score 1, 73 patients on score 2 and 22 patients on score 0.Number of rescue medications along with SLIT was remarkably reduced even during pollen season.

Conclusions: Sublingual immunotherapy showing promising results in cases of severe persistent allergic rhinitis.

0826 | Tolerance of a high-dose allergoid subcutaneous immunotherapy treatment in children

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Introduction: N/A.

Objectives: Observational retrospective study in patients under 18 years-old with dust mite allergy, comparing the tolerance of a conventional updosing schedule with a cluster updosing schedule of a high-dose allergoid subcutaneous immunotherapy (SIT). We quantified the number and severity of adverse reactions during the build-up schedule.

Results: The sample included 134 children (mean age: 11 years) with allergic rhinitis and/or asthma (23 patients in the conventional schedule and 111 patients in the cluster schedule). The median total IgE values was 2059 UI/mL and all patients had sensitization to dust mite demonstrated by a prick test and/or specific IgE (median DPT 64.8 KU/L; median DPF 44.6 KU/L). The 57% of the sample had monosensitization to dust mite. SIT treatment used was an extract chemically modified with glutaraldehyde and adsorbed on L-tyrosine (Der p1 59.9 μg/mL). The maintenance dose of 0.5 mL was reached in four doses with both build-up schedules. In the conventional build-up schedule, the patient received 0.05 ml, 0.1 ml, 0.3 ml and 0.5 ml with one week intervals. In the cluster schedule, the patient received during the first day an accumulated dose of 0.2 ml (2 doses of 0.1 mL administered 30 minutes apart). One week later, the patient received a total dose of 0.5 ml (doses of 0.2 mL and 0.3 ml administered 30 minutes apart). The adverse reactions to SIT were recorded and classified as local and/or systemic. The 23 patients who received the conventional schedule received a total of 92 doses of SIT before the maintenance dose was reached. There was not recorded any local neither systemic adverse reaction. The 111 patients who received the cluster schedule received a total of 439 doses of SIT before the maintenance dose was reached. Six patients suffered from systemic reactions, representing a frequency of 1.37% per dose administered. Eighty-three percent of patients with systemic reactions were asthmatic. All the systemic reactions were grade II according to the WAO Subcutaneous Immunotherapy Systemic Reaction Grading System and were successfully treated only with inhaled salbutamol. No grade III, IV, or V systemic reactions were observed. Twenty-four children experienced local reactions and in 16 of them (corresponding to 3.64% of the total doses administered), the size of the reaction was larger than 3 cm. All these reactions were controlled with oral antihistamines. No patients discontinued the therapy.

Conclusions: N/A.

SUNDAY, 18 JUNE 2017
TPS 18
INFECTION AND ALLERGY

0827 | Salidroside attenuates lipopolysaccharide—induced inflammatory response in rat alveolar macrophages though inhibiting NF-KB activation

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Introduction: Salidroside (p-hydroxyphenethyl-beta-d-glucoside, C14H20O7, molecular weight 300.30), which is one of the most potent ingredients of the genus Rhodiola, has been reported to have a broad spectrum of pharmacological properties. We previously reported that the extract from genus Rhodiola have remarkably preventive effect to acute lung injury (ALI), Recent a study indicates an anti-inflammatory effect of salidroside on lipopolysaccharide (LPS)-induced ALI, but the mechanisms of anti-inflammatory action are not clear.

Objectives: In the present study, anti-inflammatory activity of salidroside first was analyzed in vitro using LPS-induced inflammatory reactions in primary rat alveolar macrophages.

Results: Salidroside significantly decreases LPS-activated a few inflammatory cytokines and NO production in rat alveolar macrophages concomitantly with the suppression of inducible nitric oxide synthase (iNOS) mRNA and protein levels, and also inhibits LPS-induced increase of iNOS promoter activities. To determine the mechanism by which salidroside decrease iNOS expression, we next examined the effect of salidroside upon DNA binding and transcriptional activities of NF-κB using electrophoretic mobility shift assay (EMSA), reporter gene assays and chromatin immunoprecipitation (ChIP) assay, and the nuclear translocation of NF-κB was analyzed by western blot. The results indicated that salidroside inhibited NF-κB transcriptional activity by blocking the formation of NF-κB-DNA complexes, leading to down-regulation of the NF-κB target genes in LPS-induced rat alveolar macrophages, and also inhibited LPS-induced nuclear translocation. To further investigate how salidroside inhibits NF-κB activation, we examined its effect on LPS-induced phosphorylation of IKK-IκBa-NF-κB, and verified the anti-inflammatory effects of salidroside in rat alveolar macrophages.

Conclusions: These findings offer a potential mechanism for the anti-inflammatory activity of salidroside, which may be used as a potential anti-inflammatory agent for the prevention and treatment of inflammatory diseases.

Keywords: Salidroside; lipopolysaccharide; alveolar macrophage; inflammation. This work was supported by the National Natural Science Foundation of China No. 81173466 and 81072415.

0829 | A case of Toxocara infection as manifesting itself recurrent bronchitis

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Case Report: Background: A number of reports have shown the ability Toxocara infection has to cause clinical symptoms which suggest other diseases. The lack of a correct diagnosis prevents effective treatment and thus the symptoms may persist for a long time. We report the case of a patient who suffered from recurrent bronchitis for twenty months and was cured only when Toxocara was detected as the cause.

Methods: The patient is a 41 year-old female, with a negative history of smoking. On March 2013 she had a first episode of mucopurulent bronchitis, that was treated with Levofloxacin. Following further episodes of bronchitis at monthly intervals, all treated with antibiotics, and the occurrence of rhinitis symptoms, the patient underwent allergological evaluation (with positive response to prick tests only to ragweed pollen) and computed tomography (CT) of thorax. The latter revealed bronchiectasis with dense content, small nodular opacities with a "tree-in-bud" sign, small clumps and ground-glass opacities. On October 2014 we decided to expand the investigations to testing for parasites.

Results: The ELISA test for IgG antibodies to Toxocara was positive, therefore treatment with albendazole was prescribed. After treatment, the patients had no further bronchitis episodes. On January 2015, a new CT showed the disappearance of all radiologic abnormalities except bronchiectasis, but with a clean aspect. On October 2016, the ELISA test for Toxocara IgG proved negative.

Conclusions: This clinical case confirms the need to look for Toxocara infection in patients with persisting respiratory symptoms who are unresponsive to medical treatment. As in previous reports, anti-Toxocara treatment dramatically improved the symptoms leading to complete recovery.

0830 | An in vitro model of fully differentiated human nasal epithelial cells revealed the transcriptomic signatures of the nasal epithelium following human influenza H3N2 infection

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Introduction: The nasal epithelium is the first line of defense against invading respiratory pathogens. The physical and immunological barrier of the nasal epithelium are thus important in preventing disease escalating into infection in the lower airway. However, despite their relative importance, not much research was focused on the nasal epithelium due to its small size of model limitation. Therefore, there is an obvious demand for a model that can provide a platform for the elucidation of nasal responses at the transcriptomic level that can supplement clinical data. Our lab has previously generated an in-vitro differentiated, air-liquid interface culture of human nasal epithelial cells (hNECs) derived from nasal epithelial stem cells of healthy donors which forms a fully functioning multi-layered structure of the nasal epithelium. These differentiated nasal epithelial cells were shown to be able to sustain the infections of different respiratory viruses and showed potent innate immune responses.

Objectives: Building onto this, we performed microarray analysis on hNECs model to ascertain the potential of these cells to elucidate the transcriptomic changes in the nasal epithelium against human IAV under controlled experimental conditions.

Results: Analyses conducted revealed 253 up-regulated and 146 down-regulated genes in the nasal epithelium following infection, which may constitute susceptibility factors of individuals during an IAV infection. The gene ontology (GO) analysis identified the conserved and essential host defense mechanism including type I, II, III interferon (IFN) signaling, JAK-STAT signaling, Toll-like receptors signaling, MDA5 signaling, NF-κB signaling, inflammatory response, EGF signaling and cell death pathways. Meanwhile, the down-regulated genes indicated the impaired nasal epithelium functions due to the IAV infection, including metabolic process, mucociliary function, tight junction, and pre-microRNA processing. Moreover, differential expression of certain signatures from different individuals were also highlighted from the analysis, mirroring clinical data.

Conclusions: In conclusion, this study manages to elucidate that hNECs model has the ability to elucidate the innate immune responses of the nasal epithelium, the first line of defense against respiratory virus infections at a population level.

0831 | The role of viruses in post-bronchiolitis wheezing/asthma development—a systematic review and meta-analysis

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Introduction: Acute viral infection is a leading cause of severe wheezing during infancy and one of the most frequent causes of hospitalization in children less than 2 years old. The incidence of childhood asthma has risen within the last years. There is increasing evidence that acute viral infection during infancy can be directly linked to the development and/or incidence of childhood asthma. Whether viral induced acute wheeze causes later asthma, or is merely a marker of an asthmatic predisposition is unclear. So for example, severe respiratory syncytial virus (RSV) is considered by some, but by no means all, to be causative of later asthma.

Objectives: to investigate the association between specific viruses detected in infants with acute bronchiolitis and the development of pre-school wheezing and/or school-age asthma

Results: Infants suffering with RSV-bronchiolitis were not more likely to develop asthma as compared to infants suffering with rhinovirus (RV) bronchiolitis (OR 0.63; 95%CI (0.33-1.23)) $P = .072$) Also, RSV is strongly associated with both persistent wheezing and asthma when compared with no bronchiolitis (healthy individuals) (OR 3.63 and $P < .001$, OR 3.41 and $P < .001$), but, the risk of RSV is no different to that of other viruses (OR 0.81 and $P = .76$) for wheezing, and indeed is less strongly associated with asthma (OR 0.42 and $P < .001$)

Conclusions: Both RV and RSV are associated with the development of asthma. RV is much more strongly associated with subsequent asthma when compared with other viruses (RSV included), whilst RSV did not have a greater association with asthma development than other viruses (RV included).

0832 | Induced interferon lambda 1 helps bacterial clearance in persistent mucosal inflammation during staphylococcus aureus infection

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Introduction: Chronic rhinosinusitis with nasal polyps (CRSwNP) is mainly characterized by Th2-skewed inflammation, with an increase colonization of *Staphylococcus aureus* (*S. aureus*). Interferon-lambda 1 (IFN-λ1) is a subtype of type III interferon, with a well-known antiviral activity. Whether IFN-λ1 inhibits the bacterial clearance or increases the proliferation of bacteria especially *S. aureus* in human remains controversial.

Objectives: We aimed to explore the role of IFN-λ1 on proliferation of *S. aureus* in human nasal tissue.

Results: IFN-λ1 was induced in human nasal *ex vivo S. aureus* infection model. The colony number of *S. aureus* decreased in healthy controls, not in CRSwNP tissue in the presence of IFN-λ1. A significant increased uptake and killing rate of *S. aureus* were observed in THP-1 cell differentiated macrophages in the presence of IFN-λ1 during *S. aureus* infection compared to *S. aureus* infection alone condition. IFN-λ1 also increased the expression of lysosomal-associated membrane protein 1(LAMP1), IFN-λ1 receptor IL-28R, reactive oxidase substrate (ROS) and Janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling in differentiated macrophages during infection. Suppressing ROS activity led to an inhibition of JAK-STAT pathway activities; blocking IL-28R resulted in the reduction of ROS, LAMP1 and JAK-STAT pathway expressions. The internalization and killing rate of *S. aureus decreased* in macrophages in blocking experiments.

Conclusions: IFN-λ1 helps the clearance of *S. aureus* and IFN-λ1-IL-28R-ROS-LAMP1 and IFN-λ1-IL-28R-ROS-JAK-STAT signaling involve in the anti-bacterial function of IFN-λ1. These findings yield new insights into the treatment for viral infection or viral and bacterial co-infection in upper airway.

0833 | Growth factors play major role in maturation process of airway epithelium in presence of atopy

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Introduction: Reepithelialization of the airway mucosa is an essential step toward restoring a normal functional protective barrier during the repair of airway epithelial wounds. In the developing lung, growth factors specify patterns of branching, and control airway size and cell fate, among other functions. In the fully developed lung, these signals are presumably balanced to maintain cellular activities at equilibrium, so that normal lung structure and function are preserved. There is still a significant gap of knowledge on the maturation process of growth factors from birth to adulthood and the influence of viral infections in this balance contributing to the generation of abnormal atopic epithelium.

Objectives: The aim of the present study was to determine the role of growth factors in the maturation process of respiratory epithelium and to investigate the role of viral infections.

Results: Primary nasal epithelial cells (NECs) in all ages (0-60 years) were derived from healthy (n = 26) & atopic (n = 37) donors. NECs were cultured and infected with Human Rhinovirus 1B (RV1B) and 16 (RV16). Growth factor (EGF, FGF2, VEGFA, PDGFAA and TGFA) were measured in uninfected and infected cell culture supernatants at 48 h. Age-related reduction of remodeling and angiogenetic factors EGF, FGF2 and TGFA ($P < .05$) was observed in healthy NECs. Opposing results were observed in atopic NECs, with increasing age-related values of these factors. Direct comparison of regression lines between healthy and atopic individuals, different slopes were observed ($P < .05$) in EGF and FGF2 factors. RV1B induce higher levels of EGF and FGF2 ($P < .05$) and lower VEGF levels compared to uninfected condition ($P < .05$) in both healthy and atopic NECs. RV16 induce EGF, FGF2 and PDGFAA ($P < .05$) in both healthy and atopic NECs. The expression of TGFA do not influenced by RV1B or RV16.

Conclusions: This is the first study investigating the maturation process of growth factors in airway epithelium. Atopic epithelium don't seem to follow the same evolutionary line as healthy. The age-related reduction of basic growth factors (FGF2 and EGF) in healthy NECs reflects the temporal distancing from embryonic stages with strong developmental changes. On the other hand, the atopic NECs do not reduce these factors with age, reflecting their need of remodeling. The viral infections seem to induce strongly these factors and differentially influence healthy and atopic NECs during lifetime.

0834 | Allergic fungal rhinosinusitis: our experience in the last two decades

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Introduction: Allergic fungal rhinosinusitis (AFRS) is an underdiagnosed disease though it represents between 5 and 10 percent of all chronic rhinosinusitis (CRS). The fungus specie most often described in Spain is *Aspergillus fumigatus* as opposed to *Bipolaris* spp. in EEUU. We reviewed all cases of AFR that attended our department in the last 20 years, considering diagnosis approach and treatment.

Objectives: Descriptive, retrospective study of all the cases that attended our department from 1997 to 2016. Allergic background, sensitisation profile, specific and total serum IgE, specific serum IgG, and treatment received (glucocorticoids, antifungal drugs, specific fungal immunotherapy and surgery) were collected.

Results: Nine patients (5 males, 4 females) were included. The mean age was 32.7 $\pm$ 7.57 y. Five (56%) of them had background of asthma, 4 (44%) rhinoconjuntivitis and 1 (11%) atopic dermatitis.
Our patients were primarily sensitised to *Aspergillus fumigatus* (7/9,77%), *Alternaria alternata* (5/9,55%) and pollens (5/9,55%). The total IgE median was 418 kU/L (IQR:193-562), the median of specific IgE against *Aspergillus fumigatus* was 1.5 kU/L (IQR:0.52-6.29) and the median of specific IgG against *Aspergillus fumigatus* was 40.3 mg/dL (IQR: (30.1-125). Mean (SD) peripheral eosinophilia was 578.8 (410.77) cells/mm^3. In terms of treatment: 3/9 received oral corticosteroids and oral antifungal drugs, 2/9 received corticosteroids plus *Aspergillus sp* immunotherapy and 4/9 were treated with triple therapy of corticosteroids, antifungal drugs and *Aspergillus sp* immunotherapy. Mean of surgeries needed was 1.7 $\pm$ 1.3. Finally, mean of recurrences was 1.6 $\pm$ 1.2. No surgery was needed after combined medical treatment was performed.

Conclusions: In our experience, combined treatment (surgical and medical) is successful in the management of AFRS and reduces the number of surgical interventions. AFRS requires close follow-up to adjust treatment as necessary.

0835 | Ascaris lumbricoides induces, both, reduction and increase of asthma symptoms in a rural community

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Introduction: Several studies performed in different populations and environments have shown that severe and light helminthiases diminish and increase allergy symptoms, respectively. However, data on the simultaneous presence of these contrary effects in a single community is lacking. Filling this gap is important because it will help to better understand the role of helminthiases on allergy, avoiding the effects of relevant population and environmental differences.

Objectives: In a rural community from a Caribbean region in Colombia, we sought to evaluate the effects of helminthiases on allergy. Using an ISAAC-based questionnaire previously validated in Colombia, we determined the prevalence of asthma and allergic rhinitis in a population-representative sample of 739 subjects. Parasite infection was assessed by stool examination and Kato-Katz method. Skin prick test (SPT) to a battery of 8 allergens and *Ascaris lumbricoides* extract as well as specific-IgE to *Dermatophagoides pteronyssinus*, *Blomia tropicalis* and Ascaris *spp* (ImmunoCap) was performed in a randomly-selected and representative sub-sample (n = 301).

Results: Helminth infestation was observed in 71% of participants, mainly *A. lumbricoides* (62.5%) or *T. trichuria* (35.7%). Age and gender-adjusted prevalence of asthma and rhinitis symptoms in the last year was 14.6% and 34.1% respectively. Significant odds ratio (OR) for asthma presentation were Ascaris sensitization, as detected by specific-IgE (Adjusted OR: 2.69, 95%CI: 1.21-5.98) or SPT (aOR: 3.59, 95%CI: 1.55-8.29). Moderate/severe ascariasis (number of eggs in stool) was protective from asthma (aOR:0.34, 95%CI:0.12-0.99). Ascaris sensitization or infection did not have significant independent effects on rhinitis. The risk of *Ascaris* sensitization (SPT) was lower in subjects with moderate/severe ascariasis (aOR: 0.30 95% CI: 0.09-1.02). A positive SPT to Ascaris was almost twice more frequent in non-infected subjects (20.8%) than in moderate/severe infected (12.1%).

Asthma	Controls (n = 209)	Cases (n = 34)	OR (95%CI OR)	*P*-value	aOR (95%CI aOR)*	*P*-value
SPT						
B. tropicalis	40 (19.1)	9 (26.5)	1.52 (0.66-3.51)	.326	1.50 (0.62-3.64)	.37
D. pteronyssinus	23 (11.0)	8 (23.5)	2.49 (1.01- 6.14)	.048	2.28 (0.89-5.86)	.09
Ascaris	28 (13.4)	13 (38.2)	4.00 (1.80-8.89)	.001	3.59 (1.55-8.29)	.003
Specific IgE	(n = 203)	(n = 32)				
B. tropicalis[#]	76 37.4	16 (50.0)	1.76 (0.84-3.68)	.14	1.71 (0.80-3.71)	.17
D. pteronyssinus[#]	41 (20.2)	13 (40.6)	2.81 (1.30-6.06)	.01	2.58 (1.14-5.81)	.02
Ascaris[#]	87 (42.9)	21 (65.6)	2.60 (1.20-5.64)	.02	2.69 (1.21-5.98)	.003
ABA-1[§]	82 (39.2) [a]	20 (62.5)	2.58 (1.20-5.56)	.015	2.31 (1.04-5.12)	.04
Rhinitis						
SPT	(n = 153)	(n = 90)				
B. tropicalis	24 (15.7)	25 (27.8)	2.07 (1.10-3.90)	.025	1.91 (0.95-1.54)	.07
D. pteronyssinus	13 (8.5)	18 (20.0)	2.69 (1.25-5.80)	.015	1.70 (0.73-3.97)	.22
Ascaris	19 (12.4)	22 (24.4)	2.28 (1.16-4.50)	.017	2.21 (1.07-4.56)	.03
Specific IgE	(n = 146)	(n = 89)				
B. tropicalis[#]	54 (37.0)	38 (42.7)	1.27 (0.74-2.17)	.385	1.14 (0.64-2.05)	.65
D. pteronyssinus[#]	23 (15.8)	31 (34.4)	2.86 (1.53-5.33)	.001	2.47 (1.25-4.91)	.01
Ascaris[#]	58 (39.7)	50 (56.2)	1.95 (1.14-3.32)	.015	2.04 (1.14-3.65)	.02
ABA-1[§]	61 (46.9) [b]	40 (44.4)[c]	1.15 (0.68-1.96)	.59	1.14 (0.64-2.03)	.66

*Adjusted odd ratios were obtained in multivariate logistic regression models including age, gender, living in the municipal head and familiar history of asthma or rhinitis as co-variates. Cut-offs to define a positive IgE result were [#] >0.35 kU/L. [§] > 0.13 OD. [a] n = 209,

Conclusions: In a rural tropical village ascariasis exerts risk and protective effects on asthma symptoms, an influence associated with the severity of the infection by *Ascaris lumbricoides*. Since most environmental conditions are the same in this community, genetic factors might be determining the degree of infection and consequentially asthma symptoms.

0836 | Decline in serum cytidine deaminase activity in patients with Hepatitis C infection

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Introduction: Several pathogens have mechanisms by which they influence the host immune response, especially antibody development. Cytidine deaminase (CDA) is enzyme which responsible for finishing the somatic recombination and somatic hypermutation processes for immunoglobulin heavy chains genes. Chronic Hepatitis C (HCV) infection may alter immune responses via impact on CDA activity.

Objectives: CDA activity was measured in 126 HCV patients and compared with 47 healthy individuals (study1). CDA activity was also compared (study 2) in another group of 180 patients, studied for viral hepatitis presence and viral load (97 + HCV, 27 + Hepatitis B virus, 56 no viral hepatitis). Serum CDA levels were measured by indophenol colorimetric method of Guisti and Gallanti (with prolonged incubation time (18 h) and 10.5 mmol/L cytidine concentration). Data are presented as M±SD; CI 95%.

Results: Statistically significant differences ($P = .007$) were detected in study 1 comparing serum CDA activity (IU/L) of healthy individuals (1.7 ± 0.99; 1.4-2.0) and HCV patients (1.2 ± 0.4; 1.0-1.3). In the study 2, reduction in enzyme activity in patients with HCV infection (1.1 ± 0.65; 1.0-1.3) was seen compared with patients without PCR-detected viral load (1.7 ± 2.11; 1.1-2.3) ($P = .015$). CDA activity for HCB patients was (1.3 ± 0.65; 1.1-1.5).

Conclusions: Although the levels of CDA enzyme activity were low, there was a trend towards decrease in CDA activity for HCV patients in both studies when compared to levels of healthy individuals. Chronic hepatitis C viral presence reduced serum CDA activity potentially impacting CDA dependent immune responses.

0837 | Molecular epidemiological analysis on the human rhinovirus infections among hospitalized children in Hong Kong

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Introduction: Human rhinovirus (HRV) causes a disease spectrum of respiratory infections, ranging from mild upper respiratory tract infections to severe disease manifestations such as bronchiolitis, and pneumonia. It is also highly associated with the incidence of asthma exacerbations. HRV is classified into three species (A, B and C) within the genus *Enterovirus* of the family *Picornaviridae*. Molecular epidemiological data are usually presented in species level, while recent studies differentiate HRV down to genotype level.

Objectives: The current study provides the distribution and diversity of HRV genotype in Hong Kong.

Methods: Nasopharyngeal aspirates (n = 7547) collected from hospitalized children aged under 17 years old in Prince of Wales Hospital from September 2014 to July 2015 were tested for the presence of HRV. 20.3% samples were HRV positive (n = 1531). Positive samples were randomly selected within the study period. Their VP4/VP2 coding region were sequenced and analyzed. A comprehensive BLAST database including all ICTV confirmed HRV genotypes VP4/VP2 coding region of HRV-ABC was constructed. BLAST algorithm was used to assign these sequences into different HRV genotypes.

Results: Within 735 randomly selected samples, their VP4/VP2 region was amplified by nested PCR. 44.9% of them were HRV-A (n = 330), 6.9% were HRV-B (n = 51) and 48.2% were HRV-C (n = 354). HRV-C appeared to be the dominant species from September to July while HRV-A was more associated to the episodes identified in the spring peak. Interestingly, the genotype A23 (9.8%), A81 (7.5%), A80 (6.4%) and genotype C15 (8.9%), C2 (8.1%), C23 (7.2%) were the contributing genotypes within the HRV-A and HRV-C species, respectively. According to the phylogenetic analysis, four potential new genotypes (one in HRV-A, one in HRV-B, and two in HRV-C) were identified in this study, which required complete genome sequencing for confirmation. The p-distance indicating the interspecies distances based on the nucleotide sequences were 0.215 ± 0.053 (mean $\pm$ SD) for HRV-A, 0.214 ± 0.072 for HRV-B, and 0.260 ± 0.057 for HRV-C.

Conclusions: The phylogenetic analysis showed that the samples could be clearly divided into three different (HRV-A, B and C) clades, which is consistent with previous studies. The winter and spring dominance might infer a different transmission efficiency or ecology of HRV-A and HRV-C. The largest within group diversity of HRV-C might be beneficial to the species for their adaptation.

0838 | ROS-dependent inhibition of phosphatases is involved in disruption of tight junctions of human nasal epithelial cells induced by rhinovirus

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Introduction: Rhinovirus, which is responsible for the majority of common colds, induces the occurrence of mucus overproduction, increased vascular permeability, and secondary bacterial infection. These symptoms are primarily caused by barrier function disruption that is controlled by intercellular junctions.

Objectives: In this study, we investigated whether ROS are closely involved in tight junction disruption of primary human nasal epithelial cells induced by rhinovirus.

Methods: Primary human nasal epithelial cells grown at an air-liquid interface were infected apically with RV. Changes in the expression of tight junction proteins and protein tyrosine phosphorylation levels were determined using western blot analysis. Intracellular ROS production was analyzed by flow cytometry and confocal microscopy. Tyrosine phosphatase activity in nasal epithelial cells was measured using a tyrosine phosphatase assay system kit.

Results: When human nasal epithelial cells were incubated with rhinovirus, protein levels of tight junction were markedly decreased compared to results for medium. Pretreatment with DPI strongly recovered the disruption of tight junction proteins by rhinovirus. Indeed, significant amounts of ROS were detected in nasal epithelial cells incubated with rhinovirus. Rhinovirus-induced ROS generation was strongly diminished by DPI. In contrast, inhibitor of mitochondrial electron transport, rotenone, did not affect rhinovirus-induced ROS generation. Also, incubation with rhinovirus resulted in a marked decrease in protein phosphatases activity and increase of protein tyrosine phosphorylation levels in nasal epithelial cells. DPI inhibited the rhinovirus-induced inactivation of phosphatases and phosphorylation of protein tyrosine.

Conclusions: Our results suggest that ROS-mediated inhibition of phosphatases plays a crucial role in disruption of tight junctions of human nasal epithelial cells by rhinovirus. The data indicate that rhinovirus infection may exert a damaging effect on nasal epithelial barrier function.

0839 | Hyperbaric oxygen therapy of olfactory dysfunction following viral infection of the upper respiratory tract

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Introduction: Hyperbaric Oxygen therapy is recommended as an adjuvant therapy for neuropathy. To investigate the efficacy and safety of hyperbaric oxygen therapy in the treatment of olfactory dysfunction following viral infection of the upper respiratory tract.

Objectives: Forty patients diagnosed with olfactory dysfunction following viral infection of the upper respiratory tract were recruited in current study in the Group 1 and 2. Patients of Group 1 were administered with no treatment and patients administered with the hyperbaric oxygen therapy were incorporated into the Group 2.Before the treatment, all of them underwent T&T olfactory testing, nasal sinus computer tomography scanning and visual analog scale (VAS; 0-100), and repeated the assessment after four-week treatment.

Results: There was a statistically significant difference between Group1 and 2. before and after the hyperbaric oxygen therapy in terms of total T&T olfactory testing scoring averages and VAS Scoring averages. No side effect was found.

Conclusions: The primary outcomes suggest the efficacy and safety of hyperbaric oxygen therapy in treatment of olfactory dysfunction following viral infection of the upper respiratory tract.

0841 | The living environment shapes intestinal microbial communities and immune responses in a mouse model

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Introduction: Contact with environmental biodiversity has been suggested to be protective against allergies. In particular exposure to soil, and the rich microbiota within, is proposed to be important for health. The research performed so far provides only some clues to understanding the connection between immune tolerance and microbial colonization from the environment.

Objectives: Here we aim at gaining more direct evidence of the "environment-microbiota-health axis" by studying the colonization of gut microbiota in mice, after exposure to soil, and examining the immune status in both a steady state situation and during inflammation.

Results: The small intestinal and faecal microbiota of mice kept on a clean bedding or in contact with soil was analysed, and the data were combined with immune parameters of the mice. Both healthy mice and those exposed to the murine asthma model were used in the study. We observe marked differences in the gut microbial composition between the living environments, with a higher proportion of Bacteroidetes in the soil group. The living environment also influenced mouse intestinal gene expression as shown by up-regulated expression of IL-10, Foxp3 and CD86 in the soil group. Furthermore, using the murine acute lung inflammation model we found that exposure to soil polarizes the immune system towards Th1 and a higher level of anti-inflammatory signaling, alleviating Th2 type allergic responses. Interestingly, the inflammatory status of the mice strongly influenced the composition of the faecal microbiota, overriding for the most part the effect of environmental exposures.

Conclusions: The soil environment clearly affects the composition of murine gut microbiota and immune status. Our results provide direct evidence of the role of environmentally acquired microbes in protecting against inflammation. Moreover, our study provides additional evidence of the bidirectionality of the gut-lung axis, and the ability of these organs to influence each other's immune responses and microbiota composition.

SUNDAY, 18 JUNE 2017

TPS 19

CLINICAL PRESENTATION AND MANAGEMENT OF ANAPHYLAXIS

0842 | Patterns of anaphylaxis after diagnostic work-up: a follow-up study of 226 patients with suspected anaphylaxis at the emergency care setting

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Introduction: Most published studies on anaphylaxis in the Emergency Care Setting (ECS) are retrospective or register based. Data on subsequent allergological diagnostic work-up are sparse.

Objectives: To characterize patients diagnosed with anaphylaxis in the ECS after referral to our specialized Allergy Center (AC) for diagnostic work-up. For confirmed anaphylaxis cases, to describe co-morbidities and co-factors in relation to the anaphylactic episode.

Methods: Prospective, non-interventional study including referred patients with suspected anaphylaxis identified at the ECS, Odense University Hospital (OUH), during 1st May 2013-30th April 2014. Cases were eligible by any clinical suspicion of anaphylaxis and/or a diagnosis related to anaphylaxis according to International Classification of Diseases 10 (ICD-10) and/or if treated with adrenaline, antihistamines or glucocorticoids at the ECS or at prehospital level. In the AC, all patients were evaluated according to international guidelines. In this study, all adults were screened for mastocytosis by sensitive KIT D816V mutation analysis in peripheral blood.

Results: Among 226 patients with suspected anaphylaxis referred from the ECS, anaphylaxis was confirmed in 124 (55%), of which 20 were children. There was an equal gender distribution (64 females/60 males). Concordance between suspected elicitors at ECS and confirmed at AC was found in 85% (106/124) of the cases. The main elicitor in children was food (65%), while in adults drugs (46%) and venom (33%) were the most common. Co-morbidities were: Rhinitis (22%), atopic dermatitis (18%), asthma (18%) and cardiovascular diseases (only for adults, 25%). Mastocytosis was diagnosed in 8% of the adult patients (Venom n = 4, Drugs n = 2, Unknown n = 2) and it was significantly associated with severe anaphylactic reactions. Co-factors were: infection (30%), exercise (21%), acetylsalicylic acid and nonsteroidal anti-inflammatory drugs (16%) and alcohol (14%).

Conclusions: Only after clinical assessment according to international guidelines, the anaphylaxis diagnosis can be confirmed or excluded. Mastocytosis was diagnosed in a high number of anaphylaxis patients. In cases with confirmed anaphylaxis, co-morbidities and co-factors were present in up to 22% and 30% of the cases respectively. The presence of co-morbidities and co-factors must always be considered since they may play a role for future anaphylactic reactions.

0843 | Characteristics of patients with anaphylaxis presenting to the emergency department

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Introduction: This was retrospective case note study of adults presenting with anaphylaxis over a 1-year period (from 1 January 2015 to 31 December 2015) to the Emergency Department (ED), University Hospital Dubrava, Zagreb.

Objectives: To describe the demographic characteristics, clinical features, causative agents and administered therapy in adults presenting with anaphylaxis to the ED.

Results: Out of 23 461 records, 529 (2.25%) patients were admitted to the ED with allergic reactions, 37 patients fulfilled the criteria for anaphylaxis. The median age of presentation was 55 years. There were 43% males. Insect sting was the most common trigger (54%). Skin features were the principal presenting symptoms (92%), followed by respiratory (70%), cardiovascular (49%), and gastrointestinal signs (38%). Adrenaline was administrated in 43% of cases, the primary mode of delivery was intramuscular (44%). In all, 73% patients were discharged in the first 12 hours and 6 (16%) patients were admitted to the hospital. On discharge, adrenalin auto-injector was prescribed to 3 (8%) patients and only 5 (13%) patients were referred to an allergist.

Conclusions: There is a need for education of emergency physicians to recognise the clinical features of anaphylaxis and to treat the episode appropriately, according to the guidelines of anaphylaxis management.

0844 | Different clinical features of anaphylaxis according to the cause

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Introduction: Anaphylaxis is a life-threatening allergic reaction. Although several studies reported different anaphylactic reaction according to the causative substances, there are still few studies on anaphylaxis for each cause.

Objectives: This study was conducted to identify characteristics of anaphylactic reaction for each cause and to analyze the factors related to the severity of the disease.

Results: A total of 199 patients with anaphylaxis were analyzed. 51.8% were male mean age was 41.1 years. Food was the most common cause (49.7%), followed by drug (36.2%), bee stings (10.1%), idiopathic anaphylaxis (4.0%). In food induced anaphylaxis, seafood (28.3%), meat (18.1%), and grain/flour (18.1%) were identified as the main causes. In drug induced anaphylaxis, antibiotics (40.2%), NSAIDs (33.3%), CT radiocontrast (11.1%) were common causes. Cardiovascular disease such as syncope, hypotension was considerably more common in drug induced anaphylaxis. The incidence of severe anaphylaxis was the highest in drug induced anaphylaxis (54.2%), followed by bee sting induced (35.0%), food induced (26.3%). Skin symptoms such as urticaria were significantly more common in food induced anaphylaxis. Older age, more male predominant, more atopic tendency was observed in severe anaphylaxis. Rate of treatment with epinephrine with anaphylaxis was not high at 69.7% and 56.9% in patients with food-induced and drug-induced anaphylaxis, respectively.

Conclusions: This study analyzed the clinical features of anaphylaxis mainly caused by foods and drugs. More severe reaction was developed with drug related anaphylaxis and old atopic male was found frequently in severe anaphylactic group. Low rate of epinephrine prescription was also observed. Therefore, we need to be more careful for old man with drug allergy, and should not hesitate to use epinephrine.

0845 | Anaphylaxis in a food allergy outpatient department—one year case series

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Introduction: Anaphylaxis is an acute, potentially fatal, multi-organ allergic reaction caused by the release of chemical mediators from mast cells and basophiles. Food allergy is the most frequent cause of anaphylaxis. The aim of this study was to characterize the population with food induced anaphylaxis followed in our Food Allergy outpatient clinic (FAOC) over a 1 year period.

Objectives: Retrospective analyses of clinical files of patients with food anaphylaxis observed in our FAOC during 2016. Patients were grouped according to the age and the culprit food of the first anaphylaxis episode (some patients had symptoms with multiple foods).

Results: Sixty-two patients were included, 35 males and 27 females.

In the pediatric group (32 patients, <18 years-old), mean age 6.2 years-old (SD ± 6), the earliest anaphylaxis occurred at 14 days old (cow's milk) and the most frequently implicated food were cow's milk (n = 7), egg (n = 6) and fish (n = 6). Peanut was the culprit food in only 1 patient that also reported symptoms with fresh fruits and was sensitized to Pru p 3.

In the adult's group (n = 30), the mean age for the first anaphylaxis was 37 years (SD±17) and the most commonly identified allergens were nuts (n = 10) and wheat (n = 7). Among the patients sensitized to nuts, 5 patients were sensitized to Pru p 3, and had symptoms with other foods, mostly fresh fruits. In patients allergic to wheat, 4 patients were sensitized to ω-5-gliadin and 2 to the wheat-LTP.

The number of patients allergic to shellfish was the same in both age groups (n = 5).

Multiple combinations of symptoms were observed: urticaria (85.5%), angioedema (64.5%) and respiratory symptoms (62.9%). Cofactors were present in 20 patients, mainly exercise (60%), particularly associated with wheat allergy. Most patients (88.7%) were observed in the emergency department after the reaction, but only 29% of these were treated with epinephrine. Other allergic diseases were present in 64.5% of the patients, among those asthma and/or rhinitis were the most frequent.

Conclusions: Anaphylaxis in the adult population, more frequent with nuts and wheat, reflects the Mediterranean sensitization pattern. In the pediatric group the most frequent causes of anaphylaxis were milk and egg, as expected. The rate of sensitization to shellfish was the same in adults and infants patients. As in other studies, exercise is the most relevant cofactor. Adrenaline is still underused in anaphylaxis.

0846 | Perioperative anaphylaxis in a single tertiary hospital

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Introduction: Anaphylactic reactions during the perioperative period are non common but life threatening events. But data on its incidence and causative agents vary in different studies.

Objectives: We purposed to investigate the incidence of the perioperative anaphylaxis in a hospital with the clinical data. We conducted a retrospective chart review and identify 12 anaphylaxis cases that had possible anaphylaxis related with anesthesia between 2011 January to 2016 December. We reviewed the clinical, demographic data and the results of skin tests.

Results: Among them, 8 patients were identified as having the perioperative anaphylaxis. Overall incidence anaphylaxis during 6 years was 6.84 per 100 000 (8 out of 117 044 anesthesia). Half of the patients (4 of 8) were female, and mean age was 44.38 $\pm$ 17.85 (from 24 to 69 years). Half of the patients (4 of 8) had atopic tendency, and 3 patients had history of allergic rhinitis. According to anaphylaxis grading, 1 (12.5%) was grade A with respiratory symptoms, 6 (75.0%) were grade B with life-threatening cardiovascular and/or respiratory derangement, 1 (12.5%) was grade C with cardiac arrest. The causative drugs were identified in 6 of 8 using intradermal and prick testing. Among them, 66.7% (4 of 6) were caused by antibiotics (1 vancomycin, and 3 3rd generation cephalosporin), and 33.3% (2 of 6) were caused by neuromuscular blocking agent (1 rocuronium, and 1 both rocuronium and cisatracurium)

Conclusions: Antibiotics was the most common cause of perioperative anaphylaxis in our institute. To identify culprit agent, appropriate skin testing with standardized protocol should be performed to reduce the recurrence of life-threatening events.

0847 | Level of knowledge about food allergy and anaphylaxis of parents/caregivers, elementary school teachers and university students in Uruguaiana, RS, Brazil

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Introduction: Food allergies (AA) have become an increasingly common reality over the past few years, and have fled the family context.

Objectives: To evaluate knowledge about AA and Anaphylaxis by parents / caregivers (P), elementary school teachers (T) and university students (S) in Uruguaiana RS, BR.

Methods: Participants were 111 P children with asthma, 177 T and 300 S (Medicine, Nursing, Physiotherapy, Pharmacy and Physical Education) who answered the questionnaire developed and previously used by Polloni et al, 2013$_1$.

Results: Although participants had information about AA and anaphylaxis, this was higher in group S due to first-aid courses and health-related training. Only 39.6% of the P patients identified the foods most likely to cause food allergy although a significant portion (S: 65.9%, T: 74.7%, P: 50%) knew the most frequent symptoms of AA and were familiar with the symptoms of anaphylaxis (S: 55%, T: 61.1%, P: 50.3%). The three groups did not identify adrenaline as the drug of choice to treat anaphylaxis (S: 19%, T: 13.7%, P: 7.2%) as well as contraindication to its use in children. Few people knew how to offer allergen-free diets (S: 19.1%, T: 22.3%, P: 41.8%), although a good part found it important to read the food labels to be given to children (S: 60.7%, T: 60.6%, P: 36.9%). 71.2% were unaware of the risks of an exclusion diet. Only few participants (S:41%, T:27%, P:23%) recognized that children and adolescents with AA have emotional and relationship difficulties, and although 80.4% of respondents know that the child may have anaphylactic shock at school or picnic at school, only 6.3% think the school is prepared to attend this type of emergency.

Conclusions: The increase in the prevalence of AA requires that besides the knowledge of its signs and symptoms, the technical knowledge to provide immediate relief and the set of preventive measures to inhibit unpleasant reactions should be mandatory requirements of knowledge among all people who participate in any environment that these children will attend.

Reference: 1. Polloni L, Lazzarotto F, Toniolo A, Ducolin G, Muraro A. What do school personnel know, think and feel about food allergies? Clin Transl Allergy 2013, 3:39.

Key words: Students, teachers, parents/caregivers, knowledge, food allergy, anaphylaxis.

0848 | Declarative knowledge about anaphylaxis of primary care interns in France

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Introduction: Anaphylaxis is a clinical emergency, and all healthcare professionals should be familiar with its recognition and acute and ongoing management. The aim of this study was to evaluate the declarative knowledge of primary care interns as far as anaphylaxis diagnosis and management are concerned.

Objectives: Descriptive observational study among 650 primary care students, belonging to Nancy and Strasbourg faculties of Medicine, through an online survey.

Results: Sixty-six responses were obtained (10.2% response rate). 62.1% of primary care students considered their training is inadequate. The recommendations about the management of anaphylaxis were known only by 30.3% of them. Concerning the diagnostic, 2/3 didn't mention digestive signs as anaphylaxis and only 1/3 recognised respiratory signs as anaphylaxis.

Treatments were consistent with the recommendations for grades 1 and 3 of the classification Ring and Messmer, instead of those of grade 2, which were treated by antihistamines and corticosteroids

by oral route. Regarding patient's follow-up, 93.8% of respondents referred to an allergist.

The seniority doesn't seem to influence the ignorance of the main classifications and the recognition of the clinical signs, as well as the fact of having done the internship at the general practitioner office (realised by 80% of the interns who answered).

The severity of grade 2 symptoms is underestimated and treatment is not consistent with international recommendations, underscoring the underutilisation of adrenaline. In terminological difficulties found in the Ring and Messmer classification, such as the terms of Quincke's oedema, bronchospasm, mild hypotension, etc., may contribute to these diagnostic difficulties.

Conclusions: Our work suggests that training on recognition and management of anaphylaxis should be improved. Creation of a degree of Allergy, in France, and development of postgraduate education would participate in strengthening knowledge about this disease.

0849 | Exercise induced anaphylaxis: does it occur only with food?

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Introduction: Exercise plays an important role in IgE mediated allergy against omega-5-gliadin (w-5G) wheat protein. Thus, wheat-dependent- exercise-induced- anaphylaxis is a good model for "co-factor-mediated" anaphylaxis.

Objectives: We present a 38-year-old-male patient with recurrent anaphylaxis for the last 3 years. After three different food intake—chicken, ravioli, and toast—he experienced sudden onset of itching, generalized urticaria, dyspnea, dizziness, and hypotension in the same manner within 10-30 minutes of exercise. The patient did not have any history of atopy, allergy, and/or food intolerance No other cofactor was identified as the externally applied exercise. Similar complaints developed more mildly after exercise followed by myorelaxant and fast food intake.

Results: Skin prick tests (SPT) were negative with aeroallergens, whereas positive reactions were observed with wheat and barley, among six different flours (wheat, barley, rye, rice, corn, oat), and positive ID tests with all, except rice. SpeIgE measured by ImmunoCAP was found to be negative for gluten and wheat mix, but w-5G was positive (1.87 kUA/L). Antigliadin IgA-IgG, and tissue transglutaminase IgG-A screened to exclude Celiac disease were negative. As the patient refused to have provocation test with myorelaxants, we were unable to perform it.

Conclusions: Although no reaction was mentioned after the exercise without food intake, as well as myorelaxant use, adrenalin auto injector was prescribed as the patient observed wheat-dependent-exercise-induced anaphylaxis. This case was presented as myorelaxant can be a rare cofactor in addition to w-5G(+)/gluten(−) speIgE.

0850 | Rhabdomyolysis in the context of food-dependent exercise induced anaphylaxis

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Case Report: Background: Food-dependent exercise induced anaphylaxis is a severe generalized allergic reaction, which is more frequent in young people, with an estimated prevalence of 0.048% among teenagers.

On the other hand, rhabdomyolysis is the breakdown of muscle fibers that causes release of the contents of said fibers (myoglobin) into the bloodstream. It is extremely unusual in the context of anaphylaxis.

Methods: A 27-year-old patient was referred to our department for study. Approximately three months before he had presented an episode of pruritic wheals distributed throughout the integument, facial flushing with facial oedema sensation, occipital headache, nausea and a feverish feeling, few minutes after starting to run. He had had dinner (chicken, salad, and wholemeal bread) ninety minutes before exercising.

At the emergency room, high levels of muscle damage parameters (CK 55.000 U/L, AST 800 UI/L, ALT 450 UIl) were revealed, with decreased renal function. Intense fluid therapy was established to re-hydrate the patient and he showed rapid clinical improvement.

Results: Complementary tests were performed at emergency department (chest x-ray, brain CT and electroencephalogram) without pathological findings. Three months after the episode, skin prick tests (SPT) with common aeroallergens were all negative. SPT with common trophallergens and *Anisakis simplex*, were also negative. Total IgE (106 kU/L), basal tryptase (1.56 μg/L) and complement (C3: 110 mg/dL, C4: 33.40 mg/dL, C1 inhibitor: 31.80 mg/dL and CH 100: 401.38 U) were into normal range. Specific IgE to gliadin (rTri a 19) (ImmunoCAP) was positive (3.02 kUA/L).

Conclusion: This patient had an episode compatible with Wheat-Dependent Exercise-Induced Anaphylaxis. It was possibly not identified at emergency room because of the simultaneous episode of rhabdomyolysis. It has been mainly associated with multiple Hymenoptera stings, and it is very rarely in an anaphylaxis. In our case, rhabdomyolysis seems to have been associated to physical exercise, although it is tempting to speculate that the undiagnosed anaphylactic episode could have contributed to an increase in the intensity of rhabdomyolysis.

0851 | Cofactors of anaphylaxis

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Case Report: Anaphylaxis is an immediate systemic hypersensitivity reaction that can affect simultaneous any organ/systems(cutaneous, respiratory, cardiovascular and gastrointestinal). Its appearance is often inexplicable. Anaphylaxis includes symptoms and physical signs of the presence of the allergen and antibodies (IgE), which will induce the formation and release of chemical mediators by basophils / mast cells. The concept and definition of anaphylaxis requires explaining anaphylactoid reactions, which are symptoms that cannot be distinguished from IgE-mediated anaphylaxis, but are the result of the release of chemical mediators (particularly histamine) by non-IgE mechanisms.

We present the case of a male patient, 50 years old, who comes to allergy service for a prior reaction of angioedema at the face, developing anaphylaxis with shock and cardio-respiratory arrest in the emergency care unit, which required cardiopulmonary resuscitation. The reaction occurred late in the evening, 4 hours after playing tennis, about one hour after eating home-made beef steak with potatoes and mustard and about 20 minutes after he took an over-the-counter pill that contained flurbiprofen, for dysphagia.

The patient has a personal and family history of atopy, being diagnosed with allergic rhinitis with sensitisation to Asteraceae family pollens (Ambrosia and Artemisia).

Patient history ruled out other possible causes: other foods (possibly contaminated by pollens), alcohol, insect bites, occupational allergens, exposure to latex. Mastocytosis was excluded, serum tryptase was within normal limits; clinical examination was normal, and common laboratory investigations were also normal.

Specific IgE for mustard was weakly positive. It is known that mustard may have cross-reactivity with Artemisa pollen, but the patient had before no recommendation to avoid mustar, having no reaction until the diagnosis of rhinitis. The specific IgE to flurbiprofen is not available to perform, but the reaction may be induced by non-specific immunological mechanisms (non-allergic).

The patient received emergency kit recommendation with self-injectable epinephrine, antihistamines and oral corticosteroid, the recommendation to avoid mustard and NSAIDs.

Conclusion: In some cases it is impossible to exclude a culprit allergen or impossible to prove how much of a particular allergen is responsible for a reaction (in this case infection, mustard, flurbiprofen), which leads to lower patient quality of life.

0852 | Allergic reactions induced by cofactors in patients sensitised to lipid transfer protein

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Introduction: The aim of this work was to know the role of cofactors in allergic reactions in patients sensitised to lipid transfer protein (LTP) and the features of these reactions (cofactors implicated, type of symptoms and offending foods).

Objectives: One hundred eighty six patients (59.7 females and 40.3 males, mean age 28.3 years old, range 2 to 60 years old) were included. All of them presented with adverse reactions with any plant-derived foods and had skin prick test positive with LTP extract (ALK- Abelló).

All patients completed a questionnaire about adverse reactions with plant-derived foods (type of symptoms, offending foods and cofactors implicated: physical exercise, non-steroidal anti-inflammatory drugs (NSAID) and alcohol consumption).

Results: A total of 683 adverse reactions in relation with plant-derived foods were reported by the patients included in the study. Cofactors were implicated in 42 (6.1%) of them: 28 patients (66.7%) in relation with physical exercise, 12 (28.6%) with NSAID and 2 (4.7%) with alcohol consumption.

Symptoms reported in allergic reactions induced by cofactors were: anaphylaxis in 17 (40.5%) patients; urticaria in 5 (11.9%); angioedema in 9 (21.4%); urticaria/angioedema in 9 (21.4%); and gastrointestinal symptoms in 2 (4.8%).

Offending foods implicated in the reactions were: fruits in 25 patients (59.5%), of whom Rosaceae family in 18 (42.9%) and others fruits in 7 (16.7%); vegetables in 6 (14.3%), dry fruits in 4 (9.5%), spices in 4 (9.5%) and cereals in 3 (7.1%).

Conclusions: (i) The role of cofactors in allergic reactions in patients sensitised to LTP is poor. (ii) Physical exercise was the most important cofactor implicated in allergic reactions induced by LTP sensitisation. (iii) Fruits, specially Rosaceae family, were the most common offending foods implicated in allergic reactions. (iv) Moderate or severe symptoms were reported in these allergic reactions.

0853 | Metabolomic analysis in anaphylactic reactions*

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Introduction: Anaphylaxis is a potentially fatal allergic reaction with variable clinical manifestations and severity. Diagnosis is clinical

and serum tryptase, the only available biomarker, has limitations. Metabolomics allows the simultaneous detection and quantification of a large variety of metabolites in biological samples.

Objectives: To investigate the metabolic profiles during anaphylactic reactions in order to compare the metabolomic pattern during these reactions with the baseline state, to analyse if there are differences among the different types and severities of anaphylaxis as well as to expand the knowledge of the mechanisms involved in these reactions.

Results: 30 serum samples were analysed by nuclear magnetic resonance spectroscopy from 12 anaphylaxis episodes. Patients mean aged was 40.5 years (11-72). Clinical manifestations, evaluated according to the Sampson classification were in 9 cases (75%) a type III reaction, 2 (17%) were exclusively cutaneous and 1 (8.3%) cutaneous and neurological. Serum tryptase was elevated in 5 cases (41.7%) compared to baseline levels. Treatment for the episodes consisted in corticosteroids and antihistamines in all cases. Only 4 patients (33.3%) received epinephrine. All fully recovered.

The allergy evaluation identify diverse eliciting agents/circumstances: drug allergy (iodinated contrast, moxifloxacin, croscarmellose, dexketoprofen, metamizole and rocuronium), intraoperative reactions with negative allergic investigation (2 cases), SCIT immediate systemic reaction, food poisoning, nuts allergy and chronic urticaria (1 case, each).

The metabolomic patterns, collected at different times (30 minutes-10 hours) during anaphylaxis, differed with the baseline ones. Patterns attributable to the rescue medication and/or the eliciting agent were ruled out. The metabolomic profile varied proportionally to the time elapsed between reactions and obtaining the sample. The differences were attributed to the metabolic processes involved in the anaphylactic reactions. Comparisons among different types of reactions were not done due to the limited number of cases.

Conclusions: We have observed changes in the spectrum of signal molecules obtained in anaphylactic reactions, which were different at baseline time. As anaphylactic reactions are unpredictable and elicited by several agents, we need to increase the number of cases in order to confirm our findings.

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0854 | Use of adrenaline auto-injectors in patients at a British tertiary paediatric allergy clinic

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Introduction: Guidance regarding the number of adrenaline auto-injectors (AAIs) prescribed to children at risk of anaphylaxis is variable. The EAACI guidelines suggest children in certain risk categories should be prescribed two devices. A recent MHRA (Medicines and Healthcare products Regulatory Agency) update advised routine prescription of at least two devices whereas the BSACI (British Society of Allergy and Clinical Immunology) guideline indicates that aside from the most at risk individuals, one device is needed for most reactions and if a second is required, it can be given by a health professional.

Existing studies documenting the need to use two devices are limited. The reported results show large variations and often the indication for the second dose is unclear or not documented.

We explored the incidence of AAI usage and need to use a second device during a reaction in a population of children at a British paediatric allergy clinic.

Objectives: Anonymised questionnaires were given to parents of patients presenting to general allergy clinics at a tertiary paediatric allergy service in London over a three week period. All children aged 0-16, prescribed an AAI were included.

Results: We found that in this population, patients were prescribed between 2 and 7 devices each. Of the 52 participants, 14 (26.9%) were not carrying their devices on that day. 9 out of the 52 (17%) had needed to use their devices since they were prescribed and 8 of these were within the past 3 years. Of these 9 patients, 7 (78%) had significant airway involvement or evidence of hypotension and 3 needed to use 2 devices. In all 3 cases, the first dose given was appropriate for the child's weight and the device was administered correctly, but there was inadequate clinical response. In 2 out of 3 cases, the second dose was administered by a healthcare professional.

Conclusions: The results show that children are often prescribed multiple AAIs, which has cost implications, particularly if 27% do not carry their device. The importance of carrying the device at all times should be reinforced regularly.

Although only 17% of patients had ever needed to use the device, a third of these required a second AAI despite the first being the correct dose.

These results suggest there cannot be a blanket rule for numbers of AAIs prescribed and this decision should be based on a thorough risk assessment of the individual.

0855 | Use assessment of adrenaline autoinjectors among adults

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Introduction: Epinephrine in the form of an autoinjector device (EpiPen®, Adrenaline Auto-Injector) is often prescribed for patients who have had previous anaphylactic reactions. Correct use of the device by patients, care givers and medical staff have been reported to be low.

Objectives: Our aim was to determine the ability of patients to properly use EpiPen®.

Methods: Study was conducted between June- September 2016. Patients who had been previously prescribed EpiPen® between January 2009 and January 2016 were enrolled to our study. Patients were trained about how to and when to use EpiPen® by allergists of our clinic. The training was done at the prescription visit and repeated for some patients on follow-up visits. During the study period, patients' usage of EpiPen® was questioned, and all EpiPen® carrying patients were practically evaluated with a trainer device that does not contain medication or needle. Patients were scored in six steps on a standard form as proposed by Sicherer et al.

Results: Forty-six patients with insect venom hypersensitivity (n = 44), idiopathic (n = 1), and food (n = 1) anaphylaxis were prescribed EpiPen® of whom 39 (84.8%) had obtained the medication. Twenty patients were female (43%), and mean age of the study population was 45 ± 13 (20-67). Twenty-nine (63%) patients were still carrying the device at the time of the study. After prescription of EpiPen®, median follow up period of patients was 12 (3-72) months, and median number of EpiPen® education that patients received was 1 (1-4). No patient experienced anaphylaxis after EpiPen® prescription. One patient used EpiPen® for local skin reaction after a bee sting. Of 29 patients, 11 (38%) correctly used the trainer device. The most common reason for not carrying EpiPen® was the belief that it was not necessary (n: 6, 35%), and the most common mistake was failing to remove the cap (n:15, 83%). The median time elapsed since last training among patients who accomplished, and failed to properly use EpiPen® was 5 (1-36), and 9 (1-72) months, respectively.

Conclusions: Based on our results and previous studies, we think that repeated courses of education on how and when to use adrenaline autoinjectors should be provided to patients who need to carry the device at all times. A warning through e-mail or cell phones may be provided and regular follow-up visits scheduled.

0856 | Adrenaline auto-injector needle length: a real concern or a red herring?

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Case Report: Based on available data, intramuscular (IM) injection into the vastus lateralis muscle (i.e. outer thigh) is the preferred route of adrenaline administration. Adrenaline auto-injectors (AAIs) have different needle lengths, and there are concerns that some may be too short for IM delivery in obese patients. This concern is pertinent, considering that worldwide rates of obesity have almost doubled from 1980 to 2008; 23% of women and 20% of men are now considered obese. The aim of this abstract was to review the evidence on adrenaline delivery with the Epipen® AAI, with consideration of needle length. Knowledge of average distance to muscle is integral to this consideration and has been calculated as 0.60 cm, 0.92 cm and 1.48 cm in males, children and females, respectively.[1, 2] The EPIPEN needle lengths of 1.5 cm for the adult device and 1.3 cm for the junior one, are therefore sufficient to reach muscle for most patients. In fact with the EPIPEN, adrenaline is delivered deeper than the needle length, to a depth of 2.78 ± 0.59 cm, by virtue of both sub-cutaneous (SC) layer compression during application and propulsive force of the EPIPEN device.[1] Furthermore, assuming 25% compression of the SC layer, the EPIPEN needle tip is anticipated to reach muscle in 100% of patients with a body mass index (BMI) <25, 95% of those with BMI 25 to ≤ 30 and 83% of those with a BMI ≥30.[3] The needle length debate continues nevertheless and has been inconclusive. Some studies have shown that AAI needle lengths may be too long for some patients (i.e. risk of bone injection)[4, 5] but also too short for others (i.e. risk of SC injection).[2, 6] A recent survey of EAACI members showed that 79% of respondents considered current AAI needle lengths sufficient for their non-obese patients, but 43% were unsure whether they were sufficient for their obese patients. Clearly, optimal AAI needle length is unknown. The European Medicines Agency has requested more PK/PD studies to answer this question. Currently, the EPIPEN is the only AAI available in Europe with published PK/PD studies[7, 8] and delivers adrenaline IM in the vast majority of patients irrespective of BMI.

References:

1. Song et al. AAAI 2013;111:143-5
2. Stecher et al. Pediatr 2009;124:65-70
3. Wang et al. In: Eastern Allergy Conference. 2013
4. Kim et al. AACI 2014;10:40
5. Dreborg et al. AACI 2016;12:11
6. Tsai et al. AACI 2014;10:39
7. Simons et al. JACI 2001;108:871-3
8. Simons, et al. JACI 1998;101:33-7

0857 | Anaphylaxis management in the emergency department of a tertiary hospital in the Philippines

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Introduction: In the emergency department (ED), diagnosis and management of anaphylaxis is challenging. It has been estimated that at least 50% of anaphylaxis episodes are misdiagnosed in the ED when the diagnostic criteria of current guidelines are not used. Misdiagnosis leads to improper management.

Objectives: The objective of our study was to assess anaphylaxis diagnosis and management in patients presenting to our ED.

Results: Retrospective chart-review conducted on pediatric and adult patients presenting to The Medical City Hospital ED, Philippines from 2013-2015 was done. Cases were identified based on ICD10 coding for either anaphylaxis or other allergic related diagnosis. Only cases fitting the definition of anaphylaxis as identified by the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) Criteria were included. Data collected included demographics, signs and symptoms, triggers and management. A total of 105 cases were evaluated. Incidence of anaphylaxis for the 3-year study period was 0.03%. Median age was 19 years (range 1-71), and 44.8% were males. Food (44%) and drugs (19%) were common allergens, while 30% had no identifiable allergen. Of the 105 cases, 35 (33%) were diagnosed as "urticaria" or "hypersensitivity reaction" despite fulfilling the NIAID/FAAN criteria for anaphylaxis. Seventy-three (70%) received epinephrine, 88% via the preferred IM route. There was a significant difference in epinephrine administration between those given the diagnosis of anaphylaxis vs those diagnosed as urticaria/hypersensitivity reaction [61 (87%) vs 12 (34%), $x^2 = 30.77$ $P < .01$]. There was also a significant difference in time interval from arrival at the ED to epinephrine administration between the 2 groups, with the majority of cases diagnosed as anaphylaxis (48%) receiving epinephrine within 10 minutes, vs $\geq$ 60 minutes for most (58%) of the urticaria/hypersensitivity reaction group ($x^2 = 52.97$ $P < .01$). Only 46% of all cases were referred to an allergist, and only 1 patient was given a prescription for epinephrine from the ED.

Conclusions: Despite current guidelines, anaphylaxis is still misdiagnosed in the ED. Having an ED diagnosis of anaphylaxis significantly increases the likelihood of epinephrine administration, and at a shorter time interval. Discharge management also varied from accepted recommendations. More expansive circulation of diagnosis and management guidelines are needed.

0858 | Omalizumab for idiopathic anaphylaxis—a case series

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Introduction: Idiopathic anaphylaxis is a rare disease with no discernible cause. It is due to mast cell activation. A large specter of allergy tests and other diagnostic tests (basal tryptase, histamine intolerance, chromogranin, 5-HIAA) have to be done to exclude relevant allergen sensitization and diseases that could mimic it. According to guidelines patients with more than 6 episodes per year should be put on long term systemic glucocorticoid prophylaxis.

Objectives: Omalizumab is a monoclonal antibody, that binds to IgE and decrease mast cell reactivity. Therefore omalizumab might be helpful in prevention of the anaphylactic reactions.

Results: We present three women (56, 43 and 28 years) with recurrent spontaneous episodes of anaphylaxis (4-10 in year 2015), confirmed by tryptase elevation during episode. They were repeatedly treated by epinephrine at the emergency unit. Two patients presented with hypotension, the third with bronchospasm. Diagnostic workup didn't reveal any relevant allergy (one patient was sensitized to aspergilus, and the other with alpha-gal), neither cofactor. Two patients have concomitant chronic urticaria. Because of frequent and severe episodes, patients were started off-label omalizumab 300 mg monthly and are without anaphylactic episodes since then (9-13 months).

Conclusions: All three patients are in remission since the administration of omalizumab. Omalizumab seems an effective drug for prevention of recurrent episodes of idiopathic anaphylaxis.

0859 | Is there anything else than omalizumab allergy?

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Case Report: We present the results of security in the use of omalizumab in our hospital during the period between October 2004 to August 2016, in which 86 patients were treated with omalizumab with a total of 6054 doses, in different pathologies: asthma(60), non-allergic asthma(1), urticaria(20), polyposis(4) and food allergy(1).

In our study, we not only analyze the anaphylactic reactions produced by omalizumab but also those produced by its excipients, focusing particularly on polysorbate.

The tolerance to omalizumab in our hospital has been positive until July,21th 2016, when a patient with severe bronchial asthma, was administered the first dose of omalizumab. 30 minutes after this medication, the patient started with dry mouth feeling, dizziness, nausea and an episode of vomiting, followed by a progressive increase of dyspnea and coughing spells. Also, he presented a cutaneous level V-neck erythema. Once, in the emergency room, edema of pharyngeal pillars was observed.

Therefore, epinephrine by intramuscular injection, high-dose steroid therapy, salbutamol and ipratropium bromide nebulizations every 6 hours and serum therapy were administered.

After 4 hours, it was observed a significant clinical improvement and hemodynamic stability. Consequently, omalizumab was removed and the patient was quoted for performing the allergy study. The aim of this study is to highlight the security in the use of omalizumab by making a comparison of the data obtained in our study with the one published by the omalizumab Joint Task Force(OJTF). Taking into account the publications registered until now, skin prick and

intradermal test were performed with omalizumab and polysorbate: Skin prick test was negative for both, but intradermal test was positive for omalizumab at a concentration of 1/1000 and for polysorbate at a concentration of 1/100.

Conclusions: In our hospital, we have calculated an incidence of omalizumab-induced anaphylaxis of 0.016%: (i) We report a probable anaphylactic reaction caused by polysorbate, contained as an excipient in omalizumab. (ii) Polysorbate is a very ubiquitous excipient, commonly used in medicines, particularly for injection preparations, which would explain this reaction with the first dose of omalizumab.

0860 | Use of omalizumab for the prevention of intraoperative anaphylaxis due to ethylene oxide sensitization in a patient with concomitant latex allergy

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Case report: Background: A 1-year old male with congenital hydrocephalus and spastic quadriplegia came to our center for an episode of intraoperative anaphylaxis in 1993. Skin prick test (SPT) and radioallergosorbent test (RAST) with latex extracts were markedly positive and a diagnosis of latex allergy was made. Since then, latex-safe protocols were adopted uneventfully in further surgical procedures. In 2013 a second anaphylactic reaction occurred during surgery in a latex-safe environment, requiring resuscitation and administration of adrenaline. The patient had increasing intracranial pressure and urgent replacement of a previously implanted ventriculoatrial shunt was necessary.

Methods: SPT and RAST for general anesthetics, penicillin, gelatin, latex, Formaldehyde and Ethylene Oxide (EtO) allergy were performed. IgE antibodies against EtO were detected (6,9 kUA/l), along with latex-specific IgEs (5.9 KUA/l).

Results: Given the urgent need for surgery and the difficulty in arranging an EtO-safe surgical environment, a single pre-operative 600 mg dose of omalizumab was administered, along with IV steroids and antihistamines. The off-label use of omalizumab was approved by the Ethics Committee of the University Hospital of Ancona. Surgery was uneventful and no reactions occurred during the post-operative follow-up.

Discussion: EtO is a gas commonly used for sterilization of surgical tools and pharmaceutical components. Sensitization to EtO is rare, however subjects that have repeated contact with EtO-sterilized materials due to medical procedures (i.e. multiple surgeries, blood transfusions, hemodialytic treatment) are at higher risk of sensitization (1,2,3). Similar to latex allergy, EtO sensitization is linked to an increased risk of intraoperative anaphylaxis, therefore complete avoidance of the allergen is necessary (1). However, EtO-safe surgery is very difficult to arrange due to its widespread use, and impossible to perform in surgical emergencies (4). Omalizumab is a monoclonal antibody that binds to free IgE antibodies that has been used as pre-exposure preventive treatment in one EtO-sensitized patient with a history of intraoperative anaphylaxis (5).

Conclusion: Intraoperative anaphylaxis due to EtO allergy must be suspected and ruled out, along with latex or drug allergy, in high-risk subjects. A single peri-operative dose of omalizumab can be considered as an efficient preventive treatment in EtO sensitization when avoidance is not a feasible option.

MONDAY, 19 JUNE 2017
TPS 20
IMMUNOTHERAPY - EFFICACY, SAFETY AND INDIVIDUALISED THERAPY

0861 | Relevant patient benefit of 5-grass pollen tablet allergen immunotherapy (AIT) in grass-pollen allergic adults, adolescents and children with different clinical profiles

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Introduction: AIT with the 5-grass pollen tablet has shown its efficacy in the treatment of allergic rhinitis (AR) in several randomized controlled trials. As clinical benefit does not automatically suggest patient-reported benefit - a measurement which is becoming increasingly important for perceived benefit can be assumed to increase adherence to treatment - we investigated the benefit of 5-grass pollen tablet AIT in adults (A; 18+ years), adolescents (ADO; 13-17 years) and children (C; 5-12 years), focusing on different subgroups of pat. (male/female, poly-/monoallergic, asthmatic/non-asthmatic).

Objectives: 145 German study centers participated in this open, prospective, multicenter, non-interventional study. Pat. were observed during their 1st treatment period with the 5-grass pollen tablet. Patient-relevant benefit was measured using the standardized and validated "Patient Benefit Index - Allergic Rhinitis (PBI-AR)". The PBI-AR global score (0 = no benefit to 4 = max. benefit) was computed based on the patients' assessments of predefined treatment needs (before treatment start) and benefits (at the end of treatment) (0 = not at all important/did not help at all to 4 = very important/helped a lot). A PBI-AR global score ≥ 1 is defined as relevant benefit.

Results: Data of 981 pat. were analyzed (A: 600, ADO: 135, C: 246), for 686 of whom a PBI-AR global score could be computed. 50.3% of the pat. were female (A: 56.7%, ADO: 44.4%, C: 35.0%), 62.7% were polyallergic (A: 60.8%, ADO: 65.9%, C: 65.4%), and 26.7% had asthma (A: 22.0%, ADO: 28.1%, C: 37.4%). Across all age groups, 9 out of 10 pat. achieved a relevant benefit from AIT (% pat. with PBI ≥ 1: A: 89.2%, ADO: 90.7%, C: 94.6.0%; mean PBI global scores: A: 2.43, ADO: 2.55, C: 2.61). There were no gender differences in the PBI in any of the age groups. In C, no significant PBI differences were observed between poly- and monoallergic pat., while the PBI was higher in polyallergic A (2.53 vs 2.29) and ADO (2.76 vs 2.17). In C and ADO, there were no significant differences between pat. with and without asthma. Adults with asthma reported a lower, but relevant benefit than those without asthma (PBI: 2.20 vs 2.50).

Conclusions: In the measured period, pat. of all age groups benefited well from AIT with the 5-grass pollen tablet, regardless of their clinical profile. Successfully achieving self-defined treatment goals is an important factor which may favorably impact treatment adherence.

0862 | Efficacy of allergen specific immunotherapy in children with pollen-food allergy syndrome and different IgE profiles to recombinant component-resolved allergens (preliminary results)

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Introduction: Pollen-food syndrome (PFS) is defined by allergic symptoms elicited promptly by the ingestion of fruits or vegetables in patients with allergic rhinoconjunctivitis. Increasing prevalence of allergic rhinoconjunctivitis and high prevalence of cross-reactions to food make actual the study of predictors of antigen specific immunotherapy (ASIT) efficacy in these patients.

Objectives: To evaluate the peculiarities of PFS after ASIT among children with seasonal allergic rhinoconjunctivitis and PFS with different IgE profiles to recombinant component-resolved allergens (CRA) .

The study included 54 children (5-18 age) with PFS. The sIgE assays to birch pollen and to CRA (rBet v1, rBet v2, rBet v4, rBet v6) were performed using an automated test system. ASIT was applied sublingual with standardized commercial birch pollen extracts.

Results: 5 IgE profiles to CRA were identified. In this group 52% of patients had monosensibilization to rBet v1 component. The 48% had combinations IgE to rBet v1 and IgE to 1, 2 or 3 minor allergens (37%, 9%, 2% accordingly).

28 patients with monosensibilization to rBet v1: 20 patients had decreased rhinoconjunctivitis and PFS symptoms; 3 patients had decreased only symptoms of rhinoconjunctivitis; 3 patients had no effect; 2 patients had not finished the treatment due to negative reactions.

There are following results after ASIT.

13 patients with sensibilization to rBet v1 and rBet b6: 7 patients had decreased both rhinoconjunctivitis and PFS symptom; 5 patients had decreased only symptoms of rhinoconjunctivitis; in 1 patient ASIT hasn't been effective.

7 patients with sensibilization to rBet v1 and rBet v2: 4 patients had decreased both rhinoconjunctivitis and PFS symptoms; 3 patients had decreased only rhinoconjunctivitis symptoms.

5 patients with sensibilization to rBet v1, rBet v2, rBet v6: 2 patients had decreased both rhinoconjunctivitis and PFS symptoms; 3 patients had decreased only rhinoconjunctivitis symptoms.

There was 1 patient with sensibilization to all CRA who had no improvement after treatment.

Conclusions: As the result of the study 61% patients had visible effect of ASIT treatment with decrease of both rhinoconjunctivitis and PFS symptoms, 26% had effect on rhinoconjunctivitis symptoms. ASIT was not effective in 9% patients. 4% of patients had adverse reactions. The study needs to continue to clarify of ASIT efficacy in children with different IgE profiles to recombinant component-resolved allergens (CRA).

0863 | Short course specific immunotherapy for seasonal allergic rhinoconjunctivitis and its impact on quality of life

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Introduction: Subcutaneous immunotherapy (SIT) is indicated in patients with seasonal allergic rhinoconjunctivitis who have failed to respond to other pharmacotherapies. Conventional SIT can contain long dosing regimens leading to a significant treatment and economic burden. A short course SIT that has been reported to offer the same efficacy as conventional SIT in a shorter treatment course. We report a single centre Quality of Life data for pre-treatment and years 1 and 2 year post treatment.

Objectives: To determine the effect of the treatment on quality of life 1 and 2 year post initiation, compared to pre-treatment, using the validated Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).The RQLQ has 28 questions organised in 7 different symptom groups. The 7 symptom groups included: Activity, Sleep, Non-Nose/Eye Problems, Practical Problems, Nasal Symptoms, Eye Symptoms and Emotional Symptoms and all are scored on a 0-6 scale (0 = not impaired at all - 6 = severely impaired)

Results: All statistics were done using a 2-tailed paired *T*-test. We present the data on 47 patients who received the treatment over a 2 year period. No patients were excluded. Pre-treatment the highest average score was seen in the effect on Activity (4.99) and the lowest in Non-Nose/Eye problems (3.73), with the latter being statistically lower than all other groups ($P < .05$), except Sleep symptoms. The largest improvement was seen in Emotional symptoms (56.4%) and the least change seen with Non-Nose/Eye problems (46.1%). One year after the initial treatment every question in each group showed a drop in symptom load, which was statistically significantly different to pre-treatment level ($P < .001$). After 2 years of treatment a further drop in symptom load was seen for each question. Although the drop was lower in each case than after 1 year, individual symptoms were affected to different levels with some changes not reaching statistical significance whilst others showed significant differences up to $P < .001$.

Conclusions: Use of a short course immunotherapy in patients with seasonal allergic rhinoconjunctivitis enhances all measured aspects of their quality of life significantly, even after only 1 year of treatment. This continues to improve during the second year but to a lesser extent.

	Pre -treatment	Year 1	Year 2
Activity	4.99 ± 0.33	3.38 ± 0.27	2.51 ± 0.22
Sleep	4.12 ± 0.16	2.72 ± 0.03	1.96 ± 0.05
Non-Nose/Eye symptoms	3.73 ± 0.23	2.52 ± 0.19	2.00 ± 0.12
Practical problems	4.88 ± 0.30	3.35 ± 0.33	2.52 ± 0.12
Nasal symptoms	4.69 ± 0.16	3.14 ± 0.20	2.46 ± 0.10
Eye symptoms	4.94 ± 0.14	3.16 ± 0.17	2.38 ± 0.16
Emotional symptoms	4.68 ± 0.26	2.94 ± 0.23	2.05 ± 0.14

0864 | Tolerability of concentrated extract of house dust mite carbamylated allergoid delivered at high frequency to allergic patients in a period of 6 months

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Introduction: The practice of sublingual immunotherapy (SLIT) for allergic rhinitis due to house dust mites (HDM) has traditionally followed a continuous posology and long-term schedules for perennial allergens. Recently, the possibility to achieve rapid clinical benefit only after 4 months was shown, with parallel movement of immunological response parameters within 1 year, if the treatment schedule is adjusted with increase in allergen dose and frequency of administrations.

Objectives: Twenty-three patients (14 males, age 14-69) allergic to HDM (16 with rhinitis and asthma, 4 with asthma alone, 3 with rhinitis alone) admitted to the center in May 2016 were treated with named-patient SLIT drops, based on standardized carbamylated allergoid extract of HDM (50% Dermatofagoides pt., 50% Dermatofagoides f. at concentration of 30 000 UA/ml). The build-up phase was administered in doctor's office, monitoring patients for 30 minutes (1 drop [1500 UA]/day for 1 week, 2 drops/day for 1 weeks, 4 drops/day for 1 week, 6 drops/day for 1 week). A maintenance duration of at least 12 months (6 drops/day for 7 days a week) was planned, in order to observe a late immunological response through specific IgG4 serum dosage. The frequency of adverse events during the first 6 months is herein reported.

Results: Eleven (48%) out of 23 treated patients did not report any adverse event. Reached the maintenance phase, 2 patients interrupted without reasons related to the treatment, and 1 patient complaining drowsiness after the administration. Lingual tingling was reported by 3 (13%) subjects (for 2 till the second administration and for 1 till the fourth, of 2 drops/day). Sneezing was referred by 4 (17%) subjects (1 patient only at the first administration of 1 drop/

day, the others with 2 drops/day in 1, 3 and 4 cases respectively), conjunctival itching by 1 (4.5%) subject (in 4 circumstances with 1 drop/day) and tearing by another subject (at first administration of 1 drop/day). One subject reported face and itchy throat in 3 circumstances after 1 and 2 drops/day. All mentioned symptoms were transient, mild and not recurred in the subsequent phase of maintenance. No serious adverse events were reported and adrenaline was never used.

Conclusions: The incidence of treatment likely related adverse events appears within the expected frequency of a SLIT course. HDM carbamylated allergoid at the dose used appears sufficiently tolerated when administered on a daily basis.

0865 | Effect of immunotherapy with a subcutaneous polymerised mites extract on degranulation of basophils

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Introduction: Allergen immunotherapy has been described as the only treatment able to modify the natural course of the allergic disease. We aimed to assess the effect of immunotherapy with a polymerised extract of mites on several mechanisms involved in the development of tolerance. The main objective was to assess in CD-sens (inverse of the concentration of allergen to induce degranulation of 50% of basophils) and secondary objectives to assess changes in other laboratory, functional and clinical parameters. We show here some preliminary data of our results

Objectives: Children with asthma +/− rhinitis, sensitised to mites, received a subcutaneous product of polymerised allergens of Dermatophagoides pteronyssinus and Dermatophagoides farinae on a regular monthly basis. Data were collected on symptoms of asthma and rhinitis, use of medication, respiratory function (spirometry and impulse oscillometry), skin prick tests, serum specific IgE and IgG4, and CD-sens. Data at baseline and at a 1-year follow up visit were compared with the Wilcoxon rank test for paired samples, with the SPSS 15.0 software.

Results: We present results of the first 19 patients. There was a trend towards improvement on CD-sens (mean rank baseline/1 year: 11.2/8.0; $P = .12$). There was an increase on IgG4 in whom specific IgG4 was available for the two time points (0/3; $P = .043$). Respiratory function showed discrepant results with trends to improvement on peripheral reactance (X5) and to worsening on central airways resistance (R20) or flow (FEV1). There was no practical change on rhinitis symptoms but a mild improvement on asthma symptoms, although there was a trend to use less medication (4.8/3.5; $P = .11$).

Conclusions: The low number of patients precludes clear conclusions. Trends point to an earlier effect of immunotherapy on underlying cellular mechanisms (CD-sens), immunoglobulins (IgG4), and peripheral reactance, while changes on clinical and some functional parameters may take longer.

0866 | Effectiveness of slit for birch and house dust mite in patients with allergic rhinitis

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Introduction: Allergen immunotherapy (AIT) is immune modifying and casual treatment for allergic subjects, especially patients that do not respond well to conventional pharmacotherapy. AIT improves symptoms of allergic rhinitis and allergic asthma. By the literature, the outcome of patients treated with AIT for birch is better than AIT for house dust mite.

Objectives: Patients with allergic rhinitis treated with sublingual immunotherapy (SLIT) filled questionnaires after at least 1 year of therapy. Additional to general data we got information about sensitization, symptoms and use of additional pharmacotherapy before and at least 1 year after SLIT therapy. For evaluation of SLIT we used homogenous combined symptom medication score (CSMS). T test was used to compare improvement of symptoms and reduction of medication in both groups.

Results: We included 38 patients, 22 men and 16 women, average 37 years old. 21 have SLIT for 1 allergen, 16 for two allergens and 1 for 3 allergens, 21 of them for birch, 20 for dust mite allergen and three of them have SLIT for both. CSMS before SLIT for birch group was 3.4, for dust mite group 3.1 and after at least 1 year of SLIT it was 2.3 and 2.0, respectively ($P < .01$).

Conclusions: In our group, the most common reasons for allergic rhinitis were birch and house dust mite. SLIT for birch is as successful as for house dust mite in patients with allergic rhinitis. CSMS improved significantly for both groups after at least 1 year of therapy.

0867 | Routine clinical management of children and adolescents with house dust mite allergy in France

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Introduction: House dust mites (HDM) are the most prevalent inhaled allergen worldwide for allergic diseases such as allergic rhinitis (AR) and asthma.

Objectives: PROTECT, a nationwide, multicenter, observational, pharmacoepidemiologic study performed in France, describes the routine clinical management of children/adolescents presenting with HDM allergy by allergists, as a function of the patient's clinical profile. It consisted in 2 phases: a cross sectional and a longitudinal phases. Each physician, included the first 8 patients aged 5-17, allergic to HDM coming spontaneously in allergology clinics, who met the selection criteria and agreed to participate. Patients, who initiated sublingual immunotherapy (SLIT) with HDM at the end of the consultation, were included in the longitudinal phase. Data were collected during two consultations at inclusion (a case report form (CRF) filled out by the physician and a patient self-questionnaire) and during the follow-up visit 6-12 months after SLIT initiation (a follow-up CRF filled out by the physician and a follow-up patient self-questionnaire).

Results: 196 allergists recruited 1468 eligible patients (mean ± SD age: 10.1 ± 3.2). The mean delay for a specialist consultation was 3.5 ± 3.1 years and 38% of patients consulted directly a specialist. SLIT with HDM was initiated in 1313 patients (89%). The main reason for SLIT prescription was to prevent the evolution of the disease and to reduce allergy symptoms impacting quality of life of the patients. Among the SLIT initiated 51% suffered from at least 2 allergic manifestations (AR, 98% allergic conjunctivitis 39% and asthma 49%); 56% suffered from persistent moderate severe AR. 67% were monoallergic to HDM. Polysensitization and polyallergy were barriers to AIT prescription, 23 and 15%, respectively. The mean ± SD time interval between inclusion and initiation of AIT was 14 ± 19 days. 97% of patients were ready to start a long course of treatment and stated that the physician's explanations helped to convince them to take the treatment. According to the physician 89% of the patients on SLIT showed good adherence and 85% were satisfied or very satisfied with SLIT. 85% of the patients said that SLIT was effective, and were generally satisfied.

Conclusions: In real-life practice in France, HDM SLIT is primarily prescribed to children and adolescents suffering from persistent, moderate/severe AR and comorbidities. Both patients and physicians considered SLIT HDM as effective and were satisfied by the treatment.

0868 | Non-allergic rhinitis: new adjuvant treatment with probiotic formulation

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Introduction: Non-allergic rhinitis (NAR) is characterized by the presence of an inflammatory infiltrate and a non-IgE-mediated pathogenesis.

Objectives: This retrospective, controlled, multicentre study investigated whether a symbiotic, containing *Lactobacillus acidophilus* NCFM, *Bifidobacterium lactis*, and fructo-oligosaccharides, prescribed as complementary therapy to a standard pharmacological treatment, was able to reduce symptom severity, endoscopic features, and nasal cytology in 93 patients (49 males and 44 females, mean age 36.3 ± 7.1 years) with INAR. Patients were treated with nasal corticosteroid, oral antihistamine, and isotonic saline. At randomization, 52 patients were also treated with symbiotic as complementary therapy (group A), whereas the remaining 41 patients served as control (group B). Treatment lasted for 4 weeks. Patients were visited at baseline (T0), after treatment (T1), and after 4-week follow-up (T2).

Results: All patients completed the study; the treatments were well tolerated and no clinically relevant adverse event was reported. Adjunctive symbiotic treatment significantly reduced the percentage of patients with symptoms and endoscopic signs, and diminished inflammatory cells.

The Δ change was −34% between T1 and T0 and −52.7% between T2 and T0 in Group A ($P < .01$), and −9.4% and −26.9% at the same time in Group B ($P < .01$) in nasal obstruction evaluation. With Rhinorrhea symptom evaluation, the Δ change was −38.2% between T1 and T0 and −41.2% between T2 and T0 in Group A, with −20% and −28.5% at the same time in Group B. Group A also showed a significant decrease in the percentage of patients with hyperactive turbinate, eosinophil and mast cells (group A 39.5%, 70.4%, 88.5% vs group B 25%, 54.1, 54.5 respectively).

Conclusions: In conclusion, the present study demonstrates that a symbiotic was able, as adjuvant treatment, to significantly improve symptoms, endoscopic features, and cytology in patients with NAR, and that its effect may be long lasting.

0869 | Analysis of sensitization profile to airborne allergens of Ukrainian children and efficiency of slit to the most common allergens in the atopic dermatitis treatment

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Introduction: AD is one of the most frequent allergic disease in the first years' children. In the pathogenesis of the disease the role of sensitization to the common airborne allergens (AA) plays important role but still need more research. The aim of the study was to analyze the sensitization profile (SP) to AA of Ukrainian children with AD and determine role of SLIT in the treatment of AD.

Objectives: Under our supervision were 311 3-years children with AD. The severity of AD was evaluated by SCORAD scale. The levels of antigen specific IgE (Bet v1, Phlp1,5b, Asp fumigatus, Clad herbatum, HDM (Derp1, Derp2, Derp5), epidermis of dog and cat, Asp niger, Alt alternate, Artemisia, Ambrosia) were performed by singleplex analysis. After analyzing the SP the group of MS children were formed and SLIT were performed.

Results: 94 children were not sensitized to any AA; 81 children were MS and 136 children were polysensitized (PS) (2-5 allergens). Comparing the severity of AD and SP have shown, that PS children have more severe AD (SCORAD 31 $\pm$ 10.2) comparing MS children (19 $\pm$ 6.4) and children without sensitisation (20 $\pm$ 7.2), $P < .001$.

Group 1

	HDM sensitization			Severity of AD (SCORAD)			Bronchial asthma manifestation
	Derp1	Derp2	Derp10	Before treatment	After 6 month	After 2 years	
1.	2.15	75	0.01	55	40	28	+
2.	8.35	9.44	0.02	18	15	10	
3.	3.11	12.7	0.02	27	23	21	+
4.	10.5	0.01	0.01	31	26	21	+
5.	0.18	21.7	0.01	48	39	22	+
6.	19.8	76.5	0.02	34	30	21	
7.	48.9	0.54	0.01	36	21	20	+
8.	23.1	3.54	0.01	57	40	28	
9.	5.22	15.3	0.03	45	34	26	+
10.	0.11	18.5	0.01	19	15	10	+
11.	9.6	14	0.02	29	18	12	+

Group 2

	HDM sensitization			Severity of AD (SCORAD)			Bronchial asthma manifestation
	Derp1	Derp2	Derp10	Before treatment	After 6 month	After 2 years	+
1.	100	100	0.01	47	40	14	
2.	13.5	37.1	0.02	31	25	18	
3.	37.4	90.1	0.02	51	42	21	+
4.	87.4	100	0.04	27	24	No symptoms	
5.	14.3	32.5	0.02	43	36	17	+
6.	0.12	45.4	0.01	55	43	25	
7.	0.01	33.14	0.02	21	15	10	
8.	0.02	27.6	0.01	16	10	No symptoms	
9.	0.01	21.4	0.02	32	23	24	
10.	56.4	60.2	0.01	34	25	12	+
11.	7.12	29.6	0.02	41	33	15	
12.	16.4	36.2	0.01	24	18	No symptoms	

The study shown the high levels of sensitization to HDM (n = 93), Alt Alternata (n = 61), epidermis of cat (n = 51) and dog (n = 42). Low levels of sensitization were to pollen allergens and internal mould.

23 child were MS to the Derp1 or/and Derp2. Children were divided in two groups (Table 1 and 2) and in the second group (12 children) the treatment was supplemented with SLIT to the HDM. Children were under observation up to 5 years.

During first 6 months there were no significant difference in the severity of AD in groups.

After 1.5-2 year of treatment there are significant different in severity of AD: (3 mild and 8 moderate in the 1-st group and 7 mild, 2 moderate and 3 children without clinical signs in the 2-nd group).

Also, in the 2-nd group the presentation of dermato-respiratory syndrome was significantly lower (8 children with bronchial asthma in the 1-st and 3 children in the 2-nd group).

Conclusions: The high quantity of polysensitized children to the common airborne allergens which associated with severe AD need to research and designing the new shems of providing immunotherapy.

HDM plays the main role in Ukrainian children with sensitization to the common airborne allergens.

The role of SIT to the HDM in the treatment of AD need more investigation and could be considered like prophylactic of dermato respiratory syndrome realization.

0870 | The analysis of safety and effectiveness of allergen immunotherapy for hymenoptera venom allergy

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Introduction: Allergen immunotherapy with hymenoptera venoms (VIT) is only causal treatment of hymenoptera venom allergy (HVA). Despite many studies there is a lot of controversies about factors affecting efficiency and safety of VIT.

Objectives: To analyse the factors influencing the sting reaction severity, safety and effectiveness of VIT the study group included 246 adult patients treated with VIT in Department of Allergology at Medical University of Gdańsk. Group consisted of 119 patients who completed their 5-year course of VIT till the end of 2014 and 127 patients, who were treated with VIT in the period 2010-2014. The patients were asked for the progress of their HVA symptoms, treatment and comorbidities using constructed questionnaire.

Results: Among 246 patients 54 underwent field stings during or after VIT, 3 of them (5.5%) reacted with anaphylaxis. We observed significant improvement in the average severity of sting reactions, both in the group under (P = .001) and after VIT (P < .001). There was a significant influence of coexistence of mastocytosis (P = .0325), cardiovascular (P = .0352) and autoimmune diseases (P = .0037) on average severity of sting reactions. We also noticed correlation between severity of the reactions and age of the patients in the group during VIT (r = .23; P < .05). Therapy with bee venom in the group after VIT (P = .0042) and increased tryptase among allergic to wasp venom (P = .0317) were raising a risk of VIT adverse reactions. Effectiveness of immunotherapy was conditioned, only in the group during VIT, with bee venom therapy (P = .0187) and with length of VIT (r = −.37; P < .05).

Conclusions: Analysis of clinical outcomes of the treatment showed the effectiveness of the immunotherapy in the study group which is comparable with literature data reported in other countries. A clinical factors having a significant influence on the severity of the reaction after stinging, a safety and effectiveness of VIT were co-occurring mastocytosis, cardiovascular and autoimmune diseases, age of the patients, tryptase concentration, bee venom therapy and duration of VIT.

0871 | Efficacy of the subcutaneous immunotherapy performed in a woman with a whole body extract of pseudomyrmex ant, in Argentine

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Introduction: Although most allergic reactions to fire ants are caused by *Solenopsis invicta*, regarding ants from *Pseudomyrmex* genera, only two cases of anaphylaxis by *P. ejectus* have been described in EEUU. However, events due to the species *Pseudomyrmex acanthobius* o *Pseudomyrmex favidulus* have not been registered to date

Objectives: The aim of this work is to report a patient case with anaphylaxis by *Pseudomyrmex* ant sting, prepare an extract with the specific whole ant body, to study their biochemical and immunological properties and to validate the efficacy of the subcutaneous immunotherapy with this non-commercial extract.

Results: The argentine woman patient, 19 years old, with background of allergic rhinitis and bronchial asthma in the childhood, presented repeated episodes of anaphylaxis by non-identified insect's stings and previous immunotherapies treatment. Once identified the aggressor insect, the entomologic result revealed that it was an ant belonging to *Pseudomyrmex* genera and to two possible species *P. acanthobius* or *P. favidulus*. The biochemical determination showed high serum total levels of IgE (202 UI/ml). The in vivo intradermal test revealed a positive 6-mm wheal and flare reaction (extract dilution 1/100 000). The silver stained SDS-PAGE of the extract of this less common specie of ant showed protein bands since 20-220 kDa.

The patient sera recognized allergenic extract bands at approximately 160, 90, and a double band at 42/46 kDa prior to desensitization treatment. Interestingly, post immunotherapy the mentioned double band practically disappeared. The specific subcutaneous immunotherapy was performed by a conventional scheme of slow progression. The tolerance to the treatment was good, although she suffered an accidental sting during the ascent stage causing anaphylaxis and a second one during the maintaining stage presenting only local normal reaction. After a 6-years-treatment, the total IgE serum values strongly decreased and the specific intradermal test was negative up to 1/10 extract dilution, with histamine used as the positive control.

Conclusions: Altogether, our findings revealed that the immunotherapy performed with allergen extract prepared with whole body of *Pseudomyrmex*, ant was highly effective and that the IgE specific-double bands (42/46 kDa) present in the ant whole body extract, that disappeared after immunotherapy, were responsible for the anaphylactic shock.

0875 | Bacillus Calmette–Guérin immunotherapy enhances cellular immunity against human papillomavirus infection

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Introduction: Recurrent respiratory papillomatosis (RRP) is characterized by recurrent proliferation of benign squamous papillomas within the respiratory tract causing severe airway obstruction. More than 90% of RRP cases are caused by human papillomavirus (HPV) type 6 and 11. Classical surgery does not prevent relapses, and its combination with antiviral drugs or IFN alpha therapy has no significant success and does not completely prevent recurrence of the papillomas. Bacillus Calmette–Guérin (BCG) is a potent modulator of the immune response and has been successfully applied for treatment of superficial bladder cancer and malignant melanoma. The present study investigates the effects of BCG on antiviral immune response in RRP patients subjected to surgery and BCG immunotherapy.

Objectives: Blood samples from RRP patients ($n = 35$) subjected to surgery or combined surgery / BCG-immunotherapy on approved scheme were studied before (0), 6, 12 and 20 months after the start of immunomodulation. The percentage and absolute count of peripheral blood lymphocyte subsets and the in vitro stimulated secretion of Th1/Th2/Th17 cytokines were studied by multicolor flow cytometry in comparison to RRP patients subjected to combine surgery/IFN alpha therapy and to healthy controls. Tumor infiltrating lymphocytes (TIL) isolated from intraoperative biopsies and the cytokine secretions were studied after in vitro stimulation with BCG in comparison to lymphocytes isolated from peripheral blood of healthy individuals.

Results: In RRP patients were observed significantly increased levels of IFNg-secreting CD4 (Th1) and CD8 (Tc1) cells as compared to healthy controls (10.3% vs 5.4% and 13.7% vs 8.4% respectively). Th1 cells were normalized to control reference value after 20 months of BCG immunotherapy. The share of Th17 cells was decreased (0.8% vs 0.5%) and the regulatory T-cells was increased as compared to untreated RRP patients and healthy controls (8.0% vs 5.3% and 4.4% respectively). Also, in vitro BCG stimulation induced the proliferation of mature dendritic cells (30.3% vs 73.4%) and differentiation of plasmocytoid dendritic cells (1.4% vs 8.5%) in RRP patients. In additional, the initially decreased IFNg/IL-4, and IFNg/IL-10 ratios, were restored in the end of therapy.

Conclusions: The BCG immunotherapy stimulates maturation of dendritic cells, restores the cytokine balance and in this way enhances antiviral immune response against HPV-infections.

0876 | Effects of ß–glucan on natural killer cells and their subpopulations in patients after cancer treatment

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Introduction: NK cells and other effector cells of natural immunity are extremely important as they form the first line of anti-tumor surveillance. Immune system activity in cancer patients is endangered by cancer cells environment induced. Expression of some inhibitory molecules results in inhibition of cytotoxic T lymphocytes activity. β–glucans are one of the active natural products compounds responsible for the immunomodulatory effects in wide range diseases including immunostimulatory effects both innate and adaptive response in cancer.

Objectives: We have focused on phenotype of natural killer cells (NK) and NK cells subsets proportions after short term β–glucan supplementation in cancer patients after anti-cancer therapy.

NK subpopulations estimated: cytotoxic phenotype ($CD16^{++}CD56^{\pm}$), regulatory phenotype ($CD16^{\pm}CD56^{++}$); NKT cells ($CD3^{+}CD16^{+}CD56^{+}$) and CR3 expression on NK cells were also measured using flow cytometry with CD3, CD16, CD56, CD45 and CD11b monoclonals (BD Biosciences, USA) in the patients after complex treatment of cancer, who were supplemented with 300 mg/day of β–glucan (group G, $n = 13$) or placebo (group P, $n = 13$) for 60 days.

Results: Assumed increase of NK proportion was found in β–glucan treated patients (from 262 cells/μl to 310 cells/μl, $P < .02$); in

placebo group NK slightly decreased (from 268 cells/μl to 243 cells /μl, $P = .469$). With other estimated NK cells subpopulations there were found no significant changes after supplementation: cytotoxic NK cells in G (91.4% and 92.8%, $P < .15$) and P groups (89.3% and 89.9% $P < .52$); NKT cells in G and P groups (from 9.3% to 8.4%, $P < .12$ and from 8.8 to 6.9% $P < .38$); CR3 expression in NK (from 71.2% to 69.1%, $P < .34$ and from 71.7% to 69.3%, $P < .27$).

Conclusions: Our preliminary data could affirm positive effect of β–glucan supplementation on NK proportion in absolute WBC count. There was no positive effect found on NK subpopulations (mainly cytotoxic) proportion. Probably it would be necessary to estimate more closely the influence of β–glucan dose and time of administration.

MONDAY, 19 JUNE 2017
TPS 21
ASTHMA MECHANISMS

0877 | The anti-inflammatory effects of pentaherbs formula on ovalbumin-induced asthmatic mice model

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Introduction: Allergic asthma is an inflammatory airway disease, affecting as many as 334 million people worldwide. Inhaled steroids have long been used as the major treatment of asthma. Yet, a long-term use of steroids may bring undesirable effects. Previous studies show that pentaherbs formula (PHF), which consists of five traditional Chinese herbal medicines, *flos lonicerae*, *herba menthae*, *cortex phellodendri*, *cortex moutan* and *rhizoma atractylodis* at w/w ratio of 2:1:2:2:2 exhibited therapeutic potential in treating oxazolone-induced atopic dermatitis-like mice model.

Objectives: As allergic asthma and atopic dermatitis are immunologically related to each other, we hypothesize that PHF also poses potential anti-inflammatory and immunomodulatory activities on asthmatic mice. This study aims at investigating the potential anti-inflammatory and immunomodulatory activities of PHF in asthmatic mice model.

Methods: Acute asthmatic mouse models were established by sensitizing the BALB/c mice with an immunogen 20 μg ovalbumin (OVA) - $Al(OH)_3$ by i.p. administration on day 1 and day 15; followed by challenging the mice with the same immunogen on day 27, 28 and 29. PHF water extract (920 mg/kg/day) was administered to the mice by intragastrical delivery twice a day on day 1, 2, 3, 15, 16, 17, and/or from day 22 to 29. One day after the last challenge, the airway hyperresponsiveness was measured in the enhanced pause (penh) value with Buxco Whole Body Plethysmography. Serum were collected for the determination of total IgE and OVA-specific IgE, and inflammatory cytokines and chemokine by ELISA and Multiplex assay, respectively.

Results: Upon a 50 mg/ml methacholine challenge, the penh value of the asthmatic mice under a 14-day PHF treatment is significantly improved when compared to the sham group ($P < .05$). However, an 8-day PHF treatment did not affect the airway hyperresponsiveness of the mice ($P < .05$). Besides, intragastrical administration of PHF to the mice model twice a day does not affect the weight of the mice.

Conclusions: In this study, pentaherbs formula was found to improve the airway hyperresponsiveness of ovalbumin-induced asthmatic mice, indicating the potential use of PHF as a supplement for treating allergic diseases.

0878 | The level of adipokines at patients of young age with bronchial asthma

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Introduction: The bronchial asthma is the one of the most widespread diseases. Today the questions concerning pathophysiological bases of influences of an obesity on bronchial asthma remain open.

Objectives: The aim is to study of clinical and functional features in interrelation with the level of leptin and adiponectin at sintropia of bronchial asthma and nutritional obesity at patients of young age for optimization of antiasthmatic therapy.

133 persons were examined: 93 patients with bronchial asthma were divided into 2 groups taking into account the body mass index (BMI): BMI from 18 to 25 kg/sq.m (1st group) and BMI from 30 to 40 kg/sq.m (2nd group). Control - 40 almost healthy volunteers. Studied: existence of excess weight and definition of degree of obesity, parameters of external respiration, maintenance of a leptin and adiponectin in the peripheral blood.

Results: At all patients with BMI > 30 kg/sq.m an abdominal and visceral obesity became perceptible. According to the spirography at 26.2% of patients of the 1st group, and at 40.5% of patients of the 2nd group were registered moderate obstructive changes in the bronchial tubes ($\chi^2 = 0.53$ at $P = .467$). In group of patients with an obesity expression of obstructive changes in the bronchial tubes was more significant ($P < .05$). When studying level of adiponectin in the peripheral blood its depression in comparison with control in both groups is noted. Adiponectin level in the peripheral blood back correlates with BMI ($r = -.48$, $P = .03$) and is in positive correlation interrelation with the maintenance of lipoproteins of high density in the peripheral blood ($r = -.58$, $P = .03$). The maintenance of a leptin in the peripheral blood increased in comparison with control only at patients of the 2nd group. Positive correlation interrelations between BMI indicators, volume of a waist and leptin ($r = .56$, $r = .42$, $r = .62$ are taped at $P < .05$, respectively) that proves primary influence of fatty tissue on leptinemia level. Expression of bronchial obstruction and a systemic inflammation is interconnected with augmentation of concentration of leptin in the peripheral blood that is confirmed by results of the correlation analysis: FVC ($r = -0.51$, $P = .03$), FEV1 ($r = -0.49$, $P = .025$), IL-6 ($r = 0.69$, $P = .003$).

Conclusions: The received results demonstrate interrelation of an obesity and asthma which is provided with a set the etiopathogenetic of mechanisms, one of which is the imbalance of adipokine in the peripheral blood.

0879 | Flow cytometry analysis of surface molecule expression on in vitro differentiated human macrophages

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Introduction: Macrophages (Mϕ) are innate immune cells that play a key role in lung antiviral immune responses. A model of two major Mϕ types has been developed: M1 (classically activated) and M2 (alternatively activated). We support the hypothesis that the dominant macrophage phenotype in atopic asthmatic subjects is alternatively activated macrophages.

Objectives: Here, we investigated the expression of cell surface molecules on in vitro differentiated human Mϕ, before and after rhinovirus (RV) infection, in order to identify reliable markers for characterization of polarized human Mϕ *in vivo* in stable lung diseases, and during virus-induced exacerbations.

Results: Monocyte-derived Mϕ (MDM) obtained from peripheral blood mononuclear cells of healthy donors were polarized to M1 or M2 by treatment with IFN-γ and TNF-α or IL-4, respectively. Unpolarized MDM (M0) were treated with media alone. M1, M2, and M0 were infected with RV16 at MOI 0.1 (or treated with media alone) and cultured for 24 hours. Adherent, in vitro polarized MDM were detached and the following surface markers were assessed by flow cytometry: CD14, CD36, CD54, CD80, CD163, CD197, CD206 and HLA-DR.

Uninfected M1 cells had increased expression of CD54, CD80 and CD197 ($P < .05$, $P < .01$, and $P < .01$, respectively) relative to uninfected M2 and M0 cells and CD14 ($P < .001$) compare to M2. Additionally, CD14 was up-regulated in M0 ($P < .001$). After RV16 infection, expression of these four M1-associated markers remained increased compared to uninfected M2 cells. There were no differences in the expression of CD36, CD163, CD206 and HLA-DR between infected or un-infected M1 and M2 cells and infected or un-infected M0 cells.

Conclusions: We couldn't find any specific M2 surface markers, but our data suggest that CD14, CD54, CD197 and CD80 could be used to evaluate M1 populations *in* vivo. This work is supported by RSF grant 16-14-10188.

0881 | Activation of eosinophils interacting with bronchial epithelial cells by antimicrobial peptide LL-37 in allergic asthma

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Introduction: The role of antimicrobial peptide LL-37 in asthma exacerbation is unclear, though microbial infections, which is the most common inducer of asthma exacerbation, is accompanied by elevated LL-37 in innate immune cells.

Objectives: The present study is to evaluate the immunopathological roles of LL-37 in allergic asthma.

Results: The present study found that co-culture of eosinophils and bronchial epithelial cell line BEAS-2B significantly enhanced intercellular adhesion molecule-1 on both cells and CD18 expression on eosinophils upon LL-37 stimulation. Inflammatory IL-6, CXCL8 and CCL4 were substantially released in co-culture in the presence of LL-37. LL-37 triggered the activation of eosinophils interacting with BEAS-2B cells in a P2X purinoceptor 7/epidermal growth factor receptor-dependent manner. Eosinophils and BEAS-2B cells differentially contributed to the expression of cytokines/chemokines in co-culture, while soluble mediators were sufficient to mediate the intercellular interactions. Intracellular p38-mitogen-activated protein kinase, extracellular signal-regulated kinase and NF-kB signaling pathways were essential for LL-37-mediated activation of eosinophils and BEAS-2B cells. By using the ovalbumin-induced asthmatic model, we observed that the intranasal administration of mCRAMP (mouse ortholog of LL-37) in combination with ovalbumin during the allergen challenge stage significantly enhanced airway hyper-responsiveness and airway inflammation in sensitized mice.

Conclusions: Results therefore implicated a deteriorating and inflammatory role of LL-37 in allergic asthma. This study provides evidence of LL-37 in triggering asthma exacerbation via the activation of eosinophils interacting with bronchial epithelial cells in the inflammatory airway.

0882 | The prevalence of seasonal asthma and rhinitis in mite allergic patients

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Introduction: House dust mites are generally accepted as perennial allergens, but there are some data suggesting that there were difference in the load of the antigen between the seasons. These changes in the seasons may cause increase in allergic symptoms The aim of this study is to show that mite allergy may cause not only perennial but sometimes also only seasonal asthma and rhinitis.

Objectives: Two hundred fifteen adult patients with the diagnosis of asthma and rhinitis who admitted to adult allergy outpatient clinics between July and December 2016 and had skin prick test positivity for house dust mite antigens were included to the study.

Results: Of 215 patients, 146 were female (67.9%). Mean ages of the patients were 31.72 ± 11.75 years. 50 patients (23.3%) had asthma and rhinitis, 165 (76.7%) only rhinitis. Sixty-two patients (28.8%) had seasonal disease. Of 62 patients, 51(82%) had only rhinitis and 31% of the patients with only rhinitis had seasonal disease.

Conclusions: Mite allergy may not cause only perennial symptoms of the diseases but it can be presented with only seasonal symptoms, so that it should be considered in the patients with only seasonal allergic symptoms.

0883 | Disturbed balance of Treg cell subpopulations in late-onset elderly asthma

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Introduction: Asthma in the elderly (≥ 65 years old) is a disease of emerging concern. However, immunological characteristics of late-onset elderly asthma (asthma onset ≥ 40 years old) have rarely been studied, particularly in terms of regulatory T cells (Treg) disturbance. This study aims to investigate the relative frequencies of circulating $CD4^+Foxp3^+$Treg and subpopulations in late-onset elderly asthma compared to childhood-onset young adult asthma patients and healthy controls.

Objectives: Asthma patients and non-asthmatic controls were recruited from two tertiary hospitals, with predetermined age criteria (elderly, ≥ 65 years old; vs young adult, 18-45 years old). Peripheral blood mononuclear cells (PBMC) were isolated from each participant, and were labeled for CD4, CD25, Foxp3, CD45RA. Tregs were classified into three subpopulations, such as resting Treg (rTreg), activated Treg (aTreg), and $Foxp3^{low}$ non-Treg, according to the CD45RA and Foxp3 expression. Clinical information, such as atopy, serum IgE levels, or the level of asthma treatment required to achieve asthma control, was also collected.

Results: A total of 230 subjects (94 late-onset elderly asthmatics, 68 young adult asthmatics, 28 elderly controls, and 40 young adult controls) were analyzed. The proportion of peripheral blood whole Tregs significantly increased with aging. However, in subpopulation analyses, contrasting trends were observed between rTreg (decreased with aging; $P < .001$) and $Foxp3^{low}$ non-Treg (increased with aging; $P = .023$). No difference was found in aTreg. Within the elderly group, $Foxp3^{low}$ non-Tregs were significantly more frequent among asthma patients requiring higher level of asthma treatment, compared to those with lower level of treatment, or non-asthmatic controls.

Conclusions: This is the first study to suggest that the disturbed balance of Treg subpopulations is involved in the pathogenesis of elderly asthma.

0884 | Exercise-induced dyspnoea: results of a standardized exercise challenge in a cold chamber

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Introduction: Many patients with asthma suffer from exercise-induced dyspnoea. An important differential diagnosis to the exercise induced asthma (EIA) is exercise induced laryngeal obstruction (EILO). EILO compromises several functional disorders of the larynx causing laryngeal obstruction during exercise. The obstruction can affect the supraglottic or the glottic level, also mixed types exists. The estimated prevalence of EILO in the total population ranges from 5.7 to 7.6%. Symptoms of EILO are similar to those of EIA – dyspnoea, throat tightness, cough and inspiratory stridor during exercise. Asthma medication often has little to no effect in patients with EILO. The prevalence of EILO in children and adolescents with/without EIA is not well investigated, nor is it in adults.

Objectives: We wanted to evaluate how many suspected cases of EILO are in a group of patients suffering from exercise-induced dyspnea. Therefore we examined 99 patients aged from 10 to 45 with a standardized exercise challenge in a cold chamber. Before and 5, 10, 15 and 30 minutes after the exercise a spirometry was done.

EILO was defined as a decrease in FVC and $FEV_1 > 15\%$ with a normal FEV_1/FVC without significant change and without significant

rise of residual volume ($FEV_1/FVC > 70\%$, FEV_1/FVC change < 7.5%, RV-rise < 0.5 l).

Results: 73 of 99 patients (33 children and 40 adults; age 19.3 ± 6.0 years, FEV_1 before exercise 93.1 ± 12.0, eNO 36.8 ± 20.0 ppB) showed a significant decrease of $FEV_1 > 15\%$. On average the FEV_1 decreased to 32.3% ± 12.4 (children 32.7% ± 12.6; adults 31.9% ± 12.4; $P = .18$).

3 (9.1%) children and 4 (10.0%) adults showed a reaction fulfilling the defined criteria of EILO.

Conclusions: Prevalence of EILO in children and adults with exercise-induced dyspnoea is underestimated. Patients with asthma in all degrees can additionally suffer from EILO.

Medical history (especially localization of dyspnoea, appearance of inspiratory dyspnoea during exercise and a short time to resolution) and lung function after exercise are important components for diagnosing EILO. But the gold standard is continuous laryngoscopy during exercise.

Therapeutic options are few, little evaluated and thus of weak evidence.

0885 | Cadherin-related family member 3 expression in alveolar type II epithelial cells and primary human nasopharyngeal epithelial cells upon exposure to asthma-related stimuli

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Introduction: Human rhinovirus C (HRV-C) infection was reported to be a major risk factor for asthma exacerbations and wheezing illnesses in children. This respiratory virus has not been widely studied because it was not culturable in standard cell culture until the recent identification of cadherin-related family member 3 (CDHR3) as its cellular receptor on airway epithelial cells. We hypothesized that cellular distribution of CDHR3 in the human airways was associated with host susceptibility to HRV-C infection.

Objectives: This study aimed to investigate changes in CDHR3 expression of the human respiratory epithelial cells upon exposure to asthma-related stimuli.

Results: Both human alveolar type II epithelial cells (A549) and primary human nasopharyngeal epithelial cells were subjected to challenges with dexamethasone, lipopolysaccharide (LPS), and cigarette smoke medium (CSM). CDHR3 expression levels on these respiratory epithelial cells were determined at gene and protein levels using quantitative PCR and western blot. The localization of CDHR3 was detected by immunofluorescence staining. The effects of these stimuli on the susceptibility of respiratory epithelial cells to HRV-C infection were evaluated by the subsequent inoculation with HRV-C isolate. The replication kinetics of HRV-C was assessed by titrating the culture supernatant using CDHR3-expressing H1-HeLa cells. A549 cells incubated with dexamethasone expressed 4-fold higher CDHR3 than control cells at 24 hours post treatment, while LPS induced 8-fold increase in CDHR3 at 48 hours post-treatment. Stimulation with 0.625% CSM upregulated CDHR3 expression by 5-fold and 150-fold at 24 and 48 hours following treatment, respectively. The effects of CSM on the human primary nasopharyngeal epithelial cell culture were consistent to those observed in A549 cells, although primary nasopharyngeal epithelial cells were less responsive to dexamethasone and LPS treatments. CDHR3 expression only increased 2-fold at 48 hours after these treatments.

Conclusions: The exposure of respiratory epithelial cells to asthma-related stimuli such as LPS and CSM can enhance CDHR3 expression. Interestingly, the incubation of these respiratory epithelial cells with dexamethasone, a corticosteroid useful for suppressing asthmatic airway inflammation, can also alter the expression of HRV-C receptor. (funded by Direct Grants for Research [2015.1.055 and 2015.1.058] of CUHK).

0887 | The role of eosinophils and matrix metalloproteinases-2 in airway remodeling

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Introduction: Matrix metalloproteinase (MMP)-2 also known as gelatinase A, is a member of the MMP family of extracellular matrix degrading enzymes with important roles in many physiological and pathological conditions including organ fibrosis, cancer invasion and tissue remodeling. MMP-2 is synthesized and secreted by many cells including fibroblasts. Airway remodeling is considered to be responsible for progressive decline of lung function in asthma, however, the pathogenesis is still be clarified.

Objectives: We hypothesized that eosinophils, major effector cells in asthma, may interact with fibroblasts to release MMP-2 leading to airway remodeling.

Human eosinophils purified from normal adult volunteers and the human fetal lung fibroblast (HFL)-1 cells were co-cultured. Morphological and molecular changes of HFL-1 and the expression of MMP-2 was evaluated by zymography, immunoassays and RT-PCR. Migration of HFL-1 cells stimulated by eosinophils was evaluated using Boyden chamber system.

Results: HFL-1 expressed α-smooth muscle actin and fibronectin after coculture with eosinophils, compatible with myofibroblast phenotype. After the phenotypic change, HFL-1 expressed and released

MMP-2. Then, the transformed HFL-1 cells showed enhanced migratory activity.

Conclusions: Eosinophils may induce fibroblast-myofibroblast transformation (FMT) and stimulate secretion of MMP-2, leading to subsequent migration of fibroblasts. These observations suggest the eosinophils can promote tissue remodeling through FMT and MMP-2.

0888 | Recurrent wheezing 36 months after the first episode of bronchiolitis in infancy: the viral link

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Introduction: Viral respiratory infections are important causes of exacerbations of asthma during childhood. Acute bronchiolitis is a very common viral infection that is also associated with an increasing number of admissions at the paediatric wards. RSV consists the most common cause of acute bronchiolitis during infancy, but rhinovirus has been shown to be a very frequent cause as well. Both viruses have been associated with the development of recurrent wheezing episodes. RSV prophylaxis is already part of the prophylactic scheme in preterm infants. However, it is important to understand whether other than RSV viruses may play an equal or more important role in the development of post-bronchiolitis wheezing episodes that might be the precursor of asthma.

Objectives: To assess the relationship between bronchiolitis and recurrent wheezing development.

Results: Infants who were hospitalized with RV-induced bronchiolitis exhibited statistically more episodes of wheezing at the ages of 6, 12, 18, 24, 30 and 36 months of age ($P < .0001$). The episodes of bronchiolitis caused by both RSV/RV double infection were more strongly associated with wheezing at the above timepoints than those caused by RSV-alone ($P < .0001$), but the difference was not significant when comparing with the RV-alone cases of acute bronchiolitis ($P = .183$ at the age of 36 months old).

Conclusions: This study shows that infants with rhinovirus-induced bronchiolitis presented significantly more episodes of wheezing during the 36 months of follow up ($P < .0001$ at all time points) as compared to those who were hospitalized due to RSV-induced bronchiolitis. The profile of infants with RSV-RV double infection was comparable to those with RV but not RSV single infection. Moreover, RV positive infants reported increased need for treatment during wheezing episodes suggesting that these episodes were more severe as compared to those in the group of patients with RSV-induced bronchiolitis. Therefore, rhinovirus should be considered as an important trigger for wheezing during early toddler years in otherwise healthy term infants. More studies on the role of rhinovirus in late preterm infants who do not receive prophylaxis for RSV are eagerly anticipated.

0889 | Serum leptin and adiponectin levels correlate with mast cell activation during exercise-induced bronchospasm in asthmatic children

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Introduction: Exercise-induced bronchoconstriction (EIB), a form of bronchial hyper-responsiveness (BHR), is common in children with asthma. Hyperosmolar triggering of mast cells and possibly other inflammatory cells results in the release of bronchoconstricting mediators, e.g. cysteinyl-leukotrienes, histamine and prostaglandin D_2 during exercise challenge.

Objectives: The aim of this study was to address the correlation between leptin, adiponectin and exercise induced bronchospasm by measuring urinary metabolites of mast cell mediators such as 9α,11β-PGF_2, LTE_4.

Results: The post-exercise urinary excretion of 9α,11β-PGF_2 in the asthmatics with EIB increased significantly compared with asthmatics without EIB. The post-exercise urinary excretion of LTE_4 was not significantly difference between the two groups. The maximal decreases in % FEV_1 after exercise were positively correlated with leptin levels and negatively with serum adiponectin levels in asthmatic children. Leptin presented positive associations correlated with post-exercise urinary excretion of 9α,11β-PGF_2, LTE_4 and adiponectin presented negative associations correlated with post-exercise urinary excretion of LTE_4.

Conclusions: Serum concentrations of the adipocyte-derived hormones leptin and adiponectin are correlated with EIB/BHR and urinary metabolites of mast cell mediators induced by exercise challenge in asthmatic children.

0890 | Fixed airflow obstruction in patients with asthma

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Introduction: The aim of this study was to assess factors associated with fixed airflow obstruction (FAO) defined as

postbronchodilator $FEV_1/FVC<0.7$ in patients with asthma in real clinical practice.

Objectives: We examined 340 outpatients with mild to moderate asthma and 130 severe asthmatics (ERS/ATS definition, 2014) aged 18-82 years. Pulmonary function tests were measured by dry spirometer (2120, Vitalograph, UK). Atopic status was assessed by positive skin prick-test (>3 mm) and serum specific IgE to common inhalant allergens (house dust mite, animal allergens, pollen). FeNO was measured by a chemiluminescence analyzer (Model LR4000; Logan Research, UK). Asthma control was assessed by using Russian version of ACQ-5.

Results: Among patients with asthma 41% had FAO which was more common in severe compared to non-severe asthmatics (75% vs 29%, $P < .001$). FAO was associated with advanced patient age ($r = .37$, $P < .05$), longer duration of asthma ($r = .24$, $P < .05$), intensity of smoking ($r = .42$, $P < .05$), concomitant COPD ($r = .43$, $P < .05$) and pneumonia during lifetime ($r = .23$, $P < .05$). Patients with FAO had worse (ACQ-5 score ≥1.5) asthma control (71% vs 51%, $P < .05$), higher number of exacerbations during last year (1.8 vs 1.5, $P < .05$) and disability rate (51% vs 18%, $P < .001$). Doses of inhaled steroids (ICS) (955 mg BDP daily vs 756 mg, $P < .001$) and rescue medication use (5.2 puffs per day vs 2.5 puffs, $P < .001$) were higher in this group compared to patients with reversible airway obstruction. Body mass index, atopic status and markers of eosinophilic airway inflammation (FeNO and eosinophil counts in blood) were not associated with FAO.

Conclusions: FAO was more common in severe asthmatics, in older patients with longer duration of the disease and history of smoking. This phenotype is characterized by worse asthma control, higher exacerbation rate and frequency of disability compared to patients with reversible airway obstruction.

0892 | Exercise induced asthma: when the disease is not an excuse

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Introduction: Exercise induced asthma is a common pathology in the pediatric population, it describes the acute onset of bronchoconstriction occurring during or immediately after exercise.

Objectives: Characterize the pediatric population diagnosed with asthma and/or rhinitis who had shortness of breath with physical exercise and were submitted to a treadmill exercise challenge test.

Methods: Retrospective analysis of clinical processes of pediatric patients with asthma and/or rhinitis submitted to treadmill exercise challenge tests due to shortness of breath with physical exercise between January 2014 and December 2015.

Results: 20 patients were evaluated, aged 7-17, 60% being girls. The most common diagnostic was asthma and rhinitis (50%), followed by the patients with just asthma (40%), and finally the patients only with rhinitis (10%). In 14 patients (60%) the treadmill exercise challenge test was negative. Only 6 (40%) patients had a positive test, 4 of them were athletes, all diagnosed with asthma. 70% of the patients were treated with short-acting beta-agonists before exercising.

Conclusions: Shortness of breath, tiredness or cough can be common symptoms in the pediatric population, at different ages and athletic levels. The treadmill exercise challenge test is a fundamental tool in diagnosing exercise induced asthma, allowing us to identify the patients that have significantly decreased pulmonary function during exercise. Despite the symptoms being present in all patients, only a small percentage of tests were positive, which can be explained by the poor physical condition of the patient and not by the pathology itself. The majority of the patients was treated with short-acting beta-agonists before exercising, but after the negative results of the treadmill exercise challenge this percentage was decreased and matched the amount of positive tests. As it has already been demonstrated in other studies, there is also a high percentage of positive tests in professional athletes.

MONDAY, 19 JUNE 2017
TPS 22
NUTRITIONAL AND PSYCHO-SOCIAL ISSUES IN FOOD ALLERGY

0893 | Effects of allergenic food diversity and avoidance on the risk of IgE sensitization in the first year of life

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Introduction: The timing and effects of introducing allergenic foods into the diet of infants on allergy prevention remains unclear. We aimed to investigate allergenic food diversity and avoidance in relation to the risk of allergic sensitization during infancy.

Objectives: Subjects ($N = 272$) were enrolled from the Prediction of Allergies in Taiwanese CHildren (PATCH) birth cohort study. Detailed information about the feeding practices and food diversity toward six allergenic foods (fruits, egg white, egg yolk, fish, shellfish, and peanuts) was obtained using age-specific questionnaires for infants at 6 and 12 months of age. Fecal secretory IgA, eosinophil cationic protein (ECP), and serum levels of total and allergen-specific IgE were also measured in infants at 12 months of age.

Results: Allergenic food diversity was significantly lower in infants who were IgE sensitized at 12 months of age (3.2 ± 1.4 items vs 3.7 ± 1.3 items, $P = .006$). Compared to infants introduced to 0-2 allergenic food items, infants introduced to 5 or more (OR, 0.61; 95% CI, 0.43-0.86) or 3–4 allergenic items (OR, 0.62; 95% CI, 0.40-0.93) showed significantly reduced risks of IgE sensitization. Additionally, egg white and yolk avoidance by 12 months of age was associated with IgE sensitization (OR, 1.41; 95% CI, 1.11-1.79 and OR, 1.26; 95% CI, 1.07-1.48, respectively), as well as to food sensitization.

Conclusions: Based on our results, we suggest that increased oral antigenic stimulation through increased allergenic food diversity, particularly through introduction of eggs during infancy, confers protection against IgE sensitization.

0894 | IgE sensitization to food allergens and food allergy manifestation in children following different vegetarian diets (first results)

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Introduction: In today's world, the popularity of vegetarian diets has increased dramatically over the past few decades, and many parents encourage their children to pursue this type of diets. Increased interest in non-traditional diets (vegetarianism and pescetarianism) is observed in Russia as well. However, a nutritional status and health of children following unconventional diets have not been studied in Russia.

Objectives: To assess an IgE sensitization to food allergens and food allergy manifestations in children following different vegetarian diets.

Results: The study included 30 children aged 1-17 year following different restricted diets: lacto-ovo-vegetarian (9), lacto-vegetarian (11), ovo-vegetarian (1), vegan diet (4). The IgE levels to several food allergens (cow's milk, soy, beef, pork, egg white, fish (cod), wheat, chicken) were measured in blood samples by UniCAP.

Self-reported (or parents-reported) allergic reactions to food had 18 children from 30 (60%). 4 patients had diagnosed atopic dermatitis, 1 – oral allergy syndrome, 13 had recurrent skin symptoms. 6 patients had sIgE sensitization to 1 and more food allergens. Increased sIgE level was detected only in children with food allergic manifestations. IgE sensitization to cow's milk proteins (≤ 3.5 kUA/l) was found in 4 (13.3%) children (2 lacto-ovo-vegetarians, 1 lacto-vegetarian, 1 vegan). 4 (13.3%) children (2 lacto-ovo-vegetarians, 1 lacto-vegetarian, 1 vegan) had IgE sensitization to egg white (≤ 17.5 kUA/l). 2 patients had sensitization to soy, 2 – to wheat, 1 – to fish. Multiple sensitization was found in 3 children. One boy following vegan diet was sensitized to 5 food allergens (cow's milk, soy, fish (cod), wheat).

Conclusions: Food allergy and IgE sensitization to food allergens are common conditions in children following different vegetarian diets.

0895 | Excessive food elimination by pediatricians in food allergic infants and their mothers

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Introduction: The prevalence of food allergy (FA) has increased in recent decades. Food allergy has different clinical presentations based on the immunological mechanisms.

Objectives: In this study, we aimed to determine the clinical approach of the pediatricians for the diagnosis and management of the FA. One hundred and seventy pediatricians from different cities of Turkey fulfilled a questionnaire including 24 multiple-choice or fill-in-the-blank questions.

Results: Sixty-nine percent of the participants were pediatricians, 17% were pediatric allergists, and 13% were pediatric gastroenterologists. Ninety percent of participants claimed that they took care of FA patients. Among the participants 83% reported that they offer diet elimination for children with FA and 82% for their breastfeeding mothers. The most frequently eliminated foods in children's and mothers' diet are as follows, respectively: Cow's milk (79-86%), egg (51-50%), peanut (48-43%), hazelnut (44-36%), shellfish (27-28%), food with additives (21-26%), walnuts (29-25%), almonds (28-25%), soy (17-23%), fish (23-21%), strawberry (22-21%), tomato (20-18%), sesame (16-17%), cacao (17-14%), cow's meat (10-14%), kiwi (17-14%), orange (8-12%), blackberry (11-9%), sheep meat (4-8%), grapefruit (7-7%), mango (7-7%), bananas (7-6%), mandarin (8-6%), goat meat (3-6%), chicken meat (3-5%), gluten (8-7%), lentil (6-5%), lemon (4-5%). The subgroup analyses revealed that only 1 food was eliminated in 21% of mothers and 19% of infants' diet, 1-5 foods in 51% and 48.5%, 5-10 foods in 21% and 26%, more than 10 foods in 28% and 35%, respectively. Eighty-three of participants offer calcium supplement for the mother who are on dairy elimination and 60% consult the patients with a dietitian. Twenty-four percent of respondents postpone starting of complementary feeding over 6 months.

Fifty percent of the participants reported blood in stool as an IgE-mediated FA symptom and 19% reported anaphylactic reactions as a presentation of non-IgE-mediated FA.

Conclusions: Elimination diets are suggested by a great majority of the pediatricians for both children and breastfeeding mothers and this elimination covers a large number of food groups even the ones known to be non-allergic for most of the time. It is noteworthy that participants could not differentiate IgE-mediated and non-IgE-mediated FA findings with 100% accuracy. The introduction of interdisciplinary education programs can be proposed.

0896 | The role of a dietitian in the management of wheat-dependent exercise-induced anaphylaxis

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Introduction: Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a distinct form of food allergy, occurring when wheat consumption is combined with a triggering co-factor e.g. exercise or alcohol. Its manifestations range from urticaria / angioedema to anaphylaxis. Patient education and dietary counselling should be offered to prevent further episodes of WDEIA.

Objectives: A retrospective case series review of patients with WDEIA from 2 major UK allergy centres to determine the impact of dietitians' input and dietary changes on the overall management of these patients.

Results: Out of the 73 patients diagnosed with WDEIA only 18 (24.6%) were seen by a specialist allergy dietitian. All changed their diet; the majority (94%) started a gluten-free diet. 55 patients (75.4%) were not reviewed (not referred or no allergy dietitian available). Lack of the review was associated with a 3-fold increase in the frequency of post-diagnosis reactions ($P < .05$). Although they were mostly mild, 2 patients reported severe anaphylaxis.

Conclusions: WDEIA patients are less likely to develop further allergic reactions post-diagnosis if a dietitian is involved in their care. Specialist allergy dietitians play a key role in the management of patients with WDEIA and should be an integral part of the multidisciplinary team in all centres managing WDEIA.

0897 | Allergy service dietetic support and food challenge testing: variation in practice

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Introduction: Improving Quality in Allergy Services (IQAS) accreditation sets a minimum level of dietetic support for food allergy services. Dietetic support provides evidence based, tailored advice empowering patients to avoid inappropriate dietary restrictions, prevent nutritional deficiencies and reduce anxiety around foods.

Objectives: A multi-centre survey was completed investigating levels of dietetic support and service parameters, and also investigated practices around food challenge testing.

Results: A high level of variation was identified in the provision of dietetic input for food allergy patients ranging from no input available to varying lengths of appointment time. There was general consensus around offering food challenge to patients who were likely to reintroduce the food back into their diet. Availability of double blind challenge testing was low. There were differences with regards to the location of low risk food challenge testing; some centres performed hospital challenge for all patients regardless of risk whereas other centres supported low-risk patients to self-challenge at home.

Conclusions: Variations in levels of dietetic support and practice have been identified due to a number of underlying causes with potential impact on the provision of clinical services to patients.

0898 | Nutritional status and growth in children with food allergies

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Introduction: Food allergy is an increasing problem worldwide particularly in developed countries. Cow's milk is the most common food allergen in infants. The current treatment of food allergies is strict elimination diets. The elimination of food from the diet, especially elimination of milk, could results in poor nutrient intake and impaired growth in children because milk is the main source of nutrients and in some cases, as in children under two years, is the fundamental food.

Objectives: A systematic review of the literature was conducted and a critically analyze of the articles was established.

Results: Most of the articles consulted show that children with food allergies, and especially in children with cow's milk allergy, have a nutritional deficiencies (decreased levels of calcium and vitamin D) and / or impairment growth (shorter than controls), that in some cases are present in despite the use of hypoallergenic formulas and / or nutritional supplements.

Conclusions: Nutritional evaluation is essential in the treatment of children with food allergies.

0899 | Longitudinal study shows improved nutrient intakes and growth with an amino acid formula for children age = 1 years with cow's milk allergy and related conditions

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Introduction: CMA and related conditions require food allergen avoidance which may lead to dietary restriction, inadequacy and poor growth if persisting into childhood. This longitudinal study investigated the effect of a specially formulated amino acid feed for children ≥1y on nutrient intake and growth.

Objectives: 30 patients(mean age 2 years 7 months) already established on AAF(n = 24) or alternative milks (soya, coconut, oat, breast milk) (n = 6) for food allergy (83%, mostly multiple), intolerance (7%), reflux (7%), EOE (3%), with or without other complex conditions (autistic spectrum disorder, ventricular septal defect, microcephaly, Simpson-Golabi-Behmel syndrome, metopic craniosynostosis, duplex kidney) were recruited to receive a nutritionally complete study AAF (Nutricia) with optimised palatability and micronutrient profile for those aged ≥ 1 years (mean prescription 510 kcal/d (SD370), 544 ml/d (SD279) as 0.69-1 kcal/ml (87%); taken orally (83%) or by tube (17%)) for 4 weeks. Compliance, nutrient intakes, weight, height, and head circumference (HC)) were recorded at baseline(BL) and Wk 4.

Results: Compliance to study AAF was 92%(SD39). Energy and protein intakes were stable (+72 kcal, +2.1 g, NS). Intakes of most micronutrients improved (significant for zinc (+1.46 mg), copper (+0.19 mg), vitamin B2 (+0.46 mg), $P \leq .05$), with more patients achieving RNIs for most micronutrients at Wk 4 vs BL (significant for zinc (77% vs 53%); copper (97% v 73%); vitamins B6 (90% v 67%) and B2 (97% v 67%), $P \leq .05$). In patients not receiving BL AAF (n = 6), intakes for all micronutrients improved except vitamin B12 (−0.1 μg, NS) (significant for magnesium (+34.2 mg); zinc (+2.3 mg); copper (+0.17 μg); folate (+32.9 μg); pantothenic acid (+1.6 mg); vitamins D (+2.4 μg), C (+18.9 mg), B2 (+0.55 mg) and B3 (+5.6 mg), $P \leq .05$) and more patients achieved RNIs at Wk 4 than BL (mean 75% v 9% for all micronutrients). Weight (+0.41 kg, z-score +0.23, $P \leq .05$), height (+1.60 cm, z-score +0.34, $P \leq .05$) and HC (+1.11 cm, P = .07; z-score +0.25, P = 0.01) increased. Parents reported the study AAF was enjoyed by the patient (taste 68%; texture 72%) and preferred to any previous AAF taken(73%). Gastrointestinal and allergic symptoms remained well managed.

Conclusions: Use of a specially formulated study AAF for children ≥1 years with CMA and related conditions, improves intakes of most micronutrients and growth, due to excellent compliance and continued dietary management of allergic symptoms. Longer term, controlled studies are required to more fully assess outcomes.

0900 | Treatment of SNAS only with diet or with diet + tionickel: evaluation of the blinded challenge at T0 (start) and after 36 months of therapy

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Introduction: The SNAS (Systemic Nickel Allergy Syndrome) appears with symptoms in various organs (oculorhinits, asthma,

eczema, urticaria, abdominal pain, diarrhoea) in a fair percentage of patients suffering from proven ACD (Allergic Contact Dermatitis), caused by hypersensitivity to nickel.

Objectives: The aim of the study is to evaluate the tolerability of the oral intake of nickel in patients with SNAS through blinded challenge "in vivo" with nickel in 2 patients Group (Group A: only diet and Group B: diet + Tionickel Lofarma) at the beginning of the treatment (T0) and after 36 months of therapy.

The research was carried out on 66 patients over a period of 36 months.

62 females and 4 males aged between 18 and 68 (average age 36).

Group A: 26 patients opted to follow the mere low-nickel diet.

Group B: 40 patients chose to follow a low-nickel diet + desensitization with Tionickel.

Results: Group A (only low-nickel diet): 26 patients.

7 patients with unchanged challenge at T0 and after 36 months of therapy.

19 patients with different level of tolerability to the challenge:

T0 After 36 months.

-2 patients 10 ng —-> 20 ng.

- 13 patients 100 ng —-> 200 ng.

- 4 patients 100 ng —-> 500 ng.

Group B (low-nickel diet + Tionickel): 40 patients.

- 2 patients have interrupted the study for pregnancy.

- 7 patients have interrupted the study for side effects due to Tionickel (severe eczema).

- 31 patients with different level of tolerability to the challenge:

T0 After 36 months.

-2 patients 10 ng —-> 20 ng.

-7 patients 100 ng —-> 200 ng.

-4 patients 100 ng —-> 500 ng.

-18 patients 100 ng —-> 1500 ng.

Conclusions: Patients of Group B (diet with low-nickel diet + Tionickel) have a better tolerability (in terms of number of patients and tolerability dose of nickel) to the blinded challenge test "in vivo" after 36 months of study, compared with patients in Group A (only low-nickel diet).

In particular, Group A showed an improvement of the challenge after 36 months in 73% of the cases studied. Group B showed an improvement of the challenge after 36 months in 82% of the cases studied.

All patients of Group B who completed the study have obtained improvements in the challenge at 36 months, except for 7 patients who had interrupt the study for serious side effects from Tionickel.

0901 | The effects of individualized nutrition intervention on the disease severity and nutrition status in the children with atopic dermatitis and food allergy

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Introduction: Atopic dermatitis (AD) is the chronic inflammatory skin disease, and food allergens and nutrients are closely related to the AD in children. While elimination of causative foods is he mainstay of treatment, excessive restriction might induce unnecessary limitations in the food intake, consequently leading to nutritional deficiencies and poor growth.

Objectives: This study aimed to identify the characteristics and nutritional status in children with AD and food allergy and also investigate the effects of individualized nutrition intervention.

Methods: We retrospectively reviewed electronic medical records of 77 pediatric AD patients admitted to the department of Pediatrics, Chungnam National University Hospital, Daejeon, Korea. The patients were received 4 months of individualized nutrition intervention with food allergen elimination diet. The patient characteristics, nutrient intake status, clinical status and severity of AD using SCORAD index were analyzed before and after individualized nutrition intervention. In the anthropometric measurements, the standard deviations for weight for age (WAZ), height for age (HAZ) and weight for height (WHZ) were expressed as z-scores. The 3-day dietary diaries were recorded each month for the dietary intake analysis.

Results: Among the 77 initial subjects (boys: 54.5%, girls: 45.5%, mean age: 3.84+- 3.80)), 35 (45.5%) completed all 5 individualized nutrition interventions. Before the intervention, 48.1% of patients had experienced food restriction and 5(%) children had WHZ z-score below −2.0. The intake of n6 and n3 fatty acids, calcium, folate, and vitamin D were lower than the recommended nutrient intakes for Koreans. After the intervention, the energy, protein, total lipid, and carbohydrate intake levels were not changed significantly, but n6 and n3 fatty acids, and sodium intakes were decreased. Iron and vitamin D intake were increasing. WHZ z-score of 35 children was significantly increased ($P < .05$) and their SCORAD index was significantly reduced from 34.04 to 18.97 ($P < .05$).

Total serum IgE level and serum eosinophils tended to be decreased after intervention.

Conclusions: The adequate Individualized nutrition intervention is useful improving the growth status and for reducing the severity of AD by improving the nutrition intake.

0902 | Living healthily with food allergy

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Introduction: Health-related knowledge, skills and attitudes (KSA) are the foundation to healthy living. For those with food allergy, healthy living may be impacted by deficiencies in any of these factors. It is important to discover what it is like to live with food allergy as food in a culturally diverse society transcends social, physical and emotional wellbeing. It is more than 'just what we eat'; having food allergy creates challenges that may impact quality of life (QoL).

Objectives: With an exponential rise in food allergy worldwide this study looks at how Australian children see the world of food allergy, which is often reported through the eyes of parents. We used qualitative research methods and a KSA framework to examine how children and teenagers view food allergy and explore what they know and how they feel.

To measure QoL and KSA three age-dependent online surveys were designed. The teenager version incorporated the Food Allergy Quality of Life Questionnaire-Teenager Form (FAQLQ-TF). After obtaining Human Ethics approval the survey was principally distributed via announcements to pre-schools; Allergy Specialists; Paediatricians and the patient support organisation, Allergy and Anaphylaxis Australia. Responses were analysed.

Results: We surveyed 147 participants (4-19 years) and the most prevalent allergies were peanut (77%), tree nuts (73%) and egg (44%), with 28% having an allergy to all three. Results showed participants were able to recognise different ways to keep safe, although teenagers reported less reliance on adults, possibly reflecting greater independence. However, independence creates challenges. Concerning was the number of teenagers (27.02%) and 8-12 year olds (10.41%) who reported teasing by friends, as this may adversely affect peer engagement, confidence and delay notification of symptoms. Teenagers (38.23%) and 8-12 year olds (74.41%) also reported being scared of using auto-injectors even if having an allergic reaction.

Conclusions: Awareness and management of food allergy is important. However, fear of a bad reaction coupled with being scared to use an auto-injector can lead to reluctance in seeking assistance. With less reliance on adults, teenagers may be at a greater risk as they are not only scared but also hesitate in using an auto-injector. This outcome highlights the importance of designing educational strategies to build greater self-confidence so children do not feel inhibited in declaring their food allergy to relevant peers and adults.

0905 | Turkish validation and reliability of food allergy quality of life questionnaire-parent form

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Introduction: Food allergy affects daily lives of children and their parents in varying degrees. Food allergy quality of life questionnaire-parent form (FAQLQ-PF) is a valid, reliable instrument to assess the life quality of children from parents' perception.

Objectives: To validate and determine the reliability of the Turkish FAQLQ-PF and also to assess the life quality. In methods, children, less than 12 years-old, been diagnosed as IgE-mediated food allergy for at least 1 month were enrolled. The English FAQLQ-PF was translated into Turkish regarding World Health Organization guidelines. Food Allergy Independent Measure (FAIM) and Turkish version of the Child Health Questionnaire-Parent Form 50 (CHQ-PF50) were used for construct validity.

Results: One-hundred fifty-seven patients participated. The median age of children and food allergy duration were 2.4 years (1.2-5.2) (interquartiles) and 2 years (0.8-5.1), respectively. Ninety-six (61.1%) patients had anaphylaxis. The Cronbach's alpha coefficient was 0.88, 0.92 and 0.95 for children aged <4, 4-6 and 7-12, respectively. Intra-class correlation coefficient for test-retest reliability was found to be 0.81, 0.79 and 0.81 for groups <4, 4-6 and 7-12 years, respectively. Either patient with asthma or anaphylaxis had higher scores compared to the others. There was a clear tendency for increasing total scores of FAQLQ-PF with age; patients aged 7-12 had the highest total scores compared to others (2.2 ± 0.1, 3.0 ± 0.2 and 3.3 ± 0.3 for <4, 4-6 and 7-12 years, respectively, $P < 0.001$, P for trend $< .001$). Other factors causing poor quality of life in children with food allergy cow's milk allergy, sibling allergy and mother's age greater than 30 years.

Conclusions: The Turkish FAQLQ-PF is a valid, reliable scale. Food allergy-related life quality was worse in the presence of anaphylaxis, asthma and increasing age.

0906 | Effect of dietary elimination on psychosocial functioning status in breastfeeding mothers of infants with food allergy

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Introduction: Food allergy (FA) lead to a general decline in quality of life in connection with social, psychological and family functioning. The studies predominantly include adolescent and young adult age groups and IgE-mediated FA. However, the evaluation of the psychosocial functioning status of infants-children and their families with FA in the early life has not been evaluated.

Objectives: We aimed to define the psychosocial functioning status of nursing mothers whom are on an elimination diet for nursing infants with FA. Nursing mothers of babies (1-12 months of age) who were diagnosed with FA were included in the study. "Symptom Checklist 90" (SCL-90-R) symptom screening test was performed to measure psychosocial symptoms. SCL-90-R has 90 items and 9 symptomatic dimensions including psychiatric symptoms and complaints. The Turkish validity and reliability of the scale has been studied before. The participants filled SCL-90-R and a questionnaire evaluating the foods, which were eliminated from nursing mothers.

Results: Fifty-six mothers were included in the study between January-December 2016. The mean age of the mothers and infants was 31.2 $\pm$ 3.2 years and 5.6 $\pm$ 2.7 months, respectively. A history of psychiatric disease was not present in 82% of participants, but 4 had a history of depression, 3 general anxiety disorder, 2 postpartum depression and 1 sleep disorder. The mean duration of elimination diet was 99.1 $\pm$ 78.7 days. Food elimination rates among nursing mothers were reported as following: 4.1% eliminated 3-5 different foods, 18.3% eliminated 6-10 types of food, 34.6% eliminated 11-20 types of food and 34.6% took off more than 20 foods from diet. The depression and anxiety score of the mothers who eliminate more than 20 different foods from the diet was significantly higher than that of the ones who eliminate less than 20 foods, respectively ($P = .02$, $P = .019$).

Conclusions: The increase in the number of children with FA leads to a fear about foods in nursing mothers and the fear lead mothers to stop eating many essential foods such as milk, meat, egg, legumes, fruits and vegetables from their diet. The significant association between the degree of the food elimination and maternal psychosocial condition bring a new aspect to the follow-up of the anxious mothers which may benefit from a psychiatry support or encouraging attitude of the physicians to open the diet.

0907 | Pre-service teachers' perception of allergic students' quality of life

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Introduction: In management of allergic child in school teacher's knowledge but also perspective of child's needs is important. Health-related quality of life (HRQL) questionnaires have been applied with benefits in children with allergic diseases and in their families.

Objectives: The aim of our study was to assess the knowledge of pre-service teachers about allergies and their awareness of the impact of allergic child diseases on the quality of life in school by applying adopted HRQL questionnaires.

Participants and methods: 137 pre-service primary and lower secondary school teachers (8% male; 91% female; average age 23.9 years (SD = 1.5) participated in this study. 23% of students were allergic themselves. Participants fulfilled Allergy Quality of Life Questionnaire (AQLQ) - Teacher's Form which comprised 31 items about pre-service teachers' perception of HRQL of an allergic student (HRQLS) and 31 items about pre-service teachers' own HRQL if they had to take care for an allergic student in school (HRQLT). HRQLTs' Cronbach Alpha is 0.931. The HRQL scores were the sum of item scores divided by the number of completed items (ranging from 0-minimal impairment to 6- maximal impairment). Participants also answered edited Teachers' Health Competences Development–Allergy Questionnaire (THCDAQ[2]), which comprised 9 attitude items on managing children's health issues, 3 items about their formal education about allergies and 35 alternative knowledge items on allergic disease.

Results: The total HRQLS score was quite low, especially when assessed by female pre-service teachers (M = 4.85; SD =.71 vs M = 4.22; SD = .88; $t(116) = -2.61$; $P = .010$). The total HRQLT score was comparable low when assessed by males (M = 3.79; SD = 1.39) or females (M = 4.48; SD = 1.10) [$t(116) = -1.85$; $P = .067$]. Female pre-service teachers showed higher knowledge about allergies than males (M = 14.73; SD = 2.80 vs. M = 18.01; SD = 4.53) [$t(133) = -2.36$; $P = .020$]. Knowledge level of participants did not contribute to different HRQLS or HRQLT ($P > .05$).

Conclusions: Pre-service teachers recognised reduced HRQL of allergic children and expressed also theirs lower HRQL when taking care for allergic child. There is no significant correlation between knowledge and HRQL assessment. HRQL issues should be included in recommendation for the management of allergic child in school beside training how to prevent, recognise and manage allergic reactions.

0908 | Impact of suspected food allergy on parental anxiety

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Introduction: Food allergy is a growing problem all around the world and the psychological impacts of food allergy have been an interesting research area in recent years. It's known that the diagnosis of food allergy has a negative impact on both the children's and their parent's lives.

Objectives: Our study aimed to assess the anxiety of parents with suspected food allergy and the impact of food allergy-related internet searches on anxiety. Fifty patients visiting our allergy clinic for the first time to have their children evaluated for food allergy because of suspicion of the mother or referred us by a primary and secondary care health centers were recruited to the study. The mothers of the patients completed a study-related questionnaire form and the Spielberger's Stait-Trait Anxiety Inventory (STAI). They were evaluated with a detailed history for food allergy, skin tests and food challenge tests. Fifty mothers of healthy subjects were included to the study as a control group.

Results: The median age of the patients was 7 months (1.5-24 months), 47.1% of the patients was girl and 52.9% was boy. Skin prick tests were positive in 10/36 patients. Oral food challenges were performed to 32 patients and found positive in 15 patients. There were no differences between the patient and the control groups according to the age of children, male/female ratio, mothers' age and education and economical status of the families. The median STAI-state score was 42 (22-65), STAI-trait score was 42 (26-61), total STAI score was 82 (28-126) in the patient group. The median STAI-state score was 33 (23-51),STAI-trait score was 41 (15-58) and total STAI score was 75 (38-99) in the control group. The state and total STAI scores were found significantly higher in the patient group than controls ($P < .001$, $P = .001$ respectively). STAI-state score was significantly correlated with the number of maternally eliminated foods without medical suggestion ($P = .043$). We couldn't find any relationship with food allergy-related internet searches and parental anxiety.

Conclusions: Parental anxiety was found to be significantly high in patients with suspected food allergy and anxiety was resulted in multiple food elimination. It's important to make a correct diagnosis before multiple or unnecessary food eliminations to avoid nutritional deficiencies.

0909 | Understanding why young people with severe allergies join support groups

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Introduction: In a recent study it was found that young people who were members of an allergy support group were 2.5 times more likely to adhere to good self-care behaviours.

Objectives: The aim of this qualitative study was to explore why young people with severe allergies join support groups, areas they find important and resources offered that influence and promote adherence.

Methods: In-depth, semi-structured, telephone interviews were conducted with young people (aged between 12-21 years old) with severe allergies who belonged to allergy support groups. Interviews were audiotaped, transcribed verbatim and analysed using Burnard's structured approach.

Results: 21 young people with a food, venom or latex allergies, were recruited from a range of physical and online support groups. Of these, 18 young people joined support groups on recommendation of their parents or self-referral. Some participants highlighted that they previously had "never even realised there were support groups", emphasising that such support for young people is not widely publicised. This lack of awareness caused many young people to experience severe isolation "if I say that I want to go to a sleepover… I can never go because my friend's Mums aren't willing to take that responsibility. So I am left out on most things." Networking appeared to be the most fundamental reason for joining a support group, but young people were also interested in learning more about their allergies and how to manage these effectively. The importance of feeling included and sharing experiences was emphasised by the feelings that support groups brought "unity" and comfort in meeting with those "who understand what you're going through". Confidence was felt to increase after support group involvement and this was highlighted by reported improved self-assurance when using their AIE (auto-injectable epinephrine), the ability to disclose their allergies in restaurants and to others without allergies.

Conclusions: This study highlights the role support groups play in aiding young people to manage their allergies and adhere to positive self-care behaviours. Participants expressed how groups provide positive experiences by reducing their isolation, connecting them with others in similar circumstances and improving their confidence in managing allergies. Young people reported a need for increased awareness of support groups, as well as greater geographical distribution.

0910 | Social media and food allergy in children

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Introduction: Food allergy can severely impair the quality of life of children and their families. Education on avoidance and treatment are essential for the management of these patients. Internet and social media have become a source of information that might be useful for these purposes. The aim of this study was to describe how parents/guardians of paediatric patients with food allergy use social media in relation with their disease.

Objectives: A cross-sectional study was led in a third-level hospital in Madrid, Spain from September to November 2016. Parent/guardians of patients under 13 years of age, attended in the Paediatric Allergy Unit with a diagnosis of food allergy, were asked to fill a questionnaire about their food allergy and their use of social media. A written informed consent was obtained.

Results: The questionnaire was filled by 162 patients. Patients: median age 7.5 years (IQR: 5); sex: 59% boys, 41% girls; food allergy: 46% of them were allergic to nuts, 38% egg, 33% cow's milk and 19% to fruits; 44% were allergic to 2 or more food groups; 59% had been allergic for more than 5 years; 62% had a history of anaphylaxis. Parent/guardians: median age 42 years (IQR: 6); sex: 75% women, 25% men.

Social media was used regularly by 67% of the patients (73% of them, daily). However, only 30% used them for subjects related to food allergy. Most popular social networks used for this purpose were Facebook (79%), YouTube (27%) and Twitter (9%). Among them, 80% did it to receive food security updates, 61% for medical information and 36% to socialize with other patients.

Conclusions: Parent/guardians of children with food allergy use social media frequently. However less than 1 out of 3 do it because of their food allergy. Food security updates was the most common food allergy-related use of social media. Efforts should be directed to have caregivers of children with food allergy use social media, a potentially useful resource.

0911 | Internet use and attitudes of the parents of children with food allergy

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Introduction: Children with food allergy need special care in terms of avoiding exposure to allergic food, treatment of reactions, providing safe living places (restaurants, schools, etc.). Therefore, parents of food allergic children usually seek information on Internet to improve their knowledge about the disease and its management. However, quality and accuracy of Internet-based medical information may vary and misdirect parents in their daily practices.

Objectives: We aimed to investigate the attitudes of parents of children with food allergy whether Internet use impact their daily activities while managing food allergy. This study was conducted by using a web-based questionnaire that can be completed on the Internet in Facebook groups of families who stated that their children had a diagnosis of food allergy.

Results: Among the 234 participants, mean age was 32.2 $\pm$ 4.7 years, 96.2% were women and 81.6% had an education of high school or higher. 77.8% of the participants stated that they sought on the Internet about their children's complaints before going to a doctor. 62% of the participants stated that they use the Internet daily and 21.8% stated that they use a few times a week. Of the participants, 41.8% reported that Internet is always useful and 46.6% find Internet most of the time useful. Facebook patient groups were the most commonly preferred source for information. 86.9% of the parents found the Internet sources through Web searches by themselves. 82.8% reported that they obtain information about food allergy diagnosis and tests, 73.7% got dietary advices and 78% got information about recipes. 53.6% of the participants stated that Internet advice and doctor's advice are sometimes incompatible and while 67% accepted the doctor's information as correct, 27.9% stated that they trusted on the Internet information. In addition, 49.7% stated that they always or most of the time give advices to other patients and their families on the Internet.

Conclusions: Considering social media use is an unpreventable habit, online sources should include correct information for information-seeking parents and maybe they should be supervised or be certified by health institutions and organizations.

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0912 | Immunophenotypes of cow's milk protein allergy: new approach in predicting the development of tolerance

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Introduction: Cow's milk protein (CMP) allergy is one of the most frequent conditions among allergy diseases in early age children. Distinct predictors of the development of tolerance to CMP have not yet been defined. The development of laboratory diagnostic methods and definition of the immunophenotypes of CMP allergy will significantly facilitate the follow-up of these patients.

Objectives: To determine immunophenotypes of CMP allergy and evaluate their role in predicting the development of tolerance to CMP.

Results: 153 children with CMP allergy aged 1-18 month were included in the prospective observational study. Blood samples were taken to determine sIgE (UniCAP method) and sIgG4 (ELISA) to CMP and its fractions twice - before elimination diet and after 6-12 months of elimination diet and oral challenge of CMP.

Results: Oral food challenge procedure with CMP was performed after 6-12 months of elimination diet. 50.3% children became tolerant to CMP, of which 42 developed tolerance by the end of the first year (54.5% of all children who developed tolerance), and 35 by the end of the 2nd year (45.5% of all who developed tolerance). During evaluation of immunological markers, taken, before elimination diet, we determined 4 immunophenotypes. Tolerance to CMP developed in 97.9% of patients with 'sIgE ≤0.7 kUA/l and sIgG4 3+' immunophenotype, and in 90.1% of patients with 'sIgE >0.7 kUA/l and sIgG4 3+' immunophenotype. These results indicate a high probability of development of tolerance to CMP after 6 months of elimination diet in children with these immunophenotypes. In contrast, 19.2% of patients with 'sIgE ≤0.7 kUA/l and sIgG4 0-2+' immunophenotype, and none of the patients with 'sIgE >0.7 kUA/l and sIgG4 0-2+' immunophenotype became tolerant after 6-12 of the elimination diet ($P < .05$). Thus, these results seem to provide unfavorable evidence regarding the development of tolerance to CMP.

Conclusions: Different immunophenotypes of CMP allergy can be successfully used as new evaluation tool for predicting the development of tolerance to CMP in early age children.

0913 | Opportunities for primary prevention of food allergy in infants by the introduction of hypoallergenic commercially produced complementary foods

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Introduction: The strategies for diagnosis and management of food allergy in children are well developed. Primary prevention of food allergy includes introduction of complementary foods after the age of 4 months according to normal standard weaning practices and nutrition recommendations, irrespective of atopic heredity. The aim of the study was to evaluate the tolerance of commercially produced complementary foods (cereals - rice, buckwheat, corn; fruit purees – apple, pear, prune; vegetable purees - squash, cauliflower, broccoli; meat purees - turkey, rabbit) in healthy infants and in infants at high-risk for development of allergic disease.

Objectives: In open, longitudinal, prospective study 60 healthy infants aged 4-6 months having not received complementary foods earlier were included. 28 (46.6%) infants were exclusively breastfed, 12 (20.0%) had mixed feeding, 20 (33.4%) were bottle-fed with different milk formulas. 34 (57%) infants were at high-risk for development of allergic disease. Complementary foods (cereals, vegetable purees, meat purees and fruit purees) were introduced gradually due to the individual plan, depending on the age and nutritional status. Products tolerance was assessed 1 time per week. Identification of serum specific-IgEs for cow's and goat's milk, apple, pear, prune, squash, broccoli, cauliflower, rice, corn, buckwheat, turkey, rabbit was evaluated twice - prior to the introduction of complementary foods, and in 3-4 weeks.

Results: Mild skin reactions (hyperemia and punctate rash on the face) on the first introduction of weaning foods were observed only in 9 (15%) infants, including 6 high-risk infants. The level of specific-IgEs to studied food allergens was within normal range (0-135 IU/ml) both initially and after administration of all the studied complementary foods in all children.

Conclusions: The investigated commercially produced complementary foods have a low sensitizing potential, including infants with high risk for development of allergic disease. This allows us to describe them as hypoallergenic products.

0914 | The dark side of The poppaea'S soap

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Case report: Introduction: The donkey's milk (DM), due to its excellent cosmetic properties, was known to be used in the past by Poppaea, the Emperor Nero's wife, for her baths. This legend is supported by the current popularity of DM in cosmetology, where it is used to produce many cosmetics whose request is increasing in the developed countries. In addition to the cosmetic use, DM has recently been used as a good replacement in cow milk (CM) allergy, especially in children.

Case, objectives and results: We report a case of angioedema due to food allergy to DM proteins in a subject tolerating CM, who never drank DM before this episode, but reporting mild exacerbations of dermatitis after use of DM-based cosmetics. A direct ELISA test confirmed the presence of specific IgE reactivity against DM, but not against CM, and an ELISA inhibition test was performed to exclude potential interferences of donkey epithelial allergens. The immunoblot showed only one IgE binding band (16-19 KDa), consistent with donkey β-lactoglobulin (β-LG).

Since anaphylactic reactions to DM was documented in children with severe food allergy to CM proteins, but the cross-reactivity between CM and DM has not been clearly demonstrated, we performed an immunoblot for DM of the sera of three CM allergic adult subjects with IgEs against cow β-LG who never ingested DM. One of them, the only one reporting atopic dermatitis episodes after skin contact with DM-based products, showed an IgE binding fraction in the 16-19 KDa zone of DM, and the ELISA test of serum previously adsorbed with cow β-LG showed the presence of a genuine IgE reactivity against DM. On the contrary, the IgE reactivity against CM of pre-adsorbed serum was completely abolished.

Conclusion: To our best knowledge, this is the first case report of a genuine food allergy to DM, with CM tolerance, caused by the donkey β-LG. Furthermore, the pathway of sensitization is noteworthy, since before the food allergy, the subjects experienced dermatitis after using DM-based cosmetics.

In conclusion, our results confirm that attention must be paid to the use of cosmetics containing food proteins in patients with atopic dermatitis. Furthermore, in these subjects, the food allergy sensitization may occur, even without ingestion, through the contact of the food with the dysfunctional skin barrier.

0915 | A new strategy for diagnosing egg allergy in children with cow milk allergy

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Introduction: Milk (CMA) and Egg allergies are among the most prevalent food allergies in children. It is estimated that 40-50% children with CMA develop egg allergy, so some guidelines establish both diagnostic should be made at the same time. Avoiding all forms of milk or egg is the initial management for these types of allergies. However, such a restrictive diet has a major impact on quality of life, nutrition and social activities.

Objectives: The aim of our study is to analyzed if a written plan given to parents of children with CMA could be enough to avoid future severe reactions to egg without a previous study of sensitization. And in second term evaluate the real prevalence of egg allergy in our patients with CMA.

Results: In our Allergy Unit children diagnosed of CMA (all of them with a convincing history of an immediate allergic reaction to milk and a positive prick skin test) receive a written individualized treatment plan including: milk avoidance strategies and treatment of possible reactions at home. We also give them written instructions on the introduction of egg: a step-up procedure beginning with boiled egg (with the yolk and afterwards with white egg), continuing with omelette and finally fried egg.

From 2010 to 2016 we have diagnosed 221 children with CMA, 55 (24.9%) had a reaction during the introduction of egg in diet at home. Half of them with white egg (less than 1/4 of white egg), 30% with omelette (less than 1/4 of omelette). None of them suffered an anaphylactic reaction. 78% of the reactions were cutaneous (mostly perioral dermatitis, 12% atopic dermatitis, 10% generalized urticaria), 9% digestive (abdominal pain or vomiting) and 13% cutaneous and digestive. All reactions were solved rapidly with antihistamines and in case of urticaria with oral corticosteroids and antihistamines.

In all patients Egg allergy was confirmed after the reaction with a positive prick skin test. Those patients reacted with omelette continued tolerating boiled egg in all cases confirmed by controlled administration at our unit.

Conclusions: Written instructions on introduction of egg in CMA children seems to be a good strategy to avoid false sensitization to egg in a great proportion of patients and could be enough to avoid future severe reactions to egg at first administration.

0916 | Cow's milk-related symptom score (CoMiSS) as a screening tool for cow's milk allergy in children aged 0-24 months- a cross sectional longitudinal study in India

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Introduction: Cow's milk Protein allergy (CMPA) is a reproducible adverse reaction of an immunological nature induced by cow's milk protein. Signs and symptoms of CMPA are often nonspecific, difficult to objectify and easily missed in primary care settings. CoMiSS which considers general manifestations, dermatological, gastrointestinal and respiratory symptoms, was developed as a screening and awareness tool for cow's milk-related symptoms. However, this needs to be validated for assessment of its utility as a screening tool for CMPA.

Objectives: To measure the utility of CoMiSS in Indian children of 0-24 months of age. Methodology:-A multi centric, observational, longitudinal study was conducted over a period of 5 months (July 2016-Dec 2016). Infant and children aged 0-24 months visiting pediatrics clinic, present with one or more symptoms suggestive of CMPA were included in the study. A predesigned questionnaire was used to record information on demography, medical history, feeding pattern and clinical examination via CoMiSS. The CoMiSS score ranges from 0 to 33, score greater than 12 indicates infants at risk of CMPA. Children were followed up for confirmation for CMPA via oral food challenge or skin prick test or ImmunoCAP test.

Results: Total 83 children were enrolled in the study. Mean age and birth weight was (12.3 ± 6.4) months (2.9 ± 0.4) kgs respectively. 38.6% were presented with gastrointestinal symptoms alone whereas 38.5% of the children had an additional symptoms of cutaneous or respiratory system. CoMiSS was greater than 12 in 59% indicating the presences of CMPA, amongst them 93% were confirmed cases of CMPA via oral food challenge/ImmunoCAP test. Positive and negative predicative value for CoMiSS was 93% and 33% respectively whereas sensitivity and specificity was 77% and 66% respectively.

Feeding pattern		Total N = 83	CoMiSS Score ≤ 12	CoMiSS Score ≥12	P value
Exclusive Breastfeeding for first 6 months	yes	59	20	6	.30*
	No	24	39	18	
Introduction of complementary feeding	Less than 6 months	55	39	16	.42*
	At 6 months	21	16	5	
	After 6 months	7	4	3	

*Nonsignificant.

Conclusions: CoMiSS could potentially be used as a screening tool for CMPA in children less than two years of age, in Indian primary care setting, aiding in its earlier diagnosis. However, appropriate validation studies are need to evaluate it further.

0918 | Food allergy diagnosis: in vitro method for measurement of basophil activation and/or degranulation in children with food allergies

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Introduction: Basophil activation test (BAT) is a functional test that reflects the *ex vivo* IgE-mediated cell response induced by certain allergens and seems to be more specific and more sensitive for food allergy testing than other available in vitro tests. It represents a new tool developed to monitor basophil activation upon allergen challenge by detecting the expression of membrane surface markers (CD63, CD203c) by flow cytometry. Although some studies claimed there are advantages of CD63 over CD203c, several studies addressed the role of CD203c as the most promising new activation marker for flow-cytometry based allergy diagnosis.

Objectives: To introduce BAT to the daily routine and help clinicians in cases where other diagnostic procedures give ambiguous results, i.e. show discrepancies between skin prick test, specific IgE and patient clinical history. To test CD203c as a basophil activation marker and to determine its correlation with CD63.

Results: The simultaneous use of four different antibodies allows a better segregation and a precise measurement of basophil activation and/or degranulation. Also, the MFI for CD203c significantly differed among samples treated with different allergen concentrations although the percentage of activated basophils estimated by CD63 expression did not differ between those samples, i.e. the differences in CD203c expression are measurable during non-degranulating stimulation of basophils.

Conclusions: BAT is a reliable and useful functional test in cases demonstrating inconclusive diagnostic results. The use of anti-CD203c antibody, as an additional identification and activation marker, has been shown useful for a better resolution of the activated/non-degranulated and activated/degranulated basophils. The use of CD203c improved both the sensitivity and the specificity of BAT, resulting in an enhancement of its accuracy in the diagnosis of food allergies.

0919 | Multiple food allergy – unexpected culprits

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Case report: Introduction: Food allergy has an estimated prevalence of 6-8% in children. Multiple food allergy is less frequent, being fundamental a detailed clinical history and diagnostic workup, with special emphasis on molecular components.

Clinical case: A 5-year-old girl was referred to our department (food allergy unit), with a multiple food allergy history. She had previous history of moderate eczema, moderate to severe persistent rhinitis and moderate asthma, with sensitization to mites, mold and grass pollen, medicated with daily emollient, nasal corticosteroid, oral leukotriene antagonist, antihistamine and inhaled beta-2 agonist/corticosteroid association. Familiar history of eczema, rhinitis/asthma. Lives in an urban environment, without pets but with contact with pigeons outside and their neighbor's dog. Regarding food allergies, she had severe immediate worsening of her eczema with hen's egg (6 months; white and yolk simultaneously) and cow's milk introduction (7 months; without previous complaints with breast and formula milk). At 9 months, with meat introduction in her diet (chicken, turkey, cow, pork and rabbit), she developed eczema worsening and lip edema. The same happened with fish (codfish, salmon and fresh tuna) and tree nuts. At her first appointment in our department, she was avoiding hen's egg, cow's milk, meat (except lamb and goat), fish (except canned tuna and hake) and tree nuts. We performed skin prick tests (commercial extract and nature food) with suspected foods, being positive for hen's egg (white, yolk, ovomucoid and ovalbumin) and meat (cow, pork, chicken, turkey, lamb, goat–positive for raw meat; rabbit–positive for raw and cooked meat). Specific IgE was strongly positive for hen's egg (all components), pork, chicken meat and codfish; slightly positive for cow's milk and fractions; negative for alpha-gal. ISAC® was performed, revealing sensitization to 3 cross-reactive components (serum albumins Bosd6, Canf3 and Feld2) and specific food components of chicken's egg/meat (Gald1,2,3 and 5), cod(Gadc1), hazelnut(Cora9) and kiwi(Actd1).

Conclusion: Sensitization to cross-reactive components was responsible for most of the children food allergies, being fundamental molecular diagnosis. This is a rare case of red meat and cow's milk allergy by sensitization to serum albumins, meaning tolerance to these foods in well-cooked forms, substantially improving patient's quality of life.

0920 | Food allergy in preschools in Japan: survey of 1152 facilities in chiba prefecture

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Introduction: In these past few years, it has been reported that about 80-90% of the preschools in Japan have children with food allergies. While allergic reaction occurring at school has been shown to be a risk factor for fatal reactions, accidental events concerning allergic foods are also not uncommon in the preschool settings. This is a problem that must be solved urgently, but little is known about what the actual problem is in the preschool settings.

Objectives: The objective of our study is to grasp the actual situation of the preschools throughout Chiba Prefecture, and to analyze the underlying problems the facilities are facing.

Method: We sent questionnaires to all 1152 preschools in Chiba Prefecture from August to October 2015. Most of the questionnaires were multiple choice questions, except for those regarding accidental events or the actual anaphylaxis episodes, which were open answer questions. The questionnaires were sent to each preschools, and either the preschool nurse or the childcare worker answered them.

Results: About 90% of the preschools had children with food allergies. 76% of the facilities had more than one child with food allergies. 38% of the children eliminated more than one food, and there were a wide variety of foods that needed to be eliminated. 89% of the preschools served lunch, etc. to children with food allergies that eliminated each allergic food. About 1/4 of the facilities experienced accidental events, and 10% of the facilities experienced actual anaphylaxis. Some reported events were unique to infants and toddlers; such as reactions occurring from previously unknown allergens, children eating spilt food or food from other children's trays. Despite the fact that food allergy reactions are not rare, only half of the facilities had finished training courses for food allergy and anaphylaxis.

Conclusions: Our study showed that many of the preschools in Chiba Prefecture were at high risk of accidental events and severe allergic reactions. Considering the fact that infants and toddlers " eat each others' food", we may need to take a radically different approach to prevent children from accidental events.

0921 | Cow's milk protein allergy – a retrospective study in a pediatric clinic from Nord-East of Romania

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Introduction: Numerous researches studied food allergies components, including cow's milk protein allergy (CMPA).

Objectives: The purpose of this study was to underline the clinical course and therapeutic aspects of CMPA in children.

Methods: The study group consisted of 124 patients hospitalized in 3rd Clinic of Pediatrics, "Sf.Maria" Children's Emergency Hospital, Iasi-Romania, on a period of 5 years for symptoms suggestive of CMPA. We follow at these patients: clinical and laboratory data to establish a correct diagnosis (epidemiological data related to the onset of disease, the patient's history of atopy, age of onset, type of food, disease manifestations, biochemical diagnosis methods, intestinal biopsy, stool chemistry, specific immunoglobulin E) and the association, in some cases, of the sensitization to other proteins component supply (soy, egg, gluten, disaccharides).

Results: In the study group 60.48% of patients had gastrointestinal manifestations, 19.35% - respiratory manifestations, 8.87% - skin manifestations, 3.22% - mixed manifestations. The highest prevalence of CMPA was observed in the group aged 0-3 months (37.08%), followed by 3-6 months age group (32.25%), as confirmed by studies in the literature. From researching eating behavior of patients, revealed that at the onset of symptoms, 11 (8.87%) were natural fed, 49 (39.51%) - artificially fed, 21 (16.93%) - mixed fed, and 43 patients (36.76%) had complementary diet. It has been observed that in most cases (72.58%) symptoms started within the first 10 days after the introduction of cow's milk. In 11 cases (8.87%) the symptoms started in the early hours. 46.77% had varying degrees of malnutrition. Reducing bodies were present in the stool of 109 patients with digestive symptoms and Adler method revealed in 5 cases occult bleeding which led to the iron deficiency anemia. Intestinal mucosal biopsy performed in cases with digestive CMPA forms showed nonspecific lesions, which imposed correlation with the clinical and histological outcomes of disease evolution. Based therapy was represented by the exclusion of cow's milk protein from the diet. The response was favorable in most cases (74.20%). Failure to follow the dietary recommendations resulted in recurrence of symptoms in 25.80% of cases.

Conclusions: CMPA is a common cause of infant malabsorption, representing a complication of artificial nutrition, these patients requiring special nutritional recommendations.

0923 | Clinical and feeding behaviour assessment of egg oral immunotherapy treated children after 7 years of follow up

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Introduction: Egg oral immunotherapy (EOIT) is an active treatment option to desensitize allergic children. However, long-term studies are scarce.

Objectives: Describe the clinical situation and feeding behaviors regarding the egg intake of children who successfully completed build-up and maintenance phase of EOIT conducted seven years ago.

Results: Cross-sectional telephone survey analyzing egg reactivity and eating habits in an EOIT cohort with 7 years of follow-up. 55 of 61 (90%) subjects included in the trial successfully completed EOIT protocol started seven years ago [64% (39/61) males, current median age of 16 (range 12-25) years], 8% of patients discontinued the treatment due to digestive and/or respiratory symptoms and 2% by parents decision. 67% (41/61) achieved sustained unresponsiveness confirmed by negative egg oral challenge after 1 month of egg-free diet; 23% (14/61) are still in the maintenance phase, consuming undercooked egg at least 3 times a week, and they have not yet performed oral food challenge after egg-free diet. 89% (49/55) of patients who successfully completed EOIT answered the telephone assessment; 11% couldn't be reached. 71% (35/49) of patients were consuming egg at least 3 times/week. 69% (34/49) of patients were consuming unbaked and baked egg in any presentation, 22% consumed only baked egg and 8% consumed only foods containing egg traces. 43% of children declared/admitted that they disliked the taste/texture of unbaked egg but have good adherence and 14% were afraid to consume egg. 16% (8/49) of subjects had adverse reactions related to egg ingestion during the maintenance phase. Only 3 patients avoid cofactors before and after consuming egg. The family of one patient regretted of performing EOIT because the implied risk, however 100% of the parents would recommend EOIT to other patients.

Conclusions: Egg oral immunotherapy is an effective long-term treatment in the majority of patients. Moreover, 67% of them achieved sustained unresponsiveness along the treatment and are consuming egg without conditions. On the other hand, 8% of patients who successfully completed oral immunotherapy are consuming only foods containing egg traces with the risk of losing tolerance. Most families are satisfied with the treatment and 100% recommend it.

0924 | Tropomyosin from vertebrates as an allergen – case report

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Case report: Background: Parvalbumin is the main allergen described in fish allergy. Recently new fish allergens were identified (enolases and aldolases), but some others are waiting to be discovered and described. Tropomyosin (TM) is the *major* allergen in shellfish allergy. It is responsible of cross-reactivity between house dust mites and shellfish allergy. TM from vertebrate species, highly expressed in vertebrate muscle cells, share substantial similarity with invertebrate TM. Typically, vertebrate TMs has been considered non-allergenic proteins, however recently same articles noted the allergenic character of them. In our case, cross-reactivity between shellfish TM and fish TM helped us to understand the clinical manifestations related to the ingestion of fish.

Case report: A 11-year-old male with no family or personal history of atopy who entered the emergency room with an episode of severe anaphylaxis while eating a shrimp patty. In a later appointment of pediatrics allergology, itching and mild swelling of the mouth and throat immediately after ingestion of some fishes were referred. Serum allergen-specific-IgE (KU_A/L) levels were: shrimp >100, octopus 37.7, squid 3.57; *D. pteronyssinus* 46.10, *D. farinae* 70.1, grass pollen 4.73, codfish 2.5, hake 0.97, tuna fish 2.77, plaice 0.62, salmon 2.33, sole 1.09 and horse mackerel 0.93. A molecular allergen study was carried out using the ImmunoCAP® ISAC technique that revealed only sensitization to TM (Pen m 1, Der p 10, Ani s 3, Bla g 7) and Polcalcin (Bet v 4, Phl p 7). No sensitization was found to parvalbumin. A SDS-PAGE Immunoblotting-inhibition assay with patient serum, showed cross-reactivity between 36-37 kDa-proteins from fish (hake and cod) and shrimp (TM is a 35-38 kDa protein).

Discussion/Conclusion: Cross-reactivity between 36-37 kDa proteins from fish and shrimp (probably tropomyosin) could explain the fish allergy reaction observed. Sensitization detected to polcalcins without detecting sensitization to any specific pollen allergen could be due to in vitro cross-reactivity with TM since both are calcium transporting proteins.

0925 | Allergy to goat and sheep whey proteins without allergy to cow's milk

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Introduction: Background: Cow's milk proteins (CMP) allergy is the most frequent causes of food allergy in infants. Most children who are allergic to CMP cannot tolerate goat's or sheep's milk (GSM) either because of the high degree of cross- reactivity between milk caseins from different animals because of sequence homology between the casein fractions. The GSM allergics that are not associated with allergic cross-reactivity to CMP are rare. We present a case of a child with allergy to goat and sheep whey proteins without allergy to cow's milk.

Objectives: Case report: We report a 7 years old atopic boy developed contact urticaria touching sheep cheese. He had never ingested milk or cheese derivatives from sheep or goat. He tolerated cow's milk and their derivatives products.

Results: Skin prick tests with cow's milk and fractions (casein, β lactoglobulin and α lactoalbumin) were negative. Prick tests were positive with sheep's milk, goat's milk and with the sheep and goat's cheese. Total IgE was 627 kU/l and specific IgE to sheep and goat milk were both more than 100 kU/l. Specific-IgE to cow's milk, casein, β lactoglobulin and α lactoalbumin was undetectable. Immunoblotting sowed IgE-binding bands by 15 kDa, between 50 and 75 and 75 kDa in milk lanes.

Conclusions: The IgE -binding band by 25 kDa at cow, sheep and goat's milk lanes could correspond to α and β casein (Bos d 8); between 50-75 kDa might correspond to serum albumin (Bos d 6) and lactoferrin. In case of sheep and goat milk lanes the binding band are the same to milk but with more reactivity, specially with casein

In case of goat immunoblotting showed IgE binding bands between 14-18 kDa could be correspond α- and β-lactoalbumin (Bos d4 and Bos d 5).

0926 | Allergic reaction to whey protein powder in infancy

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Case report: Introduction: Milk allergy is one of the most common food allergies during infancy or in early childhood. We report about the case of the girl with allergic reaction to milk formula and Whey Protein Powder.

Case presentation: Two-month-old girl was admitted to the hospital for weakness, erythema and swelling of the face, ears, arms, and urticaria 10 minutes after she drank 100 ml of cow's milk formula Novalac. She had not any problems with breathing; vital functions were in normal ranges. All the symptoms were beyond the hour. We showed positive SPT to milk, and sIgE to milk, Alpha-lactalbumin, Beta-lactoglobulin and Casein. Mother and the little girl started the diet without caw's milk but occasionally girl drank small amounts without any problems.

At 5 months, her father kissed her forehead after he consumed a Whey Protein drink (Protein Whey Pro Chocolate Con Coco). She developed erythema, urticaria and swelling at forehead, which diminished in 30 minutes. Later the same months she touched with the lips the empty cup of Whey Protein drink and she developed erythema, swelling of the lips and urticaria, which again lasted for 30 minutes.

After those two reactions, the girls was clinically and diagnostically evaluated again. At first, we confirmed positive IgE sensitization to milk, and then we performed ISAC test, which was positive only for Alpha-lactalbumin and Beta-lactoglobulin. Finally, we performed basophil activation test, which was negative for cow's milk, slightly positive for Novalac formula and highly positive for Whey Protein Powder.

Conclusions: Cow's milk allergy is the most common food allergy in young children, affecting 2-3% of infants. Most allergic patients are sensitized to casein and/or whey (Alfa – lactalbumin and Beta – lactoglobulin) proteins. The girl, which was IgE sensitized to cow's milk and above mention proteins, showed in biological test negative results for cow's milk. Consequently, the girl indeed tolerated small amounts of cow's milk. However, she was highly BAT positive for Whey Protein Powder. We believe that the allergic reaction to Whey Protein was a result of IgE sensitisation to specific milk proteins Alpha-lactalbumin, Beta-lactoglobulin, which are at extremely high concentrations present in the offended Whey Protein Powder (11.25 g Alpha-lactalbumin per 100 g of powder and 34.5 g of Beta-lactoglobulin per 100 g of powder).

0927 | Case report: allergy to donkey's milk

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Case report: Background: Camel, mare and donkey milks are proposed as feeding alternative for children suffering from cow's milk (CM) allergy especially in developing countries. Monti et al. have shown that 82% of CMA patients tolerated donkey's milk (DM) (1). Several reports of allergy to goat and sheep's milk without CM allergy have been reported. Rare observations of allergy to mare milk have been also published but no case of allergy to DM until now.

Medical history: A 9-year-old girl was referred for an acute generalized urticaria after the first application of a cream containing donkey milk proteins (La Zane Attitude, Overijse, Belgium). The cream was purchased because of its reputation for beneficial effect on eczema. The girl had also an history of previous anaphylactic reactions to peanut and tree nuts. She is not allergic to horse or donkey dander and never reacted to cow's milk products or goat's cheese.

Methods: Prick-to prick tests have been performed with DM, the suspected cosmetic, CM, goat's milk (GM) and sheep's yogurth. Parents have refused to perform an oral challenge with DM. SDS-PAGE and IgE-Immunoblotting of DM and CM were carried out after incubation with the patient sera.

Results: Mean wheal sizes of prick-to-prick-test to DM, GM and the cream La Zane Attitude measured respectively 19, 2 and 10.5 mm. The skin tests to CM and sheep's yogurth were negative. The Immunoblot of DM extract showed a strong IgE-binding to a 14 kDa protein. No binding to CM proteins was observed.

Conclusion: To our knowledge, this is the first report of an IgE mediated allergy to donkey's milk without cross reaction to CM.

References:

1 Monti et al. Efficacy of donkey's milk in treating highly problematic cow's milk allergic children: an in vivo and in vitro study. Pediatr Allergy Immunol. 2007;18(3):258-64.

0928 | Anaphylactic reactions to novel foods: Case report of a child with severe crocodile meat allergy

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Case report: Availability of exotic foods is steadily increasing. We describe the first case of anaphylaxis to crocodile meat. The patient was a 13-year old boy with severe IgE-mediated allergy to chicken meat. When tasting crocodile meat for the first time he developed an anaphylactic reaction. Cross-reactivity between chicken and crocodile meat was suspected to have triggered this reaction. Basophil activation and IgE testing confirmed the boy's allergic reaction to crocodile meat proteins. Molecular analysis identified a crocodile alpha-parvalbumin, with extensive sequence homology to chicken alpha-parvalbumin, as the main cross-reactive allergen. We conclude that crocodile meat can be a potent food allergen and patients with allergy to chicken meat should be advised to avoid intake of meat

from crocodile species. Both foods and people travel around the world and accessibility to "exotic" foods is steadily growing. As a result, novel allergic cross-reactivities are likely to become a challenge in the management of food allergy and, as our report illustrates, cross-reactivity has to be considered even between foods that might not intuitively be perceived as related.

0929 | Ig-e mediated severe cow's milk allergy and salmonella carrier in a child with good weight gain

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Case report

Introduction: Cow's milk allergy is one of the most common causes of food allergy in early infancy, causing abdominal pain, diarrhea and in almost all cases failure to thrive. The correlation between rotaviral infection - development of cow's milk allergy in children is known, but no relation between the bacterial infection and the cow's milk allergy was described.

Objectives: We present the case of a 14 month male boy whose mom had urticaria, the last episode occurring during pregnancy. He received maternal milk until 4 months of age, when in error his mom received fluoroquinolones for her mastitis with staphylococus and stopped breastfeeding. In the first 4 month he developed a moderate form of atopical dermatitis, although his weight was excellent (90th percentile). It was the moment when he had the first episodes of bloody diarrhea treated with third generation cephalosporin, despite the negative coproculture and the norovirus test positive. He received a delactosate formula and after 8 days he had a severe allergic reaction with Quincke edema. It was considered a delayed allergy of milk protein, with Ig E antibodies negatives and the formula was changes with an extensive hydrolysed one. After 2 months he had a new diarrhea episode, the coproculture was positive for salmonella. He received numerous antibiotical treatment, without any success (trimetoprim+sulfametoxazol, amoxicillinum acidum clavulanicum, cefpodoxime). During this time his stools were fermented, mucosal and he had abdominal pain. For this reasons he was admitted in a hospital where he received meropenem in order to treat the Salmonella infection. In the fifth day of treatment he developed a general allergic reaction, Quincke edema, hyporeactivity. While hospitalised for the first time his Ig E for milk cow's protein where positive.

For almost another 6 month he was a salmonella carrier, who developed multiple allergies during solid food introduction (egg: prick test positive, carrot) all of them with cutaneous eruption, itching, sneeze. He had a severe diet because of all the allergic reaction, for 4 months he tolerated only chicken meat, millet, boiled pear and extensively hydrolysed milk.

Results and conclusion: Despite the prolonged dietary restrictions, his status of salmonella carrier, his cow's milk protein allergy he continued to display great weight gain (90th percentile) and less abdominal pain. For this child to have a normal diet it will be really challenging.

0930 | Watery Diarrhea Hypokalemia Achlorhydria (WDHA) syndrome may mimic celiac disease or allergic gastroenteritis

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Introduction: WDHA syndrome (Watery Diarrhea-Hypokalemia-Achlorhydria) or Verner-Morrison syndrome is a rare condition described in 1958 1 year after Priest and Alexander reported a patient with peptic ulcer, diarrhea, hypokalemia, due to an islet cell tumor. WDHA syndrome is caused by oversecretion of vasoactive intestinal peptide (VIP) or rarely peptide histidine methionine (PHM).

Objectives: A case of a 2-year old boy who presented with long-term diarrhea and failure to thrive is reviewed. This child had increased IgE and a positive blood test for a Celiac Disease associated antibody.

Results: Physical examination revealed a cachetic boy (weight – 10 kg [-3δ], height – 84 cm [10%]) who was mildly dehydrated. He had apparent excess skin with absent subcutaneous fat, and muscle wasting. Oral temperature was 98.6°F (37.0°C), pulse 120. He was initially diagnosed as celiac disease due to his history and elevated IgG antigliadin antibody. Hypochromic anemia (hemoglobin: 9.7 g/dl, RBC:4.73 $\times$ 10^{12}/l), persistent profound hypokalemia 1.8-2.4 mmol/l, elevated IgG-antigliadin antibodies: 3.149 (normal <0.9) were noted but IgA-antigliadin antibodies were normal as was chlorine levels in serum. The total IgE level was increased (611 IU/ml). Stool cultures were obtained for enteric pathogens were negative. Mucosal biopsy of the duodenum showed the initial stages of atrophy including atrophy of duodenal villi. The patient was diagnosed with malabsorption syndrome and treated with fasting with complete parenteral nutrition. He continued to experience intractable voluminous diarrhea despite treatment. He remained persistently hypokalemic despite aggressive intravenous fluid resuscitation and daily potassium replacement in excess of 4.5 mmol/kg. A tumour of the right adrenal gland was discovered on pathologic study found to be a mature ganglioneuroma, a benign tumor. Elevated levels of vasoactive intestinal polypeptide (VIP) were found. Complete resolution of diarrhea and normalization of serum potassium

occurred after tumor excision. This child has remained healthy for the last 12 years since tumor removal.

Conclusions: This case meets the criteria for diagnosis of WDHA (Watery Diarrhea-Hypokalemia-Achlorhydria) syndrome, a very rare cause of long-term diarrhea in children. WDHA can be mistaken for Celiac Disease or allergic gastroenteritis. Neuroendocrine hormone secreting tumors may mimic allergic gastrointestinal disease or celiac disease in children.

MONDAY, 19 JUNE 2017
TPS 24
CELLULAR DIAGNOSTICS AND IGE TEST DEVELOPMENT

0931 | Basophil testing contributes to the diagnosis of drug allergy in an allergy center

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Introduction: Allergic reactions to drugs are difficult to diagnose. Reagents for the first line tests skin prick test and specific IgE exist only for a limited range of drugs. Drug provocation testing is not very reproducible, as well as demanding for patients and health care staff. Basophil testing can be inserted between first line tests and provocation to aid diagnosis. Here, we describe the experience of inserting BAT in the diagnostic procedure in a tertiary hospital clinic.

Objectives: The diagnostic sequence and yield of tests in 43 consecutive patients in 2015 that required basophil tests performed for diagnosis were evaluated.

Results: Charts of patients were scrutinised for clinically relevant data and diagnoses. BAT was done with Bühlmann reagents where possible, or with an in-house test based on published recommendations. Drug, time since reaction and reaction grade according to Brown, skin prick test, sIgE, BAT, drug provocation test and clinical decision were recorded. Sensitivity, specificity, positive and negative predictive values, and 95% confidence interval (95% CI) were calculated. Variables between diagnostic tests were compared using Chi^2 test.

Drug allergy was typically diagnosed by 1. Clinical history, 2. Skin prick and specific IgE tests, 3. Basophil testing, and 4. Provocation testing.

For all 43 patients, sIgE and skin prick tests were not available or negative. Nine patients did not get a final diagnosis, 17 had no allergy, and 17 had allergy to drugs. Five were diagnosed solely on clinical history. 24 times BAT was the only test, 22 BAT were preceded by a first line test, 16 BAT were followed by a DPT and 8 diagnostic paths were more complex.

Of 70 BAT done, 9 were positive and 49 were negative. Seven patients (16%) had non-responsive basophils. BAT was the only diagnostic test performed in 18 cases. BAT was concordant with the clinical diagnosis in 14 of these cases. Eight of 16 BAT were true positive. When only BATs done within 18 months after exposure were evaluated, the diagnostic yield increased to 9 (62%).

Of 30 DPT performed 27 were concordant with the clinical diagnosis. Where both BAT and DPT were done, 2/7 BAT and 4/7 DPT (56%) were concordant with the diagnosis.

Conclusions: BAT is useful when a clear result may predict the outcome of drug provocations, both when first line tests are discordant or not available.

0932 | Lymphocyte activation test, an emerging tool in the diagnosis of drug allergy

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Introduction: The Lymphocyte Activation Test (LTT) is an in vitro technique that has been previously used in the diagnosis of delayed allergic reactions. It offers advantages over patch and intradermal tests, including absolute safety and the assessment of a T-cell response to the drug. However, it has not been yet completely standardized for many drugs.

Delayed reactions to selective inhibitors of the cyclooxygenase (COX)-2 nonsteroidal anti-inflammatory drugs (NSAIDS) are extremely rare.

Objectives: We report four cases of hypersensitivity to COX-2 NSAIDS in which these drugs were confirmed as the culprit by a positive LTT.

Results: Case 1: A 53-year-old man who presented generalized urticaria and facial edema after 15 days of treatment with daily celecoxib. Negative epicutaneous tests with celecoxib and etoricoxib were obtained. LTT was positive with celecoxib.

Case 2: An 80-year-old woman who presented generalized urticaria after 8 days of treatment with daily etoricoxib. Skin-Prick tests with a standard battery of allergens (food and pneumoallergens) were negative. No epicutaneous tests were performed. Tryptase levels were normal. LTT was positive with etoricoxib.

Case 3: A 79-year-old woman who presented generalized urticaria after 11 days of treatment with daily celecoxib. Epicutaneous tests were negative with celecoxib and etoricoxib. LTT was positive with celecoxib and negative with etoricoxib.

Case 4: A 76-year-old woman who presented DRESS Syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms) after 1 month of treatment with trimethoprim-sulfamethoxazole and etoricoxib. No cutaneous or epicutaneous tests were performed. LTT was positive with trimethoprim-sulfamethoxazole and with etoricoxib.

Conclusions: The LTT has shown to be a useful tool in the correct diagnosis of these patients. The LTT could become a good diagnostic alternative in delayed reactions with COX-2 NSAIDS and for patients with disorders that contraindicate the oral challenge test.

0933 | Toward fully leveraging the capabilities of basophil activation test in clinical research through workflow simplification and standardization

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Introduction: The basophil activation test (BAT) is a flow cytometry-based functional assay that relies on *ex vivo* basophil activation through exposure to allergenic substances. Numerous studies have demonstrated the capabilities of this test in the context of characterizing an allergic response but various parameters, such as a lack of standardization or a time-consuming and labor-intensive workflow currently hinder the field to fully leverage the capabilities of this technique

Objectives: This work aims at assessing our capabilities to simplify, standardize and miniaturize the procedure of BAT.

Method: To enable workflow simplification and standardization, we leveraged a dry and room temperature stable reagent technology. Not only staining reagents but also allergenic substances and anti-IgE for positive controls were dried. Whole blood samples (< 24 hours old) were added to the dry reagent tubes (negative controls, positive controls or test tubes); the tubes were vortexed and incubated at 37°C for 15 minutes to allow activation. After activation, red blood cells were lysed and flow cytometry data were acquired without further washing step. CD203c and CD63 expression on basophils were monitored to characterize basophil activation status in samples from allergic and non-allergic donors upon exposure to different allergenic extracts. Water soluble protein extracts of milk and peanut were prepared in house and used throughout the study. A robotic platform was also used to fully automate sample preparation when plate-based assays were considered.

Results: After optimization of the 5 color panels, flow cytometry performances as well as intermediate precision were characterized. We further demonstrated that the developed procedure can be realized on plates with a fully automated sample preparation, extending further the standardization capabilities of the method while enabling its miniaturization.

Conclusions: A whole blood based procedure for BAT, relying on the use of dry, room temperature stable and ready to use reagents was developed. Being compatible with the plate format this procedure is fully automatable, eliminates pipetting of stimulators and antibodies and does not require any washing steps. This could be a major step toward fully leveraging the capability of BAT in clinical research.

0934 | Granzyme b enzyme-linked immunospot assay in diagnosis of Stevens-Johnson syndrome induced by allopurinol

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Case report: Introduction: Allopurinol is known to cause hypersensitivity reactions including Stevens-Johnson syndrome, which is associated with high mortality. Patch tests are as a rule negative, therefore not helpful to define allopurinol as a culprit drug. Also sensitivity of lymphocyte transformation test (LTT) is limited and negative result does not exclude drug hypersensitivity.

Methods: We report a case of Stevens-Johnson syndrome that developed in a 38-year-old patient during allopurinol therapy due to gout. Based on the temporal relationship between drug exposition and clinical features, allopurinol was withdrawn because drug hypersensitivity was suspected. There was no history of any other clinically significant concomitant medications or allergy. The LTT with allopurinol and its active metabolite - oxypurinol was performed. It was followed by enzyme-linked immunospot assay detecting granzyme B (GrB-ELISpot) secreting cells from peripheral blood mononuclear cells culture. The later experiments were repeated in modified conditions: cell culture prestimulation with IL-7 and IL-15.

Results: The LTT showed borderline results: stimulation index 2 for two concentrations of oxypurinol. Results of GrB-ELISpot were slightly positive at baseline condition and clearly positive after prestimulation with interleukins.

Conclusion: In selected cases causality assessment of allopurinol hypersensitivity can be improved by GrB-ELISpot assay, especially enhanced by prestimulation with IL-7 and IL-15.

0935 | Elevated DAO in patients with histamine intolerance

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Case report: Background: Symptoms of histamine intolerance (HI) are generally associated with decreased levels of diaminooxidase (DAO), the enzyme mostly responsible for breaking down of histamine. This is the rationale behind treatment schedules of HI by means of DAO containing supplements, which could also involve second generation H1 antihistamines, cromoglycates and possibly oral steroids. We are now reporting 7 cases of histamine intolerance

in which we measured elevated DAO levels, which we believe are of theoretical and practical interest to the allergists community.

Methods: We measured DAO in the serum of 124 consecutive patients referred to our tertiary outpatient department over a period of 2 years with clinical manifestations suggestive of histamine intolerance: itching urticarial rashes and facial swelling, headache, gastrointestinal cramps, diarrhea / irritable bowel syndrome. Skin prick tests or specific IgE to the standard batch of inhalatory and food allergens were negative.

Results: We measured DAO by means of radioextraction based on measuring the conversion of 14C-labeled putrescine to delta-pyrroline by the patient's DAO (REA method). In 7 patients (2 men) out of the whole lot of 124 subjects DAO levels were between 37,5 up to >80.0 UI/ml, exceeded the upper bound of the reference normal range (14-33 UI/ml). Six of these patients experienced benefit of low histamine containing diet and standard doses of second generation H1 blocking drugs, three of them had history of atopy and clinical signs of seasonal allergic rhinitis. In the last remaining patient, who had no effect of antihistamines, intestinal microscopic colitis and mastocytosis was subsequently diagnosed. No other comorbidities to explain the increased DAO values like ovarian and prostatic cancer as suggested in the literature could be identified.

Conclusions: Since DAO is considered to be substrate-induced, its increase must prompt more detailed workup of the patients who present with this laboratory finding. If no specific conditions can be identified, we should consider conditions with increased histamine penetration (e.g. intestinal barrier dysfunction) or release (mastocytosis, unspecific histamine liberation).

0936 | Passive sensitization by transfusion with solvent-detergent treated pooled plasma in patients undergoing cardiothoracic surgery

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Introduction: Specific IgE against common airborne allergens, peanuts, wheat, and latex have been detected in solvent/detergent (SD) treated pooled plasma (Octapharma). Each batch of SD plasma is pooled from 600-1500 blood donors, and distribution of IgE specificities vary within each donor pool (batch). SD plasma is the only plasma component available for transfusion in Norway. Due to surgery or bleeding, patients may receive high volumes of plasma.

Objectives: In this study we investigate passive IgE sensitization by plasma transfusion in patients undergoing complex cardiothoracic surgery.

Results: Total IgE and specific IgE against house dust mite (d1), timothy (g6), peanut (f13), and latex (k82) were investigated by specific IgE in plasma batches and in patients before surgery and throughout hospital stay. Results are given as (mean; median; range). 23 patients were transfused with a range of 400 to 14200 ml SD treated pooled plasma. The SD plasma consisted of 13 different batches, and elevated levels of total IgE were observed in 12 of 13 batches (153; 160; 117-195). All batches had detectable specific IgE against house dust mite (3.17; 2.52; 0.81-6.28) and timothy (2.79; 2.83; 0.64-4.29), whereas 6 of 13 batches had specific IgE levels against peanut (0.60; 0.48; 0.12-1.50) and 4 of 13 IgE against latex (0.46; 0.31; 0.06-1.54). Before transfusion total IgE were below adult reference ranges (<120 kU/l) in 21 of 23 patients (80; 34; 0-834 kU/l), and in 20 of 21 patients, negative results (<0.35 kU/l) were observed when measuring specific IgE against house dust mite (0.41; 0.03; 0.02-7.51 kU/l) and timothy (0.17; 0.01; 0.09-0.10 kU/l). After transfusion, however, a significant increase in IgE concentration were observed, and the highest value measured within day 1 of surgery were for total IgE (104; 50; 15-813 kU/l), sIgE house dust mite (1.44; 0.73; 0.16-7.54 kU/l), and sIgE timothy (0.90; 0.61; 0.15-3-39 kU/l). Positive correlation was observed between the increase in IgE and the volume of plasma transfused. After transfusion a conversion to detectable levels of sIgE against peanut were observed in 4 patients (range 0.58-0.66 kU/l) and sIgE latex in 2 patients (range 0.45-0.48 kU/l).

Conclusions: We conclude that passive sensitization occurs in transfusion with solvent detergent treated pooled plasma and that IgE levels after transfusion correlate to the volume of plasma transfused.

0938 | Analysis of ICD-10 diagnosis codes of patients with hypereosinophilia

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Introduction: A great number of patients are consulted to allergy clinics due to eosinophilia. However, there are a great number of diseases in the definitive diagnosis of eosinophilia. The purpose of this study is to assess the ICD -10 (International Statistical Classification of Diseases and Related Health Problems) codes of patients who were found to have eosinophilia and to analyze their diagnosis.

Objectives: We aimed to evaluate the frequency of allergic diseases and immunodeficiency in children with hypereosinophilia who admitted to our hospital. The results of complete blood count (CBC) tests of the patients who were admitted to the general pediatric clinic in our hospital between 1 January 2015 and 31 December 2015, were analyzed. The patients who had >1500/mm^3 absolute

eosinophil count and > %10 eosinophil percentage were accepted as hypereosinophilia.

Results: 131208 CBCs were done to 66481 patients between the ages 0 and 18 within the aforementioned period. 554 (0.83%) of these patients were found to have hypereosinophilia. When ICD diagnosis codes were analyzed, it was found that of these 554 patients, 86 (15.5%) were found to have diagnoses related with allergic diseases, while 5 (0.9%) were found to have diagnoses related with immunodeficiency.

Conclusions: It was found that 91 (16.4%) who had CBC in pediatrics clinics and who were found to have eosinophilia were found to have diagnoses related with allergic diseases and immunodeficiency. This result shows that while approaching hypereosinophilia, care should be taken in terms of other diseases in definitive diagnosis as well as allergic diseases.

0939 | Determination of reference values for IgG antibodies against typical antigens of hypersensitivity pneumonitis – current data of a German multicentre study

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Introduction: Specific (s)IgG antibodies against relevant environmental and occupational antigens, especially from bacteria, moulds, yeasts, birds and chemicals play an important role for detection of hypersensitivity pneumonitis (HP). Therefore the quantitative determination of antigen sIgG has a high impact in the diagnostic procedure of HP. A frequently applied technique is the IgG Fluorescent immunoassay (FEIA) providing absolute values (mg of antigen sIgG/L). In contrast to specific IgE, the cut off values for different IgG antigens cannot be considered as a uniform value and vary in a broad range.

Objectives: The aim of this study is to establish sIgG-reference value for each recurrent antigen and/or to validate pre-existing values in a suitable healthy donor group.

Results: Therefore a study including 6 clinical centres in Germany was conducted to collect sera from 121 subjects (44% male, median age 43 years (range 21-83 years), 62% never smoker) without any signs of HP and without obvious exposure to potential HP antigens. Specific IgG to 31 typical HP antigens were centrally quantified by ImmunoCAP. For validation selected measurements were repeated, total IgG was determined, sera were tested for unspecific binding with the human sera albumin, and influence of potential confounders was analysed. Results were expressed as median, inter-quantile range and the 97.5% quantile values were evaluated as cut-off value. For three isocyanates (4 mg_A/l), three acid anhydrides (4 mg_A/l) and *Trichosporon pullulans* (11 mg_A/l) cut-off values were proposed for the first time. For several avian antigens, moulds and bacteria pre-existing cut-off values nearly could be confirmed without significant deviations, but already the 90% quantile for sIgG against *Penicillium chrysogenum*, *Aspergillus fumigatus* and pigeon antigen (Ge91) clearly exceeded the pre-existing values. In contrast, the new proposed cut-off value for *Candida albicans* was nearly half of the pre-existing value. Specific IgG-values were not significantly influenced by smoking and gender and most of them were unaffected by age.

Conclusions: For further validation comparison with sIgG values of definitely diagnosed HP patients is desirable, but realistically this will be difficult to achieve for many HP subtypes due to the small number of cases. Nevertheless we suggest considering the determined sIgG values for a better classification of sIgG concentrations in the scope of HP diagnosis.

0940 | Correlations between pollen exposure, pollen sensitization and patent pollen allergy

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Introduction: Geographical variations in the distribution of allergic sensitization in populations have been described but their relationship to pollen exposure is quite lousy. Besides, allergic sensitization is not equivalent to patent allergy. This epidemiological survey focused at the relationships between pollen exposure, pollen sensitization and clinically relevant allergy.

Objectives: 1- To assess the relationships between allergic risk (RAEP) and pollen allergy.

2-To evaluate the clinical relevance of quantitative results of skin tests and specific IgE for diagnosing patent allergy.

Results: 284 adult outpatients visiting an allergy clinic in Marseille, Bagnols/Cèze or Valence.

Skin tests to common inhaled allergens performed using the same batch in the 3 centers.

Assessment of the clinical relevance of positive skin tests by the attending allergist at the end of the outpatient visit.

Quantification of specific IgE to the same inhaled allergens.

Few correlation, except for Ambrosia, between pollen exposure and pollen sensitization.

		Ambrosia	Cypress pollen	Grass pollen	Cat danders	House dust mite
Skin tests (mm)	Relevant	7.45	7.8	3.1	6.5	7.9
NS: Not Significant	p	NS	0.02	NS	NS	NS
	Non relevant	7.57	6.6	2.7	5.9	8.2
IgE (kU/l)	Relevant	26.9	7.8	17.6	9.55	19.9
	p	0.02	0.001	NS	0.01	0.02
	Non relevant	13.1	2.5	15.7	7.22	5.1

Diameter of the wheal of skin tests was not relevant to patent allergy, in contrast to measurements of specific IgE.

Conclusions:

1. Few correlation between pollen exposure and allergic sensitization, apart from Ambrosia pollens.
2. IgE measurements, contrary to skin tests diameter, correlate with the clinical relevance of these sensitizations.

Résultats 2:

L'évaluation quantitative de la réactivité de la peau et des IgE spécifiques aux allergènes inhalés.

Diameter of the wheal of skin tests was not relevant to patent allergy, in contrast to measurements of specific IgE.

0942 | Fractional exhaled nitric oxide in elementary school children: a candidate predictor for atopy?

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Introduction: Fractional exhaled nitric oxide (FeNO) is a non-invasive and useful tool evaluating for respiratory eosinophilic inflammation. However, there have been few studies of FeNO focused on allergic rhinitis especially in children.

Objectives: We have performed a cross-sectional study to measure FeNO in elementary school children and performed group analysis according to the presence of atopy and rhinitis.

Results: FeNO of 383 elementary school children was measured. Among them 49 (12.8%) children failed to complete FeNO measurement. Remaining 334 (87.2%) children were included in the analysis. The mean age was 8.3 year (range, 6-12). The children were classified into 4 groups after completion of allergic rhinitis questionnaire, skin prick tests and physical examination: those with allergic rhinitis (group A), non-allergic rhinitis (group B), asymptomatic sensitization (group C), and healthy control (group D). Mean FeNO values in children with allergic rhinitis (15.46 $\pm$ 11.07 ppb) were the highest followed by those from asymptomatic sensitizer (12.43 $\pm$ 6.63 ppb), non-allergic rhinitis (8.75 $\pm$ 4.15 ppb) and healthy control (7.54 $\pm$ 4.35 ppb). The differences were statistically significant among groups. FeNO values were also significantly different according to age. FeNO was not correlated with the severity of allergic rhinitis, however, it was correlated with allergen/histamine ratio of the skin prick tests.

Conclusions: FeNO values are more elevated in children with atopy compared to those without atopy. They are well correlated with the results of skin prick tests. Thus, FeNO measurement may have a certain role as a predictor for children with atopy.

0943 | Do we appropriately do allergy testing in primary care?

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Introduction: There is a high demand for allergy testing as the prevalence of allergic diseases is increasing.

Different countries have their own traditions regarding allergy testing *in vivo* and in vitro in primary care and/or in a hospital setting as well. It is common in Denmark to use both prick-test and/ blood tests, but although there may be regional differences blood tests seem to be preferred tool for allergy testing.

Objectives: Our aim was to explore the pattern of allergic testing of blood samples required by primary care physicians during 2015 in Central Jutland Region and in particular in Regional Hospital Central Jutland (Viborg) geographical area to evaluate whether it was in accordance with the regional guideline for allergy testing. For this purpose we analyzed data on ordered blood allergy tests extracted from the regional laboratory information system (LAKBA II).

We offer clinicians both screening panels with IgE against most common allergens for food (FX5E) or inhalation allergens with an algorithm for automatic testing of included allergens after a positive screening test, and specific IgE analyses against single allergen.

Results: A total of 107858 IgE tests consisting of as well screening panels as panels and specific IgE, had been required from primary care in whole region. 20954 (19.42%) tests were IF and 13131 (12.17%) were FX5E. The remaining 73773 (68.39%) tests were for a specific IgE.

For children below the age of 3 years, a low frequency of FX5E tests was seen in primary care both in Viborg's area (105 tests;

3.29% out of all 3189 tests) and in whole region (819 tests; 4.6% out of all 17613 tests), respectively. Surprisingly, we observed a higher frequency of the same panel in children at age of 3-14 years (15.8% for Viborg's area and 24.5% for whole region, respectively), ordered by primary care. IF was ordered similarly often in primary care in Viborg's area (68.5%) and in whole region (74.7%).

Conclusions: Blood allergy tests in primary care in our geographical area and in whole region are not always chosen rationally despite existing guidelines. Inappropriate use of these tests could have an economic impact on regional health system as well as on quality of diagnosis, with potential impact on patient welfare. Further education of health professionals in primary care and a better collaboration with laboratory specialists is a necessary step for optimizing allergy testing.

0944 | Use of high technologies in clinical laboratory diagnostics of a seasonal allergic rhinitis

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Introduction: Based and activated basophils of peripheral blood with phenotype CRTH2 + CD203c+CD3-in SAR patients on the background of slAST were identified by a method of flowing cytometry ("Beckman Coulter Cytomics FC500", "Caltag Laboratories", USA).

Objectives: The method of slAST was applied to 60 patients of 18 up to 55 years old (15 men and 45 women) who have finished annual early treatment by pollen of a wormwood (130,930 PNU for a full course of treatment).

Results: During an exacerbation, in serious form of SAR, the activation of basophils has made 94.3 + 0.4%, decrease in activation of basophils up to 24.3 ± 2.1% ($P < .001$) was observed in use of allergens in concentration of 100 PNU, however the usage of allergen in a dose 1000 PNU an even greater decrease of active basophiles up to 10.1 ± 0.6% ($P < .001$) was observed. The maximal decrease of active basophiles in quantity in peripheral blood of patients AP up to 5.1 ± 0.2% ($P < .05$) easy and 9.2 ± 1.1% ($P < .001$) an average degree of seriousness of illness was observed when applying 100 PNU allergen and more. Thus, the maximal decrease in quantity of active basophils in peripheral blood of patients with SAR of an easy and average degree of seriousness of illness was observed when applying 100 and more PNU allergen, and at heavy 1000 and more PNU.

Conclusions: Three-parametrical flowing cytometry allows to allocate pure sub popular structure of basophils with phenotype CRTH2+ CD203c+CD3- by means of monoclonal antibodies and to reflect a degree of activation of basophils depending on seriousness of disease, and to define criteria of efficiency of applied slAST.

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Results: During an exacerbation, in serious form of SAR, the activation of basophils has made 94.3 + 0.4%, decrease in activation of basophils up to 24.3 ± 2.1% (<0.001) was observed in use of allergens in concentration of 100 PNU, however the usage of allergen in a dose 1000 PNU an even greater decrease of active basophiles up to 10.1 ± 0.6% (<0.001) was observed. The maximal decrease of active basophiles in quantity in peripheral blood of patients ?? up to 5.1 ± 0.2% (<0.05) easy and 9.2 ± 1.1% (<0.001) an average degree of seriousness of illness was observed when applying 100 PNU allergen and more. Thus, the maximal decrease in quantity of active basophils in peripheral blood of patients with SAR of an easy and average degree of seriousness of illness was observed when applying 100 and more PNU allergen, and at heavy 1000 and more PNU.

Conclusions: Three-parametrical flowing cytometry allows to allocate pure sub popular structure of basophils with phenotype CRTH2 + CD203c+CD3- by means of monoclonal antibodies and to reflect a degree of activation of basophils depending on seriousness of disease, and to define criteria of efficiency of applied slAST.

0945 | Establishment of Artificial Human Sera (ARTHUS) based on Chimeras of FcγRI and Human Immunoglobulin G4 (IgG4) Domains

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Introduction: Human pool sera are the immunologist's first choice as controls for most diagnostic applications, but are strongly limited regarding availability, varying quality and high costs. The aim of this study was to circumvent these limitations by developing a versatile tool which allows the use of polyclonal antibodies in allergen-specific IgG4 immunoassays. Allergen-specific IgG4 is a commonly used marker for monitoring of patients under immunotherapy treatment. For that purpose different diagnostic systems for the detection of specific IgG4 (sIgG4) for Dermatophagoides pteronyssinus and birch pollen were compared by the use of artificial human sera (ARTHUS).

Objectives: The extracellular domains (ECD) of the human high affinity IgG receptor FcγRI (CD64) were fused to the human immunoglobulin region of the gamma isotype, subclass 4. Recombinant adapter molecules comprising the FcγRI ECD and human IgG4 domains (CD64-IgG4) were expressed in human HEK-293 cells. Allergen-specific IgG antibodies were produced in rabbits by

immunization with Dermatophagoides pteronyssinus extract (d1) and Bet v 1, the major protein of birch pollen (t3). Pre-incubation of polyclonal IgG with CD64-IgG4 produced artificial allergen-specific reagents which were used in allergen-specific immunoassays.

Results: Assessment of CD64 immunoreactivity to human isotypes and IgG subclasses verified the reduced specificity for IgG4. After formation, the resulting IgG4-based artificial human sera were measured in established diagnostic systems of different manufacturers for the determination of sIgG4 to d1 and t3. IgG4 ARTHUS show significant reactions in all applied diagnostic systems. Comparison of results is hampered by the expression of the values in different units depending on the diagnostic system used. Our data indicate the need for standardization of different test systems for the monitoring of sIgG4 during immunotherapy treatment. The possibility to create large amounts of synthetic serum samples with a well-defined IgG4 immunoreactivity enables continuous and reliable availability of urgently needed reference material.

Conclusions: Rabbit IgG complexed with the IgG-specific CD64-IgG4 adapter molecule have the potential to provide a substitute for human reference sera with specificity for virtually any protein of interest. ARTHUS represent a suitable tool for an improved comparability of in-vitro diagnostic systems, which currently do not underlie a general standardization.

MONDAY, 19 JUNE 2017
TPS 25
COMPONENT RESOLVED DIAGNOSIS

0946 | Phylogenetic relationship according allergen sensitization pattern between 10 mites in a tropical area

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Introduction: Mites are the main source of IgE sensitization in the world. Although much is known about sensitization to *Blomia tropicalis*, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, little is known about sensitization to other species

Objectives: To evaluate the frequency of sensitization to 10 species of mites (Blo t, Der f, Der p, Aca s, Cho, Der m, Eur m, Gly d, Lep d, Tyr p) and explore the phylogenetic relationships among mites according to the most frequently reported allergens

Results: Cross-sectional study with 147 patients to evaluate sensitization to 10 mites through skin tests and serum specific IgE. Based on the reason of sensitization of each mite, the phylogenetic relationship of mites was evaluated for allergens of group 1, group 2 and group 5 according to the sequence of mRNA and amino acids with the sequences validated in the National Center for Biotechnology Information (NCBI) and alignment by CRUSTAL Omega, Version 1.2.3 of UniProt. For the construction of the phylogenetic trees, the Neighbor-Joining reconstruction method was used the Molecular Evolutionary Genetic Analysis (MEGA) program, version 6.
115 (78,2%) were sensitized to less one allergen and 110 (74,8%) to more than one. The highest frequency of sensitization was found for mites of the family Pyroglyphidae (> 70%) and the lowest frequency, for those of the family Glycyphagidae (<50%). When evaluating the prevalence ratio of sensitization to Der f or Der p increased more than 20-fold the likelihood of sensitization to mites of the Pyroglyphidae family and 10 to 20-fold to mites of other families. Sensitization to mites of the family Glycyphagidae, Chortoglyphidae or Acaridae increased the risk less than 5 times. Blo t had a low identity with allergens from other groups even with other mites from glyciphagidae family.

Conclusions: Sensitization to Pyroglyphidae mites (*Dermatophagoides spp*), increases the probability of sensitization to other mites from Glycyphagidae, Chortoglyphidae o Acaridae family. *Blomia tropicalis* allergens had a low identity with other mites including other mites of the glyciphagidae family, suggesting a low taxonomic relationship. These results should be taken into account when defining the diagnosis and treatment of allergic diseases.

0947 | Serum IgE reactivity to major Dermatophagoides pteronyssinus allergens in house dust mite allergic patients from northeast Poland

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Introduction: The spectrum of IgE response to individual allergens varies in different populations of house dust mite (HDM)-allergic patients. The aim of this study was to evaluate the IgE reactivity to natural (n)Der p 1, nDer p 2, recombinant (r)Der p 2 and rDer p 23 in HDM-allergic patients from Northeast Poland.

Objectives: The study was performed on 250 Dermatophagoides pteronyssinus (Dp)-allergic rhinitis patients (12 to 65 years of age) with (AA; $n = 135$) and without (AR; $n = 115$) asthma. The control group (CG; $n = 100$) consisted of 30 healthy nonatopic subjects (HCs), 26 allergic rhinitis patients not sensitized to Dp and 44 nonatopic asthmatics. Serum level of allergen-specific IgE to nDer p 1, nDer p 2, rDer p 2 and rDer p 23 was evaluated by direct ELISA. The cut-off for positive value was established as the mean in HCs + 3 standard deviations. Concentration of serum Dp-specific IgE was evaluated.

Results: All subjects in CG had DpIgE below 0.35 kU/l whereas all Dp-allergic patients had DpIgE above 0.35 kU/l (0.71-146 kU/l). Among all Dp-allergic patients no IgE reactivity to any of the studied allergens was found in 11 patients (4.4%) of which only 4 were AA. Serum IgE reactivity to nDer p 1, nDer p 2, rDer p 2 and rDer p 23 was demonstrated in 199 (76.9%), 206 (82.4%), 200 (80%) and 187 (74.8%) Dp-allergic patients respectively. Among AA IgE reactivity to nDer p 1, nDer p 2, rDer p 2 and rDer p 23 was demonstrated in 113 (83.7%), 116 (85.9%), 113 (83.7%) and 111 (82.2%) patients, respectively. The greatest mean serum IgE reactivity was detected for Der p 2, which was significantly greater than that of Der p 1 ($P < .001$) and Der p 23 ($P < .001$). Serum IgE reactivity was significantly greater in AA than AR patients for Der p 1 ($P = .005$) and Der p 23 ($P < .001$) but not for Der p 2 ($P = .064$). In AA not treated with inhaled corticosteroids ($n = 65$) the strongest correlation was detected between expired nitric oxide concentration and serum IgE reactivity to Der p 23 ($R = .455$, $P < .001$). Significant correlation between IgE reactivity to nDer p 2 and rDer p 2 was demonstrated ($P < .01$) but IgE reactivity to rDer p 2 in some patients was less than to nDer p 2.

Conclusions: In adolescent and adult HDM-allergic patients from Poland, Der p 1, Der p 2 and Der p 23 are confirmed to be major, serodominant allergens. Sensitization to Der p 23, in addition to Der p 1 and Der p 2, may play an important role in the pathogenesis of HDM-allergic asthma.

0948 | Regional differences in the prevalence of sensitization to lipid transfer proteins and severity of allergy symptoms in Italy: results of a multicenter study

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Introduction: Lipid Transfer Proteins (LTPs) are often causative allergens of severe allergic reactions after their ingestion (i.e.: in Rosaceae fruits or nuts) and rhinoconjunctivitis and/or asthma when it is contained in pollens. The main allergens of peach (Pru p 3) and pellitory pollen (Par j 2) are LTPs, and a certain degree of cross-reaction between them has been described.

Objectives: We analyzed geographical differences in the Italian territory, in terms of prevalence of sensitization towards Pru p 3 or Par j 2, co-sensitization towards Pru p 3 and Par j 2, and allergic symptoms (and their severity) after ingestion of peach (or other Rosaceae fruits) in Pru p 3 sensitized patients.

This is a multicenter study carried out in collaboration between the Allergy centers in South (Catania and Bari), Center (Florence) and North of Italy (Piacenza). All patients who underwent an Immuno Solid-phase Allergen Chip (ISAC) assessment of allergenic sensitizations in a 6-month period (November 2015 – May 2016), irrespectively of the clinical reason, have been included into the study. All patients sensitized to Pru p 3 were interviewed to investigate any food allergic (particularly after ingestions of peach and other Rosaceae fruits) and respiratory symptoms.

Results: 311 patients have been enrolled. The prevalence towards any LTPs was high in all the 3 macro-areas, but higher in the Center of Italy (52%) than in North (39.3%) and South (36.8%), $P = .016$. Pru p 3 sensitization prevalence was similarly high in the 3 considered macro-areas, while the Par j 2 sensitization was significantly higher in Center (26%) and South (27.7%) than in the North (7.1%), $P = .001$. 57/97 (58.8%) Pru p 3 sensitized patients had food allergic symptoms after ingestion of peach, with a higher prevalence in Center of Italy (73.3%) than in North (47.7%) and South (54.2%), $P = .027$. The prevalence of peach allergic patients was not significantly different according to Par j 2 sensitization, while in patients from South Italy, severe allergic reactions to peach (defined as the presence of anaphylaxis and/or respiratory symptoms) were more frequent in patients not sensitized to Par j 2 (16% vs 0% in Par j 2 sensitized patients, $P = .045$).

Conclusions: Geographical differences are relevant in determining the sensitization to inhalant and food allergens, and the possible combinations of food and inhalant allergens sensitizations may promote or conversely protect from the development of food allergy symptoms, affecting in particular their severity.

0949 | A comparison of IgE- and IgG-immunoreactive properties of protoplasmic proteins derived from different strains of lactobacillus genus

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Introduction: Each metabolic active bacterial cell is able to produce proteins which also can be considered as antigens. Their composition may depend on: the cell condition, bacterial taxonomic affiliation and interaction with exogenous factors. In the early life, most organisms develop tolerance and the body identifies the commensal and probiotic bacterial proteins as self-specific and nevertheless, the existence of their interaction with IgE- and IgG-class antibodies were confirmed in previous experiments of authors.

Objectives: The main aim of this study was a comparison of profile and identification of the immunoreactive proteins derived from protoplasm of five strains of *Lactobacillus* genus that are commonly used in the food fermentation process and as a popular component of probiotic formulas: 1) *L. casei* 2K, 2) *L. delbruecki* subsp. *bulgaricus* 151, 3) *L. plantarum* W42, 4) *L. rhamnosus* GG and 5) *L. salivarius* AWH.

Results: The profile of isolated bacterial proteins differs considerably in analyzed strains depending on the class of antibody and applied human serum (AL vs H) IgE ($P = .031$) and IgG ($P = .027$). It has been proven (also after identification with MALDI-TOF MS/MS method) that molecular mass of proteins plays a significant role in their immunoreactivity. Low molecular mass proteins (<15 kDa) interact stronger with IgG present in sera of healthy individuals than with allergic ($P = .029$) and molecular mass proteins (>25 kDa) are more prone to interact with IgE of allergic sera ($P = .047$). Isolation and identification of IgE and IgG reactive proteins revealed that they belong to different groups of protein characteristic for various compartments of bacterial cells.

Conclusions: *Lactobaclillus*, protoplasmic proteins profile differs significantly depending on the analyzed species and reveal different determinants with varying capacity of binding to allergic and healthy

IgE and IgG antibodies. Protoplasmic protein fraction exhibits a high usefulness in the analysis of the immunoreactivity of bacterial proteins. The application of this fraction allows the identification of not only intracellular cytoplasmic and nucleus proteins but also those that are intended to secretion through the membrane and cell wall of bacteria what may be crucial for making faster and more reliable molecular analysis of the presence of immunoreactive proteins in fermented products.

0950 | The first European allergen components profile of six main inhalant allergens in 492 atopic children. An important absence of major allergen components

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Introduction: Molecular allergology give the possibilities to build allergen components profile for every allergen source. The picture of major and minor allergens in atopic children is extremely important for diagnosis, prophylaxis and treatment (e.g. immunotherapy). In this cross-sectional, prospective study, allergen components profile in atopic children using component resolved diagnostics (CRD) was analyzed.

Objectives: Serum specific IgE to 112 allergen components were measured by using multiplex microarray in 492 atopic children (age: 0-18 years). Sensitization to six main inhalant allergens (timothy grass, birch and mugwort pollen, house dust mite (HDM), cat and dog allergens) and allergen components profile for every allergen source was analyzed.

Results: IgE reactivity to timothy components was found in 327 (66%) children and the profile from the most frequent to the most rare component was as follows: Phl p 1/5/4/2/6/11/12 and Phl p 7 (78, 57, 54, 41, 35, 23, 15 and 4% respectively), whereof in 11,3% of children the major timothy allergens Phl p 1/5 were absent. IgE sensitization to birch components was found in 259 (53%) children and the profile was as follows: Bet v 1, Bet v 2 and Bet v 4 (93, 22 and 5% respectively), whereof in 6.9% of children the major birch allergen Bet v 1 was absent. IgE sensitization to mugwort components was found in 99 (20%) children and the profile was: Art v 1 (78%) and Art v 3 (39%) whereof in 23.2% of children the major mugwort allergen Art v 1 was absent. IgE reactivity to HDM components was found in 308 (63%) children and the profile was: Der f 2, Der p 2, Der p1, Der f 2 and Der p 10 (81, 77, 73, 72 and 15% respectively) whereof in 6.5% of children the major HDM allergens Der p 1/2 were absent. IgE sensitization to cat allergens was found in 224 (46%) children and the profile was: Fel d 1 (79%), Fel d 4 (33%) and Fel d 2 (28%) whereof in 20.5% of children the major cat allergen Fel d 1 was absent. IgE reactivity to dog allergens was found in 215 (44%) children and the component profile was as follows: Can f 1/5/2 and Can f 3 (78, 50, 30 and 29% respectively) whereof in 8,3% of children the major dog allergens Can f 1/2/5 were absent.

Conclusions: CRD is critical in recognition of the reactivity to major allergens of allergen source in atopic children. A sizable part of children have no sensitization to major allergen components. This fact has an important impact on diagnosis and treatment (e.g. immunotherapy).

0951 | Assessment of allergen specific IgE to pollen allergens in allergic patients from Central Ukraine

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Introduction: New methods of allergy diagnostics make possible determination of the spectrum of antibodies induced in allergic patients to pollen allergens. The most important allergens for induction of pollen specific IgE in Central Ukraine were assessed.

Objectives: The medical records of patients of the Vinnitsa Regional Clinical Allergy Centre "Alergocentr-KPP" and Vinnitsa Municipal Hospital No1 were reviewed. Levels of allergen specific antibodies were determined using Quantitative Multiparameter Assay profiles DP 3110-1601-1 E (Inhalation 2 panel) and DP 3111-1601 E (Paediatric Inhalation panel). Records of 59 patients from September-December 2015 were analyzed. Interpretation of specific IgE antibodies including Class 0 (negative result, < 0.35 kU/l,) to Class 6 (> 100 kU/l).

Results: Patients were 15 to 58 years old with 63% females. 12 patients were aged from 15 to 21 including 10 females. All tested individuals were polysensitized. They react to fungal spores, house dust mites, food, pollen and animal dander allergens. The maximum number of sensitizations for one patient was 15. Six individuals reacted to from 10 to 15 allergens. 50% reacted to dust mites The severity of reaction was mainly significant to high (Classes III-IV) mostly. 80% of the spore-sensitive patients were sensitive to pollen. Four to one pollen type, *Secale* or *Artemisia*; one to both *Secale* and *Artemisia*, one to *Secale* and Poaceae; others were sensitized to 3-8 pollens. High antibodies (Class V, 50-100 kU/l) were seen to *Alnus*, *Corylus*, *Betula* and *Artemisia* pollen only (7.9%). Significant to high (Classes III-IV, 3.5-50 kU/l), occurred in 55% of cases. *Betula* (81%), *Artemisia* (77%) and Poaceae (75%) pollen provoked the highest number of Class III to VI results. Pollens were the main causal allergen for patients who were not fungal allergic. Severe reactions to *Phleum*, *Secale*, *Alternaria*, *Plantago* were prevalent.

Conclusions: 80% of patients reacted to up to 8 pollen types. The greatest amount of high to extremely high allergen specific IgE was provoked by *Betula*, *Artemisia* and Poaceae pollen. Pollens appeared to be the main causal allergen for patients.

0952 | Skin prick test reactivity to eighty different allergens among medical students in Birjand, Iran

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Introduction: Allergic disorders are among the most prevalent health problem around the world and have a significant negative impact on patients' quality of life. Allergens are the most common triggers of allergic symptoms and the pattern of sensitization vary in different societies because of life style and genetic background. Identification of the prevalent allergens in each area and general population has an important role in prevention and management of allergic disorders. Because of the greatness and population diversity as well as different geo-climatic conditions of Iran, the aim of this study was to evaluate the prevalence sensitivity to eighty different among medical student in Birjand, Iran.

Objectives: Demographic data and presence of allergic symptoms was evaluated by a questionnaire. Skin prick tests were performed with 80 different allergens including foods, grasses, weeds, trees, insects and molds on 144 medical students in Birjand city of Iran.

Results: 144 medical students (mean age 21.1 years, range: 19-30, M/F ratio: 0.63) randomly selected and enrolled in this study. Prevalence of asthma, allergic rhinitis and eczema was 2.77%, 40%, and 12.5% respectively. The overall rate of sensitization to any allergen was 51%. Among the food allergens, tomato, orange, walnut and pomegranate and mustard showed the highest rate of sensitization (4.82%, 3.47%, 3.47%, 3.47% and 3.47% respectively). The most common aeroallergens were Salsola kali (48.6%), common weed mix (45.3%), Chenopodium Album (40.9%) and trees mix (29.86%). There was no significant difference in rate of sensitization among girls and boys.

Conclusions: The results of present study confirmed high rate of allergic symptoms and skin sensitization to particularly weed and grass allergens among students. Further analysis with more participants needs to confirm the result of our study.

0953 | Five-years follow-up in Italian children with seasonal allergic rhinitis: preliminary data

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Introduction: The evolution of allergic rhinitis (AR) in childhood lacks of clear evidence on the spreading of allergic sensitization. The National multicenter study "Panallergens in Pediatrics" described the clinical features and allergic sensitization of more than 1200 children suffering from hay fever in the years 2009-2011.

Objectives: The aim of this study is to evaluate the evolution of clinical features and allergic sensitization of patients recruited in the previous study to identify potential predictive factors for clinical evolution (disease severity, appearance of other allergic diseases, especially asthma and oral allergy syndrome- OAS) and response to allergen specific immunotherapy (AIT). Patients were re-evaluated by performing skin prick tests (SPTs) with the same standardized panel of inhalant and food allergens used in the previous study. Clinical data were collected by using the computerized platform. Blood samples were also obtained for the determination of specific IgE.

Results: Up today, 201 patients (64.7% male, mean age 16.2 years) completed the clinical reevaluation and SPTs. By comparing the follow-up with the baseline data, it is observed a persistence of AR in 95.5% of patients, with an higher mean number of months/year with symptoms (3.4 vs 3.9, $P = .0016$), but also in the percentage of subjects with AR>4 months/year (16.4% vs 27.6%, $P = .0205$). Among allergic diseases associated with AR, we observed a slight but not statistically significant increase of patients with asthma (from 31.8% to 35.3%), and a significant increase of patients with OAS (from 22.9% to 37.3%, $P = .0023$). The mean number of positive SPT to pollen extracts was increased at follow-up (from 3.5 to 4.6, $P < .0001$), while the number of SPT positive to indoor allergens remained stable (1.2 vs 1.3). The percentage of patients with >4 positive SPT was significantly higher at follow-up (from 48.2% to 65.7%, $P = .0001$). Among the 27 patients who received AIT for grass pollens, AR disappeared in 7.4% of patients, while among patients who didn't received AIT the percentage of AR remission was 3.8%.

Conclusions: This prospective study showed an increase of sensitization and duration of AR symptoms during follow-up, but also of the prevalence of OAS, maybe linked to higher sensitization to panallergens; this data will be investigated by allergen molecular assay. Albeit preliminary data, the AIT seems to favor the remission of AR.

0954 | A cross-sectional observational study on allergen-specific IgE positivity among allergic patients in a southeast coastal versus a southwest inland region of China

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Introduction: Few studies shed light on trans-regional differences in allergen sensitization between vast regions within a similar latitudinal range but with distinct geomorphological features. We aimed to detect specific IgE (sIgE) positivity to common allergens in populations from two southern China provinces.

Objectives: Using a uniformed protocol,, 2778 serum samples collected from 1431 subjects referred by 38 hospitals in Yunnan, and 1347 subjects by 49 hospitals in Guangdong and examined for sIgE to local allergens including house dust mite, cockroach, tree pollen mix, mold mix, dog dander, crab, shrimp, egg white and milk.

Results: The overall sIgE positive rates were 58.4% in patients from Guangdong vs 61.0% from Yunnan. House dust mite (d1) was the most common allergen in both regions. Among d1-sensitized patients, only 35.7% (208/583) in Guangdong and 22.9% (147/642) in Yunnan tested positive for house dust mite alone. Among those poly-sensitized d1-positive subjects, cockroach was the most common co-sensitizing aeroallergen in either province. 41.9% of the d1-sensitized Guangdong subjects had class 4 or higher response, in drastic contrast to a very low percentage of such reactivity in Yunnan subjects. However, a high proportion of d1-sensitized patients in Yunnan (36.3%) were concomitantly positive for tree pollen mix. Guangdong subjects were more likely to have sIgE positivity to milk compared with those from Yunnan. Surprisingly, Yunnan patients showed high sIgE-positive rates for crabs and shrimps, either by an overall or by age-group analysis, compared with their Guangdong counterparts (both $P < .05$).

Conclusions: In summary, we found a high prevalence of overall sIgE positivity to local allergens among allergic patients in two southern China provinces about 840 miles apart. House dust mite (d1) was the most common sensitizing allergen in the two populations. Sensitization to d1 was frequently accompanied by co-sensitization to other local allergens, such as cockroach in both regions and tree pollens in Yunnan. Among patients in the inland Yunnan, sensitization to crab and shrimp were more common compared with those from the coastal Guangdong. These data may be associated with differences in lifestyle, climates and geomorphological features between the two regions. While further validation and interpretation are needed, our findings may add to data for evidence-based management of local allergies in China and worldwide.

Table 1 Overall and stratified rates of positive sIgE to any allergen in the study population ($n = 2778$)

	Guangdong sIgE positive rate % (n/N)	Yunnan sIgE positive rate % (n/N)
Overall rate of positivity	58.4% (787/1347)	61.0% (873/1431)
Rates of positivity by Sensitizing allergens		
1	43.6% (343/787)	30.7% (268/873)
2	18.7% (147/787)	22.9% (200/873)
3	11.1% (87/787)	16.8% (147/873)
4	16.1% (127/787)	16.7% (146/873)
5	5.8% (46/787)	6.4% (56/873)
6	4.7% (37/787)	6.4% (56/873)
Gender		
Male	63.7% (418/656)**	65.5% (408/623) **
Female	53.4% (369/691)	57.5% (465/808)
Age		
0–3 years	67.7% (197/291)	56.6% (77/136)
4–6 years	67.7% (151/223)	62.7% (69/110)
7–14 years	75.3% (146/194)	62.1% (182/293)
15–50 years	47.3% (274/579)	63.3% (468/739)
51 years	33.3% (20/60)	50.3% (77/153)

**: $P < .001$; The sIgE positive rate was significantly higher in male than in female patients in either province (Guangdong: $P < .001$; Yunnan: $P < .05$). Allergen sensitization showed significant differences among age groups in both Guangdong ($P < .001$) and Yunnan ($P < .05$).

0955 | The use of LTP's sensitization profile and protein alignment tools in food allergy management

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Introduction: Lipid transfer proteins (LTPs) are the most frequent food allergy triggers in the Mediterranean area. Cross reactivity among these allergens is considered when homology ratio is ≥70% and brings about a great challenge when recommending food avoidance to patients.

Objectives: To study the prevalence of sensitization to the most frequent LTPs and to analyse the homology ratio between different LTPs in order to stablish individual diet recommendations to avoid unnecessary restrictions.

Results: Methods: Two hundred and eighteen food allergy patients, older than 14 years were included in study. Component resolved diagnosis was performed sIgE. Values => 0.3 ISU were considered positive. LTP's FASTA aminoacids sequences were obtained from Uniprot and homology rates were obtained using protein alignment tool (BLAST).

Results: One hundred and seventy patients (78.25%) showed positive results to LTPs. Pru p 3 was detected 163 patients (74.7%, mean value: 5.5 ISU) followed by Jug r 3 (71.10%, mean value: 2.30 ISU), Pla a 3 (64.67%, mean value: 1.97 ISU), Ara h 9 (57.33%, mean value: 5.12 ISU), Art v 3 (56.42%, mean value: 1.22 ISU), Cor a 8 (55.5%, mean value: 1.17 ISU), Par j 2 (33.02%), Ole e 7 (27.52%) and Tri a 14 (20.8%). Mean number of positive LTPs per patient was 5. BLAST analysis showed >85% homology between Pru p 3 and cherry, apricot, plum, pear and apple LTPs and <60% homology between Jug r 3 and cherry, apricot, almond and peanut LTPs.

Conclusions: Peach LTP (Pru p 3) is the most frequent food sensitizer in our population with the highest specific IgE-ISU levels, followed by chestnut (Jug r 3) and peanut (Ara h 9) LT's. Plane tree and mugwort LTPs (Pla a 3 and Art v 3) behave as a food allergy marker. Pru p 3 showed the highest cross reactivity ratio and Jug r 3 the lowest. We propose the use of the LTP list of homologies ratios in order to provide an individualized diet to food allergic patients.

0957 | Different profiles of sensitization to phleum pratense: Association to response to nasal provocation test

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Introduction: Grass pollen is the most common cause of seasonal respiratory allergy. Phl p1 is a marker of true grass pollen sensitization. Although IgEs to other major grass pollen allergens are rarely observed in the absence of IgE to Phl p1, IgEs to Phl p2, Phl p5 and Phl p4 are markers of true sensitization. As we previously demonstrated, by means of Component Resolved Diagnosis (CRD), it is possible to recognize 39 sensitization profiles to Phleum pratense. Nasal Allergen Provocation Test (NAPT) is considered the gold standard for the diagnosis of allergic rhinitis.

Objectives: To investigate whether the sensitization profile to Phleum pratense is correlated to a positive NAPT to grass pollen extract.

Methods: Children with Seasonal Allergic Rhinitis were recruited between March 2016 and June 2016 in the Paediatric Allergy Unit of Sandro Pertini Hospital, Rome. Patients underwent Skin Prick testing and serum IgE assay (Multiplex); Sera were tested for the individual molecules (Phl p 1, Phl p 4, Phl p 5, Phl p 7, Phl p 12). Between November 2016 and March 2017 the patients underwent NAPT with undiluted Grass pollen extract. NAPT was considered positive if a reduction of Peak Nasal Inspiratory Flow (PNIF) greater than 40% or a Total Nasal Symptom Score (TNSS) >3 or the combination of TNSS = 2 and reduction of PNIF >20% were observed within 15 minutes from NAPT.

Results: 65 children (M/F = 40/25) (age 10-20, mean 13.7 years) were recruited in our study. All the 65 patients (100%) had positive SPT for Grass Pollen. Phl p 1 was positive in 64/65 patients (98%), Phl p 4 in 64/65 (98%), Phl p 5 in 39/65 (60%), Phl p 7 in 2/65 (3%), Phl p 12 in 10/65 (15%). NAPT with grass pollen was positive in 58 patients (89%), negative in 7 patients (11%). Phl p5 was negative in 6/7 patients (85%) with a negative NAPT, while Phl p1 resulted negative in one. We found a statistically significant association between a negative Phl p5 and negative NAPT (OR 9; 95% CI 1.149-70.474 $P = .009$), while a positive Phl p5 was associated to a positive NAPT (OR 1.267; 95% CI 1.020-1.573 $P = .009$). No statistically significant association was found between positive Phl p1 result and NAPT (OR 1.810; 95% CI 0.452-7.252 $P = .069$).

Conclusions: Phl p5 negativity has a strong association with no response to NAPT, while the association between Phl p1 and NAPT does not seem to be statistically significant.

0958 | The concordance between component tests and clinical history in British adults with suspected pollen-food syndrome (PFS) to peanut and hazelnut

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Introduction: Mild allergic reactions to peanut and hazelnut are seen in ~30% of patients with pollen-food syndrome (PFS). Component tests are considered a useful adjunct in the diagnosis.

Objectives: To determine the concordance between component tests and clinical history in patients with suspected PFS to peanut and hazelnut in a 'real world' clinical setting.

Methods: Patients were classified into PFS (Group-1; $n = 86$; 29 M; mean age ± SD- 34.5 years ± 12.8), PFS with mild systemic symptoms but not anaphylaxis (Group-2a; $n = 58$; 22 M; mean age ± SD – 22.5 ± 12.9 years) and anaphylaxis (Group-2b; $n = 17$; 7M; mean age ± SD – 28.9 ± 10 years). Since components tests are not routinely requested in cases of anaphylaxis, Group 2b were

	PEANUT					HAZELNUT			
	Arah 1	Arah 2	Arah 3	Arah 8	Arah 9	Cor a1	Cor a8	Cor a9	Cor a14
Group 1 Peanut $n = 34$ Hazelnut $n = 32$	0.04 (0.00-0.06)	0.05 (0.00-0.53)	0.02 (0.00-0.04)	2.42 (0.13-21.10)	0.03 (0.00-0.1)	12.1 (7.84-25.20)	0.00 (0.00-0.02)	0.00 (0.00-0.01)	0.01 (0.00 -0.02)
Group 2a Peanut $n = 34$ Hazelnut $n = 12$	0.07 (0.00-1.72)	0.57 (0.01-7.17)	0.03 (0.01-0.12)	0.30 (0.0-3.00)	0.01 (0.01-0.03)	2.42 (0.66-7.05)	0.00 (0.00-0.008)	0.00 (0.00-0.02)	0.01 (0.00-0.02)
*Significant by Mann–Whitney *U*	-	$P = .014$*	-	$P < .001$*	-	$P = .008$*	-	-	-

excluded from analysis to avoid bias. A sIgE of ≥0.35 kUA/l was considered positive.

Results: Group-1 Hazelnut: 85% were monosensitized to Cor a1 and 12% to storage protein/s and Cor a8. Group-1 Peanut: 41% monosensitised to Arah 8, 44% to storage protein/s or Arah 9 and 15% negative to all components. Group-2a Hazelnut: 67% monosensitised to Cor a1, 16% sensitized to storage protein/s and 17% were negative to all components. Group-2a Peanut: 19% monosensitised to Arah 8, 62% sensitized to storage protein/s and/or Arah 9, and 19% negative to all components.

SIgE to Arah 8 and Cor a1 were greater in Group 1 in comparison to Group 2a - [median (IQR); hazelnut: 12.1 (7.8-25.2) vs 2.4 (0.36-6.3); $P < .001$; peanut: 2.4 (0.10-21.1) vs 0.3 (0-3); $P < .01$)].

Conclusions: The concordance between component tests and clinical history for adults with PFS was good for hazelnut ($\kappa = 0.628$) but poor for peanut ($\kappa = -0.118$). A food challenge is the gold standard test for discordant cases.

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EARLY LIFE FACTORS IN THE DEVELOPMENT OF ALLERGIC DISEASE

0959 | Maternal effects on development of childhood allergic sensitization and associated diseases

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Introduction: We have previously shown that maternal atopic history, but not paternal, imprints the newborn's airway immune signature, whereas it is unexplored whether maternal vs paternal atopy also confers an increased risk of allergic sensitization later in childhood.

Objectives: To investigate parental effects on development of allergic sensitization and related disorders in early childhood.

Results: We investigated 605 parent-child trios from the Copenhagen Prospective Study on Asthma in Childhood$_{2010}$ (COPSAC$_{2010}$) birth cohort. Parental atopic history was determined via specific-IgE and total-IgE measurements and a structured clinical interview. The children were prospectively diagnosed with asthma and eczema at our research clinic and had specific-IgE and total-IgE levels measured at ages 6 and 18 months. Associations between parental and child atopic traits were analyzed as relative risks by chi squared tests. Increased maternal specific-IgE and total-IgE levels were significantly associated with increased specific-IgE (aRR = 2.13 [95% CI, 1.24-3.65], $P < .01$) and total-IgE (aRR = 3.89 [1.64-9.21], $P < .01$) in the children. Maternal history of asthma and eczema was also associated with asthma (aRR = 1.69 [1.23-2.32], $P < .01$) and eczema (aRR = 1.32 [1.01-1.73], $P = .04$) in their children. No significant associations were observed between father's and child's specific-IgE, total-IgE, asthma or eczema.

Conclusions: We found a consistently stronger effect of maternal vs paternal history of asthma, eczema, specific-IgE and total-IgE on the development of these traits in their offspring. This suggests that primary preventive initiatives should be directed to the pregnant mother, as maternal non-genetic factors seem to confer an additive increased disease risk to the offspring.

0961 | Relation of maternal dietary and probiotic intervention during pregnancy to the risk of atopic eczema and asthma in the offspring by the 4 years of age

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Introduction: Events in utero and in early childhood influence the health in long-term. Increasing evidence shows that allergic diseases emerge as a result of complex interactions from genetic, environmental, and microbiota-driven factors during perinatal development.

Objectives: The aim was to study the role of maternal dietary intervention with or without probiotics during pregnancy and secondly explore the effect of individual nutrients and foods in the overall prevalence of atopic eczema and asthma in children by 4 years of age.

256 pregnant women, whose unborn child had an increased risk of allergies, were randomized at the first trimester of pregnancy either to dietary counseling groups with probiotics *(Lactobacillus rhamnosus GG* and *Bifidobacterium lactis*) or placebo, or to a control group with placebo. The dietary counseling aimed at a dietary intake complying with The opposing effects of different milk products may be speculated to reflect differing protein compositions potentially contributing to allergy risk. Maternal diet was evaluated firstly as an intervention effect, and secondly by exploring the effect of individual nutrients and foods as tertiles on child's atopic eczema and asthma at 4 years.

Results: Neither dietary counseling, probiotic intervention nor intake of nutrients had an impact on the risk of child's atopic eczema or asthma. Instead, maternal milk intake in the middle category was related to reduced (OR 0.27), whereas maternal cheese intake in the middle category was related to increased risk of atopic eczema (OR 2.65) with similar trends for higher intakes.

Conclusions: The maternal dietary counseling with or without probiotics did not affect the risk of child's atopic eczema or asthma. In secondary analyses specific foods in maternal diet contributed to the risk of atopic eczema: opposing associations of milk and cheese consumption were discovered which may be speculated to reflect differing dietary protein compositions potentially contributing to allergy risk.

0962 | Early probiotic prophylaxis reduces allergic symptoms in 13-year follow-up

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Introduction: Reduced and less diverse microbial exposure in early childhood is connected to skewed maturation of the immune system and greater prevalence of allergic disease. Important part of the interaction of the immune system and microbes takes place in the gut. Using of probiotics has been proposed to beneficially affect the maturation of the immune system and therefore help to prevent allergic diseases. We carried out a study to clarify the long run effectiveness of the probiotic treatment. 1223 pregnant mothers with high risk to have allergic child were randomised to have a probiotic mixture (2 lactobacilli, bifidobacteria and propionibacteria) or placebo. Mothers received the treatment during the last month of the pregnancy and it was also given for the infants together with galactooligosaccharide during the first 6 months of their life. As it has been previously reported, there was less atopic disease in the 2-year follow-up. We have also reported, that at 5 years of age there was less IgE-associated disease in the subgroup of cesarean-delivered children, but not in the whole cohort.

Objectives: Effect of early probiotic prophylaxis on allergic morbidity in early adolescence is not well known. We have currently investigated the same cohort in 13-year follow-up ($n = 655$) using questionnaire and IgE-sensitisation analysis.

Results: No statistically significant differences were found in prevalence of eczema (32.1% vs 35.1%), asthma (13.1% vs 16.9%), rhinitis (34.8% vs 30.4%), food allergy (23.5% vs 27.3%) or all disease combined (55.4% vs 58.6%). No statistically significant differences were neither found in food specific (36.5% vs 34.4%), inhalant specific (48.0% vs 41.3%) or any specific sensitisation (54.4% vs 47.7%). Results were similar in the cesarean-delivered subgroup. To collect more specific information, a set of questions about the allergy and asthma symptoms were also asked. The ISAAC questionnaire was used as a basis for our questions. Less wheezing attacks during the last 12 months were reported (8.9% vs 15.4%) in the probiotic group. In the probiotic treated members of the cesarean-delivered subgroup there was also less exercise related wheezing (7.1% vs 20.3%) and eczema symptoms (21.4% vs 42.4%) in the last 12 months.

Conclusions: We discovered reduced symptomatology in 13-year follow-up, which can possibly predict less diagnosed allergic disease in following years.

0963 | Timing of solid food introduction and atopic dermatitis

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Introduction: The optimal timing of solid food introduction for atopic dermatitis (AD) prevention has been debated in literature.

Objectives: The aim of the study was to investigate the potential association of the moment of solid food introduction and AD.

This was a cross-sectional study aiming to investigate the potential association between early life environment and AD occurrence later in childhood. Population was represented by 1064 subjects with a median age of 110 months (IQR = 65-145). The study analysed data from questionnaires filled by mothers. The AD diagnosis was made according to ISAAC criteria. Solid food introduction was identified as the moment of food diversification declared by the mother. The association of solid food introduction (before 4 months, 4 to 6 months or after 6 months) with AD was at first evaluated using simple logistic regressions. Then, each logistic regression was adjusted for the other variables associated with AD in the database. MedCalc software (16.4.3.) was used for analysis.

Results: In the simple logistic regression analysis, the timing of solid food introduction was associated with AD (OR = 1.32, 95% CI: 1.01-1.71). When compared each period, against all other periods only the period before 4 months was associated with lower risk of AD (OR<4 months = 0.67, 95% CI: 0.45-0.98), while solid food introduction between 4-6 months and after 6 months was not associated with AD (OR4-6 months = 1.25, 95% CI: 0.85-1.83; OR>6 months = 1.42, 95% CI: 0.84-2.39). After complete adjustments, solid food introduction after 6 months was associated with increased risk of AD (OR = 1.82, 95% CI: 1.05-3.17), while introduction before 4 months was associated with a lower AD risk (OR = 0.61, 95% CI: 0.41-0.91).

Conclusions: Solid food introduction after 6 months was associated with high risk of AD, while introduction before 4 months was associated with low risk of AD.

0964 | Associations between early infant feeding with soy formula and allergic disease in adulthood

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Introduction: Choice of formula to infants, especially in the presence of allergic heredity, is debated. Whether exposure to soy protein affects the development of peanut allergy is discussed. Animal studies indicate that soy protein given early in life might prevent the development of peanut allergy.

Objectives: To investigate the association between infant feeding with soy-based formula, vs exclusive breast-feeding or cow's milk protein based formula up to 6 months of age, and sensitization and allergy to soy or peanut in adulthood.

Methods: A cohort of 235 individuals was followed prospectively from birth. Mothers of the participating individuals, all allergic, were recommended to exclusively breast-feed for at least 6 months. Of these mothers, 40% (n = 94) exclusively breast-fed, 31% (n = 74) gave soy-based formula, 27% (n = 63) gave cow's milk protein based formula and 2% (n = 4) hydrolyzate. At 27-30 years of age, 82% filled in a questionnaire, rendering a study population of 192 individuals. One hundred and seventy one of those (73%) completed a clinical examination, including skin prick test (SPT) and IgE-antibody (ab) analysis towards a number of common allergens, including peanut and soy. SPT $\geq$ 3 mm and/or IgE> 0.35 kU_A/l was regarded as positive. To identify "true" peanut and soy IgE-ab sensitization, we excluded all individuals with both birch and peanut and/or soy IgE-ab. Allergy was defined as positive SPT and/or IgE-ab in combination with reported symptoms. Maternal smoking was adjusted for.

Results: At age 27-30, 57% (n = 98) of the study population were sensitized to tested allergens. Sensitization to any of the tested allergens was 48% (n = 25) in the soy exposed group and 65% (n = 49) in the breast-fed group (P = .052). In logistic regression analyses, a tendency for reduced risk of any sensitization was observed in the soya-exposed group, aOR 0.49 (95% CI 0,24-1,01). The prevalence of peanut sensitization and allergy was 4% (n = 7) and 2% (n = 4) respectively. The corresponding numbers for soy were 1% (n = 2) and 0.5% (n = 1). No differences were found in sensitization or in allergy, to either peanut or soy between the soy-exposed group and breast-fed or cow's milk formula-exposed group.

Conclusions: Our results indicate an association between early exposure to soy and a lower risk of overall sensitization to the tested allergens. For peanut and soy specifically, our study is too small and further studies are needed.

0965 | Differences between parentally-reported and general practitioner diagnosed eczema

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Introduction: The differences in eczema as reported by parents through survey questionnaires, and doctor-diagnosed eczema has been scarcely evaluated.

Objectives: To explore the differences in eczema prevalence using different data sources.

Methods: In an unselected birth cohort, 1184 participants were recruited prenatally and attended follow-ups at ages 1, 3, 5, 8 and 11 years. Presence of parentally-reported current eczema at each follow-up was ascertained using interviewer-administered validated questionnaire (PRE). At each visit, eczema was confirmed at physical examination (CE), and the severity was graded using SCORAD. We extracted data from primary care medical records for 922 children, including the general practitioner diagnosis of eczema (GPE), and prescriptions of eczema medications. Consistency between PRE, GPE and CE was assessed using Cohen's kappa analysis. We categorized each child based on the source of diagnosis (None, PRE only, GPE only, both GPE and PRE) and compared their eczema scores and medication use.

Results: At age 1, the prevalence of GPE (46%, 432/922) was significantly higher than PRE (36%, 397/1091); mean difference 10.5% (95% CI 6.1-14.7%). The prevalence of GPE declined more steeply, and was lower than PRE from age 3 years onwards. At all ages, the agreement between PRE and GPE was poor (kappa<0.4), and it differed at different ages (fair at age 1, k = 0.31; slight at age 11, k = 0.16). Surprisingly, at all ages children with PRE were more likely to be prescribed eczema medication than those with GPE. Furthermore, the risk factors for PRE differed from those for GPE. The agreement with CE was higher for PRE than for GPE at all ages (the lowest agreement between GPE and CE was observed at age 1, k = 0.09). The proportion of children with both PRE and GPE decreased from 24.5% (213/869) at age 1 to 2.95% (12/407) at age 11 years. Children with both PRE and GPE had more severe eczema scores, and accounted for 67% of those using topical corticosteroids regularly.

Conclusions: The agreement between parentally-reported and doctor-diagnosed eczema is poor, and there is a considerable heterogeneity in relation to eczema severity, the use of anti-inflammatory treatments and risk factors. This phenotypic heterogeneity may considerably dilute any true association with environmental and genetic risk factors that would be apparent if a more precise case definition was used.

0966 | The impacts of environmental factors on the changes in individual prevalence of atopic diseases in elementary school students in Ulsan, Korea: a cohort study

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Introduction: According to a WHO report, 20% of the world population experiences allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis, and asthma is a major cause of hospitalization for pediatric chronic diseases in western countries. The prevalence of allergic diseases in Korea has steadily increased since 1990, thereby decreasing the quality of life of patients' families as well as severely increasing their socioeconomic burden. In aspect of disease management, controlling of environmental factors are more important than other factors.

Objectives: The aim of this study was the long-term variation in lifestyle and environmental factors can affect individual prevalence of allergic diseases for elementary school students in Ulsan, Korea,

Results: The study subjects were 390 elementary school students from 3 regions with different atmospheric conditions and they took both a primary survey (2009–2010) and secondary survey (2013–2014) with ISAAC questionnaire. In the comparison between schools, there was a significant difference in asthma, allergic rhinitis, and family history of atopic dermatitis prevalence among siblings. The individual prevalence changes during the follow-up period, the incidence of allergic rhinitis, and allergic conjunctivitis were increased but some cases of atopic dermatitis decreased. Items that statistically significantly increased among the changes in environmental and lifestyle factors included house income, daily use of television and computer, daily activities, construction year of house, paternal smoking, and pet ownership. Items that statistically significantly decreased were physical activities per week, daily activity at home, daily ventilation time, remodeling of house, use of insecticide, and movement to new house. Generalized estimating equations (GEE) analysis between environmental factors and allergic diseases revealed that environmental factors increasing the risk of allergic diseases included secondhand smoking and the use of humidifier for allergic rhinitis, movement to new house for atopic dermatitis, and use of insecticide and irritation symptoms of air pollution for allergic conjunctivitis.

Conclusions: Environmental and lifestyle factors affecting the prevalence of allergic diseases varied according to the type of allergic disease. Effective management of allergic diseases may be possible by properly controlling the environmental factors related to each allergic disease.

0967 | Risk factors associated with eczema throughout childhood

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Introduction: The clinical course of eczema in childhood differs between individual patients.

Objectives: To ascertain the risk factors associated with eczema at different time points during childhood.

Methods: In a population-based birth cohort study, 1184 participants were recruited prenatally and reviewed at 6 time points during childhood (ages 1, 3, 5, 8, 11, and 16 years). Presence of current eczema at each follow-up was ascertained using interviewer-administered validated questionnaire. We collected data relating to family history, prenatal and postnatal environment exposure, and coexisting allergic disease using questionnaires. We measured height and weight at each visit, and calculated body mass index (BMI). Atopic sensitization was assessed using skin prick tests. We performed genotyping for *filaggrin (FLG)* loss-of-function mutations R501X, S3247X, R2447X, 2282del4, 3673delC and 3702delG.

Results: The prevalence of current eczema was highest at age 1 (36% [397/1091]), and decreased steadily to age 16 (19% [143/745]). Maternal eczema, and child's rhinitis, asthma and atopic sensitisation were consistent associates of current eczema at each age. However, there were considerable differences in other risk factors for eczema between early and late childhood. Paternal eczema, early-life day care attendance and dust mite sensitisation were

Age of follow up	1	3	5	8	11	16
OR for current eczema (95% CI)	3.47 (2.15-5.60)	2.45 (1.52-3.94)	1.67 (1.04-2.67)	1.48 (0.89-2.43)	1.35 (0.75-2.40)	1.27 (0.66-2.44)
P-value	<.001	<.001	.03	.13	.31	.47

associated with eczema in early life (ages 1-5 years), but not later. BMI (z-score) was a unique associate of eczema in the school age and adolescence, but not in early life. The effect of *FLG* loss-of-function mutations decreased significantly with increasing age (Table); having *FLG* loss-of-function mutation was a strong predictor of eczema at age 1 (OR 3.47, 95%CI 2.15-5.60), but the size of the effect progressively decreased at the subsequent follow ups, with no significant association between *FLG* mutations and current eczema after age 8 years.

Conclusions: There are marked differences in genetic and environmental risk factors associated with eczema in early and late childhood, indicating that childhood eczema is a highly heterogeneous disease.

0968 | The lipocalin beta-lactoglobulin accumulates in stable dust: potential implications for the allergy- and asthma-protective effect

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Introduction: According to the hygiene hypothesis, living on cow farms significantly protects against asthma and allergies, which has been correlated with the immune-modulating effect of the stable microbiome. However, in addition to microbial products, also specific proteins may play a role. Beta-lactoglobulin (BLG) is a well-known bovine protein from milk. It belongs to the lipocalins, which are innate secretory molecules expressed in humans and animals. Lipocalins bind a wide variety of ligands, e.g. siderophore/iron complexes or metal ions. Our previous studies revealed that the loading state of lipocalins critically determines their immunomodulatory potential: in loaded state, the lipocalin BLG in vitro prevents release of Th2-cytokines from stimulated cells, and *in vivo* is not able to induce allergic hypersensitivity in BALB/c mice (see our companion abstract by Roth-Walter *et al*. "What makes an allergen an allergen? The sensitization capacity of the paradigmatic lipocalin allergen Bos d 5 critically depends on its ligand loading state in BALB/c mice").

Objectives: We aimed (i) to investigate whether secretory BLG is contained in cows' stable dust, and if so (ii) to reveal its source and (iii) its loading, respectively association with trace elements.

Results: Cows' stable dust and urine samples from lactating cows were collected and analyzed immunochemically. The concentration of BLG in stable dust extract (SDE) was determined by BLG-specific ELISA to be 1.18 μg/g SDE and around 20 ng/ml in bovine urine. In SDS-PAGE, protein bands at 18 and 36 kDa were detected in SDE, which subsequently could be confirmed as monomeric and dimeric BLG by specific anti-BLG monoclonal antibodies. Size exclusion chromatography-inductively coupled plasma mass spectrometry (SEC-ICP-MS) of the SDE revealed that zinc is attached to BLG. Our results thus confirm that the specific lipocalin-protein BLG is present at considerable concentrations in bovine urine as well as stable dust. Moreover, the trace element zinc is associated to BLG derived from SDE.

Conclusions: We revealed that in fact BLG is a major compound in stable dust, potentially derived from cows' urine. Whether the dose and/or the ligands of the lipocalin BLG contribute to the allergy-protective effect of certain cowsheds remains to be elucidated.

The study was supported by the Austrian Science Fund FWF (grant SFB F4606-B28).

0969 | Influence of mode of delivery on asthma, fractional exhaled nitric oxide and total serum IgE in a cohort of children aged 6 years

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Introduction: Previous studies have demonstrated a relationship between mode of delivery at birth and asthma at early childhood years, but it is still questionable whether this relationship remains at school age.

Objectives: This study aimed to evaluate whether mode of delivery is associated with asthma, fractional exhaled nitric oxide (FeNO) and total serum Immunoglobulin E (IgE) at school age.

A total of 385 children (201 boys, 54.5%; mean age, 6.2 years) born in 2010 participated in this study. The birth information of the study subjects was obtained from medical records in the Chang Gung Memorial Hospital. Allergic diseases were assessed by a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. FeNO was determined with a single-breath online method using a chemiluminescence analyzer. Total serum IgE was measured by ImmunoCAP.

Results: In this study population, 159 children (41.3%) were born by caesarean section (C/S) and 226 children (58.7%) were born by vaginal delivery (VD). Forty eight children (12.7%) had diagnosed asthma. Compared with children born by vaginal delivery (11.8%, $n = 26$), children born by caesarean section (14%, $n = 22$) did not have a higher rate of diagnosed asthma (P value > .05). The association between mode of delivery and FeNO at 6 years of age was not statistically significant (C/S: mean ± standard deviation, 13.4 ± 14.6 ppb; VD: 13.6 ± 14.2 ppb; P value > .05). No association was found between mode of delivery and total serum IgE (C/S: 297.8 ± 487.9 KU/L; VD: 346.7 ± 550.2 KU/L; P value > .05].

Conclusions: Our study indicates no significant association between mode of delivery and asthma-related traits at school age. Further studies using a larger sample size to validate the findings in this pilot study are currently ongoing.

0970 | Breastfeeding in relation to allergic diseases and total serum IgE at 6 years of age in Taiwanese children: A birth cohort study

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Introduction: Breastfeeding might confer a protective effect against childhood allergic diseases, but the evidence remains controversial.

Objectives: We investigated the effects of breastfeeding on allergic diseases and total serum immunoglobulin E (IgE) at 6 years of age in a birth cohort of children in Taiwan.

This study included 385 Taiwanese children (age 6.2 ± 0.26 years; 201 boys, 54.5%). Information about breastfeeding and childhood allergic diseases including asthma, allergic rhinitis, and atopic dermatitis were obtained using questionnaires. Total serum IgE level was measured by ImmunoCAP. Multivariable regression models were used to analyze the associations of breastfeeding with allergic diseases and total serum IgE.

Results: In this cohort, 29.4% of the children were ever exclusively breastfed. We found no significant association of breastfeeding with asthma (adjusted odds ratio [AOR], 1.39; 95% confidence interval [CI], 0.43-4.48), allergic rhinitis (AOR, 1.63; 95% CI, 0.77-3.44), and atopic dermatitis (AOR, 1.14; 95%CI, 0.47-2.77), or total serum IgE ($P = .872$), after adjustment for gender, number of older siblings, maternal prepregnancy BMI and maternal history of allergic diseases.

Conclusions: Our results suggest that breastfeeding may not have a protective effect on development of allergic diseases and IgE elevation in children at 6 years of age. We are conducting further studies with a larger sample size to confirm the findings in this pilot study.

0972 | Prenatal and perinatal risk factors for childhood asthma and asthma-like symptoms

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Introduction: Recently, prenatal and perinatal life has been considered very important in development of wheeze and asthma. The aim of the study was to examine the impact of some prenatal and perinatal risk factors on asthma in childhood in The Republic of Macedonia, as a developing country with a high prevalence of maternal tobacco smoke and a low prevalence of asthma.

Objectives: Methods: Data from 2310 children aged 5-15 years, obtained by parental-completed questionnaire on lung health, from randomly selected schools in Skopje, the capital of the Republic of Macedonia, was used. The association between maternal prenatal tobacco smoking, maternal prenatal diabetes, Caesarean section delivery, prematurity, and small for gestational age (SGA) status with asthma-like symptoms and ever-diagnosed asthma was investigated after adjustment for confounders by multiple logistic regression.

Results: The prevalence of pre- and perinatal risk factors was: maternal tobacco smoking during pregnancy = 13.7%, prenatal maternal diabetes = 1.6%, Cesarean delivery = 31.3%, prematurity = 11.3%, and SGA = 3.6%. Wheeze ever was documented in 30.3% of children, current wheeze in 6.5%, current sleep-disturbing wheeze in 3.6%, current exercise-induced wheeze in 1.7%, current dry night cough apart from a cold in 12.2%, and diagnosed asthma in 2.3%. Maternal prenatal tobacco smoking significantly increased the risk of wheeze ever (aOR: 1.40; 1.08-1.81; $P = .011$) while prenatal maternal diabetes increased the risk of dry night cough (aOR: 2.32; 1.07-5.05; $P = .034$). The association between prematurity and ever wheeze, although positive, was not statistically significant ($P = .081$).

Conclusions: The results suggest a positive association between maternal prenatal tobacco smoking and transient wheeze, but not with asthma or current asthma-like symptoms in schoolchildren. This finding further support the impact of prenatal tobacco smoke exposure on lung development and the importance of smoking secession campaign.

0973 | Birth order and pediatric allergic diseases: A nationwide longitudinal survey in Japan

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Introduction: Environmental factors are closely related to incidence of allergic diseases. Birth order is considered to be an indicator that reflects postnatal environment. However, there are few longitudinal studies on this issue.

Objectives: To examine the relationships between birth order and allergic diseases (bronchial asthma, food allergy and atopic dermatitis).We used a nationwide longitudinal survey that followed children born in 2001 (n = 47 015). We selected hospital visits for three allergic diseases (bronchial asthma, food allergy and atopic dermatitis) up to 12 years of age and conducted logistic regression analyses to evaluate the relationships between the birth order and these diseases. We adjusted for child and maternal factors and estimated odds ratios (ORs) and 95% confidence intervals (CIs) for each outcome.

Results: The associations between the birth order and asthmatic bronchitis were mixed; late birth order increased the risks in early childhood, but decreased the risks during school-age years. For example, the adjusted ORs comparing more than third- vs first-born children were 1.23 (95%CI: 1.07-1.40) between 30 and 42 months of age, but 0.76 (95%CI: 0.64-0.89) between 10 and 11 years. Late birth order had generally protective effects for food allergy, while it increased the risks for atopic dermatitis.

Conclusions: The influence of birth order depended on forms of allergic disease and age period. Childhood is unique period in its physical and immunological development, and immunological responses to postnatal environment in childhood may be inhomogeneous.

0974 | Effect of antenatal maternal supplementation with GOS/inulin prebiotics on atopic dermatitis in high-risk children (PREGRALL): Study protocol for a randomized controlled trial

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Introduction: Allergies are increasing worldwide affecting 30-40% of the population. Among this, Atopic Dermatitis (AD) is the earliest and the most common manifestation of allergic diseases (prevalence 20%). Recent studies have shown that allergies were associated with a disruption of the gut microbial 'balance' suggesting that the use of nutritional intervention very early in life may restore an optimal pattern of microflora aiming at improving the host's health. So far, most human intervention studies have mainly focused on improving postnatal infant colonization.

Objectives: Our study will test the hypothesis that a maternal antenatal prebiotics (GOS/inulin) supplementation may be superior to placebo for AD prevention in high-risk children (PREGRALL study).

Methods: The PREGRALL study is a parallel multicentre double-blind randomized controlled trial funded by the French Ministry of Health. It will recruit 376 pregnant women, at risk of having an allergic infant, from 4 centres. Participants will be randomized to be given prebiotics supplementation or placebo, from 20 weeks of pregnancy to delivery. Primary outcome is AD prevalence at 1 year old. Secondary outcomes are AD severity, quality of life, prebiotics tolerance. PREGRALL will lead a translational study based on biological samples from 100 infant-mother dyads (50 per group). Samples will be collected at different times: blood and stools from both mother and infant; cord blood; colostrum and breastmilk.

Results: We hypothesize that the intervention will (i) reduce AD prevalence in high-risk children; (ii) favourably influence maternal gut colonization and increase SCFA metabolites thereby facilitating microbiota species richness during early infant colonization; (iii) have immunomodulatory effects associated with markers of immune homeostasis (at birth and during the postnatal period) in blood of mother and offspring as well as in breastmilk. The 100 dyads will be used for an ancillary study to analyze the mechanistic effects of prebiotics on immune system, gut microbiota's and milk's composition and function.

Conclusions: To our knowledge, PREGRALL will be the first clinical trial assessing the effects of prebiotics for allergy prevention during pregnancy exclusively. It will contribute to our understanding of mechanisms involved in allergy prevention and may help to define new strategies involving prebiotics use during the antenatal period for reducing the incidence of AD in high-risk families.

MONDAY, 19 JUNE 2017
TPS 27
ASTHMA: DIAGNOSIS AND MANAGEMENT

0975 | Omalizumab for severe asthma in clinical practice

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Introduction: We analyzed omalizumab treatment for severe allergic asthma in real-life clinical setting. We report the preliminary results of clinical data.

Objectives: All patients who received omalizumab for asthma at any point between April 2006 to March 2016 were evaluated. Patient data were analyzed until December 2016. Altogether 60 patients (43 women and 17 men) had received omalizumab, 21 of them continued and 39 had finished the treatment. The age at the time of asthma diagnosis was grouped into: 0 to 4 years (9 patients), 5 to 19 years (14 patients), 20 to 39 years (17 patients) and ≥ 40 years (17 patients). Mean age of the patients was 45.2 years when beginning the treatment. The response was defined by overall control of the disease and evaluated in 50 subjects who continued the treatment for at least 4 months and did not end treatment early because of reasons not related to the response.

Results: All patients had severe asthma. Mean daily dose of inhaled corticosteroids was 1121 μg in fluticasone equivalent, 57 patients used long acting beta 2-agonists, 17 patients long acting anticholinergics, 38 patients leukotriene antagonists and 13 patients maintenance oral corticosteroids. All but 5 patients had documented IgE-mediated allergies to inhaled allergens. Nasal surgery for chronic sinusitis was carried out in 22 patients, 19 patients had current nasal polyposis, 21 patients reported food allergy. Current worsening of asthma control related to indoor mold / sick building was reported by 19 patients and to work-related exposures by 29 patients. The overall treatment effect was 60% (moderate or good response). Among subjects whose age at the time of asthma diagnosis was ≥ 40 years, 38.5% had moderate or good response compared to 60.0-71.4% in the other groups. Of patients with nasal polyposis 81.3% had moderate or good response compared to 48.5% of the patients without nasal polyposis.

Conclusions: Omalizumab was given to a severe patient group. Many of the patients had probably multifactorial causes for poor asthma control. Overall treatment response to omalizumab was 60%. Nasal polyposis was more common in subjects who had good response. Subjects with asthma diagnosed at the age 40 years or later had more seldom a good response.

0976 | The impact of long-term targeted therapy with omalizumab (more than 2 years) on the asthma control according to the registry of children with uncontrolled severe persistent asthma (Russian experience)

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Introduction: Asthma is the one of the most common chronic illness among children. However, maintain best asthma control is not often possible. Therefore targeted biological medications were developed for the asthma treatment, one of them is Omalizumab.

Objectives: To analyze the efficacy of long-term therapy with Omalizumab (more than 2 years) on the maintaining disease control according to pediatric patient registry with severe persistent asthma.

Results: The data of long-term follow-up monitoring with uncontrolled severe persistent asthma in children were analyzed. The patient registry included data of 101 children (32.67% girls) from 6 to 17 years 11 months (average age 13.4 years), receiving Omalizumab in addition to basic therapy.

The control of the disease assessed by questionnaire Asthma control test (ACT) before therapy with Omalizumab.

40 children received therapy of Omalizumab for 2 years, the average point of ACT before the therapy of Omalizumab was 14.52 ± 4.2, in 2 years of therapy - 20 ± 3.84 ($P = .000$). 13 patients (32.5%) achieved partly control, 4 (10%) became well controlled 35 children received therapy of Omalizumab for 3 years, the average point of ACT before the therapy of Omalizumab was 13.66 ± 3.87, in 3 years of therapy – 19.96 ± 3.6 ($P = .000$). 13 patients (37.14%) achieved partly control, 2 (5.71%) became well controlled.

15 children received therapy of Omalizumab for 4 years, the average point of ACT before the therapy of Omalizumab was 14.56 ± 3.82, in 4 years of therapy – 21.06 ± 3.41 ($P = .001$). 12 patients (80%) achieved partly control, 1 (6.66%) became well controlled.

6 children received therapy of Omalizumab more than 5 years, the average point of ACT before the therapy of Omalizumab was 14.33 ± 3.14, under the therapy – 21.06 ± 3.41 ($P = .018$). 4 patients (66.6%) achieved partly control, 1 became well controlled.

In 2 years under the treatment of Omalizumab the number of exacerbations and requirement of quick-relief medications have been reduced, and there was no register inpatient hospitalisations or emergency room visits.

Conclusions: Our results indicate the possibility of using the patient registry such as a tool for long-term monitoring and comprehensive assessment of disease control in children with severe

persistent asthma, receiving targeted therapy of Omalizumab. Targeted therapy can achieve best control and reduce exacerbations in these children.

0977 | The dynamics of disease control in children with uncontrolled severe persistent asthma receiving omalizumab (based on pediatric registry)

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Introduction: To achieve and maintain disease control (symptom control and risk reduction) are the main objectives of asthma treatment and severe persistent asthma is no exception. Omalizumab is a monoclonal antibody for the treatment patients with severe uncontrolled asthma, including children.

Objectives: To analyze the impact of omalizumab to improving disease control according to pediatric patient registry with uncontrolled severe persistent asthma, receiving Omalizumab in addition to basic therapy.

Results: The data of pediatric patient registry with uncontrolled severe persistent asthma were analyzed. The electronic database of clinical cases included data of 101 children (32.67% girls) from 6 to 17 years 11 months (average age 13.4 years), receiving Omalizumab in addition to basic therapy.

The disease control was assessed by questionnaire Asthma control test (ACT) before therapy with Omalizumab, in 16 weeks, in 6 month and in 1 year.

Before the therapy (n = 101), average point of ACT was 14 ± 4,5 and corresponds to uncontrolled asthma.

In 92 children received therapy of Omalizumab for 16 weeks, the average point of ACT before the therapy of Omalizumab was 13.6 ± 4.98, in 16 weeks of therapy – 16.84 ± 4.3 (P = .000). 16 patients (17.4%) achieved partly control, 1 child became well controlled.

In 95 children received therapy of Omalizumab for 6 month, the average point of ACT before the therapy of Omalizumab - 3.56 ± 5.01, in 6 month of therapy – 18.72 ± 3.6, P = .000. 24 children (25.26%) achieved partly control, in 2 children asthma became well controlled.

In 56 children received therapy of Omalizumab for 1 year, the average point of ACT before the therapy of Omalizumab – 14.74 ± 4.74, in 1 year of therapy 19.98 ± 3.06, P = .000. 25 children (44.64%) - achieved partly control, in 5 (8.9%) patients asthma became well controlled.

Conclusions: Obtained results confirm positive effects on improving and achieving asthma control in children with uncontrolled severe persistent asthma receiving Omalizumab in addition to basic therapy.

0978 | Chest high-resolution computed tomography: Clinical utility in a severe asthma unit

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Introduction: Systematic evaluation of difficult-to-control asthma includes confirmation of asthma diagnosis, management by an asthma specialist for at least 6 months, and identification of alternative diagnosis and comorbidities. Within the diagnostic algorithm, high-resolution computed tomography of the chest (HRCT) is very helpful, but its use is limited by potential risks and high costs, and clear indications are not established. The ERS/ATS guidelines on severe asthma suggest that in adults with severe asthma without specific indications, chest HRCT only be done when the presentation is atypical-excessive mucus production, rapid decline in lung function etc (conditional recommendation, very low quality evidence).

Objectives: Describe newfound associated diagnostics by means of HRCT, performed in selected patients attended in a Severe Asthma Unit.

Patients and methods: Retrospective observational study. Inclusion criteria: patients >18 years; diagnosed with severe uncontrolled asthma according to GINA and ERS/ATS 2014 guidelines after at least 6 months of follow-up in the Unit; who underwent a HRCT in 2016 for loss of asthma control and/or rapid decline of lung function in spite of good compliance to optimum treatment; who signed the informed consent for participation in the study. Excluded: patients with previous diagnosis of other lung diseases besides asthma, i.e. COPD, Churg-Strauss, bronchopulmonary Aspergillosis, monitoring of known pulmonary nodules. We recorded demographics and clinical data (smoking history, lung function, comorbidities etc).

Results: 41 patients were included, 25F, 16M, age 55.1 (18-75). Smokers 14.6%, non-smokers 51.2%, ex-smokers 34.2%. Comorbidities: Rhinitis 19 patients, Nasal polyps 14, NSAID hypersensitivity 16, Gastro-oesophageal reflux disease 11, Obstructive sleep apnoea 6. HRCT findings: Emphysema 24 patients, Bronchiectasis 15, Hiatal hernia 9, spiculated nodules 2 (currently monitored), ground-glass 3, pulmonary infiltrates 4, atelectasis 3, Pulmonary hypertension 1, Tuberculosis 2, Adenocarcinoma 1, bronchial Carcinoid 1, Lymphangioleiomyomatosis 1, granulomatous disease 5, Bronchiolitis Obliterans Organizing Pneumonia 1, coronary atheromatosis 7.

Conclusions: In our series, chest HRCT revealed significant associated diseases, justifying partly the poor outcomes. Beyond

differential diagnosis, even in patients with confirmed severe asthma and known comorbidities, HRCT should be considered when assessing poor current asthma control and future risk.

0979 | The effects of saline nasal irrigation on allergic rhinitis and asthma in children

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Introduction: There have been few studies regarding the effects of saline nasal irrigation on asthma, although it has been regarded as additional nonpharmacological treatment of allergic rhinitis (AR).

Objectives: We performed this study to investigate the effects of saline nasal irrigation on AR and asthma in children.

Results: We enrolled 20 children with AR and asthma whose age ranged 6-18 years. They were randomized into two groups: the irrigation group (8 boys and 2 girls) and the control group (8 boys and 2 girls). The irrigation group was treated with daily isotonic saline nasal irrigation as well as montelukast or inhaled ciclesonide for 12 weeks. For the control group, patients received 12 week-treatment with montelukast or inhaled ciclesonide. Levocetirizine was administered to both groups for 12 weeks. We compared Rhinitis Control Assessment Test (RCAT), Asthma Control Test (ACT), forced expiratory volume in 1 second (FEV_1), provocative concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}), and oral fractional exhaled nitric oxide (FeNO) between before and after treatment in both groups. There were no differences in baseline characteristics and medication use between two groups. During the study period, 1 of 10 patients in the irrigation group and 3 of 10 patients in the control group had a history of asthma exacerbation requiring oral corticosteroids ($P = .582$). The RCAT and ACT at week 12 were higher than baseline scores in the irrigation group ($P = .009$ and .007). No differences in the RCAT and ACT were found between pre- and post-treatment in the control group ($P = .074$ and .112). In addition, the PC_{20} at week 12 was higher than baseline measurements in the irrigation group ($P = .017$), while there was no difference in the PC_{20} between before and after treatment in the control group ($P = .333$). However, there were no differences in FEV_1 and FeNO between pre- and post-treatment in both groups.

Conclusions: Our results suggest that nasal saline irrigation is beneficial in the treatment of asthma as well as AR in children.

0980 | Impulse oscillometry (IOS) may be helpful in the diagnosis of asthma

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Introduction: Impulse oscillometry (IOS) is a novel method measuring airway resistance by superimposing sound waves in a range of frequencies to normal tidal volume breathing. IOS may be useful in the diagnosis of severe disease as it does not require effort to measure.. However, evidence for the usefulness of this method is still scarce.

Objectives: The aim of this study was to implement the use of IOS in the diagnosis of asthma. We enrolled 18 consecutive patients investigated for asthma in our out-patient clinic in a pilot study. We performed standard mannitol testing to demonstrate airway hyperresponsiveness. A decrease in the forced expiratory volume in one second (FEV1) by 20% or an increase in the airway resistance at 5 Hz (R5) by 40% was considered significant.

Results: Of the 18 enrolled patients, 4 (22%) showed bronchial hyperresponsiveness. We found significant differences in the change in post-mannitol FEV1 (median 95%, IQR 92-98%), in the negative mannitol challenges, median 80% (77-80%)) in the positive mannitol challenges, $P = .003$ and in R5 (median change in negative mannitol tests 10.5% (−7.3%-31.1%) and positive tests (median increase by 87.2% (63.5-106.0%), $P = .015$, $n = 1$ in 8. Two patients had showed only changes in the IOS measurements, these were later diagnosed with bronchiectasis and bronchiolitis, respectively.

Conclusions: We could confirm airway hyperresponsiveness in asthma patients using IOS. However, other conditions resulted in significant changes in R5 as well.

0981 | Neuropsychiatric side effects induced by montelukast in children

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Introduction: Montelukast is a selective leukotriene receptor antagonist and blocks cysteine leukotrienes. Leukotrienes are lipid mediators that are responsible for asthma clinics and show their effect by receptor binding. Montelukast is commonly used as a single or as an add-on treatment drug in patients whose symptoms cannot be controlled with inhaled corticosteroids. However it has some frequent side effects that have been increasingly reported. The most striking of these in the pediatric age group are the effects on behavior and nervous system

Objectives: In this study, we aimed to determine the frequency of these neuropsychiatric side effects that may occur during montelukast treatment.

Methods: This retrospective study performed between the years January 2013 and December 2016 included 171 children (110 boys/ 61girls, mean age 3.47) receiving montelukast therapy because of asthma and / or allergic rhinitis. Cases that showed neuropsychiatric side effects such as nightmare, hyperactivity, nervousness, restlessness and aggression were determined.

Results: Neuropsychiatric side effects were detected in 30 (17.54%) patients. Asthma was the only diagnosis in 21 patients and allergic rhinitis in 2 patients. 7 patients had asthma and allergic rhinitis concomitantly. Nightmare and hyperactivity were the most frequently observed side effects shown in 16 (9.3%) and 14 (8.1%) patients respectively. Nervousness and aggressivity were found in 3 patients each and restlessness in 2 patients. Seven of the patients had more than one side effect. Only hyperactivity were significantly higher in males (p:0.001)

Table 1. Reports of neuropsychiatric adverse events associated with Montelukast

Age (years)	Sex	Adverse events	Induction time (day)	Dose (mg/day)
4	M	NM/HA/N	60	4 mg
2	M	HA	90	4 mg
4	M	HA	60	4 mg
4.5	F	NM	7	4 mg
8.5	M	NM	7	5 mg
5	F	NM	3	4 mg
3.5	M	NM/HA	60	4 mg
4.5	M	HA/R	7	4 mg
4.5	F	R	7	4 mg
3	F	N	60	4 mg
5.5	F	NM	30	4 mg
3	F	NM	30	4 mg
3	M	HA	90	4 mg
4	M	HA/N	21	4 mg
3	M	HA	90	4 mg
5	F	NM	90	4 mg
3	F	HA	90	4 mg
3.5	M	NM	30	4 mg
5	M	NM	90	4 mg
4.5	F	HA	30	4 mg
4.5	F	NM	30	4 mg
2.5	M	NM	30	4 mg
2.5	M	NM/HA	60	4 mg
4	F	NM	90	4 mg
6	F	AGR	90	4 mg
5	M	NM	60	4 mg
3	F	NM	60	4 mg
3	M	HA/AGR	60	4 mg
6	M	HA/AGR	7	5 mg
2.5	M	HA	45	4 mg

NM, nightmare; HA, hyperactivity; N, nervousness; AGR, aggressive behavior.

Conclusions: The awareness of the frequency of this side effect profile of montelukast that is widely used in the treatment of asthma is important for the clinician conducting the treatment. It is also absolutely necessary to warn parents about these effects to prevent unnecessary diagnosis and research. Pediatricians may also recommend using montelukast carefully only in specific indication.

0982 | The results of long-term dynamic monitoring of children with uncontrolled severe persistent asthma, receiving omalizumab

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Introduction: The long-term follow-up patients' monitoring helps to receive relevant information about the clinical course of diseases, the safety and efficacy of medical technologies. Omalizumab is one of the most long used targeted therapies in children with uncontrolled severe persistent asthma.

Objectives: To analyze the efficacy of Omalizumab according to pediatric patient registry with uncontrolled severe persistent asthma.

Results: Pediatric patient registry with uncontrolled severe persistent asthma included data of 101children (67.33% boys) from 6 to 17 years 11 months (average age 13.4 years). The duration of therapy with omalizumab was from 1 to 81 months (Me 16 (10; 44) months), doses were from 75 to 600 mg, Me 300 (225; 375) mg.

All children (101) had positive dynamics of asthma during the therapy with Omalizumab. Asthma control was better: ACT-test before the Omalizumab therapy — 14 (11; 17) points, after 1-year — 20 (13; 25) points; $P < .001$. The amount of basic therapy has been reduced (before Omalizumab the average dose in term of fluticasone propionate was 629 ± 304 μg ($n = 15$), after 4 years — 524 ± 342 μg; $P = .065$). The number of exacerbations and requirement of quick-relief medications have been reduced. The severe adverse events were not registered. The local adverse events were observed rarely and stopped in their own or after taking second-generation antihistamines in age dose.

Conclusions: The registry of patients with severe persistent asthma can be used as a tool for long-term monitoring and comprehensive assessment of the efficacy and safety of different medication in children.

0983 | Changing spectrum and causes for chronic cough in children

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Introduction: Cough is a protective reflex response to inflammatory, chemical or mechanical irritation of the respiratory tract and also a social symbol, often it is called as a voice of lungs.

Depending on duration we call it as chronic and it is variable from 2 and 8 weeks in different countries. We consider chronicity if it is more than 2 weeks of duration.

Cough is not a simple thing to ignore, it has great impact on socioeconomics and causes disturbed sleep, exhaustion, nausea, vomiting, rectal prolapse, fecal soiling, urinary incontinence, hernia, subconjunctival hemorrhage, cerebral hypoxic encephalopathy, cough syncope. Parents feel frustrated, upset, stressed, helpless and feeling sorry. 80% of children have five consultation.

Objectives: To find out the prevalence and spectrum of chronic cough.

To find the causes of chronic cough and compare with previous studies from the same author.

We achieved this objectives by analysing 153 cases of chronic cough out of 720 referred patients for respiratory problem between Jan 2015 to Jan 2017 in 2 years.

Results: The prevalence of chronic cough in referred children in the age group of 2 months to 16 years is 153/720 (21.25%). Many children had wet cough, snoring, mouth breathing, bruxism and exercise induced asthma. Laryngeal dyskinesia is observed in 3.2%. The causes of chronic cough is given in the table with comparison to the study in 1999 to the current one in 2017.

Conclusions: Chronic cough is a major socioeconomic health burden, the prevalence is increased from 8% to 21.25% between 1999 to 2017 in the rapidly growing city of Bengaluru with changing demography. The most common causes are Allergic airways diseases. A detail clinical evaluation and hearing the sound of cough with basic minimal testing one can make the diagnosis in majority of cases and special tests are needed only in unusual presentation cases, localised signs and cases failed with therapeutic trails.

	1999 (n.381)	2017 (n.153)
Asthma	79	45.28
Allergic-Rhinosinusitis	10.52	70.25
Asthma+Allergic-Rhinitis	5	12.27
Pertussis syndrome	2.09	2.8
Bronchiectasis	1.05	2.8
Somatic(Psychogenic)Cough syndrome	1.05	2.8
Foreign body	0.526	
Hypereosinophilic syndrome	0.26	
Bronchogenic-carcinoma	0.26	
Impacted cerumen	0.26	
Tuberculosis	0.26	
Protracted bacterial bronchitis		0.65

0984 | Extracorporeal membrane oxygenation as emergency treatment for patients with near-fatal status asthmaticus

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Case report: Extracorporeal membrane oxygenation (ECMO) has been used primarily to treat respiratory failure due to acute respiratory distress syndrome that failed to respond to maximal medical therapy. The use of ECMO in status asthmaticus is limited to case reports. We present three cases of patients with near-fatal status asthmaticus not relieved by conventional treatment, in whom early administration of ECMO resulted in a good outcome. In case 1 and 2, ECMO was instituted because of sustained hypercapnia and respiratory acidosis within 2 hours after initiation of mechanical ventilation. Patient 3 was supported by ECMO at 10 hours after intubation because of severe hypotension and hypercapnia. The lung status in these patients was rapidly recovered within days, and they were extubated at 31, 67 hours and 4 days after initiation of ECMO, respectively. Successful weaning of ECMO was complete the next day after extubation in all patients. There was no significant complication related with ECMO in these patients. Mechanical ventilation for the patients with refractory status asthmaticus can have deleterious effects due to worsening dynamic hyperinflation and increase intrathoracic pressure. Early ECMO application is a useful treatment options for these patients failed to conventional therapy.

0985 | Biological agents in severe asthma. Blood eosinophils: les joues sont fait?

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Introduction: Severe asthma affects 20% of asthmatic patients, which were 334 million in 2014. Due to their high number of exacerbations and the difficult management, it has been calculated a direct cost per patient of 2.325$ $\pm$ 75$ every year. The best way to reduce this high economical expense is a personalized treatment approach that could also include the novel biologic drugs. Nevertheless, their high costs don't meet the idea of "sustainability" that the health systems pursue. The new monoclonal antibodies that target

IL5 / IL5 receptor are of great interest and have demonstrated promising results in the treatment of severe eosinophilic asthma (SEA) even though it is estimated that 25-30% of patients will not respond to these drugs. Hence, the choice of one of them should be strictly targeted . . .. in order to treat patients and save money.

The most studied response-biomarker is the blood eosinophil (BE) count, which is cheap and reproducible. A concentration ≥ 400 eosinophils/μl for example best corresponds with the presence of airway eosinophilia, i.e. with a sputum eosinophilia ≥ 3% that makes diagnosis of SEA. Mepolizumab requires an entry number of BE ≥ 150 cells/μl or ≥ 300 cells/μl in the last 12 months and seems to achieve best outcomes in those patients with BE ≥ 500 cells/μl. Reslizumab on the other hand requires an entry number of BE ≥ 400 cells/μl while Benralizumab requires an entry number of BE ≥ 300 cells/μl. Hence, the cutoff level is not yet clear but maybe having high BE concentration corresponds to a better response to such therapies. Even the clinical features could guide the choice of eligible patients to the new biological drugs, since for example those affected by bronchial asthma and nasal polyps have shown better results, presumably linked to their high levels of IL-5.

Objectives: To determine which could be the best eosinophil cut off to predict a treatment response in asthmatic patients. An analysis of efficacy results from pivotal studies in Reslizumab, Mepolizumab and Benralizumab.

Results: In most of the studies the concentration of eosinophils ≥ 400cells/μl seems to correlate better with the presence of airway eosinophilia.

Conclusions: Blood eosinophils (BE) as biomarker has been widely accepted even if a clear cutoff level is still under discussion. Eventually also the clinical features (i.e. patients affected by bronchial asthma and nasal polyps) could guide the choice of eligible patients to the new monoclonal antibodies.

0986 | Graves-Basedow disease in an asthmatic woman

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Case report: Objectives: To report the case of a young woman with worsening asthma in relation to the onset of clinical symptoms of hyperthyroidism, which was classified as Graves-Basedow syndrome, this being the most frequent cause of hyperthyroidism in young people and most common in females.

Method: A woman, 36 years of age, with seasonal rhinoconjunctivitis and asthma due to sensitization to olive tree and grass. She came in for a check-up due to worsening asthma symptoms of approximately three months' duration. In the latest check-ups after receiving specific immunotherapy for 4 years against olive she showed clear improvement. Currently, she reports dyspnoea almost daily with minimal effort, wheezing that won't abate with a bronchodilator, precordial pain and very frequent palpitations daily. After ordering complete blood work and spirometry with bronchodilator test (BDT) she was referred to cardiology and endocrinology.

Results: The patient sweated profusely during the examination. Normal basal spirometry and negative BDT. Electrocardiogram: tachycardia with sinus rhythm. Echocardiography: normal. Blood work: TSH: 0.0, T4L: 1.37 and T3: 4.5. Antithyroid antibodies: negative. Thyroid ultrasound: generalized hypervascularization around the thyroid. Thyroid scan: diffuse toxic goitre. Our patient was diagnosed with primary hyperthyroidism due to probably Graves' disease. Currently treated with Carbimazole and propranolol as needed, showing improvement of respiratory symptoms.

Conclusions: We report a case of worsening asthma in a clinically stable patient due to appearance of symptoms of hyperthyroidism. We recommend not underestimating any symptoms of new onset, to enable an alternative diagnosis and make new therapeutic recommendations.

0987 | Anti-IgE therapy in asthma: the western Romanian experience

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Case report: Background: Omalizumab was developed as a monoclonal antibody targeting the effector antibodies in IgE-mediated asthma. This treatment became affordable only recently for Romanian adult patients and its usage is limited by strict recommendation criteria.

Objective: We aim to examine the evolution of long-established severe asthma patients after 1 year of anti-IgE therapy.

Methods: A retrospective study of a developing case series from an Allergology Clinic in Timisoara, Romania was performed. The selection criteria were met by 4 patients. The initial assessment included prick test to indoor allergens and serological confirmation of IgE-mediated allergy and total IgE count for Omalizumab dosage calculation. Asthma severity was certified according to GINA criteria. At each subsequent study visit, a clinical examination and spirometry were performed, concomitant medications and asthma exacerbations were documented, and the ACT was administered.

Results: Despite a long-term treatment with high- dose inhaled corticosteroids (ICS) and long-acting beta2-agonists (LABA) and add-on oral corticotherapy, all patients reported frequent symptoms and presented at least 4 exacerbations in the previous year. They were proven to be allergic to dust mites and had high levels of total IgE (257 – 1058 IU/ml). Omalizumab was administered every 2 weeks in one patient, monthly in 3 patients. The baseline treatment regimen

with ICS, LABA and others was maintained. At 16 weeks, there was a significant improvement (on average 9 points) of ACT score, and 1 of the 3 patients with low baseline FEV1 had a significantly higher FEV1 (while FEV1 didn't change significantly in the other 2). There were no exacerbations up to this point. At 52 weeks, the ACT score was still better (on average 5 points) than the baseline value, while pulmonary function tests revealed distal obstruction ($n = 2$) and moderate obstructive ventilatory dysfunction ($n = 2$). Exacerbations rate ranged from 0 to 4/patient-year (total of 6 episodes, from which 3 of infectious cause).

Conclusions: A better control of asthma was achieved after 1 year of omalizumab therapy, proving its cost-effectiveness in selected patients. All the patients reported significant improvement of QoL, with respiratory symptoms reduction and less exacerbations, improved ACT score and lung function. Significant reductions in corticosteroid usage compared to the 1 year prior to treatment were noted, with no adverse reactions to Omalizumab.

0988 | Not a difficult asthma but an easy patient solution: flow-volume curve

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Case report: We herein present a case that has been referred to our clinic as a difficult asthma case but in fact which was not related to asthma.

Case: A female patient (45 years old)having a diagnosis of asthma for about 10 years. When the case was brought our attention, patient was still using beclomethasone dipropionate plus formoterol 2x2, montelukast plus desloratadine, but her symptoms were still-continuing. In particular, she has described shortness of breath with effort, and in several times, syncope after effort. Therefore, she was examined for epilepsy. In examination of the patient, mild stridor was noticed. In skin prick tests, she gave positive results for house dust mite. In spirometry, there was suppression in both inspiration and expiration loops. No pathology was recorded in otorhinolaryngology consultation. In thorax CT, subglottic stenosis was observed. According to her anamnesis, she had a history of intensive care unit hospitalization due to a traffic accident 30 years ago. The said stenosis was regarded as a sequelae of intubation. She was referred to the Thoracic Surgery, and subjected to rigid bronchoscopy therein. As a result, the symptoms of the patient showed a considerable improvement. She is still being followed-up.

Conclusion: We can improve our approach towards patients by always taking into consideration and evaluating the flow-volume curve in the spirometry, a test that we frequently use in the clinical practice.

0990 | Omalizumab safety in 91 asthmatic patients given 10,472 injections up to 9 years

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Introduction: Randomized Controlled Trials showed that omalizumab exhibited a good safety and tolerability profile in patients with moderate to severe asthma. However, safety data of long-term treatment with omalizumab are scarce.

Objectives: Our aim was to assess the safety of omalizumab in patients under long-term treatment in a real-life setting.

Results: Difficult-to-control asthmatic patients from the outpatient clinic of two regional Italian Hospitals, treated with omalizumab up to 9 years, were retrospectively evaluated. Mild to severe adverse events leading or not to discontinuation as well as any reasons for discontinuation were recorded.

Ninety-one patients (26.4% males, mean age 49.9 $\pm$ 14.9 years) were included in our study (mean omalizumab treatment length, 3.8 $\pm$ 2.6 years; mean individual monthly dose of 514.5 $\pm$ 345.7 mg, range, 150-1200 mg). A total of 10,472 administrations were given (115 single administrations per patient). Fifty-nine out 91 patients (64.8%) were treated for a period of time from 3 to 9 years, 14 of whom from 6 to 9 years. A high proportion of patients who discontinued treatment dropped out within the first year (41.3%) for reasons unrelated to treatment. Seven out of 91 patients (15.5%) discontinued omalizumab for treatment-related adverse events: arthralgia/myalgia (3 patients); urticaria, angioedema (2 patients); metrorragia (1 patient); relapsing herpes labialis (1 patient). Four other patients complained of mild adverse events (rhinitis and conjunctivitis, fatigue, thrombosis) but continued the treatment. Anaphylaxis was not reported.

Conclusions: Long-term treatment with omalizumab appears to be remarkably safe and well tolerated in the real-life setting. Prolonged omalizumab for many consecutive years did not increase the risk of side effects, including anaphylaxis.

0991 | Evaluation of quality of life and prognostic scales in patients with chronic obstructive pulmonary disease

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Introduction: This study was aimed at assessment of vaccination effects on quality of life and main prognostic scores in COPD patients.

Objectives: The study involved 362 male patients with COPD. Vaccination was done using 13-valent conjugate pneumococcal vaccine PCV13 and polyvalent pneumococcal vaccine PPV23. Quality of life was assessed using the Russian version of SRGQ and CAT questionnaire. Prognostic BODE, DOSE and ADO scores were calculated.

Results: Vaccination with PCV13 and PPV23 was associated with improvement in quality of life in 1 year after vaccination, though this effect of PPV23 decreased to the 3rd year. Quality of life questionnaires help to assess the therapeutic strategy chosen both in early and delayed follow-up. BODE, DOSE, and ADO scores have demonstrated a reliable and statistically significant decrease in 1 year after vaccination; for PCV13, this effect maintained in 3 years after vaccination.

Conclusions: The using of prognostic evaluation index BODE, DOSE, ADO are reliable a tool for monitoring the effectiveness of the conduction therapy. 2. The applying of quality of life questionnaires allows to navigate in the correctness of the chosen treatment strategy. 3.The prescription of PCV 13 vaccine for COPD patients can reliably minimize the number of exacerbations requiring outpatient and hospital treatment, as much as possible to reduce the number of pneumonia episodes and health costs of combating this nosological entity.

0992 | Bronchial methacholine challenge in children

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Introduction: Bronchial methacholine challenge is a non-specific provocation test performed to assess bronchial hyperresponsiveness (BHR). Because of its direct action on the bronchial smooth muscle, no delayed reactions are observed. Methacholine induces a bronchospasm which is reversible after administration of bronchodilators and the challenge test is performed on an outpatient basis. The most common indication for methacholine challenge test (MCT) in children is suspected asthma. This test has high sensitivity and a high negative predictive value, but a lower positive predictive value. Thus, a positive MCT does not necessarily imply a diagnosis of asthma.

Objectives: Objectives of the study were to determine the most common indications for bronchial challenge in children, to assess BHR in well controlled asthma as well as to compare the predictive values of MCT and the exercise treadmill challenge for the purpose of detecting asthma in children with postexercise symptoms.

Results: Data were extracted from a pulmonary function database prospectively generated over 2 years. A total of 533 subjects of which 292 male and 241 female, age range 6.1 years to 18 years, underwent methacholine challenge using the 2 minutes tidal breathing protocol. The provocative dose of methacholine causing a 20% drop in FEV_1 (PD_{20}) was used for determining the level of BHR.
The most common indications for MCT were suspected asthma (28,8%), recurrent or chronic cough (24.7%), uncontrolled or poorly controlled asthma (21.6%), assessment of asthma severity (12.9%), dyspnea (7.2%) and chest pain (4.8%). 72.4% of patients had a history of atopy and asthma was confirmed in 78.6% of the patients. We found no significant association of BHR level and exhaled nitric oxide levels while BHR persists in most patients with well controlled asthma. In patients with postexercise symptoms there was no correlation between the MCT results and exercise treadmill challenge.

Conclusions: MCT is the diagnostic test of choice for confirmation of asthma in patients with high clinical suspicion and normal or ambiguous spirometry. Because of its high negative predictive value, a negative MCT is highly predictive for the absence of asthma. Although relevant for asthma diagnosis, MCT is not always related to the severity of bronchial inflammation. The results of MCT should always be considered in the context of clinical symptoms and other findings of the individual patient.

MONDAY, 19 JUNE 2017
TPS 28
PEDIATRIC SKIN AND DRUG ALLERGY AND VARIA

0993 | Chemiluminescent immunoassay and LC/MS-MS methodology for the determination of vitamin D status in infants at high risk for developing allergic diseases: Is there any analytical bias?

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Introduction: Given the current interest in vitamin D status and its suggested relationship to immune and allergy outcomes, the accurate and reliable assessment of 25(OH)D levels both in research and clinical settings is imperative. Currently Chemiluminescent Immunoassay (CLIA) is routinely used to measure total 25(OH)D levels in most laboratories. For research purposes the Liquid Chromatography –Tandem Mass Spectometry Assay (LC-MS/MS) is regarded as the gold standard, due to increase in analytical specificity and the ability to quantitate 25(OH)D_2 and 25(OH)D_3 separately. Studies in adults have shown conflicting results comparing agreement of both methods, some with substantial variation in 25(OH)D levels.

Objectives: We are currently conducting the first randomized controlled trial (RCT) on vitamin D supplementation in infancy on immune function and allergic disease outcomes. We have used this study cohort as an opportunity to compare CLIA and LC-MS/MS methodologies for assessment of vitamin D status. To our knowledge no studies have investigated this in infants before.

Results: In this RCT, high risk infants are orally supplemented with either 400 IU vitamin D/day or placebo from birth to 6 months of age. Blood samples are collected at 3, 6 and 12 months of age and 25(OH)D levels are measured using both CLIA and LC-MS/MS methodologies.

Bland Altman Plots are used to identify levels of agreement between CLIA and LC-MS/MS. Correlation between difference and mean with values near zero implies concordance. Bradley-Blackwood (BB) test is used to further proof accuracy (P = n.s implies concordance).

Data on 120 infants were analysed. 25(OH) D levels from both methods were available for 69/120 infants at 3 months, 79/120 at 6 months and 73/120 at 12 months.

The highest agreement was found at 3 months (correlation between difference and mean -0.076; BB F = 0.825 (P = .44)) with good agreement at 12 months (−0.251, BB F = 2.41 (P = .097)) but no agreement at 6 months (−0.397, BB F = 12.3 (P < .001)).

Conclusions: This is the first study in infants comparing the major 25(OH)D assays currently in use. We showed a good agreement between CLIA and LC-MS/MS at 3 and 12 but not 6 months of age. Age-related differences may indicate that growth and associated immunological and metabolic changes may influence the assays. Clinicians should recognize the limitations in accuracy and precision of current assays. Further Pediatric studies comparing both assays in different age groups are urgently warranted.

0994 | Sensitized pediatric patients show lower vitamin D levels

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Introduction: Many studies have evaluated the association between allergic disease and Vitamin D. The aim of the present study was to evaluate the serum levels of vitamin D and the possible association with sensitization to main pneumo-allergens in pediatric patients possibly suffering from an allergic condition.

Objectives: We included in the present study all consecutive pediatric patients referring to the allergy unit of the Foundation IRCCS Policlinico San Matteo of Pavia (Italy) for a suspicion of allergic rhinitis or allergic rhino-conjunctivitis, from January 2015 until December 2015, only during autumn and winter. Vitamin D was dosed through radioimmunoassay methods and values expressed by nmol/l. Vitamin D was considered as deficient for values < 25 nmol/l, insufficient for values between 25 and 75 nmol/l, and normal between 75 and 250 nmol/l. Values of > 250 nmol/l were considered as toxic. For each patient we evaluated body mass index (BMI). Atopy was evaluated by skin Prick Tests for common pneumo-allergens.

Results: 227 consecutive pediatrics patients (mean age 7 years) were included in the present study. 6 patients showed deficit levels of Vitamin D, in 175 patients Vitamin D was insufficient, in 45 normal and in one we highlighted toxic levels. Mean of BMI values was 15.21 for patients deficient in Vitamin D deficit, 18.56 in insufficient patients, 17.11 in normal one and 14.81 in the patient presenting with toxic levels. Only 185 patients accepted to be evaluated through skin prick tests. 144 patients resulted positive for at least one pneumo-allergen. Vitamin D serum levels were lower in atopic patients (mean 59.62, quartiles: 44.21-67.58 nmol/l), and higher in non-atopic ones (mean 65.31, quartiles: 38.02-74.10 nmol/l).

Conclusions: In pediatrics, a proper evaluation of Vitamin D should be conducted, since we highlighted that in 181 out of 227 patients

Vitamin D levels were not appropriate. Moreover, we found that sensitized patients show lower levels of vitamin D if compared with non-sensitized patients.

0995 | The relation of gender to prevalence, severity and comorbidity of childhood allergic diseases in a cohort study in Taiwan

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Introduction: Asthma, allergic rhinitis (AR) and atopic dermatitis (AD) are major allergic diseases among children that not only pose heavy medical burden but also negatively affect daily lives of children and their families. Previous studies have shown increasing prevalence of allergic diseases in Taiwan, while the current status of childhood allergic diseases in Taiwan is not known.

Objectives: This study aimed to investigate the current epidemiology of childhood allergic diseases in Taiwan and to evaluate the relation of gender to prevalence, severity and comorbidity of childhood allergic diseases. This study was performed in 2016 on 385 children (age 6.2 $\pm$ 0.3 years; 201 boys, 54.5%) who were born in 2010 and participating in a cohort study in Northern Taiwan. All subjects were evaluated by a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and an interview conducted by board-certified pediatricians. Atopic status was determined by Phadiatop Infant.

Results: In general, the prevalence rate of physician-diagnosed asthma, AR and AD were 24.7%, 52.5% and 21.9% respectively. We found that boys were more likely to suffer from asthma ($P = .02$), AR ($P = .07$) and atopy ($P = .03$) than girls. In addition, atopic status was significantly associated with allergic rhinitis ($P < .001$) and marginally associated with asthma ($P = .05$). There were no significant gender differences in severity and comorbidity of allergic diseases. As to seasonal variation, symptoms of wheezing and rhinitis occurred more frequently in winter than in summer among both genders. The most common trigger factors of asthma, regardless of genders, were common colds (78% in boys and 88% in girls, respectively) and weather change (61% in boys and 60% in girls, respectively).

Conclusions: To the best of our knowledge, this is one of the first epidemiological studies of childhood allergic diseases using both questionnaires and physician-conducted interviews. Our study shows that the current prevalence of allergic diseases remains high in Taiwan. More boys than girls have asthma, allergic rhinitis and atopy in childhood, but there are no marked gender differences in severity, comorbidity, seasonal variation and trigger factors of childhood allergic diseases.

0996 | Sensitization profiles in children and adults newly referred to a university hospital

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Introduction: Sensitization is a risk factor for the development of respiratory allergic diseases and is influenced by many factors. A detailed knowledge of sensitization profiles in children and adults inhabiting a given area may have relevant implications for the application of prevention and treatment strategies.

Objectives: In this descriptive, retrospective study, demographic and clinical information was obtained for children (4-12 years) and adults (18 years or older) newly referred to the Cova da Beira Hospital Centre between the years of 2009 and 2015. All the patients had symptoms suggestive of respiratory allergic disease. Sensitization to inhalant allergens was assessed by skin prick tests (SPT) and specific IgE determination, and profiles in children and adults were compared.

Results: The analysis included 337 children and 589 adults. In the children's group, 44% had rhinitis, 32% had asthma, and 24% had asthma and rhinitis simultaneously. In the adult sample, 21% had rhinitis, 16% had asthma, and 63% had asthma and rhinitis.

In the adult patients, the major allergens evaluated by SPT were grass pollen (64.3%), mites (61.4%), cereal pollen (59.2%), weed pollen (56.6%), and tree pollen (49.5%). The frequency of sensitization evaluated by specific IgE tests was slightly different, but the major allergens were the same. The percentage of monosensitized patients, as assessed by SPT was 7.0%.

In the children's group, the frequency of sensitizations evaluated by SPT was 24.0% for grass pollen, 4.2% for mites, 5.6% for cat and dog dander, and 2.7% for moulds and fungi. The frequency of sensitization evaluated by specific IgE tests was very different, but the profile correlated with that of the SPT: 46.0% for grass pollen, 20.5% for mites, 12.0% for weed pollen, 8.0% for tree pollen, 14.0% for cat dander, 6.0% for dog dander, and 4% for moulds and fungi. The percentage of monosensitized patients, as assessed by SPT was 40.8%.

Conclusions: The two methods for sensitization assessment used showed consistent determination for most adult cases, but with a lower sensitization frequency for SPT in children. The prevalence of outdoor aeroallergen sensitivities was more common than that of indoor aeroallergen sensitivities. Overall sensitization profiles for both samples of the same population were similar, however mite sensitization was significantly higher in adults.

0998 | Ecthyma gangrenosum and agranulocytosis in a previously healthy child

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Case report: Ecthyma gangrenosum(EG) is a rare skin manifestation which starts with a maculopapular eruption and followed by a necrotic ulcer covered with black eschar.

EG is usually occurs in *Pseudomonas aeruginosa* sepsis and immunosuppressed patients.

We present a previously healthy 12 month-old girl with EG by *P. aeruginosa* and agranulocytosis without bacteremia.

Conclusion: It is important for allergists to culture wounds and differentiate EG from other skin disorders including Tsutusgamushi disease to initiate appropriate empiric antipseudomonal antibiotic treatment, and to evaluate for a possible immunodeficiency, even in a healthy child.

0999 | Angioedema in women of three generations: a form of hereditary angioedema type iii

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Case report: Description of the case: Hereditary angioedema (HAE) is characterized by episodes of angioedema affecting not only the skin but also other organs. The involvement of the upper respiratory tract, in some cases, poses significant risk to life. AEH type I is classically described as an autosomal dominant disease with a quantitative defect of INHC1; in type II, the level of INHC1 is normal but is not functioning. Recently, it has been reported cases of angioedema, affecting mainly females, without alteration of the level or function of INHC1 and is associated with exposure to increased levels of oestrogens – it was named AEH type III.

The authors present the case of a previously healthy 14-year-old girl who went to the urgencies due to lip and face oedema with 4 days of evolution. The airway was not compromise and had no history of trauma. She reported having started oral contraceptive (ACO) about a week before. The objective examination showed marked oedema in the upper lip, in half of the lower lip and in the left side of face. She was reassessed in an Immunoallergology appointment. She had no new episodes of angioedema after stopping with the ACO. Considering the family history, it was found that the grandmother and great-grandmother had episodes of recurrent angioedema of the face and limbs related to taking ACO and during pregnancy. For these episodes no treatment was needed. In the other hand, they described an improvement and after the menopause no episodes were recorded. Analytically, INCH1 and C4 complement tests were normal.

Discussion/Conclusions: AEH type III is a rare form of angioedema and as such, it is important to consider in the differential diagnosis. The diagnosis is a challenge and should be based on clinical findings and a detailed family history.

1000 | Hypersensitivity to antibiotics in children in Vilnius University Hospital

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Introduction: Adverse drug reactions are frequently reported in children and antibiotics are the main culprit drugs.

Objectives: This study analyses the incidence of antibiotics allergy in children who were tested for drug allergy, the culprit drugs and evaluates the clinical pattern of patients/parents reported hypersensitivity to antibiotics.

Results: Data from patients who were tested for antibiotics allergy in Vilnius University Hospital over a 3 years period (2014-2016) were analysed. 30 children (19 (63.33%) girls and 11 (36.67%) boys) were included in the analysis. The mean age of children was 7.14 ± 5.58 (3 months-17 years) years old.

44 hypersensitivity reactions to antibiotics were reported. Four hypersensitivity reactions to antibiotics were reported in one children, three reactions – in 3 children, two reactions – in 4 children. 7 (15.90%) reactions appeared during 1 hour. All (100%) hypersensitivity reactions were with skin symptoms (31 (70.45%) maculopapular rash, 16 (36.36%) urticaria). Respiratory symptoms were reported in 3 reactions (6.82%), cardiovascular and gastrointestinal symptoms were reported in 2 hypersensitivity reactions (4.55%). The main suspected antibiotics were penicillins (32 (72.73%) reactions) and cephalosporins (7 (15.91%) reactions). Amoxicillin was the most frequently reported drug (21 (47.73%) reactions), followed by amoxicillin with clavulanic acid (5 (11.36%) and cefuroxime (5 (11.36%)). Three (10%) children were confirmed as being antibiotic allergic, one patient to cefuroxime and cefotaxime and two patients to amoxicillin.

Conclusions: Skin symptoms were the most frequently reported in a suspected antibiotics hypersensitivity. The main suspected culprit drug was amoxicillin. Antibiotic allergy was confirmed for only one tenth of children so complete and careful diagnostic work-up is essential in order to confirm antibiotics allergy.

1001 | Delayed hypersensitivity reactions to beta-lactams in children: challenging diagnostic

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Case report: Background: Beta-lactams (BL) are frequently prescribed in children and hence associated with hypersensitivity (HS) reactions. Non-immediate reactions to BL can be a diagnostic dilemma in the paediatric group as infections can mimic its cutaneous manifestations.

Objectives: The authors report two cases of non-immediate allergic reaction to BL in children. The patients were submitted to skin tests (ST) with BL determinants and culprit drugs, determination of specific IgE to BL and drug provocation tests (DPT) to alternative drugs. This careful evaluation confirmed its diagnostic.

Report: Patient 1- male, 5 years old, with two previous allergic reactions: the 1st with 2 years old with maculopapular pruritic eruptions, on the 2nd day of cefaclor intake for otitis. The 2nd with 4 years old with dyspnoea, hypotension and nausea also on the 2nd day of AX administration for otitis. Denies other BL intake after these episodes. Specific IgE to BL were negative. ST with penicilloyl-polylysine (PPL), minor determinant mixture (MDM), amoxicillin (AX), penicillin, amoxicillin/clavulanic acid (AX/CL), cefuroxime, ceftriaxone and cefaclor had negative immediate reading. However, intradermal ST with AX and cefaclor showed a positive delayed reading (48 hours). DPT with alternative cephalosporin's (cefuroxime and ceftriaxone) were negative. Patient 2- female, 16 years old, evaluated 5 years after an episode of lip oedema and generalized maculopapular pruritic exanthema in the 14th day of a hospital admission for a complicated sinusitis and cerebral empyema. She was initially prescribed with ampicillin and ceftriaxone during 14 days, followed by cefotaxime and meropenem after the beginning of the complaints. She described maculo papular pruritic exanthema 48 h after AX/CL intake for a cystitis, three year later. Specific IgE to BL were negative. ST with PPL, MDM, penicillin, ceftriaxone, cefotaxime and meropenem were negative. ST with AX and AX/CL revealed positive results only on the delayed reading (48 h). DPT with ceftriaxone, cefotaxime and meropenem were negative.

Conclusions: Non-immediate HS to BL in children represents a clinical challenge. These reports highlight the importance of a systematic diagnostic workup for the establishment of a precise diagnosis of delayed HS reaction. Delayed reading of ST is essential to a correct diagnosis of non-immediate HS reaction and to avoid false labelling of viral infectious rash.

1002 | Sensitization to tiurans in a pediatric patient

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Case Report: Introduction: Tiurans are substances that are frequently used in the manufacturing of rubber items and can be found in everyday objects like rubber gloves, toys and balloons, waterproof clothes or even pesticides/insecticides, shampoos and antiseptics.

Clinical Case: Female patient with 9 years old, referred to the immunoallergology appointment with recurring episodes of angioedema and eyelid, lip and peri-oral erythema, without respiratory complaints. The first episode occurred at 5 years of age, after dental extraction (contact with local anesthetics, latex gloves and the prophylactic administration of Clarithromycin). After 2 months the patient had a similar episode, 72 hours after playing with balloons. Less than a month later, there was mention of a new episode after having contact with a rubber beach ball. In all episodes, there was a complete resolution after the administration of anti-histamines. The patient was challenged with clarithromycin and lidocaine and also submitted to skin prick tests (SPT) to aeroallergens, latex and prick-prick with latex, which all turned out negative. The patient was also submitted to Epicutaneous tests (EpiT) using a standard, dentistry and local anesthetics battery, latex glove, shampoos and lotions used by the patient. All of these tests were negative, with the exception of tiurans, perfumes mix and latex gloves. Since then, the patient keeps avoiding tiurans and remaining asymptomatic.

Discussion: Rubber contact dermatitis are late type IV reactions of hypersensitivity, mediated by cells and related to rubber additives, like tiurans, which was confirmed in this clinical case through positive EpiT to tiurans and latex gloves that have tiurans in its constitution.

Conclusion: In this clinical case, the diagnostic of contact dermatitis to tiurans would not be expectable, due to its small incidence in children. It is a more frequent pathology in adults, mostly in those with frequent exposition, namely people that work in rubber related industries. Considering the diagnosis, the patient has indication to avoid any contact with tiurans.

1003 | Guidance and preparation initiatives for participants in clinical research on pediatric allergies

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Introduction: Clinical research coordinators (CRCs) provide pediatric patients and their guardians with clear explanations of the details of a clinical study, including the risks and benefits of participation, in order to obtain informed consent and enroll patients in the study. CRCs respond to questions and concerns before the study, but doing so during and after the study is also vital to establishing a relationship of trust with the patient. In particular, simple explanations and trust-based doctor-patient relationships are indispensable to maintaining high levels of adherence to treatment regimens in pediatric allergy patients with chronic atopic dermatitis and asthma.

Objectives: We incorporated patient guidance on dealing with allergic symptoms into clinical studies and research on pediatric allergies, in addition to explanations of study details. We also incorporated guidance for patients on skin care and breathing control exercises into the studies, in addition to the conventional explanations stipulated in the protocols. In addition, we produced a seasonal, newspaper-style publication called "Allergy News" to provide information that we wished to share with our patients.

Results: The successful incorporation of patient guidance into the clinical studies allowed for better understanding of the studies, and improved the approach to pediatric patients and the rate of success in obtaining consent from their guardians. We also made specific preparations for each patient based on his or her age, and this facilitated successful communication and smooth progress of examinations and all other aspects of the studies.

Conclusions: Patient guidance and preparation by the pediatric allergy team regarding the patients' condition facilitated better understanding of the allergy and the study among the patients and their guardians.

1004 | Lithuanian allergic patient's family's experience map

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Introduction: The patient's journey mapping is a tool used by companies to help them see what their consumers truly want – the real moment's of truth and the ways in which consumers go about achieving their needs. Understanding the patients experience is the key point in our efforts to improve patients care.

Objectives: To gain a better understanding of the experiences the patient has while moving throughout the health care system and to make typical Lithuanian allergic patient's family's experience map.

Results: The live empathy and problem interviews were conducted with 50 parents of young children experiencing allergy – like symptoms. Their social economic experiences with trying to find a solution to their problem were recorded and retrospectively evaluated on the following points: causes for suspecting allergy; accessibility to doctor allergist consultation; problem – solution timeframe; money spent; and the clarity of information provided by the physician and in vitro laboratory in both: public and private healthcare sectors in Lithuania. All data was analysed using Walker's method adopted by Lean UX methodology.

The main allergy suspecting symptoms were respiratory tract (runny nose, stuffy nose, dyspnoea) (48%), dermatological (dermatitis) (36%) and gastrointestinal (diarrhoea, stomach ache) (8%). The accessibility to the doctor varies from regions, most of the specialists are based in bigger towns and the average time to get to specialist was 1-2 months. Most of the families googled and searched information in social forums instead of consulting their family doctor. 18.5% of the patient's were unconfident on diagnosis and searched for more help.

Conclusions: The illustration that maps the experience of Lithuanian family was created. The map shows emotional, socioeconomical data and the contact/interaction points where medical system improvements could be done.

1005 | A nursing protocol of assistance in a pediatric daily hospital of allergy

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Introduction: The nursing assistance to the children that attend to a daily hospital of Allergy Unit has a priority to provide the best assistance to the child with a specialized nursing cares.

Objectives: The aim of this work was to perform a nursing care protocol which summarize all the steps and actions to do in order to assess the best assistance to the children attended at the pediatrics allergy daily hospital.

Results: With this nursing protocol we avoid any mistake that could occur in the controlled administration concerning allergen-dose-patient, as well as we achieve a better compliance at home of the recommendations given to the children and their family.

Material and Methods: Reception of patients: check of the patients with name and surname, confirmation of the personal data with the family companion and introduce of the nursing staff.

Identification of patients: placement of a personal sticker on the back (if less than 1 year) or on the chest (if older than 1 year) with the name and a drawing/picture of the allergen in study (food or drug).

Interview concerning clinical aspects: questions concerning any health problems in the previous 24 hours (fever, cough, rhinitis, diarrhea, vomiting..) and any recent treatment (vaccines, antibiotics given, antihistamines taken. . .). It is also important in this step to confirm that the child has eaten anything before the procedure (children must not be in fast).

Food/Drug controlled administration: verification that the drug/food doses is the correct before each controlled administration step, and confirmation that it correspond to the one prescribed by the allergist. It also very important in this step to avoid any contamination of the food or drug given to each child with the other.

Recommendations after the procedure: this implies to assess that the parents maintain the child well observed the next 6-8 hours after the procedure and also, in those cases where necessary, a written explanation with the doses and guidelines to follow at home.

Conclusions: This protocol guarantee to the children and their families an appropriate nursing assistance as well as avoid mistakes during the procedure of study.

1006 | Outcomes of ß-lactam drug allergy challenges: a retrospective audit in a tertiary children's allergy service

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Introduction: A retrospective study of β-lactam drug allergy challenges in children attending a tertiary allergy centre. Many children are labelled as having a β-lactam drug allergy when they do not have a true drug allergy. This leads to inappropriately prescribed, second line, broad spectrum antibiotics which are more toxic, expensive and potentially exert a selection pressure for antimicrobial resistance. While the gold standard for diagnosing β-lactam allergy is a provocation challenge, initial skin prick testing to the major determinant benzylpenicilloyl (PPL) and the minor determinant mixture (MDM) is routine in our clinic followed by oral challenges with penicillin, amoxicillin or co-amoxiclav.

Objectives: To assess whether children labelled with a β-lactam allergy have a true drug allergy. If deemed non allergic, to remove the label of being penicillin allergic from patient. A retrospective review of the case notes of β-lactam drug allergy was reviewed between the years 2014-2016. After a relevant history taken, the children were seen in the drug challenge service where one dose or graded doses of triggering antibiotic given, followed by an observation period of an hour with an additional five day course of antibiotic on discharge to rule out a delayed reaction.

Results: 72 patients were challenged to penicillin. 45 (62%) male; 27 (37%) female Age mean age 5 years 4 months. The presenting symptom(s) included a viral infection with fever 13 (35%), a viral rash 25 (34%), Erythema Morbiliforme rash 21 (29%),urticarial rash 18 (25%), chest infection 11 (15%), ear infection 9(12%); angioedema 9 (12%), tonsillitis 7 (10%), Erythema Multiforme rash 4 (5%), and Macular papular rash 4 (5%).The challenge outcomes showed 68 (94%) passed with no signs of a systemic or delayed allergic reaction and 4 (5%) failed with 2 (2.5%) presenting in hospital and 2 (2.5%) post challenge with delayed symptoms.

Conclusions: Viral infections are the commonest cause of rashes in children under 5 years of age. Our study confirms that many children (94%) are falsely labelled as having a β-lactam drug allergy and can be challenged in the "one dose" clinic safely. However the severity of the presenting symptoms must be assessed in clinic to ensure severe or delayed reactions are referred to the gold standard "graded" drug challenge service if required.

1007 | Sensitization to contact allergens in a pediatric population

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Introduction: Allergic contact dermatitis (ACD) is a type IV delayed hypersensitivity reaction. Patch testing is the criterion standard diagnostic tool for confirming the diagnosis of ACD in both children and adults. Few studies have recently evaluated frequent relevant allergens in pediatric ACD.

Objectives: Determine the frequency of sensitizations to allergens in children referred for patch testing.

Material and Methods: We carried out a retrospective case series analysis of 21 children under 18 years old who performed patch tests using a standard series of 30 allergens (Portuguese Group for the study of Contact Dermatitis) between 2009 and 2016. Some patients were tested with personal products. Frequency of

sensitization and the main sensitizing substances were evaluated. Demographic data and concomitant allergic diseases were assessed. Patients with positive skin prick test (SPT) for aeroallergens were considered atopic.

Results: Sensitization was found in 14 of the 21 children tested (67%). 81% were female; median age 14 years (min 8; max 18); 16 performed SPT and 10 had positive results (62%); 12 had rhinitis/rhinoconjunctivitis, 7 had asthma and 3 had atopic eczema. Patch testing with personal products was performed in 5 patients and was negative, in all of them. The most frequent positive reactions were to nickel (78.6% n = 11), cobalt chloride (28.5% n = 4), caínas mix (21.4% n = 3); fragrance mix (14.3% n = 2) p-Phenylenediamine (14.3% n = 2). Nine patients (64% of patients with positive results) had more than one positive reaction and all of them were positive to nickel. Of the 11 patients sensitized to nickel, 10 were female and the eczema was localized predominantly to the periumbilical area, hands and eyelids. All patients sensitized to cobalt chloride were female, three were sensitized to other allergens and the eyelids were the most common localization.

Conclusions: We concluded that the diagnosis of allergic contact dermatitis to specific relevant allergens is common in children referred for patch testing. The sensitizations found in our sample are in concordance with the published data.

1008 | Use of social media for information needs in families of children with allergies

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Introduction: Social media are primarily internet and mobile based tools for sharing and discussing information amongst people. They are activities that integrate technology, telecommunications and social interaction (e.g., Twitter, Facebook, YouTube). Facebook alone has over a billion accounts. People under 25 make up between 35-45% of the population in most countries and are the majority of social media users. 84% of adolescents (in USA) have a several social media accounts. In 2010 social media accounted for 11% of all of the UK's internet usage. The total time spent on social media in the U.S. increased 37% to 121 billion minutes in July 2012, compared to 66 billion in July 2011.

Objectives: To find the information needs and use of social media of families with children with allergy. We performed a survey of adolescents and parents within a tertiary paediatric allergy clinic, a secondary care allergy clinic and parents attending an allergy support group.

Results: We had 100 respondents (58% parents and 42% teenagers) and of which 90% of respondents use some form of social media daily. Most commonly used platforms in parents were Facebook and Twitter and in Adolescents were Facebook, Youtube and Instagram. 58% of parents had used social media platforms to find allergy information however in the adolescents this was more than 75%. Most parents and children had accessed the internet for allergy information from websites and blogs (90%). The majority of patients (68%) wanted to find more information on allergy from their own clinics on social media with Facebook, YouTube and Twitter came out as the preferred methods. Only 20% of families surveyed used their own clinic's website.

Conclusions: Social media is part of nearly everyone's lives and it is important that allergy services embrace this in order to fulfill the information needs of the children and families attending their clinics. Our patients of the future will expect your clinics presence in social media. The patients of the future will expect allergy services to have a social media presence.

1008A | Move into a new house increase the severity of atopic dermatitis

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Introduction: Atopic dermatitis (AD) is the most common chronic dermatosis in children. The aim of this study is to investigate the effect of home remodeling in the severity of AD in children.

Objectives: A cross-sectional study of elementary school children (Seongnam Atopy Project 2016, n = 1591) were performed. A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to survey children of 11 elementary schools from Seongnam, Korea. SCORing Atopic Dermatitis (SCORAD) score were graded by pediatric allergic specialists, blood eosinophil count and skin prick tests (SPTs) were also measured.

Results: Parental history of AD (aOR, 3.76; 95% CI, 1.66-8.53) and past history of home remodeling (aOR, 2.09; 95% CI, 1.02-4.30) were independent risk factors for current AD. Children with history of move into a new house within 24 months after pregnancy had increased level of methylbenzoic acid (aOR = 4.49; 95% CI = 1.82-11.08). Children with high upper tertile level of methylbenzoic acid had increased risk for moderate to severe AD (aOR = 3.67; 95% CI = 1.01-13.29).

Conclusions: There was relationship between move house within 24 months after pregnancy and severity of AD in children in this study.

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TPS 29
AEROBIOLOGY EXPOSURES

1009 | Validation of a novel sampling technology for airborne allergens in low income urban homes

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Introduction: Allergen content of air samples rather than settled dust may be a better reflection of airway exposure, but current air sampling methods are noisy and require technical expertise. The Inspirotec device, based on ion capture technology, is a high-flow air sampling device that is quiet and requires no technical expertise to deploy.

Objectives: The primary objective was to compare the performance of Inspirotec air sampling technology with standard air sampling and vacuumed dust for allergen exposure assessment among twenty-five urban homes that were sampled at baseline, 17 at 3 months, and 12 at 6 months. Airborne particulate matter ≤10 μm (PM10) was collected for 5 days (flow rate: 4 L/min) in parallel with Inspirotecs (flow rates 100 ± 20 L/min), and vacuumed dust samples collected. Fel d1 and Mus m1 were analyzed by enzyme-linked immunosorbent assay (ELISA) for PM10 and dust and MARIA™ (Indoor Biotechnologies) for Inspirotec samples.

Results: Fel d1 and Mus m1 were detectable in 78% and 85% of Inspirotec and 19% and 61% of PM10 samples, respectively. Median [25th-75th%ile] mouse allergen concentrations (pg/m^3) were: Inspirotec (0.28[0.05-1.14]); PM10 (2.56[

Conclusions: Cat and mouse allergen concentrations measured by Inspirotec are strongly correlated with those measured in PM10 and settled dust samples, suggesting that the Inspirotec sampler is a valid alternative for airborne allergen monitoring.

Correlations between Inspirotec sampler and settled dust measurements of allergens

	Pearson correlation coefficient	*P*-value
Cat	0.69	<.0001
Dog	0.77	<.0001
Dust mite	0.40	.01
Cockroach	0.04	.80

1010 | Effect of meteorological parameters on pollen concentration in the city of Athens

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Introduction: Progressive climate changes may affect the quality, amount of airborne allergenic pollens, and alter the rate of allergic sensitization across long periods. The assessment of such an effect requires a long observation period in a specific geographic area, as well as knowledge of the plant biology.

Objectives: To assess variation of the three most allergenic pollens in Greece (olive, grasses, parietaria) in relation to meteorological parameters, across a 7 year period (1995-2000 and 2002) in the city of Athens.

Results

Methods: Daily airborne pollen records were collected for 7 years for the three most allergenic pollen in Greece (olive, grasses, parietaria) using a Burkard volumetric spore trap placed 20 m from the ground in Athens city center. Values were expressed as number of pollen grain/m^3 of air. The pollen parameters that were studied were: annual pollen count, annual peak daily count, growth rhythm and first day of pollination. Simultaneously daily records of the main meteorological parameters (mean daily temperature, relative humidity, rainfall, wind as well as peak daily wind) were kept and then correlated with fluctuations of the pollen concentrations. Correlations were conducted for three different periods, during winter, just before pollination and during pollination.

Results: We observed statistically significant linear correlations between meteorological factors and pollen production.

During winter, temperature and relative humidity affect negatively the production of pollen in all three species, while in the period just before pollination; only the production of olive pollen was affected.

Moreover, temperature increase just before pollination, delays the onset of pollen production in all three types of pollen, while rainfall delays only the onset of grasses pollen production.

Finally, during pollination, some linear correlations were traced between meteorological factors (temperature, relative humidity, sunshine, wind and maximum wind) and daily pollen concentration, but did not reach statistical difference, showing that during this period daily pollen count is affected by more than one meteorological factors.

Conclusions: Meteorological parameters and pollen production for all three species (grasses, olive and parietaria) correlated both at winter and just before pollination. However further analysis in a longer observation period is essential in order to quantify these correlations.

Meteorological factor	Pollen parameter	Plants	Time interval	R	R2 linear	Linear correlation
Temperature	Annual pollen count	Grasses	From 11/12 till 28/2	−0.982	0.9645	$y = -1155.4x + 13196$
Temperature	Annual pollen count	Olive	From 16/12 till 28/2	−0.934	0.8729	$y = -2256x + 26066$
Temperature	Annual pollen count	Parietaria	From 1/12 till 28/2	−0.828	0.6854	$y = -3930.3x + 44837$
Relative Humidity	Annual pollen count	Grasses	From 1/12 till 10/1	−0.758	0.5746	$y = -139.41x + 10965$
Relative Humidity	Annual pollen count	Olive	From 1/12 till 10/1	−0.821	0.6737	$y = -295.8x + 23510$
Temperature	Annual peak daily count	Olive	From 16/12 till 28/2	−0.816	0.666	$y = -189.29x + 2233.7$
Temperature	Annual peak daily count	Parietaria	From 1/1 till 31/1	−0.914	0.8346	$y = -223.93x + 2445.5$
Temperature	Annual peak daily count	Grasses	From 11/12 till 28/1	−0.814	0.662	$y = -38.78x + 457.63$
Temperature	Growth rhythm	Olive	From 16/12 till 28/2	−0.874	0.7641	$y = -11.151x + 196.77$
Temperature	Growth rhythm	Parietaria	From 16/12 till 28/2	−0.867	0.752	$y = -35.482x + 437.62$
Temperature	Growth rhythm	Grasses	From 1/12 till pollination beginning	−0.769	0.5914	$y = -20.467x + 253.46$
Temperature	First day of pollination	Olive	25 days before the last 5 days	0.896	0.8028	$y = 4.8921x + 43.379$
Temperature	First day of pollination	Olive	Last 15 days	0.907	0.823	$y = 4.1199x + 52.736$
	First day of pollination	Grasses	20 days before the last 15 days	0.866	0.7539	$y = 9.996x - 41.737$
Temperature	First day of pollination	Parietaria	15 days before the last 20 days	0.826	0.6827	$y = 5.7969x + 8.1799$
Temperature	Growth rhythm	Olive	20 days before the last 10 days	0.765	0.585	$y = 2.1534x + 48.241$
Relative Humidity	Annual pollen count	Olive	Last 25 days	0.958	0.9186	$y = 365.47x - 21104$
Relative Humidity	Annual peak daily count	Olive	Last 20 days	0.803	0.6444	$y = 32.542x - 1815.6$
Temperature	Annual peak daily count	Olive	10 days before the last 10 days	0.817	0.6678	$y = 40.675x - 349.29$
Rainfall	First day of pollination	Grasses	Last 30 days	0.89	0.7915	$y = 28.428x + 48.008$

1012 | Monitoring of plant aeroallergens in Batumi, second largest city of Georgia

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Introduction: The monitoring of aerobiological parameters is of paramount importance for the characterization of allergenic risks. The patients sensitized to pollens should read their regional pollen bulletins to keep themselves properly up-to-date on allergic disease prevention and treatment. In the last decades aerobiological studies have been developed rapidly in most part of Europe. In our country, the monitoring of pollen and fungi spores concentrations was started in 2012.

Objectives: The aims of presented study were to profile the plant aeroallergens in Batumi, second largest city of Georgia and to determine the dates of beginning of pollen seasons and their duration.

Results: The airborne pollen monitoring was performed with a Burkard Seven Day Volumetric Spore-trap (Burkard Manufacturing Co Ltd, UK) during the seasons of 2016, following the recommendations of European Aerobiology Society. Pollens concentration was calculated and expressed as the number of pollen grains per cubic meter of air (p/m^3). Pollen index was defined as the total number of pollen grains during the pollination period. The main pollen season includes 95% of the seasonal total pollen count, starting on the day on which 2.5% of total pollen was recorded and ending on the day on which 97.5% of total pollen was registered.

Results were summarized in the Table 1. Most abundant pollen type throughout the study period was *Ambrosia*, accounting for 42.9% of total annual amount. The longest pollination period was observed for *Poaceae* – season duration was 150 days.

Name of taxa	Polen index	Season start 95%	Season end 95%	Season duration (days)
Ambrosia	3458.70	23-Aug	3-Oct	41
Alnus	1466.58	25-Jan	1-Mar	36
Castanae	917.20	4-Jun	6-Jul	33
Poaceae	410.70	6-May	3-Oct	150
Pinus	378.63	29-Mar	30-Jun	94
Carpinus	298.23	4-Mar	29-Apr	56
Artemiasia	228.70	21-Aug	27-Oct	67
Cupressaceae	193.01	7-Feb	10-May	93
Ulmus	123.57	5-Feb	5-Apr	60
Fagus	115.00	19-Mar	28-May	70
Platanus	110.70	16-Mar	2-May	47
Corylus	103.39	10-Jan	18-Mar	68
Juglans	94.80	18-Mar	29-Jan	42
Quercus	74.70	19-Mar	12-Jun	85
Chenopodium	55.00	22-Jun	30-Oct	130
Cruciferae	29.30	1-May	16-Jul	76

Conclusions: The results of presented study show the variation with respect to the pollen index and number of days in the pollination seasons. The main pollen types identified in Batumi accounted for 82.3% of annual total sum and belonged to the following taxa: *Ambrosia*, *Alnus*, *Castanae*, *Poaceae and Pinus*.

1013 | Case study France: analysis of plant occupation of public green spaces

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Introduction: RNSA is part of an AIS (Aerobiological Information Systems and allergic respiratory disease management) Life project (2014-2017) N° AIS LIFE LIFE13 ENV/IT/001107.

The project aim is to develop the information base for policy on environment and health, in term of improved management of pollen-related allergic respiratory diseases in Europe.

In this project a case study has been implemented in France in order to provide recommendations for plant occupation of public green areas.

Objectives: The specific objectives of this case-study are to assess pollen counts and allergen content in public gardens and on basis of the obtained results to formulate recommendations in order to protect allergy sufferers.

Two types of pollen traps are used in this study: Hirst pollen trap and Sigma 2 Like passive pollen trap (SLT). The SLT pollen traps are used for analysis of local pollen dispersion.

Within this case study, 7 SLT have been set up in two towns of France (Paris/Lyon) during the pollen season, in order to assess pollen count. In addition to these SLT pollen traps, 4 Hirst pollen traps are also used for this case study (2 in Lyon and 2 in Paris). Statistical descriptive analysis are conducted to obtain the distribution of the pollens in the gardens according to the 2 sampling methods.

The SLT were implanted over the ground at about 70 cm in proximity position in public gardens. Every day, the slide containing biological particles was changed and sent to the laboratory to be analyzed by optical microscopy by a trained analyst. All the analysis were undertaken by RNSA in France. The first campaign of measurement was in 2015 (March-June) and the second measurement campaign in 2016 (March-June).

Results: The results of the two measurement campaigns show that there are a lot of allergenic species in the green gardens in Paris and Lyon like *cupressaceae*, Birch, plane tree, grasses. . .

Conclusions: We need to take in consideration the health impact in the choice of vegetal species to plant in green areas to avoid allergenic species.

1014 | City arboreal pollen rain is a mix of local and migrating pollen in Vinnytsia, Ukraine

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Introduction: Verdure is an important component of a city landscape but pollen of arboreal species can be produced in tremendous quantities. City pollen rain could be composed of both local and migrating pollen fractions. The contribution of the pollen inventories from Vinnytsya city and outskirts was assessed to determine the contribution of local and migrating pollens.

Objectives: Pollen counts were obtained using volumetric method using a Burkard trap mounted on the roof of the Chemical Building of the National Pirogov Memorial Medical University, Vinnytsya, Ukraine. Trees were counted in the University garden and beyond at 2 km radius; data about the plant composition in the neighboring City Park was provided by the Municipal Establishment responsible for city ornamentation; data of forest tree composition around Vinnytsya was obtained at the Regional Forestry.

Results: 2607 trees were found in the University garden including 33% linden trees (*Tilia*), 10% fir (*Abies*), 9% horse chestnut (*Aesculus*), 8% maple (*Acer*), 7% plants of Rose Family (Rosaceae), and 6% each from Cupressus Family (Cupressaceae), birch (*Betula*) and pine (*Pinus*). The main pollen producers in the Vinnytsya City Park were oak (*Quercus*), hornbeam (*Carpinus*), maple (*Acer*), ash (*Fraxinus*), poplar (*Populus*) and linden (*Tilia*).The most frequent forest trees in Vinnytsya region were *Quercus* (79%), *Fraxinus* (7%), and *Pinus* and *Carpinus* 4% each. *Robinia*, *Betula*, *Alnus*, *Abies*, *Acer* and *Tilia* were less frequent. Pollen collected in 2014-2016 was composed of the both local and migrating pollen. *Betula* contributed 19 to 76% of total tree pollen index in these years. *Alnus* contributed 7 to 25%, *Acer* contributed 2 to 15%, *Fraxinus*: 1 to 17%, *Juglans*: 3-8%, *Populus*: 2-3%, *Ulmu*:1-2%, Pinaceae:1-2%, *Carpinus*:1-6%, *Corylus*, and Cupressaceae: 1%. Linden, the most abundant tree around the University, contributed less than 1% to the annual pollen index in all years of study. In spite the fact *Quercus* is planted in the forests around the city, its pollen constituted 1-2% of the total annual amount.

Conclusions: Pollen of the birch, alder, ash, maple, walnut and hornbeam is the most frequent allergenic pollen in the air of Vinnytsya city. The ratio of tree pollen rain components does not correspond with the local composition of arboreal species. Pollen monitoring remains essential to assess risks of disease due to pollen.

1015 | Exposure to bioaerosols during fish processing on board fishing trawlers

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Introduction: Several studies in the seafood industry have shown that production workers are exposed to bioaerosols. These aerosols contain biological material as proteins including enzymes and allergens, and endotoxin, mainly from the raw material. Also shown is that exposure to bioaerosols in the seafood industry may increase the risk of developing respiratory symptoms, asthma and allergy. Despite that fishers are exposed to potentially harmful working conditions, there is insufficient knowledge about the work environment.

Objectives: The objective was to study exposure to bioaerosols among production workers on board of fishing trawlers.

Results: Four freezer trawlers producing round and Japanese cut frozen fish, and one factory trawler producing fish fillets, were included in the study. Data was collected from April 2014 to December 2014 in the Barents and Norwegian Sea. Catch consisted mainly of Atlantic cod, Haddock, Saithe and Deepwater redfish. Bioaerosol samples were collected in the fish factories during fish processing. Workers carried air samplers placed in their breathing zone, and stationary samples were placed close to work locations in the processing area. The samplers were analysed for total protein, enzymes (trypsin), endotoxin and allergens (parvalbumin).

Protein levels were higher on the three oldest trawlers (15-21 years): n = 126, range 0-257 ug/m^3, compared to the two new build trawlers (3 years): n = 126, range 0-30.7 ug/m^3. Based on a semi-quantitative scale, the highest level of trypsin was detected in 12-47% of samples in the freezer trawlers compared to 3% in the fabric trawler. In contrast the highest level of endotoxin was detected in the processing area on the factory trawler (n = 9, range 0.5-483.6 EU/m^3) compared to the freezer trawlers (n = 58, range 1.4-16.5 EU/m^3). Parvalbumin were detected in 68% of the samples on the factory trawler in contrast to 14% of the samples on the freeze trawlers.

Conclusions: Production workers processing fish on board deep-sea fishing trawlers are exposed to proteins, including trypsin and the major allergen parvalbumin. The bioaerosol levels varied between vessels, and may be influenced by different processing techniques, catch type and size of production area, season, age of the trawlers, ventilation systems as well as work load.

1016 | Allergic diseases and impacts of climate changes in children

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Introduction: As it is known allergy and allergic diseases are considered as a global problem caused due to the climate change. The climate is still changing representing not only the environment, but also a serious social and economic problem.

Objectives: The current study is aiming at investigation of the distribution of allergic diseases in children population on the background of climate changes.

Results: Retro-spectral analysis of allergic diseases revealed an increase in the rate of allergic pathologies caused by the seasonality of climate changes. Allergic rhinitis was observed in 22.9% of population ($P < .05$), bronchial asthma - 7.9% ($P < .05$), atopic dermatitis - 6.9% ($P < .05$) and food allergy - 8.9%, ($P < .05$), respectively. The boys outnumbered the girls ($P < .05$), air pollution, that has a great impact on the development of allergies, was revealed ($P < .01$) as well.

Conclusions: The study of population revealed the followings: risk factors for development of allergic disease, frequent respiratory infections, drug sensitization, hereditary load, food allergens, gender, ($P < .001$). The difference factor revealed after comparison the study results and statistical data will help to increase the accuracy for diagnostics of allergic diseases ($P < .01$).

1017 | Polcalcin sensitization in a sample of patients with respiratory allergy in Barcelona (Spain)

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Introduction: Polcalcin is a panallergen capable of sensitizing up to 10% of allergic patients to pollen.

Objectives: Patients with respiratory allergy (rhinoconjunctivitis and/or asthma) were consecutively selected for 1 month. Skin prick test (SPT) with dust mites, pollens (grass, pellitory, chenopodium, mugwort, plantago, olive tree, plain tree, cypress, birch), molds, cat and dog epithelium, latex, profilin, tropomyosin, peach LTP and polcalcin (ALK-Abelló) were performed. SPT ≥ 3 mm was considered as positive.

Results: 21 (52.5%) patients were sensitized to pollens (13 women, mean age:42 years). 17 (42.5%) were sensitized to more than one

pollen. Their sensitization profile was: grass (85.7%), olive and plane tree (52.3% each), chenopodium and cynodont (42.8% each), plantago, cypress and pellitory (28.5% each), mugwort and birch (14.2% each). 9 patients (42.0%) had positive SPT to polcalcin (6 women, mean age: 36 years). Of those, 11.1% were monosensitized to grass pollen, 88.8% presented sensitization to more than 1 pollen species and 77.7% to more than 3 pollen species. Their sensitization profile was: 100% grass pollen, olive and plane tree pollen 88.88%, pellitory pollen 55.5%, chenopodium, cynodon, plantago and mugwort pollen 44.4%, cypress and birch pollen 33.3%.

Conclusions: Almost half of pollen-sensitized patients were sensitized to polcalcin by SPT. In our area, all patients sensitized to polcalcin demonstrated grass pollen sensitization, suggesting that as expected polcalcin sensitization may depend on grass pollen. The sensitization profile and the demographic characteristics of patients sensitized to polcalcin were not different from those not sensitized to it.

1018 | Environmental tobacco smoke exposure and childhood asthma – Is it a trigger or risk factor or both?

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Introduction: Although the harmful impact of environmental tobacco smoke (ETS) on respiratory health in childhood is well known, its effect on asthma as a causal factor is still debated. The aim of the study was to examine the influence of ETS exposure at home on childhood asthma in The Republic of Macedonia, as a country with a high rate of tobacco smoking, high dietary antioxidants intake, and a low prevalence of asthma

Objectives: Parental-reported data obtained through survey of 2310 children aged 5-15 years from randomly selected schools in Skopje, the capital of Macedonia, was used. The association between maternal, paternal and alternate caregivers' tobacco smoke exposures with asthma-like symptoms and diagnosed asthma was investigated after adjustments for potential confounders using binary multiple logistic regression.

Results: Prevalence of wheeze (W) 'ever' was 30.3%, of current W was 6.5%, of current exercise-induced W was 1.7%, of current dry night cough apart from a cold or chest infection was 12.2%, and of diagnosed asthma was 2.3%. Maternal tobacco smoking during pregnancy was found to be 13.7% and postnatal was 28.5%, paternal was 34.7%, and alternate caregivers' was 9.4%. Maternal prenatal tobacco smoking was positively associated with W 'ever' (aOR: 1.43; 1.04-1.96; $P = .029$) and current W (aOR: 1.82; 1.01-3.27; $P = .045$) while alternate caregivers' exposure with current W (aOR: 1.95; 1.12-3.41; $P = .019$) and exercise-induced W (aOR: 3.57; 1.46-8.69; $P = .005$). There was no association with the outcome of asthma.

Conclusions: The results suggest that environmental tobacco smoke is a trigger factor for asthma-like symptoms, probably as a respiratory irritant, but not a risk factor for an onset of asthma.

1019 | Efficacy of air cleaners for the removal of house dust mites and dog allergens

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Introduction: Allergens derived from house dust mites (HDM) and pets are a common cause of respiratory allergic disease, and an air cleaner may be an effective tool for control of the allergens in indoor air.

Objectives: The aim of this study was to evaluate the efficacy of an air cleaner for the removal of HDM and dog dander.

Results: Samples obtained for allergen detection were composed of dust collected from homes inhabited by dogs and dried HDM culture medium that contained mite body particles and excretions. The sample dust was dispersed in a 30 m^3 chamber equipped with an air cleaner (LG Electronic). The number of airborne particles was recorded continuously by a dust spectrometer for 60 minutes and airborne particles were collected on a sampling filter at four different collection start times (0, 5, 10, and 20 minutes following dust dispersion). Der f 1 and Can f 1 concentration of the extract of collected sampling filters were measured by 2-site enzyme-linked immunosorbent assay (ELISA).

The concentrations of Can f 1 and Der f 1 in the dispersed dust were 344 ng/g and 1507 μg/g, respectively. Allergen concentrations of airborne Can f 1 and Der f 1 decreased to 71.0% and 41.6%, respectively, of the initial value 5 minutes after dispersion of sample dust.

Conclusions: An air cleaner can remove airborne HDM allergens and dog allergens more effectively than removing dust particles after a natural settle down.

1020 | Study on the correlation of airborne pollen and anti-allergic eye drops consumption in Beijing urban area.

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Introduction: Pollinosis is a common seasonal disease in daily outpatient and causes several symptoms such as seasonal allergic rhinitis, allergic conjunctivitis(AC),asthma etc. Whether pollen distribution contributes to the AC visits and eye drops usage was seldom discussed in our country.

Objectives: To study the main kind of airborne pollen in Beijing urban and the relationship between outpatient AC visits and anti-allergic eye drops prescriptions amount throughout one year in a tertiary hospital.

Methods: With a modified volumetric trap,airborne pollens were sampled from Jan 1st to December 31st 2015.Meanwhile,information of AC consultation rate per month and anti-allergic eye drops prescriptions per month in outpatient pharmacy was acquired and analyzed through information center in the same hospital. Anti-allergic eye drops which were calculated in this study include mast cell membrane stabilizer(sodium cromoglycate, pemirolast Potassium)and antihistamine (azelastine hydrochloride).

Results: Through the whole year of 2015 the total quantity of pollens amounted to 76164 grains,and the pollen dispersion period lasted 203 days from March 8th to September 26th,accounting for 55.6% of the year. Two peaks of pollen concentration in air were observed,which happened from March to April and from August to September.

The average consultation rate of AC was 80.42 $\pm$ 54.28visits per month. The average quantity of anti-allergic eye drops was 148.67 $\pm$ 148.63 bottle per month. The most common type was sodium cromoglycate.

Two peaks of anti-allergic eye drops were observed similar to AC visits which happened in march-April and August-September. The correlation index was 0.923, $P < .001$.There was a significant correlation between pollen distribution, AC visit rates and anti-allergic eye drops consumption. The drug usage and disease visit peak was higher in autumn than spring while the pollen distribution peak was higher in spring than autumn ($P < .01$).

Conclusions: The airborne pollen distribution was in accordance with anti-allergic eye drops prescription amount and AC visit rate indicating pollinosis was the major factor for this phenomenon. A stronger allergenicity was observed in weed pollen than tree pollen with the higher rate of AC visits and anti-allergic eye drops usage in autumn than spring while the pollen counts were opposite.

MONDAY, 19 JUNE 2017
TPS 30
HEREDITARY ANGIOEDEMA AND MAST CELL DISORDERS

1021 | Hereditary angioedema experience in a Belgian reference centre

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Introduction: Hereditary angioedema (HAE) is a rare heritable disorder that is phenotypically characterized by the appearance of recurrent, circumscribed, non-pitting, non-pruritic, but often painful subepithelial swellings that can be life-threatening. Various types of HAE have been described, of which we will focus on HAE type 1 and 2. Type 1 is characterized by a low amount of C1 esterase inhibitor (C1-INH) and type 2 by a normal amount, but abnormal structure and function of C1-INH.

Objectives: To describe the demographic, clinical and therapeutic characteristics of patients with HAE in a Belgian reference centre.

For this study, patients with HAE type 1 or 2, who were diagnosed at the University Hospital of Antwerp were included. Demographical data and data on symptomatology and therapeutic measures were gathered based on their medical record.

Results: A total of 20 patients (11 female; mean age 49.9 years (13.8-74.4)) from 13 different families were identified. 17/20 (85%) patients were diagnosed with HAE type 1 and 3/20 (15%) with type 2. In our population, the mean age for diagnosis of HAE was 23.9 years (0-70). Clinical data were available in 18/20 (90%) patients, of which 2 (11.1%) were asymptomatic. The other patients already experienced (an) attack(s) of angioedema that could involve many parts of the body including the gastrointestinal tract. 4/20 (20%) patients received maintenance therapy with a pdC1-INH concentrate, while the other patients only received pdC1-INH concentrate or icatibant in case of an attack of angioedema.

Conclusions: HAE is a rare but important disease. Although HAE is an inheritable disease, diagnosis is often not made at early stages of life. In order to optimize diagnostic and therapeutic measures, efforts to gain accurate epidemiological data and individual data on diagnosis, symptomatology, treatment and outcome are necessary. The development of a Belgian national registry of patients with HAE seems necessary.

1022 | Genetic study of hereditary angioedema type II in two siblings in Iran

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Introduction: Hereditary angioedema due to deficiency of C1-inhibitor protein (C1-INH-HAE) is a rare primary immunodeficiency disease which caused by mutation in the C1 inhibitor gene SERPING1, and leads to the low levels of C1-sterase inhibitor (HAE type I) or the presence of dysfunction C1 inhibitor (HAE type II). C1INH maps on chromosome 11q12-q13.1 and this inhibitor belongs to serin protease family that regulate complement, fibrinolytic, contact and coagulation systems. The aim of this study was report of genetic diagnosis of two relative patients with HAE type II.

Objectives: Two family members with clinical phenotype of repeated edema and family history of angioedema were referred to Immunology, Asthma & Allergy Research Institute (IAARI) as a main referral center for this disease. C4 level and quantitative and functional C1 inhibitor were evaluated to confirm their angioedema. Genomic DNA was isolated from EDTA treated blood samples. Subsequently, polymerase chain reaction (PCR) was performed for exon 2 to 8 of SERPING1 gene and the PCR products were sequenced and analyzed by Finch TV program.

Results: The patients were two sisters (47 and 38 years old) with past history of laryngeal edema and abdominal pain which led to hospitalization. Angioedema type II was diagnosed for them based on their decreased level of C4 and dysfunction of their C1inhibitor. Genetic analysis of *SERPING1*showed a heterozygous missense mutation in exon 8 (c.1396C>T) which cause substitution of Arg>Cys. this mutation was reported previously.

Conclusions: HAE disease is a life-threatening disease which characterized by edema in the face, upper and lower limbs, laryngeal and abdominal pain that would lead to hospitalization. Therefore, early recognition of this disease and genetic diagnosis in the patients is necessary for appropriate treatment. Also, genetic diagnosis of asymptomatic patients' family members would be helpful for prevention of occurring severe edema.

1023 | Hereditary angioedema in two sisters due to parental mosaïcism

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Case report: Hereditary angioedema (HAE) is a heritable disorder that is phenotypically characterized by the appearance of recurrent, circumscribed, non-pitting, non-pruritic, but often painful subepithelial swellings of sudden onset, that fade during 48-72 hours, but can persist for up to 1 week. Patients with HAE experience angioedema because of a defective control of the plasma kinin-forming cascade. Various types of HAE have been described of which type I and II HAE are autosomal dominant conditions resulting from mutations in the *SERPING1* gene that encodes the serpin peptidase inhibitor (C1 esterase inhibitor – C1-INH).

Here we report the occurrence of type I HAE in two sisters with unaffected parents. Both affected sibs experienced attacks of spontaneous oedema and had very low C4, C1-esterase inhibitor function and C1-esterase inhibitor plasma concentrations, consistent with a type I HAE. In contrast, the parents and the non-affected sister displayed normal C4 and C1-esterase inhibitor plasma concentrations. In the two affected sisters, the *SERPING1* gene was analysed (bidirectional Sanger sequencing and MLPA analysis). Deletions, nonsense or frameshift mutations in SERPING1 usually result in HAE type I. However, our analysis did not show evidence for deletions or duplications but revealed the heterozygous presence of a single nucleotide change in exon 3 predicted to result in a threonine to isoleucine substitution at residue 179 (c.536C>T;p.Thr179Ile) of the protein. This particular missense mutation has not been reported in databases of normal variation (ExAC, 1000 genomes, GoNL) but was previously identified once in our cohort of 50 patients analysed because of HAE. The nucleotide change was not found in both unaffected parents, which supports the hypothesis of parental gonadal mosaicism.

Somatic and gonadal mosaicism are uncommon. Nevertheless, the diagnosis of an autosomal dominant disorder in two children from unaffected parents should prompt the clinician to consider the possibility of somatic or gonadal mosaicism in one of the parents. Correct diagnosis is important since it affects further family planning. Individuals with germline mosaicism should be counselled about the increased risk of having multiple affected children despite the autosomal dominant character of the disorder and the absence of clinical signs and detectable germline mutations in the parent(s).

1024 | The impact of the introduction of icatibant on A&E attendance, hospital admissions and acute treatment episodes in patients with hereditary angioedema

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Introduction: Hereditary angioedema (HAE) is a rare genetic disorder characterised by a deficiency of C1 esterase inhibitor. Patients experience episodic attacks of subcutaneous and/or submucosal angioedema mediated by bradykinin. These attacks can be painful, debilitating and, where there is laryngeal involvement, life threatening. Rapid acute treatment results in reduced severity and duration of attack. Historically patients needed to attend A&E to receive C1 esterase inhibitor treatment and some therefore chose to not receive treatment. Icatibant, a bradykinin receptor inhibitor, is a subcutaneous injection for acute HAE attacks that can be self-administered.

Objectives: To assess the impact of the introduction of icatibant, via homecare, for acute HAE attacks on A&E attendance, hospital admissions and acute treatment episodes in one UK centre.

Results: The A&E admissions system, pharmacy records and medical notes of HAE patients on icatibant who had a Leeds area postcode were retrospectively reviewed. Data was collected for 1 year prior to a patient starting on icatibant (year 1) and for 1 year after (year 2).

A total of 20 patients were included (f = 17, m = 3; age range 25-84). Of these, 13 patients were on prophylaxis (stanozolol, danazol or tranexamic acid) the year prior to icatibant and 11 remained on prophylaxis after icatibant; 2 stopped due to trying to conceive.

The total number of A&E attendances reduced from 16 in year 1 to 3 in year 2, a reduction of 81% ($P < .02$). The total number of hospital admissions reduced from 9 in year 1 to 1 in year 2, a reduction of 89% ($P = .1$). No patient had an increase in A&E attendance in year 2.

Both patients who stopped oral prophylaxis saw an increase in acute attacks and treatment usage. However, neither attended A&E or was admitted in year 2. Their data has been excluded from the treatment episode data, as they are significant outliers.

In year 1, 21 000 units of C1 esterase inhibitor were dispensed. In year 2, 42 syringes of icatibant and 5000 units of C1 esterase inhibitor were dispensed. Icatibant use led to a 76% reduction in C1 inhibitor usage in these patients ($P < .05$). The number of treatment episodes where treatment was given increased from 17 in year 1 to 27 in year 2; a 59% increase.

Conclusions: Home treatment with icatibant for acute attacks of HAE leads to a reduction in A&E attendance and hospital admissions despite an increase in acute attacks where treatment is administered.

1025 | Identifying early HAE attack signs and symptoms: a UK nurse consensus

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Introduction: On 28th June 2016, a group of 30 immunology nurse specialists from across the UK met to agree a consensus on early attack signs and symptoms experienced by HAE patients
The purpose of agreeing such a consensus was to:

- To increase patient awareness of when attacks start
- Enabling patients to treat attacks early
- To reduce suffering during attacks
- To reduce morbidity
- To reduce the length and severity of attacks
- To reduce recovery time
- To reduce the economic impact and quality of life impact on patients

Objectives: To gain consensus from specialist immunology nurses from across the UK on what patients report as early signs and symptoms of HAE attacks, as sometimes patients report difficulty in discerning what early attack signs and symptoms are, which can lead to a delay in treating attacks.

Results: The HAE specialised nurses went into three workshops and rotated through the workshops, allowing all nurses to flipchart their patients early attack signs and symptoms. The results were subdivided into 3 categories: Abdominal, Laryngeal and extremities.

Abdominal:

- Dehydration
- Nausea
- Vomiting
- Abdominal discomfort
- Period like pain
- Cramping
- Indigestion like feeling
- Bloating
- Irritable
- Mood change
- Under the weather
- impending doom
- Extreme tiredness
- Bilious/ burping

Hands, Feet and extremities:

- Tightness
- Stiffness
- Pressure
- Pain
- Tingling
- Lethargy/ tiredness
- Erythema marginatum (redness of the skin or mucous membranes) involving pink rings on the torso and inner surfaces of the limbs which come and go
- Mood change
- Anxiety

Laryngeal:

- Cough/clearing of throat
- Change in swallow
- Voice change
- Tightness in throat
- Dehydration
- Hoarse
- Lump in throat
- Irritable
- Mood change
- Under the weather
- Anxiety

Conclusions: As a result of the workshops, Immunology nurses were able to come up with a consensus on how early attack signs and symptoms might be described by patients.
It is anticipated that the data captured can be used as a teaching aid for specialist Immunology nurses to teach and educate their patients on identifying early signs and symptoms and administering prompt treatment.

1026 | Routine abdominal ultrasonography has limited value in the care for patients with systemic mastocytosis

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Introduction: Systemic mastocytosis (SM) is a chronic myeloproliferative disease characterized by the accumulation of aberrant mast cells. Since advanced subtypes of SM can lead to organ dysfunction, it is important to screen for progression of disease during outpatient follow-up consultations. In this retrospective cohort study, we included all patients with SM who visited the Erasmus University Medical Centre from January 2009 to February 2016. Only patients who had at least 2 abdominal ultrasonography, with a minimal interval of 2 years, were included.

Objectives: The objective of this study was to determine whether routine abdominal ultrasonography is a valuable examination in this context.

Results: We included 95 patients, of whom 9 developed new hepato- and/or splenomegaly during follow-up. In this group, the mean serum tryptase level increased by 16.93 mg/L over time, compared with a decrease of −1.33 mg/L in the 86 patients whose ultrasonography results stayed normal ($P = .017$). A change in liver and/or spleen size never lead to a change in SM subtype, nor in clinical management. One patient in the 'unchanged' group progressed from

Table 1 patient characteristics, divided according to ultrasonography findings

	No new hepato- and/or splenomegaly (n = 86)	New hepato- and/or splenomegaly (n = 9)	*P*-value
Age in years (mean, SD)	58.95 (13.10)	57.44 (9.94)	NS
Male sex (n, %)	39 (46.4%)	3 (33.3%)	NS
Follow-up time in years (mean, SD)	11.4	9.56	NS
Subtype of SM			
ISM s−	17	2	N/A
ISM s+	56	6	
SSM	6	1	
SM-AHN	3	0	
ASM	4	0	
Absolute change in serum tryptase levels in mg/L (mean, SD)	−1.32 (55.2)	16.93 (26.2)	.017
Change in subtype (n)	1	0	N/A
Change in treatment (n)	0	0	N/A
Cytopenia at baseline (n, %)	6 (7.0%)	0 (0%)	NS
Decrease in bone density during follow-up (n, %)	10 (11.6%)	0 (0%)	NS

SD, standard deviation; SM, systemic mastocytosis; ISM s−, indolent systemic mastocytosis without skin lesions; ISM s+, indolent systemic mastocytosis with skin lesions; SSM, smouldering systemic mastocytosis; SM-AHN, systemic mastocytosis with associated haematological neoplasm; ASM, aggressive systemic mastocytosis; NS, non-significant, N/A, not available.

indolent systemic mastocytosis with skin involvement, to smouldering systemic mastocytosis.

Conclusions: Routine abdominal ultrasonography has limited value in the follow-up of patients with indolent SM. A combination of physical examination with serum tryptase levels can be used to screen for hepatosplenomegaly. Abdominal ultrasonography can be added on indication.

1027 | A unique presentation of pulmonary disease in advanced systemic mastocytosis, proven by the presence of mast cells in bronchoalveolar lavage

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Case report: Background: Systemic mastocytosis is a rare myeloproliferative disease which is characterized by the uncontrolled proliferation of aberrant mast cells. It has varying clinical manifestations. For unknown reasons, pulmonary localization of mastocytosis is extremely rare.

Case presentation: In this report, we describe the case of a young female with systemic mastocytosis with an associated hematological non-mast cell lineage disease with pulmonary interstitial disease directly related to mastocytosis, proven by the presence of mast cells in bronchoalveolar lavage. The treatment of her associated hematological disease (myelofibrosis with myelodysplasia) was hampered by the rapidly declining pulmonary function and progressive organ dysfunction due to the aggressive systemic mastocytosis. She died approximately 1 year after the diagnosis.

Conclusions: To our knowledge, this is the first case in which mast cells were detected in bronchoalveolar lavage. Moreover, to date, only two other cases of pulmonary interstitial disease due to mastocytosis were published. Juggling therapies for systemic mastocytosis and myelofibrosis is very difficult, however, aggressive therapy of both diseases is essential in giving these patients a chance to survive.

Figure 2 CT imaging at diagnosis and after 4 months.
The first CT of the chest showed, mainly bronchovascularly located, groundglass aspect which is most pronounced in the apical areas with a diffuse reticular aspect and widening of interlobular septa. (A+B). Next, the skeleton shows multiple focal sclerotic lesions (C+F). A CT obtained 4 months after the first showed progressive and diffuse reticular groundglass lesions (D+E).

1028 | Genotype has impact on complement proteins in patients with hereditary angioedema

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Introduction: The clinical symptoms vary widely in Hereditary Angioedema patients, and angioedema attacks' severity range from negligible to life-threatening swellings. We aimed to investigate

whether a relationship could be identified between treatment-free phenotypic characteristics and different mutation types.

Objectives: Eighty-one symptomatic patients from 47 unrelated families with HAE (89% HAE type I, and 11 HAE type II) were recruited. Blood samples were tested for complement proteins, and C1-Inhibitor function levels. Genomic DNA was isolated from peripheral blood cells. The coding exons and the exon-intron boundaries of the *SERPING1* gene were sequenced and deletion/duplication analysis with Multiplex Ligation Dependent Probe Amplification was performed.

Results: Thirty-five different mutations (38.2% missense, 20.5% deletions, 14.7% insertions, 11.8% nonsense, 8.8% large deletion, 5.9% intronic) were identified. The C1-Inhibitor antigenic levels and C1-Inhibitor functions were found to be significantly different between patients with different type of mutations. After excluding *p.R466* mutation group, C1-Inhibitor antigenic levels were at its lowest level in patients with Large Deletion and nonsense mutation ($P < .0001$). C1-Inhibitor function was at its lowest level in patients with HAE.

Conclusions: We showed that C1-Inh levels, C1-Inh function, and C1q levels were lowest in patients with large deletions, followed by nonsense mutations and deletions, and were highest level in patients with none mutations. *SERPING1* alterations are probably not the only causative factors of HAE-C1INH. In the no-mutation group, factors resulting in increased posttranslational consumption of C1INH could cause higher complement levels.

1029 | BCX7353, a once-daily oral kallikrein inhibitor, is effective and safe in the prophylaxis of acute attacks in patients with hereditary angioedema: Attack-level analysis of the APeX-1 study

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Introduction: A Phase 2, randomized, double-blind, dose-ranging, placebo-controlled, 3-part, parallel-group study (APeX-1) is evaluating the oral kallikrein inhibitor BCX7353 as a prophylactic treatment in HAE patients. An interim analysis of Part 1 (350 mg QD) is reported; additional analyses including the complete Part 1 analysis, Part 2 (125, 250 mg QD) and Part 3 (62.5, 125, 250 mg QD), currently in progress, may be provided pending completion.

Objectives: Subjects recorded details of all HAE attacks and acute treatments in a diary. A panel of HAE physicians adjudicated attacks. Assessment of efficacy was made by the number of confirmed attacks over the entire and effective dosing period (EDP, Days 8 to 29) when BCX7353 steady-state conditions were achieved.

Results: Twenty-four subjects with HAE Type I or II and a mean qualifying attack rate of 1.0 per week who completed 28 days of treatment with BCX7353 (n = 11) or placebo (n = 13) were included in the interim analysis. Confirmed angioedema attacks were reduced by 63% in the BCX7353-treated group relative to placebo (EDP; $P = .006$). The distributions of severity grade and duration of attacks were similar between placebo and BCX7353; there was a high rate of acute attack medication use to treat attacks during the study

(83% [BCX7353] and 90% [placebo] of attacks in the entire dosing period were treated). Attacks with skin swelling only were reduced by 91%, and attacks with skin swelling plus abdominal symptoms were reduced by 83% (EDP). Nine of 11 subjects on BCX7353 (82%) had no skin swelling during the EDP compared with 4 of 13 on placebo (31%). Subjects on BCX7353 had 98% of days (least-squares mean 20.6/21 days) without skin swelling; for placebo, subjects had an average of 84% of days (17.6/21 days) with no skin swelling ($P = .005$). BCX7353 had no apparent effect on reducing HAE attacks with only abdominal symptoms; however, this may be due to misattribution of BCX7353-related gastrointestinal AEs as HAE attacks. There were no serious AEs or severe-drug related AEs.

Conclusions: The clinically meaningful, statistically significant reduction in HAE attacks seen with once daily oral BCX7353, particularly those that were associated with skin swelling, strongly supports the continued development of BCX7353 as a prophylactic treatment for HAE.

1030 | Health related quality of life in hereditary angioedema patients

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Introduction: Hereditary angioedema (HAE) is a serious disease with unpredictable attacks. It has an impact on patients' health related quality of life (QOL). In this study to assess QOL of the HAE patients and investigate the relation between QOL and demographic, clinical, laboratory and psychiatric parameters was aimed.

Objectives: A semi-structured face to face interview, Hamilton depression rating scale and Hamilton anxiety rating scale were performed by a psychiatrist. Participants completed Medical Outcomes Study Short Form-36 (SF-36), Revised Form of the Multidimensional Scale of Perceived Social Support, Anxiety Sensitivity Index-3 and Adult Separation Anxiety Questionnaire. Patients' complement results were recorded and clinical data obtained by interview were crosschecked from patient files.

Results: In 33 HAE patients, subscales of the SF-36, except for physical functioning and vitality, were significantly lower compared with population norms. QOL scores were found to be correlated with depression, anxiety, anxiety sensitivity, separation anxiety, perceived social support, perceived discrimination, perceived limitation, C1inhibitor function and C1q level. Physical role functioning scores were better in the patients using attenuated androgens ($P = .006$, $t = -3.027$). HAE contributed to the marital problems and childbearing decisions of the patients.

Conclusions: HAE results in significant impairment in QOL of the patients and have an impact on family life, life style of the patients. In case of depressive and/or anxiety symptoms patients should be referred to psychiatrists for better QOL. Higher levels of C1inhibitor function seem to correlate with better QOL; these needs to be further studied.

1032 | Just syncope... are you sure?

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Introduction: Mastocytosis is rare hematopoietic disease characterized by abnormal clonal mast cell proliferation and accumulation in tissues with different clinical presentations. Mast cell activation symptoms in the absence of mastocytosis in the skin is a diagnostic challenge.

Objectives: A 60-year-old woman, in October 2010, presented palpitations, chest tightness, dyspnea and malaise without loss of consciousness. In the Emergency Room (ER) was diagnosed of anxiety. After that, repeated episodes of palpitations.

In March 2013, a few hours after eating fresh hake, she started with palms and soles pruritus, palpitations, chest tightness, malaise, sweating, nausea, hypogastric pain and loss of consciousness followed by fluctuating level of consciousness and stiffness, clonic movements, cyanosis followed by paleness, hypotension (84/47 mmHg) and oxygen desaturation. Blood test and urine analysis, EKG and cranial CT were normal (except neutrophilic leukocytosis). Neurologist diagnosed her of convulsive syncope.

In September 2013 she presented palms and soles pruritus, palpitations, malaise, dyspnea, facial flushing, vomiting, blurred vision, hypogastric pain and hypotension without loss of consciousness. In ER: tests were normal and she was diagnosed of presyncope.

Echocardiography, holter 72 h, MRI, tilt-table test, supra-aortic echocardiogram and hemogram were performed. A videoelectroencephalogram showed slowing signal and epileptiform focal activity in left temporal region (which is a normal variation in healthy people). Simultaneously an Allergy evaluation was performed: spirometry and prick test to inhalant and food extracts (normal or negative), specific IgE to anisakis was 17.4 KUA/L and tryptase was 44 and 43 μg/L (tested twice when symptom free). A densitometry showed osteopenia.

Results: With a suspicion of mastocytosis (REMA 4 points), she started treatment with Disodium Cromoglycate and oral antihistamine. An adrenaline autoinjector was prescribed. A bone marrow biopsy showed c-kit mutation restricted to the mast cell and she was diagnosed of indolent systemic mastocytosis.

Conclusions:

Syncope is a common manifestation of systemic mastocytosis but convulsive syncope is rare. This fact together with non-specific multisystemic symptoms and lack of skin involvement delayed our patient diagnosis.

Serum tryptase should always be performed in recurrent syncope.

The REMA score was useful in the diagnostic approach.

1033 | Hereditary angioedema in Neiva, Colombia

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Introduction: Hereditary angioedema (HAE) an autosomal dominant hereditary disease, is genetic disease with a frequency of 1:10000 to 1: 50000 in the general population, able to induce swelling of sudden onset in the face, neck, arms, with a duration that may last up to five days. Its complication rises when there is a laryngeal oedema, which may even cause death or a painful abdominal oedema simulating a surgical condition. HAE is divided in three types: Type I affecting C1-INH concentration or type II due to a non-functional secreted protein. Exon 8 contains the code for the reactive center with an Arginine in the 444 position (HUGO: 466), mutations in this sector makes a dysfunctional protein. There is also a type III affecting mainly women and it is related to Factor XII mutation.

Objectives: Genotypically characterize patients suffering from hereditary angioneurotic edema in Neiva, Colombia

Results: A total of three families affected by HAE in Neiva, Colombia were analyzed for the SERPING 1 gene (Table).

Conclusions: Three different mutations were found in 12 of 22 subjects participating in the study.

Number	Type	Aminoacid affected	Reference
1	c.1081C>T	p.Gln361	Ono et al 1996 (HGMD Professional 2016.2 - PMID: 8792821)
2	c.106_107del	(pSer36Phefs*21)	Verpy et al 2006 (HGMD Professional 2016.2 - PMID: 8755917)
3	c.1396 C>G	pArg466Gly	Gösswein, 2008 (HGMD professional 2016.2–PMID: 18758157
	C.1029 + 84G>A		

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1035 | Is lymphopenia overlooked in pediatric clinics?

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Introduction: Lymphopenia is an important symptom of immunodeficiency. Thus, determination of patients with lymphopenia and following these patients is important in terms of diagnosing immunodeficiency cases early.

Objectives: We aimed to evaluate the frequency of children with lymphopenia who admitted to our hospital. The results of complete blood count (CBC) tests of the patients who were admitted to the general pediatric clinic between 1 January 2015 and 31 December 2015, were analyzed. Children who had a chronic illness were excluded. Lymphocyte values of $<3000/mm^3$ were accepted as lymphopenia for children under one year of age while lymphocyte values of $<1500/mm^3$ were accepted as lymphopenia for children one year of age.

Results: Among 47.722 patients, 4182 under 1 year old and 43540 above 1 year old, were found to have CBC. One hundred and seventy-one (4.08%) patients under 1 year of age were found to have lymphopenia. Forty-six (26.9%) of these 171 patients were found to have control CBC and 5 (10.8%) were found to have lymphopenia. 2168 (4.97%) of 43540 patients above 1 year of age who had CBC were found to have lymphopenia. Four hundred and ninety of these 2168 patients had control CBC and 105 (21.4%) were found to have lymphopenia.

Conclusions: We observed that among the children who had lymphopenia, 73.1% of those less than one year old and 77.4% of those above one year old did not have control CBC. This result shows that more attention should be given on complete blood count assessment and follow-up in terms of lymphopenia.

1036 | Enteritis in a child with severe combined immunodeficiency (SCID)

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Case report: SCIDs are rare diseases that result from severe defects of T and B and/or NK cells, and may present with different phenotypes according to affected cell lines. The symptoms usually occur in the first months of life and can be fatal, so early diagnosis is essential for the implementation of directed and prophylactic therapy. A 7 year old boy with medical history of stomatitis, chronic diarrhea and poor staturo-ponderal progression from the first year of life, complicated pneumococcal pneumonia of empyema at 22 months when hypomorphic SCID was diagnosed. Linphopenia CD4 and naïve CD8. Normal B and NK cells, proliferations to normal mitogens, absent to antigens. Genetic confirmation of defect linked to X at 5 years (defect of the common gamma chain). Initiated replacement therapy with immunoglobulin and prophylactic cotrimoxazole. Admitted to hospital for diarrhea and fever with 3 days of evolution. Treated with Ceftriaxone, Metronidazole and Azithromycin. At the 4th day of illness he became apyretic but maintained diarrhea (5-8 episodes/day). On the 5th day presented exuberant gingivostomatitis and candidiasis. Started Vancomycin, Fluconazole and Acyclovir. Hemocultures, coprocultures, virus and parasite research in feces and nasopharyngeal secretions were negative. Blood: EBV positive PCR, with negative viral load. At the 6th day, he had abdominal distension and severe pain. Radiography and Ultrasound: "abdominal aerocolia, colic parietal edema with pure ascites in moderate volume". Transferred to pediatric intensive care unit (PICU) on the 7th day, in food pause. He kept the remaining therapy and started Meropenem and Metronidazole. Food pause until D5 of internment in the PICU. He received parenteral nutrition until D11, continuous enteral feeding (neocate®) from D5 to D8, then bolus with tolerance. Diet without residues since D13. Initiated IGIV 1 g / kg and Rituximab 375 mg / m2. During the hospitalization he remained stable and the colic distension slowly decreased. EDA and colonoscopy were scheduled. Still waiting for the results of bone marrow donor.

Clinical manifestations of SCIDs include severe and recurrent infections, particularly at the intestinal level and often associated with important malabsorption and malnutrition states, the resolution of which often involves prolonged hospitalization.

1037 | Clinical features and effectiveness of intravenous immunoglobulins in patients with primary antibody production deficiencies in the middle urals

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Introduction: primary immunodeficiencies (PID) are clinically manifested infections, a tendency to the appearance of autoimmune diseases and malignant neoplasms. According to the literature defects mainly affecting the humoral immunity make up about 60% of all PID. The prevalence of primary antibody production deficiencies varies depending on the detected defect.

Objectives: To identify the clinical features and evaluate the effectiveness of replacement therapy with standard intravenous immunoglobulins (IVIGs) in patients with primary antibody production deficiencies in the Middle Urals.

Methods: The study included patients of a regional primary immunodeficiency register, where 81% (n = 91) of patients has defects in antibody production.

Results: Selective IgA deficiency is the most common form of PID in the Middle Urals (n = 48). Clinical features of selective IgA deficiency are concomitant allergic diseases and infectious processes of mild to moderate course, which do not require special treatment. The other forms of primary antibody production deficiencies (n = 37) in the register of the Sverdlovsk region are submitted to common variable immunodeficiency, agammaglobulinemia, hyper-IgE-syndrome. Severe recurrent infections are characteristic for patients with these forms of PID. Chronic rhinosinusitis (n = 18), bronchiectasis (n = 18), pneumonia (n = 18) are most often detected in PID patients in the Sverdlovsk region. The majority of patients with humoral immunodeficiencies requires lifelong replacement therapy with donor immunoglobulins. The frequency of relapses and exacerbations of chronic rhinosinusitis was 2,7-fold decreased in our patients receiving replacement therapy with standard IVIG as pathogenetic treatment (n = 19).

Conclusions: The prevalent clinical forms of PID in the Middle Urals are defects in antibody production: selective IgA deficiency and common variable immunodeficiency. The most common clinical manifestations of PID are recurrent, resistant to usual therapy, infectious diseases of respiratory system, which require special treatment. The only and highly effective method of primary antibody production deficiencies treatment is replacement therapy with standard IVIGs.

1039 | Hyper-IgE syndrome: a case report

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Case report: The hyper-IgE syndrome is a rare disorder characterized by elevated levels of IgE, pruritic dermatitis, recurrent staphylococcal abscesses, sinopulmonary infections and skeletal disorders. The autosomal dominant form is associated with mutations in the DNA-binding domain of signal transducer and activator of transcription 3 and the autosomal recessive form with a mutation in tyrosine kinase 2 and in the dedicator of cytokinesis 8. A five-year-old-boy with non-consanguineous parents with history of a severe atopic eczema since de first year of life, a moderate persistent asthma since two years old, recurrent suppurative otitis media (eight or more episodes per year), familial hypercholesterolemia, poor staturo-ponderal progression and delay in psychomotor development. In the investigation carried out cell, granulocytic or complement deficiency was excluded and elevation of IgE (2379kU/l) was found. It is a child in need of daily medication with antileukotrienes, inhaled corticosteroids, antihistamines, topical corticosteroids, emollients and early antibiotics or anti-fungal agents as required for specific infections. He has multidisciplinary follow-up in Immunoallergology, Dermatology, Otolaryngology and Developmental Consultation. Clinical and immunological diversity make diagnosis and therapeutic guidance of this syndrome difficult. Early diagnosis can be lifesaving and can lead to a significant reduction in morbidity.

1041 | DOCK2 deficiency in one Iranian patient

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Case report: Introduction: Combined immunodeficiencies (CID) is a group of disorders in which defects in adaptive and humoral immunity leading to severe bacterial, viral and fungal infections in early childhood which may result in early death. The aim of this study is to report a one year old girl with DOCK2 deficiency (a rare type of CID).

Case properties: The patient was a one-year-old girl of consanguineous parents who referred to Immunology, Asthma and Allergy Research Institute (IAARI). She had several times of administration to hospital 2 months after birth due to high fever. She also developed diarrhea, leukopenia, anemia and thrombocytopenia from 3 months old. Initial and advanced screening tests for immunodeficiency

including evaluating the lymphocyte markers, serum immunoglubolin and complement levels, NBT and isohemagglutinins tests were done for the patient. To detect underlying genetic defect, Next Generation Sequencing (NGS) was applied.

Results: She had significant reduction in her CD4+ T and CD19+ B cells but her CD8+ cells were increased markedly. Her IgM level was higher than normal (796 mg/dl) while she had normal IgG and IgA levels. Quantitative PCR (QPCR) was confirmed her CMV infection. She had received IVIG and GCSF treatments from 4 months old but she died at 12 months old. NGS results revealed a reported homozygote missense mutation (c.C3310T, p.R1104W) in exon 33 (NM_004946) of the dedicator of cytokinesis (Dock2) gene. The detected mutation was confirmed using PCR. Her parents were heterozygote for this mutation.

Conclusion: DOCK2 deficiency or Immunodeficiency-40 (IMD40) with an autosomal recessive pattern of inheritance is a type of combined immunodeficiency caused by genetic defects in DOCK2. This finding is helpful for further diagnosis of the disease as well as prenatal diagnosis. To determine type of CID and the responsible genes, NGS can be a useful diagnostic approach.

1042 | Deficiency of glucose 6 phosphatase: the importance of screening for primary immunodeficiency (PI)

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Case report: The deficiency of glucose 6 phosphatase results from mutations in the G6PC3 gene and is characterized by severe congenital neutropenia, recurrent bacterial infections, intermittent thrombocytopenia, superficial venous circulation, and congenital cardiac and urogenital abnormalities. The phenotypic spectrum is broad and encompasses Dursun's syndrome which includes other rare manifestations such as growth retardation, primary pulmonary hypertension (PPH) and minor facial dysmorphism. An 8 year old boy from Pakistan with parental consanguinity. Medical history of productive cough, dyspnea for small efforts and hospitalizations for respiratory infections and cutaneous abscesses. Poor staturo-ponderal progression and delay in psychomotor development. Follow-up in Pediatric, Pulmonology and Cardiology with the following conclusions: Partial chronic respiratory failure; Obstructive pattern; HPP; Pansinusitis; Cardiopathy with slight tricuspid regurgitation; Microcytic anemia, hypochromic and suspected PI by IgM hypoglobulinemia with global lymphopenia and intermittent neutropenia, facial dysmorphia, microcephaly and short stature. Hospitalization for exacerbation of dyspnea and aggravation of hypoxemia, being diagnosed with interstitial Pneumonia to RSV and Haemophilus influenza. Medicated with salbutamol, aminophylline, methylprednisolone and cefuroxime. Myelogram (hypercellular marrow) and pulmonary biopsy were performed by minithoracotomy (friable gray lung, fibrin adherent to the lung). Isolation after in the Pediatric Intensive Care Unit ventilated in VCPR. Hb 5.5 g/dl; Leukopenia with severe neutropenia (100), PCR 49.1. He made erythrocyte concentrate, piperacillin/tazobactam and gentamicin, analgesia with alfentanil. Extubated in D1. Dependence of O2 and severe persistent neutropenia at admission. Diagnosed glucose deficiency 6 phosphatase. Initiated granulocyte colony stimulating factor (G-CSF) with clinical improvement. The glucose 6 phosphatase deficit should be considered in the differential diagnosis of congenital neutropenia, since the absence of treatment can be fatal. Treatment with G-CSF allows the increasing of neutrophil count, as well as prevent infections and improve the quality of life of patients. In patients with milder forms of the disease it is possible to control only with prophylactic antibiotic therapy; on the other hand, the prognosis is reserved for patients who are more severely affected and do not respond to G-CSF.

1043 | Optimal response to canakinumab in a patient with chronic recurrent multifocal osteomyelitis

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Introduction: Chronic recurrent multifocal osteomyelitis (CRMO), also known as chronic nonbacterial osteomyelitis, is an orphan disease whose prevalence is estimated at 1-2/10^6. CRMO is a rare autoinflammatory disease that mainly affects children. It is characterized by multifocal bone inflammation, with a subacute or chronic affectation. The diagnosis of CRMO is made by exclusion of infectious and tumoral causes through minimal invasive biopsy. NSAIDs are the accepted first-line medications for CRMO and other treatment options are bisphosphonates and TNF antagonists.

Objectives: We present a 15-years-old boy sent to the Pediatric Immunology and Allergy Department, diagnosed with severe CRMO at 11 years of age. At the beginning he was treated with NSAIDs and corticosteroids with a poor response. The patient was treated with other drugs as bisphosphonates, TNF antagonists and intravenous immunoglobulins but there was no response. Anakinra (interleukin 1 receptor antagonist) was administered for 28 months with an initial improvement but a late clinical and radiological worsening. Finally, Canakinumab (human monoclonal antibody targeted at interleukin-1 beta) was requested as a compassionate use showing an optimal response.

Results: Canakinumab has been well tolerated by the patient and no secondary effects have been detected. The patient is

asymptomatic and without new outbreaks of disease for since the treatment started ten months ago.

Conclusions: This encouraging result observed in this patient, can define canakinumab as a new therapeutic strategy in the treatment of CRMO.

1045 | Tolerance of rapid intravenous immunoglobulin (IVIG) infusion

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Introduction: Intravenous Immunoglobulin (IVIG) is a highly purified pooled blood product collected from 1000-20 000 persons, purified for their antibodies (immunoglobulins), and carefully screened for transmissible diseases. It is an essential therapeutic treatment for individuals with life-threatening antibody deficiency. Though a critical treatment, adverse events can occur. Rapid infusion rates have been thought to be a key factor in adverse reactions as well as the dose of IVIG with each infusion. For several decades, IVIG infusion rates in the infusion center at National Jewish Health have been up to 600 mL/h in most patients and well-tolerated. To establish the validity of the assumptions and confirm the safety of rapid infusion rates, we compared our findings on rates of severe adverse reaction events to published data.

Objectives: This retrospective chart review studied patients aged 2 months to 80 years old who have been seen at National Jewish Hospital and treated with Privigen (a 10% liquid IVIG preparation) who have completed at least 3 infusion cycles. Patients were divided into Rapid Infusion Protocol, modified fast infusion, and conventional rates (for an 80 kg person, averages 185 mL/h over 2 hours). Rapid Infusion Protocol was defined as: 100 mL/h for 25 mL, then 200 mL/h for 50 mL, then 400 mL/h for 100 mL, then 600 mL/h until done without regard to weight (average of 462.5 mL/h over 2 h). Chart data was used to define the clinical factors that could be linked to possible adverse reactions.

Results: Since 2015, 28 of the 29 patients administered Privigen at fast infusion rates were well-tolerated. Nineteen of these individuals were on our Rapid Infusion Protocol and doing well. Nine were on a modified fast infusion rate that reaches a maximum of 100 to 300 mL/h (4 required decreased infusion rates due to minor reaction from the Rapid protocol, 5 due to physician preference). One patient is on a conventional infusion rate protocol for minor reaction to faster rates.

Conclusions: Conventional rates of IVIG infusion are time intensive. Our Rapid Infusion Protocol and modified fast infusion rates with Privigen was well tolerated in individuals (65.5% and 31% respectively) in both men and women. Only minor reactions were noted to have occurred.

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1046 | C1-inh-hae: the relationship between parents and children's emotional status, children's disease activity and health related quality of life

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Introduction: The severe life threatening characteristics of Hereditary Angioedema with C1-inhibitor deficiency (C1-INH-HAE) may elevate the anxiety of pediatric patients and their parents. This emotional burden together with the physical restrictions of C1-INH-HAE may decrease children's health related quality of life (HRQoL).

Objectives: (1) To examine the relationship between parents' emotional status, children's emotional status and disease activity (2) To examine the prediction of children's HRQoL by their anxiety, disease activity and parental C1-INH-HAE disease.

Results: Thirty-four children with C1-INH-HAE (aged 4.48-18 years), recruited from Israel and Hungary participated in this study. Disease activity was defined as the number of attacks in last year and the sites of angioedema attacks. All children completed the State Trait Anxiety Inventory for Children (STAIC) and the Pediatric quality of Life Inventory (Peds-QL). Fathers and mothers completed The State Trait Anxiety Inventory (STAI) and The second version of the Beck Depression Inventory (BDI-II). Among the study group, 3 children had healthy parents; 13 children had fathers with C1-INH-HAE and 18 children had mothers with C1-INH-HAE. Children's anxiety trait significantly correlated with mothers' anxiety trait ($r = .39$, $P = .04$) and sites of angioedema attacks ($r = .53$, $P = .003$). Fathers' depression significantly correlated with child's C1-INH-HAE number of attacks ($r = .48$, $P = .02$). Sites of angioedema attacks predicted 23% of children's physical HRQoL. Children's anxiety trait predicted 51% of their emotional HRQoL. Site of angioedema attacks predicted 22% of their social HRQOL and 51% of school HRQOL. Sick parents added 15% to school HRQOL prediction and children's anxiety trait added additional 6% to this prediction.

Conclusions: The emotional status of children with angioedema may be related to their parents' emotional status and to site of angioedema attacks. HRQoL of children with angioedema is mainly predicted by site of HAE attacks, child's anxiety trait and a parent with angioedema. Intervention should consider children and parents' emotional status, disease characteristics and their impacts on child's HRQoL.

1047 | Safety of diverse treatment modalities in pediatric patients with hereditary angioedema

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Introduction: Hereditary angioedema with C1-INH deficiency (C1-INH-HAE) is a rare, potentially fatal, genetic disease that often presents in childhood. For pediatric patients (pts), several therapeutic strategies are approved or are in late-stage development for acute, long-term and pre-procedural prophylactic treatment of HAE attacks

Objectives: Data were compiled from pediatric pts (age < 18) from 2 clinical trials evaluating icatibant (Shire, USA) (NCT01386658, NCT01034969) and 6 clinical trials evaluating intravenous (IV) C1-inhibitor (C1-INH) (Shire, USA)(NCT00289211, NCT01005888, NCT00438815, NCT00462709, NCT01095510, NCT02052141). Pts were grouped by whether they were treated acutely (on-demand), or for long-term and pre-procedural prophylaxis. Demographic, disease history and safety data are presented

Results: Overall for on-demand treatment, icatibant was administered to 37 pts and IV C1 INH was administered to 36 pts. For long-term and pre-procedural prophylaxis, IV C1-INH was administered to 39 and 9 pts, respectively. Demographic and safety data are summarised in Table 1 (Footnote: [1]NCT01386658; [2]NCT01034969; [3]Studies NCT01095510), NCT00289211 and NCT00438815 except for pts treated for pre-procedure; [4]Studies NCT01005888, NCT00462709 and NCT02052141; [5]Two pts from NCT00289211, and 7 pts from NCT00438815)

Conclusions: C1-INH HAE is a disease with dire consequences and treatment requires a comprehensive management plan. In order to provide pediatric pts the best opportunity to lead a normal life, safe, well-tolerated and efficacious therapies are required. Data presented on icatibant and IV C1-INH highlight the favorable safety profile for both acute treatment and prevention of angioedema attacks.

Treatment	HAE attacks			Prophylaxis	Pre procedure
	Icatibant[1]	Icatibant[2]	C1 INH[3]	C1 INH[4]	C1 INH[5]
Study Phase	3	Registry	2, 3	3	3
N	32	5	36	39	9
Age at screening, median (range)	12 (2, 15)	17 (16, 18)	11 (2, 17)	11 (3, 17)	10 (6, 17)
Female, n (%)	13 (40.6)	3 (60.0)	23 (63.9)	27 (69.2)	6 (66.7)
Family history of HAE, n (%)	29 (90.6)	5 (100)	28 (77.8)	25 (64.1)	6 (66.7)
Monthly Number of Attacks before enrollment, median (range)	2.2 (0.2, 22.7)	0.3 (0, 1.6)	1.0 (0.0, 29.4)	2.5 (0.5, 29.4)	0.5 (0.2, 1.0)
Moderate or severe as the most frequent severity of previous attacks, (n, %)	21 (65.6)	1 (20.0)	24 (66.7)	38 (97.4)	7 (77.7)
Adverse Events, patients (n, %)	9 (28.1)	2 (40.0)	5 (13.9)	26 (66.7)	5 (55.6)
Adverse Events, events (n)	32	7	6	223	12
Related adverse events, patients (n, %)	1 (3.1)	0	1 (2.8)	7 (17.9)	0
Related adverse events, events (n)	2	0	2	43	0
Serious AE, patients (n, %)	0	1 (20.0)	0 (0)	4 (10.3)	0
Serious AE, events (n)	0	4	0	11	0

1048 | Hereditary angioedema in Slovakia – results from national pilot study

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Introduction: Hereditary angioedema (HAE) is a prototype of rare disease. The global awareness of HAE is still increasing and new therapeutic options significantly improved the management of this rare disease. Slovakia is a country in eastern central Europe with population over 5 million people. The first publication of HAE case series from former Czechoslovakia was reported by Starsia et al. (1988). However, actual exact data about the prevalence of hereditary angioedema (HAE) in Slovakia were missing.

Objectives: The national study about the number of HAE patients and their selected characteristics was performed through the questionnaire-based survey in Out-patient clinics for allergy and clinical immunology. The study was conducted by Center for HAE in Martin.

Results: Based on the achieved questionnaires, all together 94 living patients with HAE (aged 37.52 ys.; 55% males) from 42 families were found in Slovakia. 21 patients already died due to laryngeal oedema. The most prevalent form was HAE type I (86%), followed by HAE type II (9%) and III (5%). The diagnostic delay between the first symptoms and diagnosis estimation (29.52 ys.) was approximately 8 ys. In majority of the patients (67%) combination of various clinical symptoms (skin, gastrointestinal, laryngeal, genital) was observed. However, 17% patients suffered from isolated skin symptoms, 7% from gastrointestinal and 3% from laryngeal angioedemas. Six patients are still asymptomatic. Molecular-genetic analysis was performed in 69% of patients and 12 new previously non-described mutations were detected. Regarding the prophylaxis, 39% were without prophylactic treatment, 44% took attenuated androgens, 13% tranexamic acid, and 2% either pd-C1-INH or rh-C1-INH. Acute attacks were treated in 30% with danazol, in 26% with icatibant, in 23% with pd-C1-INH and in 21% with rh-C1-INH.

Conclusions: This is the first report about HAE epidemiology in Slovakia with estimated prevalence of 1:57 700. The survey is still ongoing and is aimed on improvement of HAE diagnosis and management in Slovakia.

1049 | Hereditary angioedema: analysis of 287 attacks treated with C1 esterase inhibitor in the French cohort cobra

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Introduction: The COBRA registry reports clinical data and treatment response with C1 esterase inhibitor Berinert® in the French population of patients with Bradykinin mediated Angioedema (AE): Hereditary AE (HAE) with and without C1Inh deficiency, idiopathic non histaminergic AE, drug induced AE.

Objectives: We conducted an analysis of patients with HAE included in the *Cohort Berinert Angiœdème* (COBRA) registry study from 2007 to November 2016, which aims to collate information on all Berinert®-treated patients with HAE throughout France. The analysis included retrospective data extracted from patients' medical record and prospective data directly recorded in the electronic registry. Data on treatment response was only available for documented attacks after COBRA enrollment.

Results: 132 type I-II HAE patients, 34.4 ± 17.8 years old, (66.7% women) are today included in the registry. They were 13.4 ± 10.8 yo when they had the first attack and 18.4 ± 14.6 when the diagnosis was made. They have been treated with Berinert® during the last 3.7 ± 4.4 years and the first treatment was received when they were 30.2 ± 17.1 yo. 47.8% of them were genotyped and 92.7% were presenting a Serping1 mutation. Among them 105 patients (79.5%) presented at least an attack treated with Berinert®. These patients presented 287 attacks: abdominal (29.0%), facial (22.0%), laryngeal (14.0%), peripheral (10.0%) and multi-location (25%). 60.0% of the attack were rated "severe", 38.0% "moderate" and 2% "low". A trigger event was described in 25.4% of crisis in relation with stress or trauma for 15.0% of the cases. 39.8% (98) of attacks have been treated with 20 UI/kg, 54% (135) with 10-20UI/kg. On available data, symptoms began to be improved in less than 1 hour in 35.0% and in less than 2 hours in 27%. Symptoms disappeared in less than 24 hours in 68.5%. A treatment failure occurred for 8 out 287 attacks (11.1%): 4 attacks were treated with a low dose (<20UI/kg), 1 attack was treated 8 h after starting, no precise information are available for the 3 remaining attacks. Patients' satisfaction rate was 94.6%.

Conclusions: COBRA registry affords the opportunity to systematically describe type I-II bradykinin mediated AE patients treated with Berinert® and to monitor its efficacy in attack treatment.

1050 | Elderly vs younger patients (pts) with hereditary angioedema type I/II: safety analysis from the icatibant outcomes survey

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Introduction: Hereditary angioedema with functional C1-esterase inhibitor deficiency (C1-INH-HAE) is characterized by recurrent swelling in subcutaneous or submucosal tissues. Symptoms often begin by 5-11y and worsen during puberty, however attacks may occur at any age and reoccur throughout life. Disease course in elderly pts is rarely reported.

Objectives: The Icatibant Outcomes Survey (IOS) is an observational study evaluating safety/tolerability and efficacy of icatibant. We conducted descriptive analyses in younger (<65y) vs elderly pts (reaching ≥65y at any time during IOS enrollment); safety-related findings are reported herein.

AE, by system organ class	Elderly Pts (n = 73) Events n, %	Elderly Pts (n = 73) Pts n, %	Younger Pts (n = 593) Events n, %	Younger Pts (n = 593) Pts n, %
Any Event	13 (100.0)	2 (2.7)	49 (100.0)	15 (2.5)
General Disorders/Administrative Site Conditions	13 (100.0)	2 (2.7)	15 (30.6)	9 (1.5)
Vascular Disorders	0 (0)	0 (0)	13 (26.5)	7 (1.2)
GI Disorders	0 (0)	0 (0)	5 (10.2)	3 (0.5)
Investigations (Weight or blood pressure decreases)	0 (0)	0 (0)	5 (10.2)	2 (0.3)
Skin/Subcutaneous Tissue Disorders	0 (0)	0 (0)	4 (8.2)	4 (0.7)
Nervous System Disorders	0 (0)	0 (0)	3 (6.1)	2 (0.3)

Results: As of August 31, 2016, 666 pts with C1-INH-HAE type I/II were enrolled, of whom 73 (11.0%) were ≥65y. Throughout the study, icatibant was used to treat 3785 attacks in 500 pts, with 55 elderly pts (11%) reporting 405 icatibant-treated attacks. Occurrence of ≥1 adverse events (AEs) was similar for elderly (24.7%) vs younger pts (20.2%; $P = .371$). Serious AEs (SAEs) were more likely to occur in elderly pts (17.8% vs 9.6%; $P = .0312$); the most common SAEs in the elderly were gastrointestinal (GI) disorders and neoplasms (18.5% of events each). However no SAEs in elderly pts were possibly related to icatibant, whereas 2 younger pts reported 3 possibly related SAEs. Excluding off-label use and pregnancy (evaluated for regulatory purposes), percentage of pts with ≥1 possibly/probably related AEs was similar between age groups ($P = .7087$). All related events in elderly pts were attributed to general disorders/administration site conditions, whereas related events in younger pts occurred across various system organ class designations (Table).

Conclusions: Our study revealed similar AE rates (overall and possibly/probably related) in icatibant-treated elderly vs younger pts, with a larger percentage of treated elderly pts experiencing an SAE. No new safety concerns were identified.

1051 | Presence and family distribution of SERPING1 mutations in macedonian HAE type I patients

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Introduction: HAE is a rare genetic disorder with potentially fatal episodes of swelling, caused by heterogeneous SERPING mutations.

Objectives: To investigate the presence and family distribution of SERPING1 mutations in Macedonian HAE type I patients.

C1-INH-HAE diagnosis was established based on clinical and anamnestic criteria in 23 patients from 15 families; 4 patients are silent carriers. Genetic studies were carried out using PCR and sequencing to detect *SERPING1* mutations in promoter, noncoding exon 1, the 7 coding exons, and exon-intron boundaries. Multiplex ligation-dependent probe amplification was performed in order to search for large deletions/duplications in *SERPING1* gene.

Results: Disease-causing mutations in SERPING1 were identified in all patients. In C1-INH-HAE type I, we identified 13 different mutations, and 2 large deletions. Five novel mutations were identified. Two of the mutations (c.813_818delCAACAAC>T and c.1188_T>G) are reported here for the first time. Depending on the type of SERPING1 gene mutation, patients were divided into two groups: group 1 (nonsense, frameshift, large deletions/insertions, splicing defect, and mutations at Arg444) or group 2 (missense, excluding mutations at Arg444).

Conclusions: Authors have identified 13 different disease-causing mutations, including five novel mutations, contributing the heterogeneity of mutations in the SERPING1 gene.

1052 | The international registry for angioedema without wheals

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Introduction: Angioedema is a disabling and potentially lethal disease, characterized by the appearance of self-limiting edema that last 1-5 days and affect the subcutaneous tissue and/or gastrointestinal and oropharyngeal mucosa. It can appear as part of the urticaria angioedema syndrome, but there are forms that occur without wheals and can be either hereditary or acquired. These angioedema are identified based on etiology, mediator, or just clinical presentation. An overall classification of these forms of angioedema was published in 2014 (Allergy 2014; 69:602-16).

Objectives: To gathering in a single registry, clinical and laboratory data related to the different forms of angioedema and detect the therapy options used to manage this pathology.

Results: In November 2016 representatives of angioedema centers from 18 counties (Serbia, France, Spain, Italy, Hungary, Greece, Macedonia, Brazil, Romania, Mexico, Colombia, Canada, Greece, Poland, Bulgaria, Poland, Bulgaria, Canada) met in Sofia (Bulgaria) to

agree on the final structure of the registry. It is a web based international multi-center illness registry. It includes patients with confirmed diagnosis of acquired or hereditary angioedema with or without C1 inhibitor deficiency able to provide informed consent. The following data are gathered: 1. Patients' personal and demographic data; 2. Clinical and laboratory characteristics finalized to confirm the diagnosis; 3. Major comorbidities listed according to International Classification of Diseases (ICD-9); 4. Angioedema treatments; 5. Prospectively gathered data related to duration, gravity and treatment of angioedema attacks and to prophylaxis of angioedema. At this writing, the registry contains entries from 17 different centers with 927 patients and 4139 different angioedema attacks. All patients have confirmed diagnosis of hereditary angioedema with C1-INH deficiency.

Conclusions: We created the first international disease registry for patients with different forms of angioedema without wheals. Most of these forms of angioedema are still without diagnostic test or approved treatment. Pooling together data on this disease is the first step to provide a tool for understanding pathophysiology and developing diagnostic tests and specific therapies.

1053 | A novel prophylaxis in hereditary angioedema with C1-inhibitor deficiency: administration of C1-inhibitor during erythema marginatum

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Introduction: Hereditary angioedema with C1-inhibitor deficiency (C1-INH-HAE) is a rare, autosomal dominant disorder. The characteristic episodes of subcutaneous/submucosal edema formation may be preceded by erythema marginatum (EM) – the occurrence of a 'map-like' pattern on the skin. Nevertheless, EM can occur as an isolated finding or accompanying a hereditary angioedema (HAE) attack as well. Based on the data of the Hungarian HAE Registry, 49 among 173 C1-INH-HAE patients (28.3%) from 32 family had EM in their life. Nevertheless, it is unknown whether a HAE attack can be prevented by the proper prophylactic treatment during EM.

Objectives: Our aim was to introduce a safe and effective novel prophylactic treatment during EM in patients who's HAE attacks are preceded by EM in a considerable proportion of the cases. Written informed consent were obtained from both subjects.

Results: According to the data of the Hungarian HAE Registry and our clinical data, we selected two patients (Patient 1, Patient 2) who frequently had EM as a prodromal symptom. Regarding this data, we instructed both patients to administer plasma-derived C1-inhibitor concentrate (pdC1-INH) as soon as possible after the onset of EM, in order to prevent the development of HAE attack. Interestingly, HAE attacks never developed if pdC1-INH was administered within 6 hours from the occurrence of EM in both patients. In contrast, without pdC1-INH treatment, in Patient 1 and Patient 2, 97.0% and 44.3% of the EM were followed by a HAE attack, respectively ($P < .0001$, Fisher's exact test).

Conclusions: As a novel prophylaxis in C1-INH-HAE, intravenous administration of pdC1-INH concentrate during EM might be an effective, individual therapeutic strategy in those patients who's HAE attacks are often preceded by EM. Besides it can improve the quality of life of these selected patients, pdC1-INH administration during EM provides the lowest effective dose for the prophylaxis of their HAE attacks.

Table 1 R = randomized, D-B = double-blind, S-B = single-blind, X = cross-over, P-C = placebo-controlled, S&E = safety and efficacy, D-R = does-ranging, ST&P = safety, tolerability, and pharmacokinetic, OLE = open-label extension; mos. = months; N = total number of patients

Company; Drug; ClinicalTrials.gov identifier	Shire; C1-INH; NCT01005888	Shire; C1-INH; NCT02052141	Shire; C1-INH; NCT00462709	Shire; C1-INH with recombinant human hyaluronidase; NCT01756157	CSL Behring; C1-INH; NCT01912456	Shire; lanadelumab; NCT02093923
Phase; Design; Patient age, years; Baseline number of attacks/month	3; R, D-B, P-C, S&E; ≥6; ≥2	3; R, S-B, X; 6-11; ≥1; ≥2 in Germany	3; OLE; ≥1; ≥1 or any laryngeal edema;	2; R, D-B, D-R, X; ≥12; ≥2 moderate or severe	3; R, P-C, X, S&E; ≥12; ≥4 over 2 mos.	1b; R, D-B, D-R, P-C, ST&P; ≥18; ≥2/year with at least 1 in the past 6 mos.
Dose; Formulation; Treatment/study duration	1000U every 3-4 days; IV; 12 weeks	500U or 1000U, every 3-4 days; IV; 12 weeks	1000U every 3-7 days; IV; Median of 248 days	1000U or 2000U every 3-4 days; SC; 8 weeks	40 IU/kg and 60 IU/kg twice weekly; SC; 16 weeks	30 mg,100 mg, 300 mg, or 400 mg; SC; 6 weeks
N; Patients attack-free (%)	22; 18%	500U: 6; 50% 1000U: 6; 50%	146; 35%	1000U: 22; 23% 2000U: 22; 45%	40 IU/Kg: 45; 38% 60 IU/Kg: 45; 40%	300 mg: 5; 100% 400 mg: 11; 82%

1054 | The goal of prophylaxis against hereditary angioedema attacks is no attacks: a summary of findings for approved and investigational products

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Introduction: Hereditary angioedema (HAE) with C1 inhibitor (C1-INH) deficiency is a rare disease characterized by episodic subcutaneous or submucosal swelling and attacks on the larynx can be fatal. Prophylaxis aims to completely prevent HAE attacks or significantly reduce their frequency, severity, and duration.

Objectives: We present data on the proportion of attack-free patients from the latest trials of 3 human plasma-derived C1-INH concentrates (IV C1-INH [Shire, USA], subcutaneous [SC] C1-INH [Shire], and SC C1-INH [CSL Behring]), and an investigational fully human monoclonal antibody (lanadelumab [Shire]) against plasma kallikrein (Table 1).

Results: Across the C1-INH studies, the proportion of attack-free patients varied from 18%-67%. In the early phase lanadelumab trial, 82-100% of treated patients were attack-free.

Conclusions: Many patients benefit from these therapies, but an unmet need for therapies that produce consistent attack-free results in HAE patients still exists.

1055 | Approaches to estimate plasma kallikrein inhibition levels required for attack prophylaxis in hereditary angioedema

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Introduction: Hereditary angioedema (HAE) is caused by a deficiency in C1 esterase inhibitor (C1-INH), a serine protease inhibitor that targets multiple proteases in pathways including intrinsic coagulation, complement, fibrinolysis, and the plasma kallikrein-kinin system. It was previously demonstrated that dysregulated plasma kallikrein (pKal) activity due to C1-INH deficiency leads to edematous attacks in HAE.

Objectives: We evaluated approaches to assess the extent of pKal inhibition needed for HAE attack prophylaxis.

Results: In vitro pKal activity was measured with synthetic peptide substrates in the presence of C1-INH protein at levels approximating that in healthy subjects (16-33 mg/dL or 1.6-3.3 μmol/L) and HAE patients (≤30% of normal). Inhibition by C1-INH and lanadelumab, a fully human monoclonal antibody pKal inhibitor in clinical development for HAE attack prophylaxis, was compared in vitro. The association between inhibition and both lanadelumab levels and reduction in cleaved high molecular weight kininogen, a biomarker associated with attack reduction in a phase 1b study in HAE patients, was also evaluated. In vitro data suggests that the high level of endogenous C1-INH in healthy subjects required to prevent dysregulated contact activation is likely due to its relatively slow association rate constant (1.7×10^4 M^{-1} s^{-1}). In contrast, the association rate constant for lanadelumab is ~200-fold faster (3.4×10^6 M^{-1} s^{-1}), which could explain the observed clinical efficacy of lanadelumab at drug levels that are 26- to 54-fold lower than endogenous C1-INH levels. We also estimated levels of active pKal generated during an attack (30-110 nM). The Cmax of ecallantide (30 mg, SC), a Kunitz domain inhibitor of pKal, is ~80 nM and is effective for acute attack treatment. However, the inhibitor concentration needed to prevent attacks could be lower than that required to treat an ongoing attack. It is expected that lanadelumab plasma concentrations are sufficient to prevent attacks in the ongoing Phase 3 program following 300 mg at the designed dosing intervals. Since lanadelumab (Ki = 125 pM) is a potent, stoichiometric pKal inhibitor, drug levels that approximate the amount of active pKal are expected to provide sufficient inhibition of pKal activity.

Conclusions: These approaches suggest the approximate levels of potent pKal inhibitors required for HAE attack prophylaxis. These are being used in the ongoing clinical development of lanadelumab.

1056 | Novel high-resolution follow-up of the coagulation and fibrinolytic parameters in a single angioedematous attack of a C1-INH-HAE patient

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Introduction: Hereditary angioedema due to C1-inhibitor deficiency (C1-INH-HAE) is a potentially life-threatening rare disease, characterized by recurring and spontaneously resolving angioedematous attacks. Previously many studies published on the activation of the plasma enzyme systems during hereditary angioedema (HAE) attacks, nevertheless kinetic follow-up has never been performed.

Objectives: For the first time, we aimed to study the kinetics of parameters in the coagulation and fibrinolytic systems in a

spontaneously resolved HAE attack of a C1-INH-HAE patient. Furthermore, we aimed to study the kinetics of these parameters in a healthy subject during a 24-hour period, served as control. Written informed consent were obtained from both subjects.

Results: After a 24-hour symptom-free period and another 19-hour prodromal period, the patient had a 29-hour-long HAE attack in multiple skin locations, and was followed up for another day. Altogether 12 blood samples were obtained through the 96-hour observation period. We measured levels of D-dimer, prothrombin fragment 1 + 2 (F1 + 2) and thrombin-antithrombin (TAT)-complex. It is remarkable that during prodromal stage - which was characterized by erythema marginatum - the levels of all three parameters were as constantly low as those levels measured in the healthy control. Levels of F1 + 2 and TAT-complex were significantly elevated at the moment of the onset of edematous symptoms whereas level of D-dimer was elevated after 6 hours. Levels of all three parameters reached maximum 12 hours after reaching the maximum severity score. Highest level of D-dimer was almost 100-fold higher than the levels measured during prodromal stage. Fibrinogen levels were constantly elevated during prodromal stage whereas during HAE attack, fibrinogen levels were similarly low as levels were measured in the healthy control. In the healthy control subject, all measured parameters were stable during 24-hour observational period.

Conclusions: This study was a part of a project aimed to the better understanding of the mechanisms leading to the onset and to the resolution of HAE attack. Real-time monitoring of F1 + 2 and TAT complex suggest that thrombin contribute to the development of edema formation. We confirmed that D-dimer is a prominent biomarker of an ongoing HAE attack. Elevated levels of fibrinogen before the onset edematous symptoms raise the possibility of using it as a predictive marker.

1057 | Prevention of Hereditary Angioedema (HAE) attacks with subcutaneous C1-INH (SC) preparation of CSL830 in the COMPACT study: Effects on severity and attack location

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Introduction: Prophylactic C1-INH (SC) treatment in a Phase 3 study (COMPACT, NCT01912456) recently reported up to a 95% median reduction of the overall HAE attack rate compared to placebo.

Objectives: The objectives of these post-hoc analyses were to determine the number, severity and location of HAE attacks that occurred during the treatments and the same are presented here.

Methods: Ninety patients (pts) were randomized (1:1) to receive 40 IU/Kg or 60 IU/Kg of CSL830 and their corresponding high-volume (HVP) or low-volume placebo (LVP) doses (ITT Population). Study composed of 4 sequences, each with 2 treatment periods, where pts received either CSL830 followed by placebo or vice-versa. Descriptive statistics were used to report the proportion of pts with HAE attacks, total number of attacks, investigator-graded severity (mild, moderate or severe) and the location of the attacks.

Results: Of the 45 pts randomized to receive either dose of CSL830, a lower proportion of pts had at least 1 HAE attack on the 60 IU/Kg (n = 25, 55.5%) and the 40 IU/Kg (n = 26, 57.8%) dose than on placebo (LVP: n = 42, 93.3%, HVP: n = 40, 88.9%). Also, a lower proportion of pts had at least 1 severe attack on the 60 IU/Kg (n = 4, 8.9%) dose than on the 40 IU/Kg (n = 9, 20.0%) dose and placebo (LVP: n = 31, 68.9%, HVP: n = 33, 73.3%). The proportion of pts with at least 1 moderate attack were similar between the 2 CSL830 doses (60 IU/Kg: 28.9% vs. 40 IU/Kg: 26.7%) but the proportion of pts with at least 1 mild attack was higher on the 60 IU/Kg (17.8%) dose compared to the 40 IU/Kg (11.1%). A majority of pts on the CSL830 doses had attacks in the abdominal region (≥40 IU/Kg: n = 35, number of attacks = 120); while a majority of the pts on placebo had attacks in the peripheral region (Combined placebo: n = 75, number of attacks = 480). The overall number of pts who had HAE attacks in the abdominal, peripheral, laryngeal or facial regions were at least 2-fold higher on placebo than on CSL830 (Combined placebo: n = 73, 75, 25, 19 vs. ≥40 IU/Kg: n = 35, 29, 5, 8). Similar outcomes were observed for the number of attacks in each of the anatomical regions. No pt had a laryngeal attack on the 60 IU/Kg dose compared to 9 pts on LVP, 5 pts on 40 IU/Kg and 16 pts on HVP.

Conclusions: Prophylactic CSL830, a C1-INH (SC) preparation reduced the number of pts experiencing HAE attacks as well as the number of attacks at all anatomical locations per patient and reduced the overall severity of HAE attacks compared to placebo.

1058 | Real-world outcomes in C1 inhibitor hereditary angioedema: experience from the icatibant outcome survey in Spain

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Introduction: Hereditary angioedema (HAE) is a rare, potentially fatal, bradykinin-mediated disease. The Icatibant Outcome Survey (IOS; NCT01034969) is a Shire sponsored international observational study monitoring safety and effectiveness of icatibant, a bradykinin B2 receptor antagonist approved for the acute treatment of HAE in adults. Using IOS data from patients (pts) with C1-INH-HAE, we compared disease characteristics and icatibant-treatment outcomes between IOS pts from Spain and other IOS countries.

Objectives: A descriptive, retrospective comparative analyses of IOS data from centers in Spain vs those from centers in Austria, Brazil, Denmark, France, Germany, Greece, Israel, Italy, Sweden and the United Kingdom (July 2009 - August 2016). Icatibant treatment outcomes were retrieved from pts with complete attack outcome data for time to treatment, time to resolution and attack duration.

Results: A total of 666 IOS pts with C1-INH-HAE (84 from Spain and 582 from other IOS countries) provided demographic data. No meaningful differences were identified between pts from Spain and other countries with respect to gender (53.6% vs 60.0% females), median age at enrollment (39.4y vs 39.4y), median age at symptom's onset (14.0y vs 12.0y) and median age at diagnosis (22.2y vs 20.5y). Spanish pts reported fewer severe or very severe HAE attacks (43.1% vs 56.9%) than pts from other countries respectively and differences in the percentage of pts reporting "very mild, mild, or moderate" symptoms (Spain: 251/441; Other: 1171/2714) vs "severe or very severe" symptoms (Spain: 190/441; Other: 1543/2741) were significant ($P < .0001$). Icatibant treatment outcomes were derived from 109 attacks in 84 Spanish pts and 1258 attacks in 582 pts from other IOS countries. The median time to treatment (2.9 h vs 1.0 h; $P = .0049$), time to resolution (17.0 h vs 5.5 h; $P < .0001$), and attack duration (24.0 h vs 8.3 h, $P < .0001$) in Spanish pts vs pts from other countries, were all significantly longer. The majority of pts self-administered icatibant (79.7% in Spain and 89.8% in other countries)

Conclusions: C1-INH-HAE general disease characteristics were similar in Spanish IOS pts and pts from other IOS countries, however Spanish IOS pts report fewer severe attacks, administer icatibant significantly later, and their attacks last longer, perhaps indicating differing HAE management practices, pt selection or reporting procedures.

1059 | A phase 3 open-label extension study of the efficacy and safety of lanadelumab for the prevention of angioedema attacks in patients with hereditary angioedema: trial design

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Introduction: Lanadelumab (DX-2930/SHP-643) is a long-acting, highly-specific, potent, human monoclonal antibody targeting plasma kallikrein that received fast track and breakthrough therapy designations. Results from a Phase 1b study (NCT02093923) did not identify safety signals and supported efficacy of lanadelumab in preventing hereditary angioedema (HAE) attacks. A pivotal randomized, double-blind (DB), placebo-controlled, parallel arm study (NCT02586805) is ongoing, and an open-label extension (OLE; NCT02741596) is currently enrolling patients (pts).

Objectives: To describe the design of a Phase 3 OLE study to evaluate the long-term safety and efficacy of lanadelumab for prevention of angioedema attacks in patients with HAE.

Results: This OLE will include pts (≥12 years old; Type 1/2 HAE) rolling over from the DB study and an additional 50-100 pts who did not participate in the DB study (non-rollover). The non-rollover population will include pts switching to lanadelumab from another prophylactic therapy. Rollover pts will initially receive a single 300 mg subcutaneous dose of lanadelumab and will not receive

another dose until after their first HAE attack. Thereafter, lanadelumab 300 mg q2 weeks will be administered until Day 350, followed by a 4-week safety follow-up. Non-rollover patients will be dosed q2 weeks regardless of their first attack. Pts may qualify to self-administer lanadelumab. The primary objective of the OLE will be to assess long-term safety. In the phase 1b study, 25% pts had local adverse effects following lanadelumab treatment vs 23.1% following placebo. Secondary objectives include evaluation of efficacy (time to first HAE attack to determine outer bounds of the dosing interval, attack rate, number attacks requiring acute treatment, are moderate/severe, or are associated with high-morbidity). Lanadelumab 300 and 400 mg was associated with a 100% and 88% reduction in attacks, respectively, in the Phase 1b study. Immunogenicity, pharmacokinetics/pharmacodynamics, quality of life, characteristics of breakthrough attacks, self-administration and safety/efficacy in pts switching to lanadelumab from another prophylactic therapy will be evaluated. Results of the OLE are expected in 2018.

Conclusions: Results of this study will provide additional important data on the long-term safety, efficacy and dosing frequency of lanadelumab, a first-in-class subcutaneous therapy for prevention of angioedema attacks in patients with HAE.

MONDAY, 19 JUNE 2017

TPS 33

MANAGEMENT OF ATOPIC DERMATITIS AND OTHER SKIN DISEASES

1060 | Cyclosporine in the management of patients with refractory severe atopic dermatitis to conventional treatment

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Introduction: Severe childhood atopic dermatitis refers to the presence of recurrent, widespread, eczematous dermatitis that significantly interferes with the daily activities and/or the quality of life of the affected child and family. The vast majority of child severe, long-standing atopic dermatitis can be managed with the appropriate use of topical treatment, including long-term maintenance therapy and adjunctive treatments.

Objectives: Describe the clinical evolution of patients with severe atopic dermatitis (SAD) in treatment conventional and Cyclosporine.

Results: Series of cases of patients with SAD, in follow-up by the clinical of Dermatitis atopic of the Hospital Infantil de México Federico Gómez.

Was conducted an initial assessment with clinical history, general tests, and assessment of objective/subjective SCORAD (o/s). According to international guidelines started conventional treatment or Cyclosporine (5mgkgdia), in addition to the general measures. The tracking is performed every 2 weeks in the first 2 months e included levels of Cyclosporine, creatinine, pressure blood and valuation of SCORAD o/s.

Included 15 patients of 7.3 years (±3. 8 years). Patients are divided into 2 groups: 1) treatment with Cyclosporine from income and 2) conventional treatment with later onset of Cyclosporine. In Group 1, the middle of SCORAD basal o/s was 40.8 and 51.7 respectively, with a decrease at the end of the follow-up period 34.1 and 44. Group 2 during conventional treatment showed an increase of basal SCORAD (46.5/54.7) after treatment conventional 58.06/80.06 points on such a scale, it was decided to start Cyclosporine, at the end of the period the SCORAD o/s decreased 22.8 and 31.6. Adverse effects were not reported.

Conclusions: The treatment with Cyclosporine is an alternative useful and safe in patients with severe atopic dermatitis. The Improvement clinic is evident in the first weeks. It requires of a greater number of patients to generalize results.

1061 | Antroquinonol inhibit keratinocyte apoptosis and attenuate skin epithelial cell inflammation in mice model of atopic dermatitis

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Introduction: *Antrodia camphorata*, a parasitic fungus on rotting trees of Cinnamomum kanehirai Hay in Taiwan, is used as a folk medicine for the treatment of diarrhea, abdominal pain, hypertension, and itching of the skin, and has been shown to have several pharmacologic effects, including inhibition of the inflammatory response, antioxidant and free radical scavenging activities, and anti–tumor cytotoxicity activity.

Objectives: To evaluate the effect of antroquinonol (AQ), a pure compound and major active component of *Antrodia camphorata*, on atopic dermatitis.

Results: We established *Dermatophagoides pteronyssinus* (Der p)-induced AD mouse model through epicutaneous challenging (EC) in SKH1 hairless mice. The skins of EC-sensitized mice were dry and trans-epidermal water loss (TEWL) was higher than control mice indicated that the skin barriers were damaged by repeated EC sensitization. In histology, their skins developed lesions characterized by epidermal and dermal thickening, inflammatory cells and eosinophils infiltrations. Also, thymic stromal lymphopoietin (TSLP), a cytokine secreted from keratinocytes triggering dendritic cell-mediated T helper (Th) inflammatory responses, was highly expressed and associated with Langerhan's cells migration in EC-sensitization mice. Oral administration with low (5 mg/kg), middle (15 mg/kg), and high (45 mg/kg) dose of AQ, respectively for consecutive 14 days after EC sensitization with Der p. We found the thickness and eosinophils infiltrations in epidermis and dermis of AQ-treated AD mice were decreased as compared to non-treated AD mice. Moreover, the expression of TSLP from keratinocytes was decreased, and Langerhan's cells migration was also limited in epidermis area in the treated AD mice. There were significantly decreased IL-17 and IFN-γ but increased anti-inflammation cytokine IL-10 after oral administration with AQ. Moreover, in vitro study showed that AQ pre-treatment could inhibit Der p induced HaCaT cells apoptosis through up-regulating Nrf2 expression and diminishing allergic inflammation.

Conclusions: These findings suggested that AQ inhibited Th1、Th2 and Th17 by increasing the expression of anti-inflammation cytokines IL-10, and inhibited keratinocytes apoptosis in AD mice, which may provide a new therapeutic option for AD patients.

1062 | Seminal plasma hypersensitivity in female atopic dermatitis patients

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Introduction: Seminal plasma hypersensitivity (SPH) is a rare allergic condition. To date more than 100 cases have been reported whereas the causative allergens represent are heterogeneous group of seminal plasma (SP) non-specific and specific proteins. Recently, a subgroup of SPH cases have been linked to a sensitization against prostate-specific antigen (PSA) from human or dog. Canis derived PSA (Can f 5) represent a major allergen in dog allergy and it is in part cross-reactive to human PSA. It is known that atopic dermatitis (AD) patients are frequently sensitized to dog allergens and especially Can f 5. However, little is known about their tendency to react to human seminal fluid.

Objectives: The objective of the study was to analyse the frequency of sensitization towards PSA-specific IgE in female AD patients and investigate symptoms against human SP. For this reason 57 female AD patients with an average age of 36 years were interviewed for local and systemic allergic reactions after sexual intercourse by a questionnaire. Moreover, specific IgE against dog dander, Can f 5 and o70 (seminal fluid) was analyzed. The questionnaire scores were also compared to those of an aged matched control cohort consisting of skin healthy females. All enrolled participants gave written informed consents and the study was approved by local ethical committee.

Results: 60% of female AD patients were sensitized to dog dander. Of these patients, 35% had also IgE against the major dog allergen Can f 5 representing dog PSA. Moreover in 25% of Can f 5-positive female AD patients IgE against seminal fluid could be detected. Interestingly, IgE against seminal fluid could not be detected in Can f 5-negative individuals suggesting that seminal fluid test substance contains PSA. Indeed blocking sera with human PSA significantly reduced binding to seminal fluid. In the questionnaire results, total symptom score with an average above 6 was high without significant differences in Can f 5-positive and -negative AD patients. However, compared to control cohort female AD patients experienced significantly more symptoms towards SP.

Conclusions: IgE sensitization towards components of human SP is quite frequently in female AD patients. Moreover, female AD patients often experienced reactions after contact with human seminal fluid. Further studies are necessary to investigate the clinical relevance.

1063 | The beneficial effects of an insect protein based elimination diet on clinical signs of food allergy in dogs

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Introduction: Entomophagy (the food consumption of insects) is traditionally practiced in many parts of the world. Edible insects are discussed to be an adequate new protein source for canine diets, of which yellow mealworm protein showed the highest in vitro digestibility.

Objectives: To investigate the benefit of an insect protein based diet on clinical signs of food allergy in dogs. Twelve dogs with previously diagnosed food allergy by a strictly and exclusively fed elimination diet (with improvement in clinical signs, deterioration on food provocation and subsequent improvement on the elimination diet again), were fed with the test diet for two weeks. Dogs were re-evaluated on days 0 and 14. Concomitant therapy was not changed during the study period. Clinical changes were evaluated by a validated quality of life score, a pruritus visual analogue scale, an owner evaluated coat quality form and a validated canine atopic dermatitis lesion index. Possible adverse reactions were recorded.

Results: Twelve dogs completed the study. Most of the dogs had residual mild clinical signs. None of the dogs deteriorated with the insect protein-based diet, eight of those even improved their clinical signs.

Conclusions: An insect protein based elimination diet showed clinical benefit for food allergic dogs. As a balanced complete diet, it might be considered a suitable alternative to hydrolysed or home-prepared diets for food allergic patients.

1064 | Successful treatment with mepolizumab in a patient with refractory wells syndrome

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Case report: Wells syndrome is a rare condition of unknown etiology presenting with pruritic, often papular and nodular, cellulitis-like skin lesions and typical histologic features. Here, we report the case of a 74-year old patient who suffered from highly pruritic, sometimes papular and nodular, sometimes urticarial eruptions as well as cellulitis-like lesions for a period of eight years. The changing clinical presentation and histological findings have led to different diagnoses in the past, including atopic dermatitis, prurigo and bullous pemphigoid. Recently, typical flame figures have been observed in histology, helping to establish the diagnosis of Wells syndrome. During

the course of the disease, the patient received different treatments such as antihistamines, dapsone, systemic and topical glucocorticoids, UV therapy, methotrexate and cyclosporine, and he was hospitalized many times because of the very intense pruritus. None of the treatments were successful or they had to be discontinued due to side effects. Recently, the patient reported about suicidal thoughts because of the severe and treatment refractory pruritus. Among many other comorbidities the patient developed severe refractory eosinophilic asthma, for which a treatment with mepolizumab was initiated. Mepolizumab is a humanized monoclonal antibody directed against IL-5, licensed for the treatment of severe asthma with an eosinophilic phenotype as an add-on treatment. After two injections of 100 mg mepolizumab, there was a marked improvement in skin lesions, followed a few weeks later by a complete resolution of pruritus. After a total of three injections, the skin lesions disappeared completely. Patient related outcomes such as pruritus VAS and the DLQI reflected this impressive improvement. Blood eosinophils, which had been elevated up to 10fold pre-treatment, normalized after the first injection. A biopsy of residual skin lesions taken after the second injection showed a sparse lymphocytic infiltrate with absence of the preexisting eosinophils and flame figures. Discontinuation of treatment due to logistic reasons let to a relapse of highly pruritic skin lesions, and retreatment of mepolizumab again resulted in resolution of the skin lesions followed by improvement in pruritus. Taken together, this case indicates that IL-5 is involved in the pathogenesis of Wells syndrome and that eosinophils are likely to play an important role in the associated severe chronic pruritus.

1065 | Adult Henoch-Schönlein Purpura: clinical and histopathological predictors of systemic disease and profound renal disease

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Introduction: A major challenge in managing adult Henoch-Schönlein purpura (HSP) is difficulty assessing the risk of systemic involvement. There is a paucity of data and previous study results have been conflicting.

Objectives: This study sought to determine specific clinical and histopathological features associated with systemic involvement in adult HSP.

Methods: We reviewed the records of 99 adult HSP patients who presented at our centre between January 2008 and May 2015.

	Bivariate analysis			Multivariate analysis		
	Not indicated for Nephrology Referral (n = 43)	Indicated for Nephrology Referral (n = 56)	*P*-value	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	*P*-value
Age, 10 years						
Mean ± SD	3.75 ± 1.57	4.81 ± 1.20	<.01	1.56 (1.10-2.21)	1.62 (1.02-2.57)	.04
Median (min-max)	3.1 (1.8-7.2)	4.8 (2.9-6.7)				
Age, years						
Mean ± SD	37.5 ± 15.7	48.1 ± 12.0	<.01	NA	NA	NA
Median (min-max)	31 (18-72)	48 (29-67)				
≤30	40 (50.0%)	1 (5.3%)	<.01	NA	NA	NA
>30	40 (50.0%)	18 (94.7%)				
≤40	46 (57.5%)	6 (31.6%)	.04	NA	NA	NA
>40	34 (42.5%)	13 (68.4%)				
≤50	59 (73.8%)	12 (63.2%)	.06	NA	NA	NA
>50	21 (26.3%)	7 (36.8%)				
≤60	73 (91.3%)	16 (84.2%)	.36	NA	NA	NA
>60	7 (8.7%)	3 (15.8%)				
Lesions on trunk	68 (85.0%)	12 (63.2%)	.03	3.31 (1.08-10.09)	4.80 (0.85-27.15)	.08
	12 (15.0%)	7 (36.8%)				
Lesions on upper limbs	54 (67.5%)	8 (42.1%)	.04	2.86 (1.03-7.95)	1.90 (0.46-7.91)	.38
	26 (32.5%)	11 (57.9%)				
Cutaneous bullae and/or necrosis	64 (80.0%)	10 (52.6%)	.01	3.60 (1.25-10.33)	5.98 (1.43-25.00)	.01
	16 (20.0%)	9 (47.4%)				
Fibrinogen on immuno-histology	68 (85.0%)	11 (57.9%)	.01	NA	NA	NA
	12 (15.0%)	8 (42.1%)				

Results: Renal involvement was found in 56 patients (56.6%), joint involvement in 21 (21.2%), and gastrointestinal involvement in 13 (13.1%). Age >30 years was an independent predictor for renal involvement, with an adjusted odds ratio of 2.97 (95% CI: 1.08-8.16, $P = .04$). Risk factors for significant renal involvement necessitating nephrology referral were further evaluated: the odds were 60% higher for every 10-year increase in age (95% CI: 1.02-2.57, $P = .04$), and patients with cutaneous bullae and/or necrosis had 6-times higher risk (95% CI: 1.43-25.00, $P = .01$).

Limitations: This study was limited by a lack of long-term data.

Conclusions: Adult HSP patients older than 30 years have 3-times increased risk of renal involvement. The risk of significant renal disease necessitating nephrology referral rose significantly with age and the presence of cutaneous bullae and/or necrosis.

1066 | *Malassezia* spp and *Candida albicans* allergic sensitization are associated with increased severity of atopic dermatitis

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Introduction: Atopic dermatitis (AD) in an inflammatory disease characterized by skin microbiome dysfunction. Fungal species such as *Malassezia* and *Candida* may foster allergic inflammation.

Objectives: We aimed to assess the impact of *Candida albicans* and *Malassezia spp* sensitization in the severity of atopic dermatitis.

Results: A cross sectional evaluation of 75 patients (60% female, 77% atopic), mean(sd) aged 29 (13), with a previous medical diagnosis of AD and without other skin-immunomediated diseases or significant comorbidities was performed. AD severity was classified according to SCORAD index into mild <25, moderate 26-49 or severe >50, and need of oral immunosuppression (IS) to attain disease control in the last year. Accordingly, 18 patients had mild, 32 moderate and 35 severe AD, and 34 (45%) had used oral IS. Serum levels of *inhalant Phadiatop*™, total and specific IgE to *Malassezia spp* (Mspp) (n = 75) and *Candida albicans* (n = 52) (IMMUNOCAP-FEIA, Thermofisher®) were determined. Non parametric statistics (Kruskal-Wallis), Spearman correlation and ROC curves were determined (SPPS.22 software).

We found a significant correlation between total IgE levels, specific IgE to *Malassezia spp* and value of SCORAD ($P = .006$ and $P = .004$ respectively), severity classes of AD ($P < .001$ e $P = .049$) and need of IS ($P < .001$ e $P < .001$). SpIgE to *Candida* was positively correlated with the need of IS ($P = .028$), but not with SCORAD ($P = .388$) or their classes ($P = .689$). The AUC for spIgE to Malassezia and need of IS was AUC=0.768, with a cut-off point of 0.35 KuA/L.

Conclusions: Our study provides support the role of specific IgE to *Malassezia* and *Candida Albicans* as a marker of disease severity in AD patients.

1067 | The effects of a homeopathic combined preparation on clinical signs of atopic dermatitis

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Introduction: A commercially available preparation containing homeopathic ingredients improved clinical symptoms of atopic dermatitis in individual human and canine patients.

Objectives: To investigate the clinical benefit of a homeopathic combined preparation on canine atopic dermatitis in a case series of ten dogs.

Ten dogs with diagnosed canine atopic dermatitis were treated with the study medication orally for three weeks. Atopic dermatitis was previously diagnosed by clinical findings, a compatible history and ruling out differential diagnosis. All dogs were kept on the same diet and a non-flavoured antiectoparasitic treatment during the study period. Concomitant therapy had to remain unchanged for the three weeks. The clinical benefit was evaluated via a pruritus visual analogue scale, a validated quality of life score and a canine atopic dermatitis lesion index (CADLI). A coat quality score was evaluated by the owners. Before and after the study, all dogs were cytologically checked for secondary pyoderma. Possible adverse reactions were recorded at each visit.

Results: There were no significant changes in CADLI (Wilcoxon test, $P = 1.0$), pruritus scores (paired t test, $P = .34$) and coat quality (paired t test, $P = .34$)) over the duration of the study. Only one patient had a mild decrease in pruritus and a mild increase in coat quality.

Conclusions: In this case series, the tested homeopathic preparation did not improve clinical signs of canine atopic dermatitis.

1068 | Current management of moderate-to-severe atopic dermatitis: a survey of physicians in Korea

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Introduction: There is lack of evidence for the treatment of moderate-to-severe atopic dermatitis (AD), resulting in variation in strategies in patient management.

Objectives: We collect data on current practice of moderate-to-severe AD as reported by allergist, pediatricians, and dermatologist in Korea.

Results: A total of 93 physician members of Korean Academy of Asthma and Allergy participated in questionnaire-based survey. Sixty five percent were pediatricians and 31% were dermatologists. The major patients' age group was less than 5 years for 89.8% of pediatrician and 6- 12 year-olds for 38% of dermatologists. The proportion of moderate-to severe AD was higher in dermatologists and allergists compared to pediatricians. The respondents agreed the necessity of education including demonstration of basic skin care and applying topical medicines, psychological, and nutritional support in 88.2%, 75.3%, and 83.9% respectively. However, less than half of physicians conducted education and counseling in real practice. There were distinct differences in preference in choosing first-line treatment for moderate-to-severe AD according responder's specialty. The order of preferred systemic treatment for moderate to severe AD was wet wrap therapy, systemic corticosteroid, cyclosporin in pediatrician. However, dermatologists ranked cyclosporin, phototherapy, and systemic corticosteroid as the first-line regimen for moderate-to-severe AD. The major factors quoted as barrier for proper management of AD were steroid phobia, unproven complement-alternative medicine, lack of education, and unreasonable insurance system.

Conclusions: Our findings suggested distinct differences in moderate-to-severe AD treatment exist among physician's specialty. Moreover we suggest there is still an unmet need for personalized, evidence-based, and multi-disciplinary approach including therapeutic patient education in AD in real practice. For moderate-to severe AD, consensus in approach of management should be implemented for the best outcomes based further randomized controlled trials.

1069 | Burden of illness in atopic dermatitis (AD) patients by self-reported severity: analysis of national health and wellness survey data from France, Germany, Italy, Spain, and the UK

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Introduction: Moderate-to-severe AD is an under-recognized public health concern with a high disability burden. Data on the disease burden in this population are limited, especially in Europe.

Objectives: To assess the burden of illness in adult AD patients in 5 European countries based on self-reported disease severity.

Methods: Patients with diagnosis of AD from France (n = 341), Germany (n = 198), Italy (n = 457), Spain (n = 683), and the UK (n = 184) of the 2016 National Health and Wellness Survey were stratified by self-reported AD severity (mild, moderate or severe). Patient burden was compared for severe AD vs mild AD, and severe AD vs moderate AD, respectively. Multivariable analyses (controlling for demographics, including country) were conducted to measure differences in HRQoL (SF-36v2 mental and physical component summary scores, SF-6D health utilities and DLQI scores), work productivity and activity impairment and healthcare utilization. Pairwise comparisons (Chi-square tests) were conducted on prevalence of atopy-associated comorbidities (asthma and nasal allergies/hay fever), mood disorders (anxiety and depression) and sleep disorders.

Results: Mean age of patients was 43.9 years; 70.5% were female. Severe AD patients had significantly lower HRQoL ($P < .001$) on SF-36v2 mental and physical summary component scores and SF-6D health utilities (39.2; 47.2; 0.63) vs mild AD (43.2; 50.4; 0.68), respectively. DLQI score was significantly higher for severe AD (8.4) vs both mild AD (3.1) and moderate AD (5.5) ($P < .001$; higher scores representing greater impairment). Activity impairment was greater for severe AD (38.2%) vs mild AD (27.8%) ($P < .001$); in employed patients overall work impairment was greater in severe AD (35.0%) vs mild AD (21.7%) ($P < .001$). Asthma was more frequent in severe AD (34.1%) vs both mild AD (18.1%) and moderate AD (20.4%) and nasal allergy/hay fever was more frequent in severe AD (61.9%) vs mild AD (44.5%) (all $P < .001$). Severe AD vs mild AD was associated with 3.5 (mean) more healthcare provider visits during the prior 6 months ($P < .001$).

Conclusions: Statistically significant differences on HRQoL, work productivity, activity impairment, comorbidities, and healthcare utilization were found between AD severity levels in adult patients in Europe, suggesting that AD burden generally increases with severity.

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1070 | The effect of dupilumab on the pharmacokinetics of cytochrome P450 substrates in adult patients with moderate-to-severe atopic dermatitis: an open label phase 1 trial

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Introduction: Dupilumab, a fully human anti-IL-4Rα mAb, potently inhibits both IL-4/IL-13 signaling, key drivers of type 2/Th2-mediated inflammation, implicated in atopic diseases such as atopic

dermatitis (AD) and asthma. It is currently unknown if blockade of IL-4/IL-13 signaling through IL-4Rα impacts the activity of cytochrome P450 (CYP) enzymes and affects the pharmacokinetics (PK) of concomitant medications.

Objectives: This single sequence, cross-over study assessed the effect of dupilumab on the PK of 5 CYP isoform-specific substrates, as well as safety and efficacy of dupilumab in an open-label phase 1 trial (NCT02647086). Adults with moderate-to-severe AD received an oral cocktail consisting of midazolam, omeprazole, S-warfarin, caffeine, and metoprolol (probe substrates for CYP3A, CYP2C19, CYP2C9, CYP1A2, and CYP2D6, respectively), on Days 1 and 36. Subcutaneous dupilumab was administered as a 600 mg loading dose on Day 8, followed by a weekly dose of 300 mg from Day 15 to 50. PK parameters included Geometric Mean Ratios (GMR) of AUC_{last} (area under the plasma concentration-time curve from time zero to time of last quantifiable concentration) and C_{max} (maximum observed plasma concentration) measured at Days 1 and 36, while efficacy assessments included changes in Eczema Area and Severity Index (EASI) scores (scale 0-72).

Results: A total of 14 patients were enrolled in the study (baseline mean EASI score [SD] = 29.2 [14.2]), and 13 completed the study. GMRs and 90% confidence intervals for both AUC_{last} and C_{max} (Table 1) indicate no meaningful effect of dupilumab on the PK of midazolam, omeprazole, S-warfarin or caffeine. Based on a slight increase in metoprolol exposure, blockade of IL-4/IL-13 signaling by dupilumab may have a small numerical effect on the activity of CYP2D6. A total of 3 patients had at least one adverse event (AE); there was 1 serious AE leading to treatment discontinuation (systemic inflammatory response syndrome). Mean EASI (SD) scores decreased by 59.3% (37.6) and 87.2% (13.4) at Days 35 and 50, respectively.

Conclusions: This study showed that blockade of IL-4/IL-13 signaling by dupilumab through IL-4Rα does not have a meaningful effect on the activity of CYP3A, CYP2C19, CYP2C9, CYP1A2 or CYP2D6 in adult patients with moderate to severe AD. Consistent with previous studies, dupilumab had an acceptable safety profile and provided substantial clinical benefit to patients with AD.

Analyte	Pharmacokinetic parameter	Geometric mean ratio	90% CI
Midazolam, n = 13	C_{max}	1.13	0.93-1.36
	AUC_{last}	0.98	0.89-1.09
Omeprazole, n = 13	C_{max}	0.98	0.83-1.15
	AUC_{last}	1.00	0.88-1.12
S-warfarin, n = 13	C_{max}	0.96	0.83-1.11
	AUC_{last}	0.90	0.83-0.98
Caffeine, n = 12	C_{max}	1.05	0.95-1.17
	AUC_{last}	1.12	0.87-1.45
Metoprolol, n = 13	C_{max}	1.22	1.05-1.41
	AUC_{last}	1.29	1.10-1.51

90% CI, 90% confidence interval; AUC_{last}, area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration; C_{max}, maximum observed plasma concentration.

1071 | Unraveling a case of junctional epidermolysis bullosa in a newborn: tragic coincidence of a novel mutation of the ITGA6 gene and trisomic rescue

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Introduction: Epidermolysis bullosa is a genetical disorder of varying severity that affects the skin and mucosal membranes, causing mechanical fragility and blistering. Depending on the ultrastructural level of blister formation, epidermolysis bullosa is classified into four major forms: simplex, junctional, Kindler syndrome and dystrophic.

Objectives: In this study we attempted to investigate the genetic cause in a female newborn with progressive, fatal epidermolysis bullosa. In the prenatal analysis of amniotic fluid cells, which had been conducted due to developmental abnormalities in the embryo, low-level fetal mosaic trisomy 2 was detected.

Methods: Prenatal amniocentesis, immunofluorescence mapping, transmission electron microscopy and genetic analysis were used for diagnostic evaluation.

Results: Immunofluorescence mapping disclosed junctional split and absence of immunoreactivity for integrin a6. Sequence analysis of the ITGA6 gene on chromosome 2 revealed a homozygous mutation, leading to a premature termination codon. This mutation was found in heterozygous state only in the mother, but not in the father. Segregation analysis with chromosome 2-specific short tandem repeat (STR) markers exhibited exclusive maternal inheritance of chromosome 2, thus demonstrating evidence for uniparental disomy (UPD2).

Conclusions: Full trisomy 2 as well as high-level mosaicism would lead to spontaneous miscarriages or severe fetal malformations. Due to a very rare event of trisomy rescue a uniparental disomy can lead to the manifestation of a recessive condition in case of mutation transmission by only one parent. This case demonstrates uniparental disomy 2 as cause for a severe form of fatal junctional epidermolysis bullosa.

1072 | IL-17A-producing ILC3 is increased in HDM-induced AD mice model

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Introduction: Atopic dermatitis (AD) is generally characterized as a Th2-mediated inflammatory skin disease. Group 2 Innate lymphoid cells (ILC2s) is known to induce AD by producing type 2 cytokine. However, several recent studies have been reported that IL-17A is also increased in patients with AD as well as murine AD model.

Objectives: To address the roles of ILC3s in AD, we used house dust mite (HDM)-induced AD models using NC/Nga mice.

Results: Interestingly, both type 2 and type 3 cytokines (IL-13 and IL-17, respectively) were increased in the skin-draining lymph nodes and skins of AD mice compared with control mice. ILC3s in AD mice produced IL-17A but not IL-22. Adoptive transfer of ILC3 into the recipient NC/Nga mice accelerated the development of AD compared with the PBS-injected mice. Finally, neutralizing IL-17A delayed the development of AD.

Conclusions: Taken together, our results suggest that ILC3s play critical roles in the pathogenesis of AD by orchestrating the production of both type 2 and type 3 cytokines.

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URTICARIA AND ANGIOEDEMA MANAGEMENT

1073 | Management of chronic refractory urticaria

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Introduction: Chronic urticaria (CU) that continues for a period of six weeks and longer should be considered refractory when symptoms are not controlled by higher dose H1 antihistamines up to fourfold dose in combination with first-generation antihistamines and/or antileukotrienes and short-term use of systemic corticosteroids.

There is no standardized approach to the management of severe refractory CU and therapy must be individualized.

The aim of this study was to investigate underlying causes of chronic refractory urticaria and find best treatment options.

Objectives: 13 adult patients (>18 years old) with chronic refractory urticaria were investigated and treated according to The EAACI/GA2 LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria (2013 update) and The diagnosis and management of acute and chronic urticaria (2014 update by JTFPP of AAAI/ACAAI). To differentiate atopic and non-atopic patients Phadiatop and Specific IgE to the food allergens were analyzed by ImmunoCAP Phadia (ThermoFisher Scientific). All other possible reasons of CU were investigate: viral infections (hepatitis B and C, EBV), bacterial infections (*Helicobacter pylori*, etc.), parasitic infections (Lambliosis, Ascaridosis, Toxocara, Lyme disease), complement component deficiencies, connective tissue diseases, neoplasms (lymphoproliferative disorders), autoantibody-associated urticaria (thyroid autoantibodies and IgE receptor autoantibodies) etc.

Results: The study revealed that chronic refractory urticaria was caused by: *Helicobacter pylori* – 4 cases; Hepatitis C – 1 patient; Autoimmune thyroiditis – 2 cases; Lyme disease – 1; Idiopathic urticaria – 5. Treatment was based on above-mentioned sources and BSACI guideline for the management of chronic urticaria and angioedema (2015). Patients were treated for the different causes, as well with anti-inflammatory (corticosteroids) and immunosuppressant drugs (methotrexate), omalizumab (150-300 mg three injections administered monthly, independently from total serum IgE).

Conclusions: Chronic refractory urticaria is a serious problem of modern allergological practice. When symptoms are refractory and standard anti-allergic and anti-inflammatory therapy is useless, all possible causes should be considered. Treatment could be based on individual most effective combinations of antihistamines, antileukotrienes, rational doses of glucocorticosteroids and immunosuppressants (with minimum side effects), as well as, if needed, omalizumab.

1074 | Treatment of patients with chronic urticaria in Europe: findings from visit 1 of the worldwide prospective observational aware study

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Introduction: Chronic urticaria (CU) is characterised by repeated occurrence of itchy and sometimes painful hives and/or angioedema for 6 weeks or longer. Treatment guidelines are available (EAACI/GA^{2}LEN/EDF/WAO), but data are lacking on the actual therapies prescribed to European CU patients.

Objectives: To present current treatment data from CU patients residing in Europe (EU) collected at enrolment in the ongoing observational AWARE study, alongside quality of life (QOL) measured by the Dermatology Life Quality Index (DLQI). Patients were aged 18 years or older and refractory to at least one course of H1-antihistamines (H1-AH). Data were split into regions for comparison: United Kingdom (UK), Nordic countries (Sweden, Norway, Denmark), Southern Europe (SE: Belgium, France, Portugal, Spain, Italy, Greece), Germany, and Russia.

Results: At enrolment, 3733 patients provided data (UK, n = 261; Nordic, n = 160; SE, n = 922; Germany, n = 2247; Russia, n = 141), and 58% were receiving treatment. Among those, 57% were treated with a second-generation H1-AH; escalation to recommended third-line therapy was observed in 32% (26.2% omalizumab, 0.9% ciclosporin, 4.5% montelukast, 0.8% combination). Nordic patients were most likely to be receiving treatment (74%) followed by Germany (61%), SE (58%), UK (52%), and Russia (39%). Among Nordic patients receiving treatment, second-generation H1-AHs were taken by 38%, while 59% had already escalated to a third-line therapy. Corresponding numbers were as follows: Germany, 63% and 27%; SE, 47% and 40%; UK, 43% and 40%; and Russia, 66% and 22%. Combination treatment with corticosteroids alongside third-line therapy was rare (2%), as was treatment with other non-guideline medications (6%). UK patients were much more likely to receive non-guideline recommended treatment (21%) compared with Nordic (3%), German (4%), SE (8%), or Russian (13%) patients. The effect of urticaria on QOL

was reported as moderate, very large, or extremely large in 54% of Nordic patients, 51% of SE patients, 56% of German patients, 61% of UK patients, and 85% of Russian patients.

Conclusions: A substantial proportion of European CU patients are currently not prescribed any CU treatment, despite being under medical care. Many CU patients appear to be refractory to H1-AH and show a substantial burden in QOL. Moreover, only a third of enrolled patients had been escalated to recommended third-line therapies.

1075 | Aware-amac: first results from a large non-interventional study on the management and clinical impacts of chronic urticaria in patient refractory to h1-antihistamines in Asia, Middle-East and Africa

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Introduction: Chronic Urticaria (CU) is characterized by the repeated occurrence of red, swollen, itchy and sometimes painful hives and/or angioedema for six week or longer. Most data on CU originate from specialized centers located in western countries.

Objectives: The objective of this study is to describe real-life clinical outcomes, treatment patterns, resource utilization and quality of life in patients with Chronic Spontaneous Urticaria (CSU) and/or Chronic Inducible Urticaria (CINDU) in countries from Middle East, Africa and Asia. The disease characteristics of CU patients from these countries at baseline are presented for the first time.

Results: Methods: Observational, prospective, multinational (15 countries) study. Diagnostic or monitoring procedures and visits intervals were performed according to routine practice with the exception of patient-reported outcomes and UAS7 assessments. Baseline characteristic are summarized by descriptive statistics.

Results: 926 patients aged 18 + with the diagnosis of CU, refractory to H1-antihistamine therapy were analyzed: CSU 908, CINDU 18.

Mean age (SD) at baseline was 39.6 (12.3) years: CSU 39.8 (13.3), CINDU 33.3 (12.1).

69.8% of the CU patients were female, 53.7% Caucasians, 37.6% Asian. The majority of CU patients (80.9%) reported no family history of urticaria. 45.6% of CSU patients reported presence of angioedema. In 36.7% of them angioedema was present at baseline: 35.5% mild, 46.0% moderate, 18.4% severe. 62.6% of Caucasian patients were diagnosed with CSU with angioedema vs 25.4% of Asians. The mean duration (SD) of the current episode of urticaria at baseline was 27.0 (44.9) months in CSU patients with angioedema, 30.0 (52.4) in CSU patients without angioedema and 15.9 (18.6) in CINDU patients.

At baseline the current treatment of CU patients was reported as follows: 36% with H1-antihistamines alone, 20.6% with omalizumab, 0.9% with cyclosporine, 2.7% with montelukast (omalizumab, cyclosporine and montelukast were given as monotherapy or in combination with H1-antihistamines), 39.1% received other classes of treatment (such as steroids) or various combination of omalizumab, cyclosporine or montelukast.

Conclusions: CU characteristics at baseline explored in this large real-life study confirmed the need of adequate treatment in patients in Middle East, Africa and Asia.

1076 | Patient characteristics and associated conditions to define treatment responses in chronic spontaneous urticaria: a study evaluating treatment responses by urticaria control test

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Introduction: Chronic spontaneous urticaria (CSU) treatment can be challenging both for the physician and their patients. Guidelines recommend a stepwise approach for the treatment. Establishing a treatment plan on a stepwise basis may lead to time constraints and quality of life impairments for the patients. There is a lack of knowledge to define basic characteristics or associated conditions to determine which patient responds to a particular treatment. That is why we sought to describe special characteristics to define which patients will response to step treatments.

Objectives: This was a retrospective study including a total of 213 CSU patients. The patients were treated in a stepwise treatment regimen; step 1 standard doses of H1-antihistamines, step 2 high doses or combinations of H1-antihistamines and step 3 omalizumab (300-600 mg). Treatment responses were evaluated by urticaria control test (UCT) (UCT < 12 not controlled; ≥12 under control); 1st month UCT was used for step 1&2 treatments and 3rd month UCT was used for step 3 treatment. The demographic characteristics of the patients and laboratory results including anti-TPO, ASST, total IgE, ESR, CRP, associated infections, systemic diseases, stress, family history, NSAID intolerance, associated inducible urticaria, autoimmune diseases and in-clinic UAS scores were recorded. The characteristics of the patients responding to step 1& 2 and step 3 treatments were compared.

Results: Two hundred and thirteen patients (94 males and 119 females) were recruited. A hundred and twenty-one (%56.8) patients were on step 1-2 treatments while 86 (%43.2) were on step 3 treatment. Thirty-seven (%59.7) of the patients on step 1 and thirty-three (73.3%) of patients on step 2 were found to be under control in the first month UCT evaluation. Of the 86 patients in step 3, 64 (74.4%) were under control in the 3rd month UCT evaluation. When we compared the demographic characteristics, laboratory results and associated conditions in the step 1-2 responsive vs step 3 responsive patients, we found that the only parameter that differed between groups was in-clinic-UAS ($P = .001$). Patients with in-clinic-UAS < 3 responded better to step 1-2 treatments.

Conclusions: Urticaria activity score should be used as a parameter when making treatment plans in CSU patients.

1077 | Mean wheal diameter and presence of angioedema in chronic spontaneous urticaria linked to values of D-dimer, CRP, ESR and disease duration

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Introduction: Chronic spontaneous urticaria is a mast-cell driven disorder characterized by recurrence of wheals and/or angioedema (AE) for more than 6 weeks. D-dimer, fibrinogen, ESR and CRP have been investigated as biomarkers for CSU diagnosis and treatment. However, it is not clear yet whether the levels of these can help to better characterize the subgroups of patients distinguished on clinical grounds.

Objectives: Here, we evaluated the association between mean wheal diameter (MWD) and presence of AE and values of D-dimer, fibrinogen, CRP and ESR, disease activity and quality of life scores.

Materials and Methods: We retrospectively assessed the data from 171 CSU patients. Episodes of AE were documented over a period of four weeks. MWD was calculated as a mean of largest diameters measured in 5 different wheals. CU-Q2oL, DLQI and UAS results were obtained and D-dimer, CRP, ESR and fibrinogen were evaluated in blood on the same day. UAS was assessed once retrospectively based on the mean intensity of the itch and number of wheals reported by the patient for previous 4 weeks. The patients did not take immunosuppressants and systemic steroids at the time of the study. Autologous serum skin test (ASST) was performed. Statistical analysis was carried out using SPSS 22, Spearman coefficient being employed for measuring the correlation between parameters, Mann-Whitney test – for comparing the groups ($P < .05$ was seen as statistically significant).

Results: Median of MWD was 1.5 cm (interquartile range: 1-3 cm). One hundred thirty-two (77.2%) CSU patients had AE. We found that MWD is higher in CSU patients with angioedema ($P = .004$). MWD positively correlated with duration of CSU ($P = .004$), DLQI, ESR ($P = .04$), CRP ($P = .01$) and D-dimer ($P = .03$), and negatively – with CU-Q2oL. Presence of AE was associated with higher values of ESR ($P = .03$), CRP ($P = .04$), D-dimer ($P = .01$) and longer disease duration ($P = .02$). Patients with AE and high MWD tended to have a higher UAS ($P = .06$ and $P = .07$, respectively).

Conclusions: We found that elevated values of D-dimer, CRP and ESR and longer duration of CSU are linked to higher MWD and presence of AE. The elevation of these parameters might point to more marked inflammation and activation of coagulation cascade in patients with AE and large wheal diameter. The mechanisms behind different clinical patterns of the disease require further investigation.

1078 | Acquired angioedema in a patient with adrenal insufficiency and marginal zone lymphoma: A challenging diagnosis and management

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Case report: Background: A 61-year old female, with previous diagnosis of adrenal insufficiency (AI) and splenic marginal zone lymphoma (MZL), came to our attention for recurrent abdominal pain since 2015. In 2016 the patient had multiple ED visits and each time abdominal ultrasound examinations showed diffuse endoperitoneal effusion, thickening of the small bowel wall and splenomegalia. Mean blood pressure on admission was 90/50 mmHg, with no marked alteration of electrolyte and metabolic panels. Specific therapy for suspected adrenal crisis (hydrocortisone, IV fluid replacement) was administrated, with no improvement of the abdominal symptoms. Familial history was negative for angioedema, allergy and autoimmunity. Laboratory tests showed marked reduction of serum C4, C1q, quantity and functional activity of C1-inhibitor protein (C1INH). Based on clinical and laboratory features a diagnosis of Acquired Angioedema (AAE) was made.

Method: Bradykinin B2-receptor antagonist therapy (Icatibant) was prescribed to the patient, to be administered in case of abdominal, cutaneous and/or laryngeal attacks. On-attack rescue treatment with steroids and IV fluids was also recommended in case of AI symptoms or no response to icatibant therapy.

Results: The patient experienced abdominal attacks that were treated with icatibant, with resolution of abdominal pain in less than 24 hours. During the attacks the patient had no need for AI rescue medications. Long term prophylaxis treatment with danazol or tranexamic acid is currently being evaluated.

Conclusion: AAE is a condition frequently associated with malignancy, in particular with B-cell disorders like MZL (1). In patients with recurrent abdominal pain and malignancy, AAE diagnosis has to be ruled out, given the risk of life-threatening laryngeal edema (2). To date, no cases of AAE patients with concomitant AI were documented. Adrenal crises in AI may occur in stressful conditions, presenting with nausea, vomiting, low blood pressure, electrolytes imbalance, hypoglycemia and resulting in metabolic acidosis and shock if not promptly treated with corticosteroids (3). The recurrence of endoperitoneal effusions and the lack of response to steroid therapy, however, were not typical signs of an adrenal crisis. AAE attacks may elicit adrenal crises in patients with AI if unrecognized and untreated. Icatibant therapy is a well-tolerated treatment option for AAE, although treatment of the underlying B-cell disorder is recommended (4).

1079 | Localized heat urticaria: a report of 2 cases

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Case report: Introduction: Localized heat urticaria (LHU) is one of the less frequent physical urticarias. It's developed by skin direct contact with hot air, water or other elements with high temperature and this causes cutaneous itch and weals in contact area. We report 2 cases of LHU with progressive worsening of their life's quality.

Methods: Case 1: A 57-year-old woman, hypothyroid, who presents itching symptom and localized weals 5 minutes later after taking contact with several daily hot objects (radiator, cup of coffee) since two years ago. Case 2: A 50-year-old woman, cook, who has no personal history. She presented self-limited erythema and cutaneous itch after sunbathing 9 months ago. She leaned on a hot rock then and weals appeared in back, which required oral ebastine and prednisone. Since then, she has a similar clinic when she contacts a heat source. Both tolerate sun exposure while they are walking, they also take antihistamines with partial response and avoid heat exposures as far as possible. In first case we value treatment with omalizumab. We carry out the following study: blood test, heat application at different temperatures in the forearm, intradermal reaction skin test with autologous serum at room temperature, 40 and 60°C, intradermal reaction skin test with methacholine, exercise test and visible light exposure.

Results: Results are shown in the Table 1.

Conclusions: (1) We report 2 cases of infrequent LHU in which we have found trigger umbral temperature and discarded other physical urticarias such as cholinergic and solar. (2) Due to profession of one the patients (cook), it could be considered as professional LHU and it could be included as professional dermatosis like other physical urticarias are.

Complementary tests		Case 1	Case 2
Blood test (hemogram, biochemistry, thyroid study, immunoglobulin profile, complement, ANA, tryptase)		Normal	Normal
Heat application (hot water tube at different temperatures) in the forearm during 5 minutes, with 10-minutes reading after removing	45° C	Positive	Positive
	40° C	Positive (UT)	Positive
	35° C	Negative	Positive (UT)
	30° C	Negative	Negative
IDR skin test with autologous serum at room temperature (during 24 hours), and 40 and 60°C (with room temperature during 20 minutes) with 1-hour and 24-hour reading	60° C	Positive	Positive
	40° C	Positive	Positive
	Room temperature	Negative	Negative
IDR skin test with methacholine	Negative	Negative	
Exercise test (static bicycle or march) during 20 minutes, with immediate reading and at 10 minutes after finishing	Negative	Negative	
Dermographism (blunt object skin application)	Negative	Negative	
Visible light exposure (5, 10 and 15 minutes), with immediate and late reading	Negative	Negative	

IDR, Intraderm reaction; UT, Umbral temperature.

1080 | Population-based age-adjusted incidence and prevalence of chronic urticaria in a united states locale

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Introduction: The Rochester Epidemiology Project (REP) is a unique research infrastructure system that links together nearly all of the medical and pharmacy records of the residents of Olmsted County, MN for approved medical research. This infrastructure makes it possible to conduct population-based descriptive, case-control, historical and prospective cohort, and cross-sectional research studies of most diseases and medical conditions. In recent years, the project has expanded the area over which the records linkage program extends, to the point that the project now encompasses 27 counties of southeast Minnesota, with almost a million population covered.

Objectives: To define the incidence and prevalence of chronic urticaria in a defined population.

Results: The overall prevalence of acute urticaria in this population for the time interval 1995-2015 was 17%, while the overall prevalence of chronic urticaria over the same time frame was 2.6%. Age-adjusted incidence graphs over this time interval will be presented. The incidence of chronic urticaria appeared to be rising over this time interval.

Conclusions: Previous studies of chronic urticaria incidence and prevalence have been difficult to accomplish, and in all other published instances have involved distribution of questionnaire instruments to a target population, with ascertainment based on relatively low response rates to the questionnaire, followed by extrapolations of difficult-to-define accuracy. A strength of the current study is that it provides comprehensive coverage of physician-level diagnostic information for a highly stable target population that is independent of any specific level of cooperation from the subjects included in the population. This study also highlights the need for change in the coding structures used for this diagnosis, since for quite some time in the American coding systems [ICD-9] the same codes were used for both acute and chronic urticaria.

1081 | Clinical presentation, classification and approach to angioedema in an emergency department: four years' retrospective study

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Introduction: Angioedema is an acute condition that can lead patients to the emergency department (ED). However, diagnostic and prognostic predictors are lacking.

Objectives: Assess clinical presentation, classification and management of all patients that attended the ED of a Central Hospital for angioedema and compare histamine-mediated(HMA) and non-histamine mediated(nHMA) angioedema.

Methods: A review of all ED episodes with diagnosis of angioneurotic edema (ICD-9 995.1), edema of larynx (ICD-9 478.6) and conjunctival edema(ICD-9 372.73) presenting to the Centro Hospitalar de São João ED between January 2012 to June 2016 was performed. Demographic and clinical characteristics and management approach were collected via a standardized form. Of the 355 ED episodes identified, 309 matched a clinical history of angioedema. Classification was performed accordingly to previous guidelines (*Cicardi et al*. Allergy 69 (2014) 602-6). Data is presented in % or median interquartile range. For comparison, patients were classified in HMA and nHMA angioedema. Chi-square test or Mann-Whitney U test used, as appropriate.

Results: Patients had a median age of 49[34;67] years, 59% female, 6% had asthma, 7% rhinosinusitis, 3% chronic urticaria, 4% history of oncologic and 8% of autoimmune disease. More than half were triaged as very urgent (*Manchester Triage System*). Regarding classification, most had acquired angioedema: 23% related to ACEI, 22% idiopathic histaminergic, 16% allergic and 13% idiopathic non histaminergic. Hereditary angioedema (HA) was present in 26 patients. Due to lack of data, 17% were not classified. Regarding presentation, 20% had associated respiratory symptoms, 11% urticaria and 8% abdominal pain (all with HA). Swelling affected the face in 42% of the patients, 47% lips, 20% the tongue,18% periorbital region, extremities and neck in 5% and pharyngo- laryngeal region affected in <3%. More than two thirds were treated with corticosteroids and antihistamines. Icatibant was used in 13 patients and C1 inhibitor in 22. Presentation with lips edema and concomitant presence of urticaria were significantly more frequent in HMA. Older age, neck involvement and abdominal pain were more frequent in nHMA ($P < 0.05$). Most of the patients were discharged, 10% were admitted (68% nHMA).

Conclusions: Clinical presentation, age, location of angioedema, differs between non-histamine and histamine mediated angioedema. This could be useful for predicting treatment and prognosis.

1082 | Synergistically expressed tissue factors on vascular endothelial cells by histamine and LPS trigger the extrinsic coagulation pathway followed by inter-cell gap formation

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Introduction: Chronic spontaneous urticaria (CSU) is a common skin disorder characterized by daily recurring skin edema and flare with itch. The increase of plasma histamine concentration and the effectiveness of histamine H_1-receptor antagonists suggests crucial role of histamine in the pathogenesis of CSU. Moreover, various plasma or endogenous factors have been identified to release histamine from basophils and/or mast cells. The involvement of the coagulation cascade, especially the extrinsic coagulation pathway, being triggered by the exposure of plasma to tissue factor (TF), has also been demonstrated in the pathogenesis of CSU by a number of observations. However, the mechanism of TF expression in CSU has not been clear. On the other hand, it has been suggested that infections by bacteria and/or virus may be complicated as an underlying cause in many cases of CSU.

Objectives: We here investigated the expression of TF by human endothelial cells in response to histamine and lipopolysaccharide (LPS), an agonist of toll-like receptor (TLR). We also evaluated the potential of histamine- and LPS-induced TF expression on the cells

for the activation of the extrinsic coagulation pathway and the increase of inter-cell gap formation.

Results: Histamine, either added at indicated concentrations or released from adjacent basophils by anti-IgE antibodies induced TF expression in synergy with LPS on human endothelial cells, via histamine H_1 receptor and TLR-4. This reaction produced thrombin (FIIa) in human plasma, which is cleaved from prothrombin by FVIIa and FXa in the cascade of the extrinsic coagulation pathway. Moreover, FXa and FIIa, but not FVIIa, induced contraction of HUVEC. Furthermore, the reactions were inhibited by an antagonist against protease activated receptors (PAR)-1. Finally, the expression of TF was terminated by the exposure to AMP or adenosine.

Conclusions: Thus, a small amount of histamine and LPS may induce the expression of TF by vascular endothelial cells, triggering the cascade of the extrinsic coagulation pathway followed by the increase of vascular permeability, and eventually induce robust degranulation of mast cells together with other plasma derived histamine releasing in CSU. Combined application of antagonists against histamine H_1 receptor, TLRs, PAR, adenosine receptors and/or inhibitors of activated coagulation factors, such as FXa, could be effective therapeutic measures for patients with severe and refractory CSU.

1083 | Major basophil chemotactic factor CCL2 is increased in chronic urticaria patients and correlates with basopenia

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Introduction: Chronic urticarial (CU) is associated with basopenia, but the underlying mechanism for reduced basophil numbers remains unknown. Our recent study indicates substantial reduction in circulating basophils during acute allergic reaction, which correlates with a significant increase in the major basophil chemotactic factor CCR2 ligand CCL2.

Objectives: The aim of our current study was to investigate relationship between CCL2 levels and basophil numbers in CU patients. To achieve this, concentration of CCL2 and absolute basophil count were measured in 64 patients with CU. Comparison group of 24 healthy controls was also included. CCL2 was determined with ELISA (R&D Systems, USA) and the absolute basophil count (CD123 + HLA-DR− cells) was determined with flow cytometry (BD, USA)

Results: Serum CCL2 concentration was significantly increased ($P = .0002$) in patients with CU (median 279 pg/mL) compared to healthy controls (median 191 pg/mL). A significant negative correlation ($r = -.24$, $P = .025$) between serum CCL2 concentration and the absolute number of circulating basophils was demonstrated.

Conclusions: Our study indicates increase in the level of major basophil chemotactic factor CCL2 in CU patients, which is associated with a decrease in the number of circulating basophils. CCL2-mediated migration may represent a mechanism for the selective migration of human basophils in CU. Additional studies will help clarify the importance of these observations.

1084 | Becoming chronic urticaria remission after the first injection of omalizumab

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Case report: The drug preparation *Omalizumab* initially designed to treat severe bronchial asthma, at the present time has been licensed for the therapy of chronic urticaria. The drug's mechanisms involved in that conditions, as well as urticaria forms where it proved to be effective, are intensely investigated. Cases of anaphylaxis in asthmatic patients and episodes with a lack of efficiency in patients with chronic urticarias were described before.

A case of patient K, male, 21 years old. The patient presented to the Allergy department in November 2014 for the aggravation of his chronic urticaria. It is seen from the medical history that skin eruptions started to emerge in early childhood, at the age of 4 years; the patient was followed with a diagnosis urticaria and Quincke's disease; the symptoms persisted until the age of 16. Then a spontaneous recovery occurred. The patient sought medical advice, allergy testing had been made with no underlying conditions revealed. The present aggravation started from the September 2014 with recurring of swellings and daily skin eruptions, mostly in the evening period, resolving within 24 hours. No relations with external triggers were observed. A general work-up were made with a conclusion: apparently healthy. Autologous serum test was positive.

The patient was diagnosed with recurrent angiooedema, moderate chronic urticaria.

After the patient informed consent was signed, a therapy with elevated dosing of *antihistamines* has been started (fexofenadine 180 mg 4 tab. a day), combined with H2-antihistamine and antileukotrienes (*Ranitidine* 150 mg and *Montelukast* 10 mg), in the course of the treatment pruritus (intensity of itch scored 4-5) and swelling in the face area persisted, rashes appeared every day. We attempted to replace the antihistamine preparation, with no therapy effects observed. In the backdrop of a marked aggravation of rashes in the course of the mentioned therapy, the patient was given *Metypred* 3 tab. a day for 3 days, with a moderate positive effect: swelling persisted but itch resolved.

The therapy with *Omalizumab* has been recommended to the patient; starting with 300 mL subcutaneous in the upper arm area.

The patient remained under medical supervision 30 minutes with no complications and no abnormalities at the injection site observed. Within four hours of the injection, the patient registered an intense exacerbation of rash, swelling in the face and hands areas and a

substantial itching. He sought medical advice. On presentation, his state was of moderate gravity, with swelling of the eyelids, lips, and hands areas, and an abundant hot pink confluent rash. There were wheals up to 3 cm in diameter, on body and limbs. Vital signs within normal limits. Swelling and rashes resolved on the therapy with system glucocorticosteroid preparations and antihistamines within 24 hours. No recurrent of rashes were observed hereafter; the patient kept to take antihistamine (*Loratadine* 40 mg daily). Two weeks on he by himself reduced the dosage to 20 mg and within a month discontinued the therapy. Until the present moment (for more than one year) the remission is preserved. Causes of the sharp exacerbation of rash and of the whole disease aggravation remained unclear; mechanisms of the complete remissions are to be investigated as well. The recovery was reached "through exacerbation"; it would not be correct to interpret that exacerbation as an allergy reaction.

1085 | Chronic urticaria difficult to treat

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Introduction: We present the case of a 38 year old woman, with urticarial repeated episodes from 2 years, that were initially amenable after therapy with antihistamines, but then they persist.

Objectives: We conducted allergy skin prick tests and we showed intense cutaneous sensitization to mites. It was tried therapy with high-dose antihistamines, but without effect.

Results: Therapy with Omalizumab 150 mg/month was initiated for six months with favorable evolution. Therapy was discontinued for two months, and symptoms were recurrent. It was then administered biological therapy with 75 mg/month for 2 months, but also with recurrent symptoms.

Conclusions: Currently the patient is under chronic biological therapy with 150 mg/month with favorable evolution.

1085A | Benefit from mepolizumab treatment in a patient with chronic spontaneous urticaria

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Case report: Mepolizumab is a humanized monoclonal antibody directed against IL-5, and is licensed for the treatment of severe asthma in patients aged ≥12 years (EU only adults) with an eosinophilic phenotype as an add-on treatment. Here, we report the case of a 27 year old woman with severe refractory eosinophilic asthma, who was treated successfully with 100 mg mepolizumab every 4 weeks. The asthma control test (ACT) increased from 13 points before treatment to 23 points 4 weeks after the first injection of mepolizumab, further improving to the maximum possible 25 points another 8 weeks later, showing a complete control of her asthma. At the first visit in our clinic, the patient reported to also suffer from recurring wheal and flare-type skin reactions for several years, and chronic spontaneous urticaria (CSU) was diagnosed. The patient reported that her CSU symptoms were periodically triggered by infections and have been treated with antihistamines, with only limited effect. Despite treatment with antihistamines, the CSU episodes led invariably to sick leaves for at least two weeks, indicating a very poorly controlled urticaria. From the day after the onset of treatment with mepolizumab, the patient reported a dramatic and sustained improvement of her urticarial symptoms, both, the spontaneous wheals as well as the infection-triggered episodes. Four weeks after the first injection, the urticaria control test (UCT) was 12, indicating a well-controlled urticaria. The UCT ranges from 0 (no control at all) to 16 (complete control), a score of 12 or higher indicates controlled disease. Another 8 weeks later, the UCT was 16, and the patient reported about an ongoing and complete absence of the urticarial lesions, despite several infectious episodes during the winter time. Interestingly, a mild acne in the face improved under treatment with mepolizumab, too.

To our knowledge, this is the first report of a therapeutic response to mepolizumab in a patient with CSU. Interestingly, the number of eosinophils in the skin of CSU patients has recently been reported to be higher than in healthy controls, and eosinophils have been proposed to contribute to the pathogenesis of CSU. Our findings call for further studies of the role of IL-5 and eosinophils in chronic urticaria.

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TPS 35
IMMUNODEFICIENCY

1086 | Immunological deficits in children with recurrent pneumonia

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Introduction: As a part of routine diagnostics performed at our Department, most of the children submitted to immunophenotyping are suspected of having primary immunodeficiency. These immune disorders characterized by the loss of innate and/or adaptive immune system might account for recurrent pneumonia, defined as two or more episodes of pneumonia in a six-month period or tree or more episodes in a lifetime. The aim of this study was to evaluate if a partial or a complete lymphocyte deficit is seen in children with recurrent pneumonia received at our Hospital.

Objectives: Flow cytometry-based immunophenotyping of peripheral blood was performed in children suffering from recurrent pneumonia, and screened for T cells, NK cells, B cells (our basic panel) as well as for the eight B cell subpopulations (expanded panel). A retrospective study of the immunophenotyping analyses performed within one year involved 22 patients (age 3-13, both sexes equally represented) and the results were summarized according to the corresponding referent age values.

Results: Fourteen patients had a decreased number of double-negative B cell subset, nine had a decrease of plasmablasts, and six patients were deficient in the switched memory B-cell subpopulation, as compared to the reference values of their respective age. In some patients, an increase of naive (4 patients), transitional (4 patients) and non-switched (4 patients) B cell subsets was present. Furthermore, among the T lymphocyte population, activated T lymphocytes (mainly involving CD8 T cells) showed an increased frequency (5 patients), while both an increase (2 patients) and a decrease (2 patients) was noticed in the NK-cell population.

Conclusions: Immunophenotyping by flow cytometry remains a valuable and indicative method for the diagnosis and monitoring of primary immunodeficiency in children affected by recurrent pneumonia. As suspected, most patients presented with a deficit of the B-cell population, namely terminally differentiated B-cell subsets, while the accumulation of less differentiated B-cell subsets was pronounced. This immunologic pattern reflects a defective progression of the B-cell differentiation process and implies a genetic mutation as an underlying mechanism of the immunodeficiency disease. Therefore, these patients qualify as candidates for the genetic analysis by the next generation sequencing technique that is being introduced at our Department as an inevitable part of translational and clinical research.

1087 | Clinical phenotypes associated with common variable immunodeficiency (CVID)

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Introduction: Common Variable Immunodeficiency (CVID) is a polymorphic disorder characterized by low serum levels of immunoglobulin (IgG, IgM and IgA) that causes recurrent infections, autoimmune diseases and an increased risk of hematologic and solid cancer.

Objectives: We tried to identify common phenotypes associated with this disorder to better define and manage clinical manifestations and complications. We retrospectively analysed 40 patients (27 male and 13 female) with diagnosis of CVID, according to ESID criteria. We divided them in five categories according to clinical presentation: infection only (I), polyclonal lymphoproliferation (L), autoimmunity and cytopenia (A), enteropathy (E), solid or hematologic neoplasia (N). Some patients presented with overlap-manifestations.

Results: The most common phenotype was the I (40%), followed by the phenotype A (35%) and E (20%). 17% of patients presented with overlap phenotype. In the 80% of the patients with N phenotype an autoimmune disorder recurred. We also identified some peculiar differences between the five phenotypes: the onset of CVID was early in the N phenotype; splenomegaly and splenectomy were more commons in the A phenotype; bronchiectasis affected especially the patients with phenotypes I or A (increasing their mortality); chronic lung disease were more represented in the patients with overlap features. Finally we observed that the N phenotype was characterized by an higher mortality (RR 14).

Conclusions: CVID is a very heterogeneous disease which presents a great variability of clinical presentation. Several phenotypes may be associated with the disorder, with the I and A type being the most represented. Bronchiectasis are present in half of affected patients. Moreover, each different phenotype presents a different mortality risk and this confirms the importance of an accurate diagnosis, since early Ig replacement therapy could prevent further complications.

1088 | 20% subcutaneous immunoglobulin (20%SCIg): long-term evaluation in a population of adult patients with CVID

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Introduction: Common variable immunodeficiency is the most frequent symptomatic immunodeficiency of the adulthood characterized by low level of serum immunoglobulin, recurrent infections and others complications. Treatment is based on replacement therapy with immunoglobulin administered by the intravenous or the subcutaneous route.

Objectives: The aim of our study was to evaluate in a real-life population of patients with CVID the efficacy, safety of treatment with 20% SCIg (Hizentra ®) during a mean follow-up period of 30 months. We enrolled a cohort of 16 adult patients with CVID, diagnosed according to ESID criteria. They were 10 females and 6 males with a mean age at diagnosis of 40 years. 20%SCIg was administered every 7 days changing every time the site of administration. The median dose of Hizentra administered was 0.15 g/kg/injection. In each patients we collected data about efficacy, reporting annual infections rate and severity of infections described and IgG serum levels; safety, registering the presence of adverse reactions and type of reactions and. A specifically designed questionnaire evaluated the satisfaction of patient with the treatment

Results: No patient withdrawn the treatment. All patient achieved and maintained protective serum IgG levels (median 780 mg/dl). No severe bacterial infections were observed during the follow-up period. Despite the achievement of IgG protective levels, one patient (M/46 years-old) still presented recurrent pneumonia. We thus introduced antibiotic prophylaxis with macrolide, with benefit. We documented an yearly rate <2 of mild infections, especially at the upper respiratory tract. No systemic adverse reactions to SCIg were observed. We documented local reactions on infusion site (swelling in the injections sites, redness) without pain, especially during the first infusions, which gradually disappeared subsequently. Treatment was well-tolerated. Using the semi-quantitative Likert scale, we documented patients' satisfaction with treatment mostly related to contact with health professionals and administration modalities. All patients preferred also the subcutaneous route of administration to the intravenous one, with several advantages reported: no need of venous access, no need of hospitalization, home-self administration, increased independency and less interference with social and familiar life.

Conclusions: Our data reported the efficacy, safety and tolerability of 20% SCIg in patients with CVID during a long-term period.

1090 | Cytomegalovirus infection in a patient with leukocyte adhesion deficiency type 1

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Case Report: Leukocyte adhesion deficiency type 1 (LAD-1) is a rare autosomal recessive immunodeficiency disorder, characterized by recurrent bacterial and fungal infections without pus formation. Herein, we represent an 11-year-old girl with the chief complaint of periumbilical abdominal pain, nausea, vomiting, and bloody diarrhea since three months, who was born to first cousins consanguine parents. The diagnosis of LAD-1 was made at 2 months of age. There was a family history of LAD-1 in her sibling who died in 11th year of life with the diagnosis of intestinal non-Hodgkin lymphoma. On physical examination, generalized abdominal tenderness was noted which was most marked in the periumbilical region. Abdominal X-ray showed minor dilatation of small intestine loops and horizontal colon. Abdominopelvic ultrasonography demonstrated increased thickness of right intestinal loops. On the suspicion of inflammatory bowel disease, mesalazine (Pentasa), albumin infusions, as well as the intravenous (IV) antibiotic in the form of amikacin were initiated. She received blood transfusion as well. Subsequently, laboratory data showed WBC of 96600/mm^3, hemoglobin of 8.4 mg/dL, hematocrit of 27.6%, RBC count of $3.66 \times 10^6/mm^3$ (normal range: 4.0-4.9 $\times$ $10^6/mm^3$), mean corpuscular volume (MCV) of 75.4 fL (normal range: 72.7-86.5 fL), and platelet count of 203000/mm^3. The patient's symptoms continued. Her antibiotic regimen was substituted by the combination of metronidazole, vancomycin and amikacin on the 7th day. Five days later, the patient developed fever, and intravenous immunoglobulin (IVIG) replacement was commenced, consequently. In addition, IV antibiotics in the form of ciprofloxacin, vancomycin and meropenem were started. On investigation, the hemoglobin level of 7.4 mg/dL, platelet count of 395000/mm^3, and total leukocyte count of 8600/mm^3 were reported. Her ESR was 142 mm/h and the CRP level was 111 mg/L. The endoscopic examination of the gastrointestinal tract was performed, through which, mild to moderate esophagitis, moderate gastritis, moderate duodenitis, together with erosive colitis were reported. CMV IgG as well as the herpes simplex virus 1 (HSV-1) IgG were found to be positive (their levels were 100 U/mL, normal range < 14, and 36.9 U/mL, normal range < 1.1, respectively), while the CMV IgM was shown to be negative. CMV polymerase chain reaction (PCR) was also positive in the colonic biopsy specimens. Subsequently, a diagnosis of CMV infection with LAD-1 was made. IV ganciclovir was added in view of

the aforementioned results. The child recovered in a 4-week period and the condition was established by the negative CMV PCR in the colonic biopsy specimens and was asymptomatic for 6 months.

Our case underscores the importance of exploring the possibility of gastrointestinal CMV infection as a possible complication in LAD-1 patients with obvious gastrointestinal manifestations. Development of CMV infection in LAD patients could provide insight into the probable role of β2 integrins in the host immunity against viral infections.

Table 1 Initial laboratory data

Laboratory test	Reported values	Reference values
Complete blood count		
WBC/mm^3	104200	4700-10300
Neutrophils (%)	76	33-61
Lymphocytes (%)	10	28-48
Band cells (%)	14	0-11
Hemoglobin (mg/dL)	6.6	10.9-13.3
Hematocrit (%)	22.2	33.0-39.6
Platelet count/mm^3	298000	183-369
Liver function tests		
AST (U/L)	11	8-50
ALT (U/L)	5	7-45
Alkaline phosphatase (U/L)	409	115-437
Albumin (g/dL)	2.5	3.7-5.6
Stool analysis		
Ova	Not seen	Not present
Parasites	Not seen	Not present
WBC	18-20	Not present
RBC	8-10	Not present
Calprotectin	20	0.1-15
Stool culture	Negative	
Other tests		
Serum total protein (g/dL)	7.8	5.9-8
ESR (mm/h)	142	1-8
CRP (mg/L)	122	0-10
Amylase (U/L)	25	23-85
Lipase (U/L)	10	0-160
Urinary sediment	Inactive	
Urine culture	Negative	
Rapid urease test	Positive	
Histopathologic examination of the gastric mucosa	Peptic ulcer with the aggregation of lymphoid follicles	

Abbreviations used: WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; RBC, red blood cells; ESR, erythrocyte sedimentation rate; h, hour; CRP, C-reactive protein.

1091 | Hereditary angioedema laryngeal attacks: Report from the Czech national registry

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Introduction: Hereditary angioedema (HAE) is a rare, autosomal dominant disorder characterized by recurrent attacks of subcutaneous or sub-mucosal oedema. Symptoms are extremely variable in frequency, localization and severity. Laryngeal attacks are potentially life threatening, the patients are at risk of suffocation during the attack.

Objectives: The goal of this study was to analyse laryngeal attacks in the Czech Republic (CR) between March 2012 to December 2016. Data were collected from the Czech National Registry of Primary Immunodeficiencies.

Results: The data of 150 HAE patients (81 females, 69 males, 130 with type I HAE; 20 with type II HAE) were available. 220 (142 in HAE type I patients, 78 in HAE type II patients) laryngeal attacks in 41 patients (23 females, 18 males; 34 patients with HAE type I patients, 7 patients with HAE type II) were recorded. There was no significant difference in laryngeal attack frequency between HAE type I and type II (P = .4256, Fischer's exact test). The triggering factors described by the patients included infection in 12 (5.5%) attacks, stress in 11 (5%) attacks, injury in 10 (4.6%) attacks and menstruation in 3 (1.4%) attacks. In 180 attacks (82.2%), the triggering factor was not identified. Prodromal symptoms (most often erythema marginatum or weakness) were reported in 21 (9.6%) attacks. 170 (77.6%) of laryngeal attacks were treated with icatibant, 35 (16.0%) with recombinant C1-INH, 11 (5%) plasma derived, highly purified, nanofiltered C1 inhibitor, 1 (0.5%) with plasma derived, nanofiltered C1 inhibitor and 2 (0.9%) by increase in androgens dose. Treatment had to be repeated in 32 attacks (14.6%). The drug was self-administered in 169 (77.2%) attacks, 40 (18.3) attacks were treated in the emergency, 4 (1.8%) attacks were treated in GP's or local hospital and only 4 (1.8%) attacks were treated in HAE centre. Hospitalization was necessary in 4 (1.8%) attacks, in intensive care unit in 2 attacks (0.9%), Emergency medical service (EMS) was used in 5 attacks (2.3%). No patient died in consequence of the attack.

Conclusions: Although laryngeal attacks are a life-threatening condition in HAE, no death as a consequence of the attack was recorded in CR in the follow-up period. More than ¾ attacks were

treated by well-trained patients, hospitalisation was almost exceptional. Modern treatment and adequate training may prevent fatal consequences of this still life threatening HAE complication.

1092 | Severe congenital neutropenia: two case reports and literature review in Vietnamese patients

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Case report: Background: Severe congenital neutropenia (SCN) is a genetically heterogeneous immunodeficiency disease characterized low blood neutrophils counts, early bacterial infections, and risk of leukaemia development. SCN is associated with mutations of ELANE (ELA2), HAX1, GFI1, WAS, CSF3R or G6PC3.

Case presentations: We report an 6- month-old boy who was admitted due to severe abscess in his left leg. His medical report has showed severe neutropenia (neutrophils count below 0.5G/l) since after birth and he was misdiagnosed with myelodysplastic syndrome. Mutation analysis revealed ELANE gene mutation within Exon 3 at nucleotide position 301 (c.301G>A), resulting change of the 101 codon (Valine to Methionine), which has been reported to cause severe neutropenia. The second case of 5-year-old male presented with necrotizing abscess in his scalp. His past medical history showed recurrent infections (pneumonia, mastoiditis otitis, perianal abscess) from 7 months of age with severe neutropenia (neutrophils count always below 1G/l) for many times. He also has physical and mental retardation. His bone marrow showed maturation arrest of granulopoiesis at the promyelocyte stage. Family history revealed an older brother died of septicemia and another older sister died of meningitis in childhood. Genetic analysis of this second patient is pending. Both patients were treated with wide-spectrum antibiotics and granulocyte colony stimulating factor (G-CSF) with dose 5mcg/kg/day. Hematopoietic stem cell transplantation are considering in the first case.

Conclusions: In Vietnam, infectious diseases are the most common disease which cause fatal for children under 5 years old. Patients with primary immunodeficiency disease, including severe congenital neutropenia are usually misdiagnosed; therefore they died due to severe infections. Our report aims to increase the awareness of Vietnamese doctors about primary immunodeficiency disease.

1094 | A report of two new mutations in RAG1 and ADA genes in severe combined immunodeficiency disease

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Introduction: Severe combined immunodeficiency (SCID) is a rare heterogeneous group of primary immunodeficiency disease (PID), caused by different genetic mutations. At least fourteen genes have been known as responsible genes for SCID including interleukin-7 receptor-a (IL-7Ra), recombination-activating gene 1 (RAG1), recombination-activating gene 2 (RAG2), and adenosine deaminase (ADA). In this study, we investigated two gene mutations in five infants suspected to PID who referred to Immunology, Asthma and Allergy Research Institute (IAARI) between March 2012 and January 2017.

Objectives: Following observations of complete immunological evaluation results and clinical features of five patients and taking informed consent, genomic DNA was extracted from EDTA-whole blood samples of patients and their parents. Based on immunophenotyping results, exon-intron regions of target genes were amplified by polymerase change reaction (PCR) technique, and PCR products were analyzed by direct sequencing method.

Results: Sequencing results revealed three reported homozygous mutations including one frame shift mutation in exon 3 (c.361dup A) besides one substitution mutation in splicing site in exon 4 of IL-7Ra gene (c.534 + 1 G>A), and one missense mutation in exon 5 of RAG1 gene (c.2570 C>A). Two new mutations were also found; one substitution mutation in exon 7 of ADA gene (c.778 G>C) and one deletion mutation in RAG1 gene (c.834 C del). Heterogeneous results were confirmed in parents.

Conclusions: Genetic diagnosis is necessary for definitive diagnosis of PID patients which could help physicians to move towards their appropriate treatments and approaches such as gene therapy. Moreover, identifying mutated genes could be also effective for prenatal and early diagnosis of other family members.

1095 | Situation of care for patients with systemic autoinflammatory diseases - results of an expert survey

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Introduction: Systemic autoinflammatory diseases (sAIDs) are rare debilitating disorders with limited awareness, significant delay in diagnosis and high morbidity. Most patients are seen in specialized expert centers. Due to a lack in standardized management guidelines, there is currently no uniform approach in diagnosis and treatment of these disorders and the real life situation of sAID patient care is ill characterized.

Objectives: In this cross-sectional study we consulted 123 university departments of dermatology, pediatrics, rheumatology and other sAID expert centers in German-speaking countries regarding the epidemiology, situation of care and perception of their sAID patients.

Results: A total of 35 centers participated in the survey and completed the questionnaires. Most centers managed both adult and pediatric patients with a variety of monogenic and acquired sAIDs. For well-characterized monogenic sAIDs such as Cryopyrin-associated periodic syndrome and Familial Mediterranean fever, the diagnostic and treatment strategies were similar between the centers and included inflammation markers and genetic testing as well as IL-1 blockers and colchicine as first line treatment. For multifactorial sAIDs, we observed great heterogeneity in diagnostic and therapeutic approaches. As a major unmet need, diagnostic delay was identified with a mean time to diagnosis between 1 and 10 years. The overall situation of care for sAID patients was rated to be excellent or good by only 13% of centers, and to be poor or non-sufficient by 39% of centers.

Conclusions: This study demonstrates a high need to improve the situation of care and to harmonize diagnostic and treatment strategies for sAID patients.

1096 | Nutritional and bone mineral density state in patients with primary immunodeficiencies

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Introduction: In humoral primary immunodeficiencies (PID) recurrent respiratory infections (RRI) are a major cause of morbidity and mortality, despite appropriate immunoglobulin replacement therapy. In these patients, the chronic inflammatory state (IS) represents a potential risk factor for osteoporosis and malnutrition (MN). Furthermore an unhealthy dietary pattern may contribute to IS and worsen potentially alterations of bone mineral density (BMD).

Objectives: The aim of this study is to investigate potential MN state and BMD alterations in pediatric patients with PID and to evaluate possible association between IS markers, BMD alterations and dietary pattern.

Results: We evaluated 13 children divided into two groups (7 patients with Agammaglobulinemia X linked or Common variable immunodeficiency and 6 controls) and we assessed their nutritional status by measuring BMI, body circumferences (arm, wrist, waist, hips), body fat % (BF %) through the thickness of the body skinfold, and impact of adhering to a Mediterranean diet (MD) through the KIDMED score. We also determined inflammatory biomarkers (IL1, IL6, IL10 and TNFα) through a multiplex based flow cytometric assay, and the number of respiratory infections during the last year. We finally assessed BMD through dual energy X-ray absorptiometry scan.

The PID group vs CS was characterized by: age 8.6 $\pm$ 4.2 years *vs* 6.8 $\pm$ 2.1 years; no RRI 38.3 $\pm$ 7.5 *vs* 4.63 $\pm$ 6.12 ($P < .001$); TNFα 13.04 $\pm$ 6.9 vs 0.1 $\pm$ 0.3 ($P < .001$); IL1β 0.87 $\pm$ 2.45 vs 0 ($P = .300$); IL6 13.9 $\pm$ 39.54 vs 0($P = .030$); IL10 4.6 $\pm$ 2.9 vs 0 ($P = .001$); BMD: Z score L1-L4 -.035 $\pm$ 1.55 vs -0.113 ± 1.24 ($P = .742$); BMI 18.8 $\pm$ 2.9 kg/m2 vs 19 $\pm$ 2 kg/m2; BF% 22.66 $\pm$ 7.8% vs 23.7 $\pm$ 9.2% ($P = .248$); KIDMED 7.8 $\pm$ 2.6 vs 6 $\pm$ 2.5 ($P = .248$); with regard to the body circumferences, there were no differences between the two groups.

Conclusions: Appropriate immunoglobulin replacement therapy, according to international guidelines, and good adherence to the MD could explain the balance between pro (IL6 and TNFa) and anti inflammatory (IL10) cytokine levels, the normality of BMD and the absence of differences in the nutritional state between the two groups, despite a statistically significant difference of the RRI episodes. The extention of the study with a larger population could confirm this hypothesis and investigate possible predictors of the risk of malnutrition and bone alterations in adults.

1097 | Adenosine deaminase severe combined immunodeficiency (ADA-SCID): Profile of efficacy and safety in long-term peg-ada replacement therapy

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Introduction: Adenosine deaminase (ADA) deficiency is a rare, autosomal-recessive systemic disorder of purine metabolism characterized by severe combined immunodeficiency (SCID). Mutations in

the ADA gene are responsible of elevated serum and urinary concentrations of adenosine metabolites that impair lymphocyte differentiation and function. This disorder occurs in 1 in 200 000 to 1 000 000 newborns worldwide and it is responsible for approximately 15% of SCID cases. Patients with ADA-SCID have lymphopenia, failure to thrive and recurrent, opportunistic infections, potentially fatal if not promptly treated. Three therapeutic options are available: hematopoietic stem cell transplantation (SCT) from an allogeneic HLA-compatible sibling donor, enzyme replacement therapy (ERT) with polyethylene glycol-modified bovine adenosine deaminase (PEG-ADA) and more recently gene therapy (GT).

Objectives: In the past 3 decades, PEG-ADA replacement therapy has been the alternative therapeutic option to SCT when compatible sibling donor is not available. ERT allows a rapid normalization of immune system function and prevents systemic metabolic manifestations due to the accumulation of adenosine metabolites. The limitations of PEG-ADA therapy include primary failure to recover protective immune function, the development of neutralizing antibodies that reduce efficacy, immune dysregulation, development of lymphoproliferative disorders. The aim of this study is to describe the efficacy and safety of long-term PEG-ADA therapy in 2 patients diagnosed with ADA-SCID.

Results: Two siblings diagnosed with late onset ADA-SCID (respectively at age 4 and 1) at Pediatric Department of Policlinico Umberto I (Rome) undergone ERT for 6 years. ERT efficacy was proven by a dramatic improvement in immunologic parameters with a marked increase in immunoglobulin concentration and lymphocyte count after three weeks of therapy. Assays for immunoglobulin concentration, lymphocyte subsets, urinary metabolites (Ado, dAdo), yearly performed, showed normal results to date. Therapy was associated with a reduction in infections without development of autoimmune or lymphoproliferative disorders.

Conclusions: PEG-ADA therapy showed a long-term efficacy and safety in 2 siblings diagnosed with ADA-SCID. A 6 year follow up showed a stable immune reconstitution, persistent reduction of infections, no systemic complications. ERT can therefore be considered a valuable alternative option when curative HSCT is not possible.

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LESSONS FROM SOCIETY AND PATIENTS

1104 | The association between perceived immune status, general health, and well-being

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Introduction: As several diseases and illnesses are related to deficiencies in immune system functioning, it is suggested that perceived immune functioning may be closely related to various general health outcomes, and may thus have an impact on daily functioning and mood.

Objectives: The purpose of this study was to examine the relationship between perceived immune function, general health, daily functioning, and well-being in young adults.

N = 2489 Dutch students (16.8% men, mean ± SD age 21.2 ± 2.1 years old) completed an online survey. To assess general health status, the Short-Form General Health Survey (SF-20) was completed. The SF-20 has six subscales, measuring physical functioning, daily functioning, social functioning, psychological functioning, perceived health, and physical pain. The WHO-5 Well-Being Index is a questionnaire consisting of 5 non-invasive questions, and was completed as measure of psychological well-being. Perceived immune functioning was rated on a scale ranging from 0 (very poor) to 10 (excellent).

Results: Perceived immune functioning correlated significantly with subscales on physical functioning ($r = -.253$, $P = .000$), daily functioning ($r = -.254$, $P = .0001$), social functioning ($r = .360$, $P = .0001$), psychological functioning ($r = .196$, $P = .0001$), perceived health ($r = .514$, $P = .0001$), and physical pain ($r = -.276$, $P = .0001$), as well as the WHO-5 Well-Being Index ($r = -.244$, $P = .0001$).

Conclusions: Significant associations were observed between perceived immune function, general health, daily functioning, and well-being.

1105 | Twitter use during the Spanish allergy and clinical immunology society annual meetings (2013-2016)

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Introduction: Twitter™ is a popular social media platform. It has been documented to be a useful tool for engaging attendants of medical conferences into conversation. There is no information available on its utility for European allergists. We have studied the twitter activity generated during the Spanish Allergy and Clinical Immunology Society (SEAIC) annual meetings from 2013 to 2016.

Objectives: A prospective, observational study was performed, including all the tweets published under the official hashtags for the 2013-2016 SEAIC meetings. Tweet transcripts, participating users, tweets per user and impressions were recorded from the Symplur database. Tweets were analysed and categorized based on their content. Users were identified and categorized as physicians, nurses, patients, pharmaceutical companies, organizations, SEAIC members and congress delegates. Demographic information was taken from twitter profiles.

Results: A total of 11578 tweets were published by 476 unique users. The number of participants in the conferences via twitter increased from 198 in 2013 to 741 in 2014, 3016 in 2015 and 7623 in 2016. The growth of twitter users went from 32 in 2013, to 105 in 2014, 108 in 2015 and 342 in 2016. Tweets contained more frequently logistical information in 2013 (67%) and 2014 (47.8%), while scientific session-related messages were posted more often in 2014 (70.5%) and 2016 (72.1%). Organizations were responsible for most of the tweets in 2013 (50.5%), and physicians led participation from 2014 and on, up to 86.7% in 2016. Congress delegates and SEAIC members represented always less than 40% of the participants. Up to 5% of the tweets were generated by non-Spanish users in 2016.

Conclusions: Twitter has demonstrated its usefulness as a live-communication tool during a national Allergy meeting. Its use has increased dramatically in the last four years. A small number of participants can publish a number of tweets enough to reach a large audience, even crossing the national borders. Spanish allergists have progressively become aware of all these opportunities.

1106 | Online microblogging providing information dissemination of anticholinergic therapy in asthma

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Introduction: The inhaled anticholinergic tiotropium by soft mist inhaler (SMI) is approved by EU and US regulatory authorities, and is the only long-acting muscarinic antagonist recommended by recent GINA updates, as add-on asthma therapy for adults or adolescents. Online microblogging allows users to update condensed information

in informative platforms with the potential of continuous medical awareness for asthma.

Objectives: In order to assess information dissemination regarding anticholinergic therapy in asthma on a free popular online microblogging platform, as the study objective, a detailed search of the Twitter social network and a parallel literature search in the Pubmed database of citations for biomedical literature were conducted in January 2017, for the previous three years, using three lexical items: 'Asthma' and 'Tiotropium' and the registered trademark name of the only SMI available for use in asthma. Content analysis of the shared short messages of up to 140 characters called tweets and of the accounts which posted them was also carried out.

Results: A number of 232 tweets detected were analysed: 40.95% posted in 2014 (the year in which tiotropium SMI in asthma has been accepted by EU regulatory authority), 38.79% in 2015, and 20.26% in 2016. Tweets were posted on various accounts: 37.5% specialists, academic physicians, recognized experts or editors of medical journals, 31.47% health care or biotechnology news, 15.08% patients, family members and other individual bloggers or patient support organizations, 9.05% health institutions/organizations or professional medical societies, and 6.9% company-sponsored accounts. 34.91% of tweets announced the indication for tiotropium SMI in asthma and its acceptance by official regulatory authorities, 31.03% of tweets contained citations of clinical studies with results published in medical journals, 27.16% of tweets contained direct links to clinical studies in bibliographic databases, while few consisted in other comments or opinions. All 15 randomized clinical trials and 2 meta-analysis regarding tiotropium SMI in asthma, published between 2014-1016 and identified by the computerized literature search of the electronic database PubMed, are cited as direct links in tweets posted in that period.

Conclusions: Twitter online microblogging platform targeted search and its responsible use may provide near real-time communication of updated information and concise quality scientific data dissemination regarding anticholinergic therapy in asthma.

1108 | Similarities and differences between dog and cat allergy. The quasar group. pet-all project

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Introduction: To develop a consensus document including a set of recommendations based on the available evidence and on the experience of clinical experts in allergy to dog and/or cat. This part is focusing on differences in several aspects of cat or dog allergy.

Objectives: Consensus was developed according to RAND/UCLA methodology. Literature review and list of indications were sent to members of panel. Panelists rated each of indications twice, in a two-round "modified Delphi" process. In first round ratings were made individually at home, without interaction among panelists. In second round, panel members met for 2 days under the leadership of a moderator experienced in using the method. Consensus agreement: ≥80% of the expert panel agreed. Discrepancy: When <80% of the expert panel agreed. Levels of evidence according to the OCEBM Levels of Evidence Working Group.

Results: *Course of Illness*: Cat exposure is associated to higher levels of IgE at two years of age and to lower risk of sensitization to household allergens at 8 years while dog exposure was not significantly associated with IgE levels or sensitization. (NE:1)*Atopic dermatitis:* No protective effect or increased incidence of atopic dermatitis in children exposed to cats. Exposure to dogs from birth does not increase the risk of atopic dermatitis.(NE: 1). Regarding remission of atopic dermatitis, it has not been demonstrated a protective effect of exposure to cat or dogs. (NE: 5) *Exposure:* patients allergic to cats exposed to several cats and concentration of Fel d 1 greater than 44 micrograms per gram of powder can tolerate the presence of animals. (NE:5). No such data are available in dog allergy. *Associated syndromes:* Cat-pig syndrome: patients sensitized to cat allergens present symptoms of IgE-mediated anaphylaxis after ingestion of pork(NE: 4); sensitization to Can f 5 has been related to sensitization to human seminal plasma. (NE: 4) *Hypoallergenic animals*: Genetically modified cats exist whilst we are not aware of the existence of genetically modified dogs. There is no scientific evidence to support naming "hypoallergenic" to a particular breed of dog or cat. (NE:5)

Conclusions: Some differences do exist between dog and cat sensitization, with different influences on other allergic diseases.

1110 | Allergodermia and other related obsolete terms improperly used for various skin disorders

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Introduction: Although the diagnosis of 'allergodermia' does not exist in the tabular list of the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, in use in Romania, nor in the EAACI and WAO current nomenclature, some primary care physicians improperly use it in our country. Moreover, it is not lexicographically present in Romanian language dictionaries.

Objectives: The study objective was to assess the inaccurate use of allergodermia and related terms for various cutaneous disorders. A literature search in the Pubmed database, comprising more than 26

million citations for biomedical literature from the premier bibliographic database of the U.S. National Library of Medicine, life science journals, and online books, was performed in January 2017 using the following terms: 'allergodermia' or 'allergodermias' or 'allergoderma' or 'alergodermie'. A search in the medical records of our allergy clinic in a six-month period in 2016 was also conducted to select cases in which the referral notes from the family doctor used the diagnosis of 'alergodermie' and a correlation was made with the diagnosis mentioned in the structured allergy consultant reply letters.

Results: In the literature search, the term 'allergoderma' was found in only two articles (one in German and English, 1959; one in French language, 1967) referring to severe bullous skin conditions. We identified the terms 'allergodermia' or 'allergodermias' in four non-English language articles published more than four decades ago (Serbian, 1954; German, 1959, 1960, 1968), and the term 'alergodermie' in one Romanian article from 1985, referring to drug-induced generalized dermatitis. The assessment of selected patient records from our clinic revealed that the diagnosis of 'alergodermie' was improperly used by general practitioners in 21 referral notes for the following conditions: chronic spontaneous urticaria with or without associated angioedema, physical urticaria or cholinergic urticaria (57.14%), drug-induced urticaria and/or angioedema (23.81%), contact dermatitis, facial dermatitis or ocular allergy (19.05%), according to the allergy specialist diagnosis.

Conclusions: Some primary care physicians still persist in using the very old and obsolete term of allergodermia. The practice of using such inaccurate terminology, constituting an obstacle to medical communication, is confusing and deplored, and must be combated through educational actions.

1111 | Not every syncope is allergy - false labelling of patients as drug hypersensitive

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Case report: Background: The diagnosis of anaphylaxis is challenging as is based on probability and pattern recognition. Therefore, when signs or symptoms are incorrectly interpreted as an allergic reaction, patients are at risk of being erroneously labelled as allergic. Non-steroidal anti-inflammatory drugs (NSAID) are reported to be one of the most common causes of drug hypersensitivity, being oral provocation challenges the gold-standard for its diagnosis.

Objective: To describe a case where a precise diagnostic work-up was essential to solve a wrongly labelled drug hypersensitive patient.

Case report: Female, 43 years old, teacher, living in the south of Portugal, with previous history of allergic mild intermittent rhinitis with pollen sensitization and mild protein S deficiency was admitted in our outpatient clinic in 2016. She reported two episodes, in 2007, of syncope that occurred after standing up after a night sleep. In the first she took ibuprofen 6 hours before for a headache and in the second she was prescribed with paracetamol for a viral infection. The patient did not remember any other associated symptoms. By that time, there were performed intradermal test with acetylsalicylic acid that revealed a positive result and the patient was labelled as aspirin allergic. Due to the need of being treated with aspirin, the patient was admitted, later, in our department to aspirin desensitization protocol. Results of our diagnostic work-up were: normal physical exam, normal results also for laboratory analysis, electrocardiogram, exercise electrocardiogram and echocardiogram. Oral provocation challenges with paracetamol, ibuprofen and aspirin were performed according to EAACI/ENDA guidelines and were all negative. Due to tests results and the unprecise clinical history, the patient also made a Tilt table test which diagnosed a neurocardiogenic syncope.

Conclusion: Intradermal skin testing with aspirin can be associated with false positive results. This report is an example where a detailed diagnostic work-up can remove a false label of drug hypersensitivity and that differential diagnosis of anaphylaxis should always be considered when the clinical history is not strongly suggestive.

1113 | Protective and anti-inflammatory effect of resveratrol in right ventricle failure

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Introduction: Right ventricle failure is a status that occurs, when the heart can't maintain it's pump function and deliver enough blood to the lung arteries. Resveratrol is a non-flavonoid polyphenol, found in plants. Previous studies showed its positive effect on cardiovascular system, and inflammation. The mitochondria have a big role in inflammation, and it's membrane's injury can result the development and progression of several diseases, like pulmonary hypertension causing right ventricle heart disease, and also other illnesses caused by oxidative stress.

Objectives: The aim of the experiment was to prove the anti-inflammatory effect of resveratrol in heart muscles and mitochondria protecting effect.

Methods: The induction of pulmonary hypertension (PH) was carried out by monocrotaline subcutan injection which resulted in right heart failure. Male Wistar rats were randomized into four groups:

1. control (0.1 mg/kg saline, once, subcutan)
2. control + resveratrol (0.1 mg/kg saline, once, subcutan; 20 mg/kg/day resveratrol, orally)
3. PH (60 mg/kg MTC, once, subcutan)
4. PH + resveratrol (60 mg/kg MTC, once, subcutan; 20 mg/kg resveratrol, orally)

The experiment was stopped after 28 days, the rats were euthanized, their organs were removed and processed. We analyzed the heart muscle mitochondrial lesions with electronmicroscopy and the biochemical changes with Western blot analysis.

Results: Mitochondrial lesions were visualized by electronmicroscope. As we expected, the mitochondria of the PH group were damaged, while the PH + resveratrol group contained both damaged, normal and fusioned mitochondria. The signaling pathways were analyzed with Western blot. The protecting PI3K-Akt, GSK-3β, ERK 1/2 pathways were induced by resveratrol, while the p38MAPK, NFκB pathways were suppressed. The balance of the mitochondrial proteins (Mfn 1/2, OPA-1, FIS1, TOM20) have been pushed in PH on the side of mitochondrial fission, while in the PH + resveratrol group on the fusion's side, meaning that the PH group there were a huge mitochondrial loss, while in the PH + resveratrol group the cells managed to restore bigger part of their mitochondria.

Conclusions: The resveratrol reduced the severity of the right ventricle heart failure, we could detect changes in the signaling pathways towards anti-inflammatory pathways as an effect of resveratrol and the defense of mitochondria.

1114 | Sisters but not twins

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Case report: We describe here the case of two sisters, MGV and MG with the same pathology but different presentation of their disease. MGV is a mild ex-smoker (1 pack/year, with abstention from smoking for 30 years) 69 years old woman, ex-employee with exposure to passive smoking, accessed to our clinic because of worsening of her breathing for a few month. The diagnostic examination of her chest evidenced a reduction of breath sounds without pathological noises, functional tests show a not reversible moderate grade of obstruction, and chest X-ray an accentuation of vascular-Bronchial pattern. Because of the mild smoking history and the functional results we dosed the quantitative levels of alpha-1 antitrypsin, then found to be 0.151 g/L. For a better diagnostic assessment has been performed a qualitative dosage of alpha-1 antitrypsin positive for the "PI*ZZ" mutation. After diagnosing alpha 1-antitrypsin deficiency we decided to extend the diagnostic screening also to her sister MG. She's a 68 years-old never smoked ex-employee without passive smoke exposition, with no breath symptoms. Also her quantitative dosage of alpha-1 antitrypsin has been found to be reduced 0.25 g/L, following the low level of this protein we required a genetic screening, with a positivity, as already shown in her sister, for "PI*ZZ" mutation. The biggest surprise concerned the results of MG's lung function tests, although both have the same genetic mutation for alpha 1 antitrypsin MG, unlike her sister, showed no pathological spirometric tests, carrying out functional tests found to be above normal.

This case report emphasizes some aspects still not very understood of a, nowadays, not completely known pathology, leaving open several questions such as the possible protective or worsening function of environmental factors, or the possible presence of other genetic co-factors not currently known.

1116 | Psychological distress and mood in young Dutch women with reduced perceived immune functioning

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Introduction: Reduced immune functioning may cause psychological distress and disturbed mood. Furthermore, it has also been suggested that increased stress levels have a negative impact on immune status.

Objectives: This study examined psychological distress and mood in young Dutch women with reduced perceived immune functioning vs women with a normal immune status.

Dutch young women were invited to complete an online survey. Perceived immune functioning was assessed with the Immune Function Questionnaire (IFQ). Higher IFQ-scores indicate worse immune status. They were asked whether they experienced reduced immune functioning at this moment. Mood was assessed with the Profiles Of Mood Scale - Short-Form (POMS-SF), consisting of five subscales, assessing tension/anxiety, depression, anger/hostility, vigour/activity, and fatigue. The DASS-21 has 3 subscales, assessing stress, depression, and anxiety.

DASS-21 and POMS-SF subscale scores were compared between women with and without perceived reduced immune functioning, using the Independent-samples Kruskal-Wallis Test. The relationship

between IFQ and DASS-21 and POMS-SF subscale scores was examined using nonparametric Spearman's rho correlations.

Results: N = 1443 women (means (SD) age 21.2(2.1) years old) completed the survey. Relative to women with a normal immune status (N = 921), those reporting reduced immune functioning (N = 522, 36.2%) had significantly higher scores ($P < .0001$) on the DASS-21 subscales of depression, anxiety, and stress, and significantly lower scores on the POMS-SF subscales assessing tension/anxiety, depression, anger/hostility, vigour/activity, and fatigue. Perceived immune functioning was significantly associated ($P < .0001$) with DASS-21 subscale scores of depression ($r = .175$), anxiety ($r = .228$), and stress ($r = .254$), and the POMS-SF subscales of tension/anxiety ($r = .222$), depression ($r = .194$), anger/hostility ($r = .220$), vigour/activity ($r = -0.238$), and fatigue ($r = .324$).

Conclusions: Better perceived immune functioning is associated with lower levels of stress, anxiety, and depression, and less disturbed mood.

1117 | Reduced perceived immune functioning and sleep

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Introduction: A bi-directional relationship between sleep quality and immune functioning has been established.

Objectives: The purpose of this study was to compare the severity of sleep complaints (i.e., scores on insomnia, narcolepsy, and circadian rhythm disorder scales) among healthy young adults who report experiencing reduced immune functioning with those reporting a normal health immune status.

Dutch students were invited to participate in an online survey. Subscales of the SLEEP-50 questionnaire were completed to assess narcolepsy, insomnia, and circadian rhythm disorder. Total Sleep Time, number of nightly awakenings, and sleep quality were also assessed. Whether or not participants perceived reduced immune functioning was determined via a single yes/no question. Differences in sleep outcomes between those who perceive reduced immune functioning and those who reported a normal / healthy immune status were compared using the nonparametric Independent-Samples Mann-Whitney U test.

Results: A total of 2041 students completed the survey. Those who reported reduced immune functioning (33.5%) scored significantly higher ($P < .0001$) on SLEEP-50 subscales of insomnia (18.0 ± 5.7 vs 15.6 ± 5.0), narcolepsy (6.0 ± 1.9 vs 5.5 ± 1.6), and circadian rhythm disorder (5.8 ± 1.9 vs 5.2 ± 1.8) compared to participants reporting a normal immune status. Participants perceiving reduced immune functioning also had significantly more nightly awakenings (1.1 ± 1.2 vs 0.8 ± 1.0, $P < .0001$), and reported significantly poorer sleep quality (6.5 ± 1.6 vs 7.1 ± 1.4, $P < .0001$). No significant difference was found on total sleep time.

Conclusions: Perceived reduced immune functioning was associated with poor sleep quality and more sleep disturbances. Acquiring a healthy immune status may contribute to improved sleep, and vice versa.

1118 | Irritable bowel syndrome, perceived immune functioning and general health perception

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Introduction: Irritable bowel syndrome (IBS) can have a significant impact on quality of life and wellbeing. Research has pointed at the involvement of the immune system in the development of IBS.

Objectives: Purpose of this study was to investigate the association between IBS complaints, perceived immune function and general health.

An online survey was completed by Dutch university students. Perceived immune functioning was assessed via the Immune Function Questionnaire (IFQ), which assesses past year presence of 19 immune-related health complaints, including flu, fever and infections. Higher scores on the IFQ reflect poorer immune functioning. In addition, perceived immune functioning and general health were rated on 1-item scales ranging from very poor (0) to excellent (10). The presence and severity of IBS complaints was determined with the Birmingham IBS Questionnaire, a 14-item scale, which each item rated on a 6-point Likert scale, ranging from 0 ('none of the time) to 5 ('all of the time'). Higher total IBS scores indicates a greater likelihood of the diagnosis IBS. Nonparametric Spearman's rho correlations were computed to investigate the association between IBS, perceived immune functioning and general health.

Results: Data from N = 1950 students were included in the analyses (83.6% women). IBS scores were significantly associated with perceived immune functioning assessed with the IFQ ($r = .400$, $P = .0001$) and the 1-item rating ($r = -.251$, $P = .0001$). The correlation between IBS and perceived general health was also significant ($r = -.303$, $P = .0001$). The associations were significant for both genders, and the strength of the associations did not significantly differ between men and women.

Conclusions: Irritable bowel syndrome complaints are associated with reduced perceived immune functioning and a poorer perception of general health.

1119 | What are the key influencers on patient's decisions about their allergic rhinitis management?

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Introduction: Allergic rhinitis (AR) management is frequently complicated by delayed diagnosis and sub-optimal management. This is partly due to patients self-medicating with over-the-counter (OTC) medicines without consulting a health care professional. It is unknown what factors influence a patient's decisions regarding AR management and medicine choices.

Objectives: This study aimed to identify and understand the key factors influencing AR management, from the patient's perspective.

Methods: Explorative semi-structured qualitative interviews were conducted with adults with self reported allergic rhinitis. Participants were recruited via traditional print media, social media and invitations to a volunteers database. Interviews were transcribed and analysed thematically.

Results: People with severe and persistent AR who had symptoms since childhood relied mostly on their own experimentation with OTC medicines, as they felt that over their lifetime they had exhausted all HCP recommendations with limited perceived benefit. They felt that they would only revisit a HCP about their AR, if they were alerted to a breakthrough in AR treatment via media outlets. They were also more likely to explore alternative therapies because they felt traditional medicine was unable to provide adequate relief. People with milder and intermittent AR were more likely to consult a general practitioner or pharmacist for advice on medicine selection. They reported an influence by the media with regards to searching for a particular product that had been advertised but the ultimate selection would be made based on perceived effectiveness. People with mild and severe AR reported being heavily influenced by their immediate family and friends, particularly if they were a fellow AR sufferer. Few people reported consulting reputable resources or materials that provided information on AR and its management.

Conclusions: Many people with AR heavily rely on their own experimentation with over the counter medicines to find a treatment which they feel effectively controls their symptoms. Although health care professionals are a wealth of knowledge and can facilitate a patient with optimal management of AR, they are often not consulted. There is an overwhelming need to develop resources for patients to learn about their AR and make informed decisions with regards to its management that are available at point of purchase of OTC medicines for AR.

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1120 | Rapid desensitization for hypersensitivity reactions to chemotherapeutic drugs; a case series

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Introduction: Adverse drug reactions are frequent and occur in 10 to 20% of hospitalized patients and approximately 7% of the general population. In the last decades, there has been a considerable increase in the frequency of hypersensitivity reactions (HSR),especially in patients with cancer and chronic inflammatory diseases, due to their exposure to new and more powerful chemotherapy drugs[2].

Objectives: Here we report 4 patients with anaphylaxis to chemotherapeutic agents, who have been successfully desensitized by using a standardized 12-step protocol. A 10-year old girl, with anablastic T cell lymphoma, developed anaphylaxis while receiving VP16 injection. The second case was an 8 year-old girl presented with Wilms tumor. She had anaphylaxis following VP16 infusion as well. The third case was a 12-year-old with ALL he developed anaphylaxis after receiving methotrexate (MTX). The 4th case was an 11 year-old boy with ALL. He developed anaphylaxis while receiving Elaspare.
An IgE-mediated drug allergy was confirmed by skin test in all cases.

Results: A 12-step protocol was generated by Castells, that gradually increases the infusion rate and drug concentration to achieve the target dose over 5.8 hours. The final step 12 maintained a constant rate of infusion to deliver the remainder of the total dose. Mild reactions including pruritus or pruritic rashes occurred in patients number 2 and 4. In patient number one, due to more symptoms in step 12, we reduced the rate, and then after symptom relief the protocol was maintained constant at step 11 to deliver the remainder of the total dose. She received all her medication with no other reactions. In the next courses of her chemotherapy the same protocol was applied. all the patients were desensitized successfully.

Conclusions: Drug hypersensitivity reactions are adverse events resembling allergy, which occur at therapeutic doses. Anticancer chemotherapeutics have the potential for acute HSR. RDD is effective when used appropriately. It is both an acceptable approach and a high-risk treatment modality in patients in whom the first line chemotherapy agent is offended. The reactions were often mild and the majority of them occurred during step 12, when patients were receiving the drug at the maximal rate and full concentration like in patient number 1.
Basic research is needed to clear the underlying mechanism of temporary tolerance, so that further interventions can improve the safety and efficacy of this approach.

1121 | Dabrafenib: a safe alternative in two patients with vemurafenib-induced dress

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Introduction: Skin toxicity appears in more than 90% of patients treated with vemurafenib, a BRAF inhibitor. Most reactions are mild to moderate and can be managed with dose reductions. In contrast, severe adverse reactions are rare but continuation of the culprit drug is strictly contraindicated. In those cases it is important to use a safe first-line alternative since survival rates in BRAF-mutated tumors are notably increased with the treatment with BRAF inhibitors.

Objectives: To assess the clinical safety of dabrafenib in two patients with vemurafenib-induced DRESS.

Results: We present two patients who developed a drug reaction with eosinophilia and systemic signs (DRESS) during the treatment with vemurafenib for BRAF-mutated metastatic tumors. A 50 year old male patient was diagnosed of metastatic melanoma in intestine and lymph nodes with BRAF V600 mutation in July 2016. First-line treatment with vemurafenib was initiated at 960 mg twice daily and, seven days later a diffuse generalized maculopapular eruption appeared. During the following four days he also developed facial edema, fever (39°C), bilateral inguinal lymphadenopaties and a generalized purpuric morbilliform eruption with pustules .Vemurafenib was then withdrawn. Laboratory tests revealed eosinophilia (2900 x10E9/L), lymphopenia (500 x10E9/L) and increased GGT (97 UI/L) and. Clinical remission was achieved after methyl- prednisolone 1 mg/kg and cetirizine 20 mg/day. A 71 year old female was diagnosed of double colorectal cancer, with a BRAF V600 mutation. Despite Cisplatin-VP16 and RDT+5-FU treatment there was a rapid peritoneal progression and vemurafenib was initiated in June 2016 at 960 mg twice daily. Twenty-five days later, she initially presented a maculopapular rash that progressed to a generalized purpuric and vesicular exanthema with facial edema. Peripheral eosinophilia (2200 x10E9/L), lymphopenia (400 × 10E9/L) and acute renal failure (creatinine 2.59 mg/dL) was observed. Vemurafenib was withdrawn and corticosteroids initiated at 1 mg/kg with clinical remission and improvement of laboratory parameters. In both cases dabrafenib was introduced gradually with the following schedule: 75 mg/day during 3 days, 150 mg/day during 3 days and 150 mg/12 h under strict clinical and blood test monitoring with good tolerance and no analytical abnormalities.

Conclusions: Dabrafenib is a safe alternative in patients with vemurafenib-induced severe cutaneous reactions.

1122 | Desensitization to rituximab: results of a case series from a tertiary referral centre

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Introduction: Rituximab is a monoclonal antibody primarily indicated for treatment of hematologic malignancies and autoimmune disorders. Hypersensitivity reactions to rituximab are not rare and may be IgE or non-IgE mediated. IgE-mediated hypersensitivity to rituximab has been reported to occur in 5-10% of infusions. Desensitization may represent a valuable approach in this setting, especially when other treatment alternatives are inadequate or unavailable, and is based on administration of gradually increasing doses of the culprit drug until the total cumulative dose is achieved.

Objectives: We herein report six cases of successful desensitization to rituximab in patients with a history of hypersensitivity reactions to this agent. Desensitization procedures were performed in the Allergy Department of Sotiria Athens General Hospital between January 2015 and October 2016, using a standardized 12-step protocol.

Results: We retrospectively reviewed the medical records of all patients who underwent desensitization to rituximab during the study period. Six cases (2 males, 4 females), submitted to 37 desensitizations in total, were retrieved. Their mean age was 69 years (range 57-83 years). They all had a history of immediate systemic reactions after the infusion of rituximab for treatment of hematologic or rheumatic disorders. SPTs/IDs were performed in all patients with negative results. Before desensitization, all patients received pretreatment therapy with antihistamines, corticosteroids, montelukast and paracetamol. Administration of the total scheduled dose of rituximab was completed successfully. Three patients experienced mild to moderate reactions during the four final steps of the procedure and the protocol was modified accordingly, by lengthening or adding steps.

Conclusions: Desensitization to rituximab was well-tolerated, with only mild to moderate reactions, and successfully completed in all our patients, allowing uneventful continuation of treatment. This procedure may represent an effective and safe alternative for patients with a history of hypersensitivity reactions to rituximab.

1123 | Desensitization to temozolomide, experience in a tertiary allergy unit

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Introduction: Temozolomide is an oral alkylating cytotoxic agent used in the treatment of newly diagnosed glioblastoma multiform as well as in recurrent or progressive malignant gliomas, such as glioblastoma multiform or anaplastic astrocytoma. The most common adverse effects include nausea and vomiting, constipation, headache, and fatigue, as well as myelosuppression, which may be dose limiting.

Objectives: To evaluate the effectiveness of a desensitization protocol to Temozolomide in patients with hypersensitivity to this drug

Results: Patients referred to our service from January 2009 to January 2017 with suspected allergic reaction to temozolomide and who were subsequently desensitized to that drug were analysed. Medical History, skin prick tests (SPT), oral provocation tests (OPT) and desensitization protocols were evaluated.

11 patients were enrolled (female: 5, male: 6, mean age: 48 years). All of them presented an inicial delayed cutaneous reaction, including exanthema (6), urticaria (4) or angioedema (1). In 3 patients, adverse reaction occurred in the first cycle of chemotherapy and in the rest, in successive cycles. 6 patients presented recurrent symptoms in the next cycle of treatment when temozolomide was readministered. Skin prick test with temozolomide was performed in three patients, all with negative result. OPT was carried out in two patients, experimenting a similar cutaneous reaction as they have suffered in the initial reaction. Before desensitization, all patients received treatment with antiH1, antiH2 and antiemetic and in 7 out of 11, antileucotriens was also included. Patients who hadn't received antileucotriens, presented mild cutaneous adverse reactions during the first desensitization protocol, but only in one of them pretreatment was modified not being necessary to change the protocol.

A total of 84 oral desensitizations were successfully completed in the 11 patients.

Conclusions: Rapid desensitization protocol is showed to be safe and effective for patients with adverse reactions to Temozolomide. Rapid desensitizations protocols could be considered in patients with delayed reactions.

1124 | Negative predictive value of typing safe iodinated contrast medium

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Introduction: Iodinated contrast media (ICM) are pharmaceuticals widely used in diagnostic procedures. Adverse effects associated

with their administration are mostly non-allergic. Although only minority of the reactions are IgE-mediated, they are often severe and potentially life-threatening. So far patients with the history of anaphylaxis related to ICM have been routinely advised to avoid procedures with their use what sometimes makes diagnosing and treatment quite problematic.

Objectives: The aim of the study was to determine negative predictive value of typing safe iodinated contrast medium in patients with the history of anaphylaxis related to ICM.

Results: Out of 48 patients reporting adverse reactions after ICM 18 (8 women and 10 men, aged 52-80) were selected with the history suggesting immediate anaphylactic reaction. All the patients had health problems requiring procedure with ICM administration in the near future. The diagnostic work-up aiming at finding safe ICM consisted of skin prick tests, intracutaneous tests and intravenous challenge with alternative ICM (iomeprol or iopromide).

Allergologic work-up was conducted in 16 patients. 2 patients were positive in skin tests for both tested ICM and in 14 cases it was possible to find a safe alternative ICM (12- iomeprol, 2 – iopromide) including 10 cases in whom ICM was later administered in a real life procedure (coronarography or computed tomography) and in all of them was proved to be safe. Thus, negative predictive value of the protocol was 100%.

Conclusions: Stepwise approach including skin prick tests, intracutaneous tests and provocations with iodinated contrast media allows finding safe alternative ICM for future procedures in significant number of patients with the history suggesting anaphylaxis related to other ICM.

1125 | Program for optimizing the use of antibiotics (proa) and beta-lactam hypersensitivity. a prospective analysis

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Introduction: PROA aims to provide first-choice antibiotics to all inpatients, including Betalactam-hypersensitivity-labelled-inpatients (BHLP). These patients may receive alternative antibiotics associated with antibiotic resistance and higher healthcare costs. Systematic assessment by allergists has been shown to be useful.

Objectives: To assess the usefulness of implementing Allergy assessment in PROA by reporting: Prevalence of BHLP. Effectivity and safety of rapid drug desensitization (RDD) when urgent therapy with the culprit drug is needed. Data on programmed studies to confirm or exclude betalactam hypersensitivity. Prospective, observational, longitudinal study including BHLP, during a 6-month period (Sep/15-Mar/16), at Ramon y Cajal University Hospital. PROA members were able to freely refer BHLP to Allergy Division. Referred patients underwent systematic study including: anamnesis, risk assessment, specific-IgE (sIgE), skin testing (ST), and drug provocation test (DPT). Gold standard for positive hypersensitivity diagnosis: positive sIgE and/or positive ST and/or positive drug provocation test (DPT). Gold standard for negative diagnosis: negative DPT. BHLP in need of urgent treatment with betalactams received their therapy by means of RDD.

Results: Out of 16.960 inpatients during this 6-month period in our Hospital,262 (1%) patients were BHLP.

Out of 262 BHLP, 5 (2%) were in need of urgent therapy with betalactams, and received their first choice therapy by means of RDD. All patients tolerated the required drug with no reactions.

Out of 262 BHLP, 26 (10%) completed full Allergy assessment and reached a final diagnosis: POSITIVE (confirmed hypersensitivity): 23%; NEGATIVE (excluded hypersensitivity): 77%.

Out of 262 BHLP, 236 (90%) did not finish full Allergy assessment and could not reach a final diagnosis due to different reasons: Loss of patient due to bureaucratic reasons (42%). High risk (20%). Allergy study performed in another Hospital (12%). Hospital discharge before assessment (7%). Death (6%). Patient failing to attend appointments (5%). Did not consent study (3%). Other reasons (4%).

Conclusions: Implementing Allergy assessment in PROA may benefit many patients (up to 1% of all inpatients in our Hospital).

RDD is an effective and safe technique for urgently administering betalactams to BHLP.

In 10% of the referred patients, betalactam hypersensitivity could be confirmed or excluded. Measures to improve the completion of Allergy assessment should be implemented.

1126 | Successful desensitization to cyanocobalamin using an ultra-rush protocol

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Case report: Background and aim: Allergy to cyanocobalamin (vitamin B12) is uncommon. In patients allergic to vitamin B12 and with clinical indication for its replacement therapy, desensitization is mandatory. There are two protocols published for desensitization, designed with slow schemes from 3-5 days up to 7 weeks, with a total cumulative dose of 1000 μg. These protocols are time consuming and therefore not cost-effective. We have developed a shorter protocol with only one-day duration.

Clinical case: We report a case of a 61 years-old male patient, with atopic asthma and rhinitis and with vitamin B12 deficiency (Barrett's metaplasia) on replacement therapy for the last 5 years. At 6 February 2016, two hours after the last administration of cyanocobalamin (Permadoze®, 1 mg) the patient developed for the

first time, face and hands angioedema with generalized pruritus and urticaria, that remitted with oral levocetirizine (10 mg) and deflazacort (30 mg). The patient was referred to our Department, and we have performed a diagnostic work-up that included skin tests with injectable cyanocobalamin and cobamamide that were negative, with non-diluted solution (1 mg/mL and 5 mg/mL respectively). Subsequently, intradermal tests have been made, starting at 1:1000 dilutions and with 10-fold progression. Positivity was observed in the immediate reading, performed at 20 minutes, at a concentration of 1:10 for both. There were no late reactions. Both tests have been performed in two healthy volunteers, being negative. We have scheduled a desensitization protocol for a one single day reaching 1 mg vitamin B12 (cyanocobalamin - Labesfal™ 1 mg/mL) - (Table). Written informed consent was obtained. The total protocol took approximately 2 hours and 30 minutes. A total of 9 subcutaneous injections were administered, with a total cumulative dose of 1010 μg. No local or systemic adverse reactions were observed, and the patient was discharged 4 hours after the last injection. A phone contact of the medical team has been provided within 24 hours. This desensitization protocol has been kept every two months without adverse reactions, maintaining serum vitamin B12 at normal levels.

Conclusions: To our knowledge, this is the first report of a cyanocobalamin rush desensitization protocol with only one-day duration, reaching a total cumulative dose of 1 mg. It allows the maintenance of an indispensable and very effective treatment. This protocol has proven to be safe, cost-effective and highly convenient.

Table. Cyanocobalamin desensitization ultra-rush protocol (modified from Caballero MR, *et al*. Allergy 2007;62:1341-2).

Dilution/ Concentration	Administered amount (mL)	Cumulative dosage (μg)
1:100 (10 μg/mL)	0.1 mL* → 0.3 mL* → 0.6 mL*	10
1:10 (100 μg/mL)	0.1 mL* → 0.3 mL* → 0.6 mL*	100
1:1 (1000 μg/mL)	0.1 mL**→ 0.3 mL** →0.5 mL	900

*Interval between subcutaneous injections of 15 minutes, ** Interval between subcutaneous injections of 30 minutes.

1127 | Desensitization to irinotecan. A case report

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Case report: Background: Irinotecan is an antineoplastic drug that prevents DNA from unwinding by inhibition of topoisomerase I. It is widely used in the treatment of gastrointestinal malignancies, but despite the frequent use only few cases of allergy has been reported.

Material and Methods: A 52-year-old man with a personal history of asthma, isolated episodes of supraventricular tachycardia, pityriasis lichenoid and no history of allergy; was diagnosed in March 2015 with rectal cancer stage III (T2N0M0). XELOX (capecitabine and oxaliplatin) in combination with bevacizumab was initiated. Seven months later, he had lung, lymph node and pelvic progression, so it was decided to administer FOLFIRI (folinic acid, 5- fluorouracil and irinotecan) and cetuximab.

The first time he was exposed during the administration of irinotecan and 1 hour after the administration of cetuximab, the patient presented urticaria in neck and chest that required hydrocortisone IV for treatment with improvement minutes later.

Results: The SPT with irinotecan 20 mg/mL; was positive with papule 5 mm and erythema 30 mm (with negative control). The SPT 1/1 and ID 1/1000, 1/100 and 1/10 with cetuximab were negative.

Drug desensitization was programmed using a 12-step protocol, which enabled a cumulative dose of 382 mg of irinotecan to be administered (Table 1). Premedication was acetylsalicylic acid, montelukast, bilastine, ranitidine and prednisone. Desensitization was successful and the patient did not experience a reaction during the infusion nor during the following hours.

Conclusions: We present a case with a hypersensitivity reaction by caused by irinotecan with positive SPT that suggests a IgE

Step	Solution	Rate (mL/h)	Time (min)	Volume (mL) administered (mL)	Dose administered (mg)	Cumulative dose infused (mg)	% Total dose
1	Dilution 1/50	2	15	0.50	0.01528	0.01528	0.004
2	Dilution 1/50	4	15	1.00	0.03056	0.04584	0.008
3	Dilution 1/50	10	15	2.50	0.07640	0.12224	0.02
4	Dilution 1/50	25	15	6.25	0.19100	0.31324	0.05
5	Dilution 1/50	50	15	12.50	0.38200	0.69524	0.10
6	Dilution 1/50	100	15	25.00	0.76400	1.45924	0.20
7	Dilution 1/50	200	15	50.00	1.52800	2.98724	0.40
8	C	10	15	2.5	3.78300	7.48330	0.99
9	C	20	15	5	7.56599	15.04930	1.98
10	C	40	15	10	15.13199	30.18129	3.96
11	C	75	15	18.75	28.37248	58.55376	7.43
12	C	75	171	213.75	323.44624	382.00000	84.67

mediated mechanism. We used a successful and rapid protocol for desensitization to irinotecan

	Doses (mg)	Solution Volume (mL)	Solution Concentration (mg/mL)
Dilution 1/50	7.64	250	0.031
Solution C	378.30	250	1.513

1128 | Effectiveness and safety of a readministration protocol in patients with immediate type hypersensitivity reactions due to anti-tuberculosis drugs

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Introduction: Immediate-type allergic reactions from antituberculosis drugs are not rare and causes treatment interruptions. We have already defined a successful protocol for readministration for culprit drugs in a small group of these patients. In this protocol, the culprit drugs were reintroduced with gradually increasing dose protocols consisting of 6 to 8 steps on consecutive days to induce tolerance.

Objectives: This study is aimed to determine the effectiveness and safety of this readministration protocol in a real life setting.

Method: The patients with immediate-type drug reaction from antituberculosis drug in which the culprit drugs were readministered with the defined protocol were included in the study. Demographics, the reaction characteristics due to antituberculosis drugs and the details of readministration protocol (effectiveness and safety data) were recorded.

Results: 76 cases were included in the study. The hypersensitivity reactions were developed during isoniazid, rifampicin, pyrazinamide, and ethambutol therapy in 73 cases; isoniazid, rifampicin, and ethambutol therapy in one case; isoniazid, and ethambutol therapy in one case; and isoniazid therapy in one case. The severity of the reactions were grade 1 in 60 cases, grade 2 in 10 cases and grade 3 in 6 cases. In 44 (57.9%) cases, readministration procedure was completed without any reaction. Thirty four reactions detected in 32 cases during the procedure. All of these reactions were in grade 1 and could be easily controlled. Most of them (% 73.5) were due to pyrazinamide. Of these 32 patients, in 20 patients the procedures were stopped according to the decision of the primary responsible doctor or the patient. The procedure was continued in 12 and was completed successfully in 9 of these cases. In 3 cases, we couldn't manage to complete the procedure. The culprit drug was again pyrazinamide in all of the 3 patients. To sum up, when we exclude 20 cases who didn't continue the procedure, culprit drugs could be resumed in 53(94.6%) of remaining 56 cases.

Conclusions: The readministration protocol used in this study seemed to be effective and safe.

1129 | Successful desensitization to intravenous immunoglobulin: Report of two cases

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Case report: Background: Intravenous Immunoglobulin (IVIg) is mainly used for primary and secondary immunodeficiency but also for neurologic, hematologic, dermatologic disorders, solid organ transplantation, infectious and rheumatologic diseases. Adverse effects such as headache, nausea, flushing and tachycardia occur up to 40% of intravenous infusions of IgG while anaphylactoid reactions and anaphylaxis occur less frequently.

Method: We present a desensitization protocol used in two patients who were referred to the Department of Allergy at Sotiria General Hospital of Athens for further evaluation of adverse reactions to IVIg treatment. Patient 1: A 73-year-old female with a clinical history of non-Hodgkin lymphoma, had been treated with IVIg for 15 years with no adverse reactions, followed by temporary discontinuation of treatment for a 5-month period. Within minutes after re-administration of IVIg, the patient presented generalized non-pruritic erythema, epigastralgia and a general sense of distress. Patient 2: A 57-year-old male, treated with IVIg for chronic lymphocytic leukemia, presented flushing, difficulty in breathing and chest tightness within 1 minute after receiving the first dose of the drug. Skin prick tests performed with IgG at dilutions 1/10 and 1/1 were negative, while intradermal tests, carried out with undiluted drug were positive. Histamine and saline were also used as positive and negative controls, respectively. Skin tests to 5 control subjects were negative and non-irritating. Laboratory results showed very low levels of IgA. A desensitization protocol with IVIg was conducted. Premedication for 3 days was administered in both cases.

Results: The desensitization protocol consisted of 7 steps of rapid pulses of 0.25, 0.5, 1.25, 2.5, 5, 10, 15 mL administered at a rate of 1, 2, 5, 10, 20, 40, 60 mL/hour respectively, every 15 minutes, and 1 step of drip infusion at a final rate of 80 mL/hour until completion of the infusion. Patients were able to tolerate multiple sessions of IVIg desensitization protocol with no adverse reactions.

Conclusions: Systemic adverse reactions to IVIg are common and of variable pathogenesis. Desensitization to IVIg may be useful in

patients with adverse reactions to the drug, regardless of the underlying mechanism.

1130 | Chronic pruritus caused by intravenous levothyroxine sodium treated with off-label omalizumab

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Case report: Omalizumab is a humanized monoclonal antibody that inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils. It is licensed for use in severe allergic asthma and chronic urticaria The off-label use of medicines is a common clinical practice. Patients with hypothyroidism require lifelong treatment with thyroid replacement therapy. Levothyroxine is usually orally administered but can also be administered as intravenous infusion.

A 40 years. woman presented with a severe form of hypothyroidism and intestinal malabsorption disorders that requires chronic treatment with levothyroxine. After using high doses of different oral drugs with no effective result, iv levothyroxine was administrated reaching the control of her symptoms. After 3 years. of treatment two times per week with 450 mcg, she stopped it for 3 weeks suffering a very symptomatic hypothyroid state with headache, dizziness, tiredness and muscular pain. After restarting the administration with half dose, she develops generalized itching without urticaria and absence of systemic symptoms that increases with each administration. Her Endocrinologist reduced levothyroxine to 200 mcg 2 days/week and began antihistamines without clinical improvement. She was referred to our Allergy Unit where a follow up for urticaria was performed, including total IgE measures 212 KU/l. IgE levels 3 months earlier was 120 KU/l. She received high doses of antiH1 and montelukast with poor response. Corticosteroids couldn't be used because of patient comorbidities. Treatment with levothyroxine stayed the same, without increasing the dose although the patient was suffering. Omalizumab was prescribed at a dose of 300 mg/4 weeks.

First dose of omalizumab was administrated 2 days before her next dose of iv levothyroxine with no pruritus exacerbation. On the 4th day after omalizumab itching began to decrease and after the 2nd dose antiH1 were reduced gradually and levothyroxine could be increased reaching levels of 450 mcg. Actually the patient can get the drug with any side effects.

We present a case of drug allergy to a chronic essential treatment that can be administrate through the concomitant use of omalizumab. Omalizumab can increase the threshold of sensitivity to levothyroxine as it has been observed in other studies with oral food challenges and chemotherapic desensitizations. This may be an effective option in those patients with drug allergy and limitated therapeutical strategies.

1131 | Anaphylaxis during reevaluation with skin testing for amoxicillin allergy

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Case report: Background: B-lactams are among the most frequent causes of hypersensitivity drug reactions. Amoxicillin is reported to be the most commonly consumed β-lactam in many countries. In the literature, generalized reactions after β-lactam skin testing are exceptionally rare.

Method: We report a case of anaphylaxis during intradermal tests (IDs) with β-lactam antibiotics in a patient with a history of anaphylactic reaction to amoxicillin. A 68-year-old female was referred to the Department of Allergy at Sotiria General Hospital of Athens for further evaluation of amoxicillin-induced anaphylaxis. The patient had had an episode of anaphylactic reaction 10 minutes after oral administration of first dose of amoxicillin for treatment of periodontal abscess ten years ago. She was transferred to the emergency department where she recovered after receiving standard treatment. The patient reported that she had tolerated amoxicillin in the past with no adverse reactions. Her medical history was significant for COPD.

Results: Initial diagnostic workup included in vitro (specific IgE, total IgE, serum tryptase) and in vivo (skin prick tests, intradermal tests) assays, with negative results. Due to high index of clinical suspicion, the patient was reevaluated by repeating skin testing 1 month later. Approximately 5 minutes after performing IDs, the patient started complaining of pruritus of the tongue, palms and the head quickly followed by dizziness, blurred vision, tachycardia, nausea, retrosternal pain and generalized urticaria. She was immediately treated with adrenaline, corticosteroids, antihistamines, intravenous fluids, oxygen and nebulized salbutamol with gradual recovery. An increase of serum tryptase was detected, 1 hour after the onset of symptoms (25 mg/L). Baseline serum tryptase level obtained at 2 weeks follow-up was found to be within normal limits (7.7 mg/L). An electrocardiogram was conducted with normal findings. IDs performed for amoxicillin and ampicillin were positive.

Conclusions: Our reported case of a severe anaphylactic reaction during performing IDs highlights that clinicians should be aware of the possibility of severe adverse reactions during the procedure of reevaluation by repeating IDs in patients with a previous history of allergic reactions. Precautions during β-lactam skin testing should be taken to prevent these potentially life-threatening events.

1132 | Immediate type hypersensitivity to low molecular weight heparin (enoxaparin)

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Case report: Objectives: In this report we describe a patient with allergic urticaria after administration of Enoxaparin.

Materials and methods: A 57-year-old woman, without allergic antecedents, was referred to our clinic from emergency department because of pharyngeal pruritus and urticarial lesions on ears, chest and abdomen. No angioedema, dyspnea or nausea were described. She started with these symptoms immediately after the first injection of subcutaneous low molecular weight heparin (LMWH) (Enoxaparin). She received this treatment as prevention of thromboembolic disorders as she was immobilized with ferula after an ankle sprain. There weren't any other factors implicated in the reaction.

The patient responded to antiallergic treatment with intravenous diphenhydramine and hydrocortisone.

Total tryptase levels were measured in serum at 15 minutes (2.86 ng/mL) and 2 hours (2.73 ng/mL) following the reaction.

We performed the following allergy study: skin prick tests (SPT) with standard of urticaria including foods, latex, plant food panallergens and anisakis; prick and intradermal tests (IDT) with enoxaparin and other LMWH, unfractioned heparins (UFH-Heparin Sodium) and Fondaparinux; "in vitro" study with basophil activation test and drug provocation test.

Results: SPT and IDT were positive with LMWH [Bemiparin (6 × 4), Tinzaparin (6 × 4) and Enoxaparin (9 × 7)] and Heparin Sodium (8 × 5). Negative with the rest LMWH (Dalteparin, Nadroparin), Fondaparinux, food allergens and latex. Basophil activation test was negative with Enoxaparin, Dalteparin y Nadroparin. Drug provocation test with subcutaneous Fondaparinux was tolerated by the patient at full doses.

Conclusions: Heparins are important anticoagulants, used in the prophylaxis and treatment of thromboembolic disorders. Although heparins are drugs widely used, hypersensitivity reactions are uncommon. Most of the reactions that have been described correspond to cutaneous delayed hypersensitivity reactions. In the literature reviewed, immediate reactions have rarely been reported. We present a patient with urticaria caused by allergy to Enoxaparin demonstrated by positive IDT. The positive test with other LMWH and UFH (Heparin Sodium) suggests possible cross reactivity. We propose Fondaparinux as an alternative treatment for this patient.

1133 | Slow aspirin desensitization in a patient with aspirin exacerbated respiratory disease

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Case report: Aspirin exacerbated respiratory disease (AERD) is characterized by chronic rhinosinusitis with nasal polyps (CRSwNP), asthma and aspirin intolerance. Aspirin (ASA) desensitization is indicated in patients with AERD who have suboptimally controlled asthma or sinusitis, those required multiple revision polypectomies, and patients who require COX-1 inhibitors for antiplatelet therapy.

A 25 year old man presented to our facility with complaints of nasal obstruction and shortness of breath. He experienced anaphylaxis after ASA consumption 5 years ago. He was on inhaled corticosteroid + LABA, montelukast, oral antihistamine and nasal corticosteroid therapy for 3 years. He required multiple surgical and medical polypectomies in the last 4 years.

He was referred to us for aspirin desensitization.

ASA desensitization was performed twice, both failed to succeed. First desensitization was started with 30 mg. He developed urticaria and mild nasal congestion 30 minutes after the second dose (45 mg). The patient was treated with 45.5 mg pheniramine and 40 mg methylprednisolone. High serum tryptase level was detected (34.9 ng/dL). Nasal congestion resolved at the same day while urticaria lasted 3 days. Six weeks after the complete resolution of the symptoms aspirin desensitization starting with a lesser dose (15 mg) was initiated. 30 mg and 45 mg ASA were given with 3 hours intervals. At the 30th minutes of 45 mg ASA, urticaria and mild nasal congestion reoccurred and patient was treated accordingly. Since the conventional treatment modalities were not sufficient to prevent polyp regrowth, ASA desensitization was crucial for the patient. A different desensitization protocol starting from a lesser dose was adapted to the patient and desensitization was achieved in 9 days. The patient has been on 625 mg 2 × 1 ASA therapy for the last

Aspirin Desensitization Protocol

	1. dose	2. dose	3. dose	4. dose	total daily dose
Day 1	0.1 mg	1 mg	3 mg	10 mg	14.1 mg
Day 2	10 mg	15 mg	15 mg		40 mg
Day 3	10 mg	20 mg	20 mg		50 mg
Day 4	25 mg	25 mg			50 mg
Day 5	50 mg				50 mg
Day 6	50 mg				50 mg
Day 7	30 mg	45 mg			75 mg
Day 8	60 mg	90 mg	150 mg		300 mg
Day 9	325 mg	650 mg			

3 months without any hypersensitivity reactions. Endoscopic polyp examination revealed no signs of polyp regrowth.

Conclusion: ASA desensitization is an effective therapeutic tool in the management of AERD. But desensitization is not without risk; specific protocols and recommendations exist to mitigate the risks. Sometimes tailoring of the desensitization protocol according to the drug and the patient's previous reaction may be required.

1134 | 6 - hour successful desensitisation protocol to intravenous immunoglobulin (IVIG) in a case of common variable immune deficiency (CVID) with severe panhypogammaglobulinemia

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Case report: Introduction: CVID is a rare disease characterised by low levels of at least two immunoglobulin isotypes, including IgG and impaired specific antibody response. Substitutive therapy with IVIG is now considered the main treatment for CVID. Infrequently patients can develop adverse reactions (AR) during IVIG therapy which can be classified as: mild, moderate or severe; anaphylactic and nonanaphylactic. The exact cause for the AR is largely unknown although there are several proposed mechanisms such as: complement activation and the presence of IgE or IgG antibodies against IgA in IVIG product. The relevance of the IgG presence is unclear as there is a lack of correlation with the occurrence and the severity of the AR. Risk factors for AR such as large dose or rapid dose IVIG have also been described. Information regarding desensitisation protocols in patients with AR to IVIG is scarce and nonstandardised.

Objectives: We present the case of 39 year old female who was diagnosed with CVID with severe panhypogammaglobulinemia (including hypoIgE) in 2001. The patient received multiple administrations of IVIG (200 mcg/mL, 25 mcg/mL IgA content) until 2009 and has experienced three nonconsecutive episodes of hypotension with associated dyspnea occurring during the first 30 minutes of infusion which required treatment with adrenaline and systemic corticosteroids. Interestingly the same preparation was tolerated after an episode regardless of its IgA content and apparently all three episodes where related to the infusion rate and the temperature of the infused preparation. After the third AR (2009) she only received, once in three months, at low rate infusion, an IVIG with 1 mcg/mL IgA content unfortunately not available in our country and quite expensive.

Results: As the AR could not be explained by an IgG or IgE response to the presence and the level of IgA in IVIG, using the available data in the literature we decided to set up a desensitisation protocol to IVIG (900 mcg/mL IgA content), available in our hospital. The patient was premedicated and transfer to the Intensive Care Unit where incremental doses of IVIG, starting with a rate of 1 ml/h until a rate of 30 mL/hour, were successfully administrated, during a 6-hour protocol.

Conclusions: We present a case CVID with severe panhypogammaglobulinemia, in which severe AR during substitutive therapy with moderate IgA IVIG occurred. A 6-hour desensitisation protocol to IVIG was developed and successfully administrated.

1135 | Aspirin desensitization in a patient with chronic Eosinophilic pneumonia: After unsuccessful desensitization 5-year follow-up

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Case report: Background: Chronic eosinophilic pneumonia (CEP) diagnosis is typically made based on clinical and chest radiographic findings of predominantly peripheral opacities and identification of eosinophilic infiltrates in the lungs. CEP is accompanied by asthma in more than 50% of cases. The presence of CRS with nasal polyps, severe asthma, and female gender are all associated with higher prevalence of aspirin hypersensitivity reactions. Desensitization to aspirin is well described in the allergy but there are no any data in patients with CEP.

Method: A case of a 43-year-old female patient with a 3-year history of asthma, rhinosinusitis and chronic idiopathic urticaria (CIU) was admitted to our clinic with respiratory and nasal symptoms. One year later, she noticed swelling of eyes, nasal symptoms, bronchospasm and cyanosis 10 minutes after taking the Aspirin 500 mg for headache. After 3 months and 5 months later the first reaction, she experienced similar reactions with flurbiprofen and paracetamol. respectively. Laboratory findings showed peripheral blood eosinophilia. Paranasal sinus computed tomography (PNSCT) showed chronic pansinusitis. A chest CT scan showed bilateral fibrotic, peripheral pulmonary infiltrates, Histopathology of the mucosal biopsy revealed dense eosinophilic infiltration in the bronchial wall without evidence of vasculitis.

Results: To confirm aspirin hypersensitivity placebo-controlled, oral aspirin provocation procedure was performed. After the oral administration of 50 mg of the drug, the patient developed nasal symptoms. Two months later, she underwent bilateral nasal polypectomy. After 2 months surgical excision, she underwent 5-days oral aspirin desensitisation protocol which was successful. Maintenance dose was kept at 600 mg twice daily. Despite aspirin desensitization, two months after nasal polypectomy the recurrence of pansinusitis and nasal polyposis was shown with PNSCT. Therefore, aspirin treatment was discontinued. During 5 years of follow-up, her asthmatic symptoms have been well/partially controlled only an ICS/LABA inhaler as maintenance medication and nasal steroids. The patient had three courses of oral corticosteroids.

Conclusion: The present case demonstrates that aspirin desensitization may not be possible in patients with a history of aspirin sensitivity and CEP. Despite clinical similarities, different mechanisms for

induction of eosinophil might operate in CEP and aspirin-exacerbated respiratory disease (AERD).

1136 | A case of ganciclovir desensitization

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Case report: A nine year old girl having high temperature and stomach ache symptoms was diagnosed with primary hemophagocytic lymphohistiocytosis. During the treatment she had neutropenic fever, dyspnea and bronchospasm. Laboratory tests revealed a 7 189 566 CMV-DNA copies/ml. Ganciclovir therapy was started for CMV pneumonia. At the first dose of ganciclovir she had urticaria and at the second dose dyspnea, bronchospasm, tachycardia with urticaria. Adrenaline, antihistamines and corticosteroids were administered for anaphylaxis. And treatment was replaced with valganciclovir but there was no clinic or laboratory regression.

Because valganciclovir was ineffective and foscarnet couldn't have been provided we decided to apply systematic desensitization for ganciclovir without performing skin prick tests because the reaction was anaphylaxis. Total dose was calculated 350 mg, for the patient with a 35 kg weight according to 10 mg/kg daily dose of ganciclovir. A(1/1000 dilution), B(1/100 dilution), C(1/10) dilution) and D(no dilution) solutions including 3 dilutions were prepared. Desensitization was applied with a 1/10 000 beginning dose as 14 steps by increasing doses every 30 minutes and lasted 6.5 hours. There wasn't any reactions during desensitization. Patient was treated with ganciclovir every day without any problem for 21 days. After the treatment clinic symptoms revealed and CMV DNA copies was found <31 IU/mL.

In conclusion, we present a rare case with ganciclovir allergy and a new protocol of ganciclovir desensitization.

1137 | Amoxicillin-clavulanic acid desensitization: clinical report and schedule employed

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Case report: Background: Betalactam allergy is a very common consultation problem in our Allergy Departments, and there are commercialized several alternatives in order to recommend in patients with a positive result in the allergological study. The problem begins when these patients need an antibiotic because the alternative treatment isn't enough to erase the culprit bacteria. Our aim was to show a desensitization protocol with amoxicillin-clavulanic acid in a patient with a confirmed diagnosis of betalactam allergy.

Patients and methods: A 35 years old female patient came to our Allergy Department referring general pruritus without urticaria or angioedema one hour after the first amoxicillin-clavulanic dose intake prescribed for tonsillitis, and needing amoxicillin-clavulanic acid in order to treat a resistant Helicobacter Pylori infection to alternative treatments. A clinical report focused in other allergies and pathologies was performed and an in vivo study (including a Drug Provocation Test with amoxicillin-clavulanic acid) was performed too, with a positive result of DPT after one hour (general pruritus and mild urticaria). We performed a desensitization following the protocol showed in table 1 in order to offer this treatment to erase the infection.

Results: Our patient tolerated the desensitization protocol with only mild pruritus after an accumulated dose of 525 mg, being well controlled with conventional treatment (without adrenaline). She followed with the treatment at home without any problems

Conclusion: We present a patient with a confirmed amoxicillin-clavulanic acid sensitization and a desensitization protocol to this drug. In a future, a reduction of this schedule may be studied in order to improve this treatment method.

Table 1 desensitization schedule

Step	Solution	Ml/h	Time (minutes)	Administered dose (mg)	Accumulated dose (mg)
1	A	2	15	0.01	0.01
2	A	5	15	0.025	0.035
3	A	10	15	0.05	0.085
4	A	20	15	0.1	0.185
5	B	5	15	0.25	0.435
6	B	10	15	0.5	0.935
7	B	20	15	1	1.935
8	B	40	15	2	3.935
9	C	10	15	5	8.935
10	C	20	15	10	18.935
11	C	40	15	20	38.935
12	C	100	500	836.065	875

1138 | A desensitization case of recombinant factor VIIa

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Case report: A 26 month old boy was diagnosed with factor 7 deficiency with a 1% factor 7 level when admitting hospital because of gingival bleeding at November 2014. His sister also had factor 7 deficiency. When he was 10 month old, he admitted to emergency department with petechia all over the body and bloody stool. Recombinant factor VIIa was used for the first time and after the medication confusion and tachycardia had occurred. Cranial computerized tomography performed for intracranial bleeding was normal. After developing a swollen eye, a diagnoses of anaphylaxis was taught and symptoms revealed with adrenaline therapy .

For recombinant factor VIIa allergy we performed skin prick test which was negative. But intradermal test with 1/1000 dilution ended with a 8 mm reaction. Because the patient had to be treated with recombinant factor VIIa and there was no alternative, we planned to apply systematic desensitization. Total dose was calculated 410 mcg, for the patient with a 13.5 kg weight according to 30 mcg/kg dose of Factor 7. A(1/1000 dilution), B(1/100 dilution) and C(1/10) dilution) solutions including three dilutions were prepared. Desensitization was applied with a 1/410 beginning dose as 13 steps by increasing doses every 20-30 minutes and lasted 5 hours. There wasn't any problem during desensitization and repeated doses following days. Factor 7 desensitization was also performed two more times, one for head injury and second for a swollen knee with the same protocol because the period between the doses was longer as three months.

In conclusion, we present a rare case with recombinant factor VIIa allergy and a new protocol of recombinant factor VIIa desensitization

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NEW PROBLEMS IN OCCUPATIONAL ALLERGY

1140 | Questionnaire-based evaluation of occupational hand eczema among health-care providers in hospitals and out-patient clinics in Romania

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Introduction: Occupational skin diseases have an unknown prevalence in Romania. Occupational allergic or contact hand eczema is rarely reported due to lack of diagnosis. Specific questionnaires may be applied as useful tools in evaluation point prevalence of these disorders.
We developed a work-related questionnaire, simple and short (3 pages), easy to understand and to fill in, with yes or no answers to specific questions. Questionnaire is focused on clinical aspects related to direct work exposure: contact with chemical agents (detergents, disinfectants, soap, liquid soap, shampoo and other personal hygiene products or skin cleanser);use of latex gloves or other type of gloves (plastic, cotton, natural or synthetic rubber); other relevant exposures; frequency of hand washing; atopic or allergic background of each individual; the presence of comorbidities, chronic treatments or other exposures (such as UV radiation).

Objectives: To realize the first Romanian self-reported questionnaire for evaluation of occupational hand eczema among health-care providers in hospitals and out-patient clinics in Romania.

Results: A large cohort of persons (approximately 1500) were involved in the study. Data was statistically analyzed.
The study permits the identification of susceptible persons to develop occupational skin diseases, recognition of work-related risk factors and may contribute to elaborate preventive measures to specific occupations and risk-profiles.

Conclusions: This questionnaire can be applied as useful tool for the evaluation of occupational hand eczema among health-care providers in hospitals and out-patient clinics in future epidemiological studies.

1141 | Occupational exposure to ionizing radiation in a hospital context

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Introduction: The use of ionizing radiation (IR) of the X- ray type in medical interventions is a growing practice in the daily routine of health professionals. The benefits that x-rays brought to medicine are unquestionable even though the increasing knowledge about the adverse effects of occupational exposure of health care professionals. In order to follow radiologic protection principles and international recommendations, it is crucial that health professionals exposed to IR learn about the dangers associated with their daily exposure and how to prevent and minimize adverse effects.

Objectives: Evaluate the knowledge of operating room health care professionals from CHVNG/E exposed to IR regarding the danger they are exposed as well as the need of adequate protection equipment.
A questionnaire was applied to all health professionals working on the operating room of CHVNG/E, independent of their professional category. The questionnaire evaluated the socio-demographic and professional profile of the workers, exposure to IR, use of personal protective equipment, adequate professional profile training concerning IR protection and symptoms associated with their work. A cross sectional descriptive study was performed and all answers were carefully analyzed using de SPSS software. The comparison of percentages between groups was performed using the qui-square test followed by a Mann-Whitney post-comparison.

Results: The population of health professionals studied with an average age of 43 years, was manly male (69.4%) nurses (63.9%). They worked in the CHVNG/E for 12.57 ± 8.3 years. Almost all professionals (94.4%) did not had any specific education on IR. Less than half, 47.2 and 29.2%, used protection equipment such as lead apron and thyroid shields, respectively. Although 71% considered very important the use of individual dosimeter, only 29.2% used it always. The most referred clinical symptoms associated to IR were hand erythema (23%) and bone or joint pain (36%).

Conclusions: This study demonstrated that the frequency of use of personal protective equipment and dosimeter was low among professionals which may be related with the lack of specific education of the professionals on the topic of IR. Furthermore, the low frequency of personal protective equipment use during exposure to IR could be associated with the existence of cutaneous manifestations and bone pain found in the studied population.

1142 | Occupational respiratory diseases in mosque workers

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Introduction: Content of mosque as a workplace environment might carry a risk for occupational diseases. The aim of this study

was to investigate the frequency of asthma and rhinitis in mosque workers.

Objectives: Outcomes were measured by questionnaire, spirometry, skin prick test (SPT), serum specific IgE (ImmunoCAP), exhaled (FeNO) and nasal nitric oxide (nNO)(NIOX-Mino). Participants were workers of mosque for at least 1 year, in Kirikkale city.

Results: Mean age of employees was 46.04 ± 10.39 years (all male, n:61), and 73.8% of them had a university degree. Frequency of atopy was 11.4% in SPT/sIgE with a highest rate for house dust mites. According to the survey, prevalence of asthma and rhinitis symptoms (11.5% and 42.6%) increased after working in mosque (44.3% and 60.7%). We diagnosed a higher frequency of asthma and rhinitis (36.1% and 63.9%) than reported in the questionnaire (23% and 21.3%). In ear-nose-throat examination, 27.9% of the participants were diagnosed as sinusitis. 26.2% of the employees stated that their symptoms started immediately in the mosque, and 19.7% of them had improvement at weekends/vacations. The time interval of starting work related respiratory symptoms was 5.20 ± 5.09 years. Employees diagnosed as asthma and/or rhinitis were more atopic, had higher FeNO and nNO levels than healthy workers. In the logistic regression analysis, FeNO levels were related with work related respiratory symptoms.

Conclusions: These results indicated that employees working in the mosque environment were at risk of allergic diseases, and preventions in this regard should be taken. Exhaled nitric oxide might be useful as a diagnostic tool for occupational asthma.

1144 | Occupational rhinitis caused by green coffee beans in coffee roastery worker

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Case report: Introduction: A 45-year-old previously healthy non-smoking laboratory technician who had worked in a coffee roastery for 23 years presented with watery rhinitis and sneezing associated with handling green coffee beans (GCB) for several years. Since one year she complained about dyspnoea without cough, too. The patient had been removed from work tasks with GCB contact two years before referred to us, but still had visited production areas sometimes.

Results: Skin prick testing (SPT) with common aeroallergens showed no sensitization. SPT with a sample of raw coffee powder from the patient's workplace gave a positive result of 9 mm (Histamine 7 mm, Diluent control negative). Specific serum IgE for GCB was positively high at 1.27 IU/L (normal <0.35 IU/L). X-ray of thorax and paranasal sinuses were within normal variation. Fractional exhaled nitric oxide (FeNO) level was high at 114.2 ppb (normal <30 ppb). Baseline spirometry showed mild obstruction and positive bronchodilatation response. The histamine challenge test showed nearly strong bronchial hyperresponsiveness (PD_{15} FEV_1 was 0.106 mg). These findings with an asthma positive serial peek expiratory flow (PEF) monitoring allowed us to diagnose asthma. PEF monitoring at the workplace showed no differences between work days and free time. The specific inhalation challenge test for 10% raw coffee for 30 minutes in a challenge chamber showed no reactions. The specific inhalation challenge test for 100% raw coffee for 45 minutes was positive for occupational rhinitis (OR) with rhinorrhea 1.22 g, bilateral nasal volume change −16% and bilateral nasal resistance change +47%. No changes in lower airway functions i.e. forced expiratory volume in 1s (FEV_1), PEF or FeNO were observed and occupational asthma was not diagnosed. Regular asthma medication was initiated. Measured raw coffee dust concentration in the specific challenge test was 69 mg/m^3 (10% raw coffee dust in lactose dust in 30 minutes).

Conclusion: Green, raw coffee dust is dust of unroasted, green coffee beans. According to epidemiological data, immediate IgE mediated allergic rhinitis to GCB in coffee roasteries is not very common in non-atopic workers. Here, we report a case of OR confirmed by a specific challenge test in a non-atopic patient.

1145 | Occupational rhinitis due to locust bean gum

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Case report: Background: Locust bean gum (LBG) is a galactomannan vegetable gum obtained from the seeds of the carob tree *(Ceratonia siliqua)*. It is used, in food technology, as a thickening and gelling agent (E-410). Carob tree belongs to *Leguminosae* family. A 44-year-old woman, who worked in an ice cream factory, complained of ocular and nasal itching, runny nose, nasal congestion and sneezing, while handling Cremodan® SL29, a powder used as a stabilizer. She related no symptoms with oral intake of ice cream and other legumes during the first year, but then developed pharyngeal itching, eyelid angioedema and dyspnoea after chickpea ingestion, and cough after oral intake of almonds, pistachio and sunflowers seeds.

Methods: Skin prick tests (SPT) were performed with Cremodan® SL29 (prick by prick), with each component of Cremodan® SL29 (LBG, dextrose, milk protein, gelatin, pectin and carrageenan) and the extract from carob tree seed (CTS), legumes (lentil, soybean, pea, chickpea, and white, red and green bean) and nuts (peanut, nut, almond, cashew, hazelnut, pistachio, pinion and sunflower seeds). SDS-PAGE immunoblotting was performed to study the molecular mass of the IgE-binding bands in LBG and extracts from Cremodan® SL29 and CTS. Cross reactivity between Cremodan® SL29, CTS,

LBG, chickpea and almonds was studied by SDS-PAGE immunoblotting inhibitions assays.

Results: SPT were positive to Cremodan® SL29, CTS and LBG. Legumes SPT showed positive results to extracts from chickpea, soybean and lentil. Nuts SPT were positive to extracts from peanut, nut, almond, cashew, pistachio, pinion and sunflower seeds. SDS-PAGE immunoblotting with Cremodan® SL29, LBG and CTSs extracts showed a similar IgE binding profile: bands of 69, 55, 50, 35, 34, 28, 22 and 19.5 kDa were detected. Immunoblotting-inhibitions assays showed that LBG and CTS extracts produced a complete IgE-binding inhibition to extracts from Cremodan® SL29, chickpea and almond. Cremodan® SL29 was able to achieved a total IgE-binding inhibition to chickpea extract and a partial inhibition to almond extract.

Conclusion: We present a case of occupational rhinitis due to IgE-mediated allergy to Cremodan® SL29 due to presence of LBG among its component. IgE cross-reactivity between proteins from carob tree seed, chickpea and almond has been demonstrated.

1146 | Occupational asthma due to carmine (E120) inhalation in a candy factory worker

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Case report: Background: Carmine (E120) is a natural dye extracted from the dried female bodies of insect *Dactylopius coccus* (cochineal). It is frequently used in the cosmetic, pharmaceutical and food industries, and it has been involved in hypersensitivity reactions such as food intolerance or occupational asthma.

Case report: A 44 year old woman with history of allergic rhinoconjunctivitis by pollens (olive, grasses and Chenopodiaceae) reported episodes of dyspnoea, chest tightness, cough and wheezes related to work in a candy's factory. The patient related the episodes only with the manipulation of red marshmallows, but she tolerated exposure to marshmallows of other colours. Symptoms began at 30 minutes of exposure and improved with inhaled terbutaline, although on 2 occasions she had to go to Emergency Department. The patient improved on vacation and got worse when she returned to work. She needed oral corticosteroids and inhaled budesonide and formoterol for control of symptoms. Finally she was moved to other activity in the factory being asymptomatic. Examining the composition of the different candies manipulated by the patient, the only ingredient that differentiates them was the E120 present in the red marshmallows. The patient had no contact with E120 in the production line of marshmallows, but she suffered an asthma crisis needing treatment in Emergency Department after opening a container with this product to take a sample for our study.

Methods and results: At the first visit, the patient presented obstructive spirometric pattern, positive bronchodilator test, high FENO level (126 ppb), chest x-ray and CT scan without pathological findings, eosinophilia of 24.7% (1500 E/mm3) and IgE 407 UI/mL. Serum specific IgE against carmine and bovine gelatine were negative. Prick test to carmine was positive at 5 mL/mL and 10 mg/mL and negative with corn flour. The patient refused to perform bronchial provocation test with E-120.

Conclusion: We report a case of occupational asthma due to carmine (E120) inhalation in a candy factory worker, a finding no previously reported. Unlike other cases published in other work environments, our patient did not have direct exposure to this substance since she worked with the final product.

1147 | Occupational rhinitis caused by guar gum

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Case report: Introduction: Guar gum is the nutritional reserve polysaccharide of the *Cyamopsis tetragonoloba* seed's plant of the legume family. Purified guar gum fiber is a white powder that when mixed with water generates a viscous and tasteless gel and is used as a thickening agent mainly in the food industry, in juices, ice cream, sauces, pet food and baking.

Clinical case: A 42-year-old male who worked in a chemical company was referred to our Service with a one year history of nasal hydrorrhea, sneezing, ocular itching and nasal obstruction about 30 minutes later of manipulating guar gum powder with a mask. He tolerates all the legumes (quinoa, soy, chickpea, beans, etc). He has been treated by specific mite's immunotherapy in 2003 and currently complaints from slight rhinitis during spring and autumn months.

Methods and results: Skin prick test to legumes (chickpea, white bean, pea, bean) and guar gum to the 0.1, 1.5 and 10 mg/mL concentrations were negative. Total IgE was 12.5 U/mL. Specific IgE to guar gum, carob gum and bromelain (recombinant) were <0.10 kU/L. Sodium dodecyl sulfate polyacrylamide gel electrophoresis immunoblotting according to Laemmli procedure with gum guar didn't revealed IgE-binding bands proteins. In order to demonstrate guar gum powder caused symptoms to our patient we made a specific nasal provocation test with an extract of guar gum which were positive (ATM decrease in 29.9%) to the 11.01 mg/mL concentration.

Conclusion: We report a case of occupational rhinitis after manipulation of guar gum powder in which we have not been able to

demonstrate allergy to the proteins from the plant species *Cyamopsis tetragonoloba*. Those proteins accompany as contaminating molecules to the polysaccharides of guar gum purified powder. In this case the sample for electrophoresis with the guar gum powder may not contain enough proteins to be detected by the patient's serum. Besides, in vitro allergy to carbohydrate determinants were negative.

1148 | Occupational allergic contact urticaria due to aerosolized peach (prunus persica) lipid transfer protein

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Case report

Background: Peach allergy is the most common allergy to fresh fruits in Spain. Allergy to peach lipid transfer protein(LTP) Pru p 3 affects over 60% of the patients allergic to peach in the Spanish population.

We present a case of an allergic contact urticaria due to aerosolized Pru p 3 in a fruit industry worker.

Methods and patient: A 34 year-old woman with history of mild persistent perennial rhinoconjuntivitis and OAS to peach, cherries and walnuts. She works at a factory packing fruits using cotton protective gear and latex gloves. Our patient refers when she packages peaches exclusively without any direct contact with the fruit, she presents immediate pruriginous wheals and papules in exposed distant areas. The symptoms usually disappear in 24 hours.

Skin prick tests (common aeroallergens, latex, Prunus persica extract and profilin), prick to prick test with fresh fruit, specific IgE, rubbing test and open- food challenge test (OFCT) were performed.

Results: We obtained positive skin prick tests to house dust mite Dermatophagoides pteronyssinus, Olea europea pollen and Prunus persica. Prick to prick test with cherry, walnut and peach yielded a wheal of 4 mm, 11 mm and 5 mm respectively. Specific IgE was positive to Pru p 3 (11.1 kUA/L), Der p 1(2.97 kUA/L), Der p 2 (7.12 kUA/L) and Ole e 1(0.75 kUA/L).

Rubbing test with raw peeled peach and peach peel was performed. It was positive to the peel (a wheal of 9 mm) and negative to the pulp.

OFCT with 90 g of raw peeled peach was performed, presenting oral pruritus without any systemic symptoms.

Conclusion: We present a case of an occupational allergic contact urticaria due to sensitization of aerosolized peach LTP Pru p 3.

1150 | Food allergy in workers sensitized to peach leaves

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Introduction: Inhaled sensitization to peach leaf proteins has been described in isolated case reports and has been related to rPru p 3 (peach LTP).

Objectives: The objective of this study is to describe the food allergy presented in a series of patients with symptoms of occupational respiratory allergy (rhinoconjunctivitis and/or asthma) due to sensitization to peach leaves.

Results: We studied 57 patients (39 women and 18 men). Prick test with peach leaf extract was positive in 35 patients (61.4%) and serum specific IgE against that extract was positive in 44 patients (77.2%). Thirteen patients (22.8%) presented prick test positive with rPru p 3 and all of them were sensitized to peach leaves. In the immunoblotting studies without 2-mercaptoethanol, sera from 20 patients (35.1%) identified a double band of 10-16 kDa. It could correspond to LTP isoforms present in the peach leaves according to the results of the blotting inhibition tests performed.

Fifteen patients (26.3%) reported food allergy to fruits, especially fruits of the Rosaceae family (12 patients). Nine patients presented symptoms with fruits from other families and/or nuts. The most frequent clinical presentation was oral allergy syndrome (OAS) both by Rosaceae fruits (peach: 9, plum: 4, nectarine: 3 and pear: 2) and non-Rosaceae fruits (melon: 5, watermelon: 1 and mango: 1). There were 2 anaphylactic reactions in the same patient (one with kiwifruit and another one with nectarine) and 2 patients suffered acute urticaria after almond ingestion.

All patients with food allergy to Rosaceae fruits presented positive prick-prick with these fruits (peel and pulp). The patient with anaphylaxis by kiwifruit presented positive prick with commercial extract and high specific IgE (6.02 kU/L), and those sensitized to almond, positive prick with commercial extract.

Conclusions: In our study, peach leaves sensitized the majority of patients who had respiratory symptoms with occupational exposure to these trees and we showed that peach leaves could be a source of ns-LTP isoforms.

The most frequent form of food allergy in our sample was the oral allergy syndrome (OAS), both by Rosaceae and non-Rosaceae fruits.

1151 | Soybean allergy in relation to the presence of soy at the riverbank of the tajo river

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Introduction: Different episodes of asthma in specific geographic regions (Barcelona, Tarragona, Cartagena and New Orleans) happened throughout history were associated to the discharges of the ships that transport soybean and to certain meteorological conditions like the humidity, the temperature and the direction of the winds.

The hull of the soybean seed (*Glycine max*) was the main source responsible for these events.

Objectives: The aim of this study is to determine that proteins present in different soybean species were involved in the patient's symptoms

Results: We present the case of a 50 year old sailor with asthma from the age of 10, with no other relevant antecedents, referring angioedema and urticaria after ingestion of some legumes and soy drinks. He tolerated soybean sprouts (*Vigna radiata*).

From 2014 onwards, he presented symptoms of dry cough, dysphonia, dyspnoea and wheezing in the workplace (riverbank of the Tajo River) coinciding with the discharge of the soybeans in the port.

The skin tests carried out were positive to *D. pteronysinnus*, *D. farinae*, *L. destructor*, grasses and soybean. The specific IgE values were positive against D. *pteronysinnus*, *D. farinae*, soybean (*Glycine max*), maize, conglycinin and glycinin.

Proteins from pea, bean, white kidney beans, green soybeans (*Vigna radiata*), soybean (*Vigna radiata*), yellow soybean flour (*Glycine max*), hydrosoluble soybean extract (*Glycine max*) and extract of the liposoluble fraction of soybean (*Glycine max*) were transferred to a PVDF membrane and then incubated with the patient's serum, revealing a greater binding of IgE to different proteins of the extracts of pea, white bean, soybean flour and both fractions of the yellow soybean seed.

Conclusions: The differentiation of the soybean species involved in the patient's symptomatology and the possible cross-reactivity between the proteins of different species of the family fabaceae (conglicinins and glycinins) made possible the differential diagnosis of the patients

1152 | Occupational asthma to the mussel anemone, actinia equina

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Introduction: Charles Richet and Paul Portier described anaphylaxis when experimentally using anemone venom. Even though anaphylaxis caused by anemone has been recently described, occupational asthma has not. We describe below, two cases of IgE-mediated occupational asthma caused by the mussel anemone, *Actinia equina*.

Objectives: Case 1: A fisherman from Cangas (Pontevedra) specialized in loading and unloading mussels for a mussel farm. He has a 10-year history of episodes of skin pruritus, hives on exposed areas of skin, sneezing, oculonasal itching, cough and wheezing dyspnoea. These symptoms only occur when he is loading and unloading the mussels. When he is not working, he is symptom- free.

Case 2: A woman who has worked for 40 years at a mussel treatment plant in Moaña (Pontevedra). In November 2015, she began to suffer episodes of sneezing, oculonasal itching, cough, wheezing dyspnoea and nocturnal dyspnoea. Her symptoms worsened at work and improved at home during the weekend.

Both related their symptoms to exposure to the anemone found on mussel shells (*Actinia equina*). We performed an occupational asthma study.

Results: Specific bronchial provocation test using anemone extract:

Case 1: Positive at a concentration of 1:100 p/v, with a 28% fall in FEV_1 after 10 minutes. Spontaneous recovery after two hours and no late response.

Case 2: Positive at a concentration of 1:10 p/v, with a 43% fall in FEV_1 after 5 minutes, and a late response after 8 hours with a 26% fall in FEV_1. • Negative provocation in 2 asthmatic patients used as control.

Skin prick tests using anemone extract:

Case 1: *Actinia equina* 9 mm (3+); Histamine (10 mg/mL) 6 mm; Glycerol saline 0 mm

Case 2: *Actinia equina* 7 mm (2+); Histamine (10 mg/mL) 8 mm; Glycerol saline 0 mm • Controls: negative in 5, non-atopic people.

Battery of common inhalants and food extracts, including mussel: Negative in both patients.

Immunodetection:: Case 1: 3 IgE binding bands were detected with a MW of 20, 32 and 40 kDa.

Case 2: 3 IgE binding bands were detected with a MW of 25, 30 and 40 kDa.

Conclusions: We present two cases of IgE-MEDIATED, OCCUPATIONAL ASTHMA to the mussel anemone, *Actinia equina*.

1153 | Occupational asthma caused by poppy seeds (papaver somniferum)

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Introduction: Some cases of occupational allergy due to CPS (concentrate of poppy straw), and anaphylaxis due to the ingestion of

poppy seeds have been published, but there is nothing in the literature regarding occupational allergy caused by the manipulation of poppy seeds. We now describe a case of occupational asthma caused by the manipulation of poppy seeds.

Objectives: Case: A 27 year-old male who works in a morphine company (Alcaliber) manipulating CPS, separating the straw from the poppy seeds. The patient was asymptomatic until 5 months before visiting our clinic, referring ocular and nasal congestion and respiratory problems twice a week. The patient reported a worsening of symptoms some minutes after starting work, requiring the use of rescue bronchodilators 3 to 5 times a day during his work shift. The patient mentioned an 80% improvement in symptoms during vacations. Occupational asthma and allergy study tests were performed.

Results

Skin prick tests: Inhalants: Dog and cat dander, *D. pteronyssinus*, *Dactylis*, *Trisetum*, *Olea*, *Platanus*, *C. arizonica*, *Quercus*, latex: negative. *Alternaria* 13 mm^2 (1+). Glycerol saline: negative. Histamine 37 mm^2

CPS: 4 mm^2 (1+); Poppy seeds: 12 mm^2 (3+). Glycerol saline: negative. Histamine: 10 mm^2

Specific Bronchial Provocation Test: Poppy seed extract: positive [PC_{20}= 7, 14 mg/mL]. Poppy straw extract: negative (decrease in FEV1 < 20%).

Methacholine Test: PC_{20} (mg/mL) 0.87.

FE_{NO} (ppb): Poppy extract

Pre-provocation test: 18 ppb.

Post-provocation test: 47 ppb.

ELISA (Poppy seeds): negative.

Western Blot: Molecular weight bands compatible with allergens described in *Papaver somniferum* (Pap s1 17 kDa y Pap s 34 kDa).

Conclusions: We describe a case of IgE-mediated occupational asthma caused by allergy to poppy seed proteins (*Papaver somniferum*).

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ASTHMA EPIDEMIOLOGY

1151 | Impact of omalizumab on healthcare utilization among patients with uncontrolled allergic asthma followed in Canadian clinical settings

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Introduction: In Canada, it is estimated that asthma affects 8.5% of the total population. It is the leading cause of hospital admissions, the third leading cause of work loss, and results in 146 000 emergency room visits annually in the overall population. Severe uncontrolled asthma contributes to about 50%-94% of asthma-related expenditures. Omalizumab is indicated for the treatment of adults and adolescents with moderate to severe persistent asthma whose symptoms are inadequately controlled despite optimized standard therapy. RCTs have consistently shown that administration of omalizumab is associated with fewer asthma exacerbations per patients translating into less health care utilization (HCU). Real world effectiveness data assessing the HCU in the Canadian context is limited.

Objectives: This study is a retrospective, pre-post cohort, observational study. The primary objective was to evaluate the impact of omalizumab on health care utilization (HCU) as assessed by the reduction in number of hospitalizations, emergency room (ER) visits, and oral corticosteroid (OCS) use in patients covered in Ontario. The number of night awakenings was an exploratory endpoint. Omalizumab was added for drug coverage to the Ontario Trillium Drug Program's Exceptional Access Program list on January 19, 2012.

Results: 148 patients (mean age 57.6; female 62.2%) formed the study population. Omalizumab was associated with a 74.4% reduction in the number of hospitalization (pre- vs post-omalizumab 12 month treatment period: 0.7 vs 0.2 $P < .001$). 89.9% of patients did not have any asthma related hospitalization. There was a reduction of 87.5% in ER visits (7.3 vs 0.9 $P < .001$), 66.2% of patients did not have any emergency visit. A 74.7% reduction of the number of high dose OCS by (4.23 vs 1.07 $P < .001$), 52.7% of patients did not need to take any courses of high dose OCS. The mean number of night awakenings / per week decreased from 6.1 (8.03) to 1.3 (2.79) following 12 month treatment with omalizumab.

Conclusions: Treatment with omalizumab of patients with persistent uncontrolled asthma is associated with a significant decrease in the number of hospitalizations, ER visits, oral corticosteroid use, and QoL parameters such as number of night awakenings in a Canadian real-world setting. The results are consistent with outcomes observed in previous large real-world trials such as the experience registry.

1155 | Non-utilization of medical rehabilitation before the occurrence of early retirement due to asthma bronchiale in Germany– prevalence and sociodemographic correlates

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Introduction: In Germany the statutory pension insurance fund covers the cost of rehabilitation treatment for employees whose working capacity is endangered due to health problems. The underlying principle called "rehabilitation over retirement" is the concept to avoid early retirement due to health problems by rehabilitation.

Objectives: The aim of the study is to describe the utilization of medical rehabilitation before the occurrence of early retirement due to asthma bronchiale in Germany from 2003 to 2014 and to investigate potential sociodemographic determinants. Analysis based on 20% random samples of administrative pension records from the Research Data Centre of the German Federal Pension Insurance, which include of all new cases of early retirement. We used logistic regression models to investigate the risk of non-utilization of medical rehabilitation during five years before the occurrence of early retirement. Age, sex, marital status, non-German citizenship, school and vocational education, professional career and annual income were considered as potential risk factors.

Results: Among all early-retired patients due to asthma bronchiale 46.7% (428 out of 917) did not utilized medical rehabilitation during five years before the occurrence of early retirement.

Risk for non-utilization was higher among men (compared to women, adjusted OR: 1.4; 95% CI: 1.0-1.9) and increased with age (60 to 64 years compared to 25 to 44 years, 2.8 [1.6-4.9]). Further risk factors for non-utilization were to be unmarried or widowed (vs married, 1.3 [1.0-1.8]), unknown or low educational level (vs median educational level, 1.7 [1.2-2.5]), as well as low annual income (1st quartile vs 4th quartile, 6.3 [3.9-10.2]).

Conclusions: Despite the importance of medical rehabilitation among patients with asthma bronchiale more than 46% of them obtained no medical rehabilitation during five years before the occurrence of permanent work disability, worst affected are deprived persons.

1156 | Costs of exacerbations in asthma in a French tropical island (Reunion Island)

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Introduction: Asthma is one of the most common chronic and disabling diseases worldwide, and exacerbations affect resource burden and health costs.

Objectives: This study was to examine the costs of asthma exacerbations in relation to differing degrees of severity. Patient clinical history records were reviewed from 452 patients who had one or more visits to our clinic due to asthma between 2013 and 2015. Exacerbations were divided into different levels of severity according to the GINA spirometric criteria: mild (self managed), mild/moderate (antibiotics and or without systemic corticosteroids), moderate (healthcare center visits) and severe (emergency care visits or hospital admissions).

Results: 152 subjects (34%) reported at least one exacerbation. A significant relationship was found between severity of exacerbation and costs. The mean annual total cost, valued in Euros at price level 2015, per exacerbation was 44 (mild), 69 (mild/moderate), 335 (moderate) and 3015 (severe). The prevalence-weighted cost of all exacerbations for an average subject with asthma was about 275, according for about 40% of the direct costs: 80 (mild), 210 (moderate), 3100 (severe) and 5700 (very severe).

Conclusions: The costs for exacerbations increase considerably by different levels of severity in asthma. Prevention of asthma exacerbation could thus be very cost effective.

1157 | Correlation between the age of onset of asthma and the severity of asthma in elderly patients

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Introduction: Introduction: In the elderly, asthma is underdiagnosed and involves several factors such as aging, lung and immune system disorders, epigenetic factors, exposures, various comorbidities and psychosocial effects. There are at least two major adult asthma phenotypes; those of early onset, where asthma is typically atopic with predominant Th2 inflammation. In contrast, patients with late-onset asthma are often non-atopic, more likely to develop a persistent airflow limitation.

Objectives: To correlate the severity and the different late onset asthma phenotypes versus early onset in older adults, various comorbidities and psychosocial effects.

Material and method: We studied 75 patients from 60 to 86 years of age. Divided into: Asthmatics with early onset (<40 years) and late onset asthmatics (≥40 years).Classified as Intermittent Asthma, Mild Persistent, Moderate and Severe, according to GINA. Serum IgE, absolute eosinophilia, FEV1 pre- and post-bronchodilator were determined for each patient. We performed Asthma Control Test (ACT), and skin prick test with aeroallergens, which were divided into Negative, Monosensitized and Polysensitized.

Results: Mean age was 64.7 years (SD ± 5.8), 24 were male and 51 female. Early-onset Asthma patients were: female 64.1% and male 35.9% ($P = .078$). ACT ≥20 53.85% and lower 46.15% of patients ($P = .631$). Eosinophilia: they had> 400cel/cc 17.95% and <400 82.05% ($P = .000062$). IgE<154 IU/dL 52.41% and ≥154 43.59% ($P = .4233$). FEV1 was 46.15% <80 and 53.85% ≥80 ($P = .6310$). ($P = .00023$). Skin prick test: 35.9% monosensitized ($P = .0781$), negative 2.56% ($P < .0000001$) and polysensitized 61.53% ($P = .1495$). In Late Onset Asthma, we found: Female 72.22% and male 27.77% ($P = .0076$). ACT ≥20 55.55% and 44.44% fewer patients ($P = .505$). Eosinophilia: 33.33% had> 400cel/cc ($P = .0455$), <400 66.66% ($P = .0455$). IgE<154 IU/dL 58.33% and ≥154 41.66% ($P = .317$). FEV1 50% was<80 and the other 50% ≥80 ($P = .99$). Skin prick test: Monosensitized 22.22%, negative 22.22% ($P = .00085$) and polysensitized 55.55% ($P = .505$).

Conclusions: In late-onset asthma, women predominate, pulmonary function is reduced and is more frequently related to COPD overlap than early-onset asthma. Sensitization to aeroallergens is more frequently negative in late than early onset.

1158 | Level of control of patients with severe asthma at a tertiary hospital

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Introduction: Severe asthma (SA) prevalence in Spain is between 5% to 10% of asthmatics, with a high resource consumption related to level of control.

Objectives: Analyze the level of control of the severe asthmatic population older than 14 years in a tertiary hospital.

Results: All clinical histories of patients evaluated at external and specialty consultation, diagnosed as SA older than 14 years, during 2015, were reviewed. Level of control was analyzed according to American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria. Hospital and Intensive Care Unit (ICU) admissions whose primary or secondary diagnosis (according to CIE-9-MC) was extrinsic asthma, intrinsic, chronic obstructive, other ways of asthma,

and non-specified asthma; as well as asthma exacerbations treated at emergencies, were counted during 2013-2015.

Fifty-four of the 123 patients (44%) included in the study were well controlled. The number of admissions in 2013, 2014 and 2015 were 145, 127 and 119 respectively. When the incidence density rate (ID, defined as the number of events divided by the amount of person-time observed) was analyzed for hospital admissions, no significant differences were found; neither for the admissions at the ICU (3.56, 4.21 and 5.44 at 2013, 2014 and 2015, respectively; $P > .05$). On the other hand, a significant decrease in the ID rate for asthma exacerbations assisted at emergencies in 2015 (239.5, 275.7 and 340.9 in 2013, 2014 and 2015, respectively) was observed. Therefore, it suggests that exacerbations had the severity enough to justify the admission.

Conclusions: Our control data of SA do not differ from other reviews, but should be increased. Furthermore, the lack of decrease of admissions observed, force the specialists to re-evaluate the assistance of the affected population.

1159 | Older adults with asthma: characteristics and outcomes of long-standing versus late-onset asthma

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Introduction: Asthma in the elderly is under diagnosed and under treated and there is a paucity of knowledge.

Objectives: To examine the effect of age of onset on clinical characteristics and outcomes in a cohort of older patients with long-standing (LSA) and late-onset asthma (LOA). In all, 148 patients 60 years of age and older with persistent asthma were recruited. We defined LOA as asthma developing at age 40 or later and LSA as developing before age 40. We compared airway obstruction as assessed by spirometry, as well as asthma control using the Asthma Control Test and asthma-related emergency department visits and hospitalizations among patients with LSA vs LOA. Information on age at onset, demographics, heredity, and home and occupation exposure was also collected.

Results: Patients with LOA, were less likely to have FEV1 < 70% of predicted (41% vs 60%, $P < .05$), to have FEV1/FVC<0.7 (51% vs 67%, $P < .05$), and were also less likely to report a history of allergic conditions (39% vs 81%, $P < .05$). Higher emergency department visit and hospitalization rate were observed in patients with LOA ($P < .05$). Also asthma control was worse in patients with LOA. No differences were noted in demographic information, medical comorbidities, and compliance between LSA and LOA subjects.

Conclusions: Older adults with LOA have different clinical and physiological characteristics and outcomes compared to those with LSA. Some of these differences may represent sequelae of long-standing disease, however LOA may also represent a different clinical phenotype.

1160 | Variability in assessment of severe asthma at a tertiary hospital

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Introduction: Severe asthma (SA) prevalence in Spain is between 5% and 10% of asthmatics. A correct approach and re-evaluating diagnosis is critical in this population, trying to exclude other or additional respiratory diagnosis, and to identify unrecognized triggers such as allergens.

Objectives: Analyze and compare SA patients assisted at outpatient clinic and specialty consultation of Allergology and Pneumology of a tertiary hospital, focusing on the approach followed and basic diagnosis techniques.

Results: All clinical histories of patients evaluated at outpatient clinic and specialty consultation of Dr. Peset University Hospital, with a diagnostic of severe asthma or bronchopulmonary aspergillosis (BPA) during 2015, were reviewed. The age, sex, duration of symptoms, atopic background, admissions in the previous year, emergency consultation, smoking habit, nasal polyposis, aspirin-sensitive asthma (ASA) syndrome, BPA, treatment and level of control were registered. Furthermore, methods used for the diagnosis of asthma (pre and post-bronchodilator spirometry or methacholine challenge) and for detection of sensitization to inhaled allergens (skin prick tests and/or specific IgE antibodies) were registered. Patients attended by Allergologist and Pneumologist did not differ on anthropometric characteristics, duration of symptoms, smoking habits, polyposis, and presence of ASA syndrome or BPA. Drugs prescribed in both specialities were similar, except for glycopyrronium which was more used in patients treated at Pneumology, and omalizumab used more frequently in Allergology. Most relevant findings were observed at the basic study for diagnosis. In the group of patients (n = 59) controlled by an Allergist, the diagnosis of asthma was based on pre and post-bronchodilator spirometry or methacholine challenge in 55 (93%), whereas this only occurs in 69% of patients controlled by a Pneumologist ($P < .001$). Studies to identify allergic sensitization were performed in 100% of the group controlled in Allergology, but only in 55% of the group controlled in Pneumology ($P < .001$).

Conclusions: Important differences were perceived, especially on the diagnosis of populations with severe asthma assisted at both specialties, fact that supports the importance of decrease the variability in clinical management by establishing multidisciplinary teams in each hospital.

1161 | Prevalence and seasonal variation of airway hyper-responsiveness in asthmatic children in Taiwan

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Introduction: Airway hyper-responsiveness(AHR) is a key feature of asthma and could be detected through various bronchoprovocation tests. Methacholine acts directly on the airway smooth muscle receptor and has both high sensitivity and specificity compared to other tests in diagnosis of asthma. In pediatric population, the percentage of positive methacholine challenge test(MCCT) in asthmatic children varies among studies and some have also reported seasonal variability. However, these studies were mostly performed in temperate region.

Objectives: The study aims to evaluate the prevalence of airway hyper-responsiveness and its seasonal variation in asthmatic children in Taiwan, a subtropical country.

Methods: A total 276 asthmatic children and their methacholine challenge test (MCCT) results were retrospectively reviewed. All of them were diagnosed with asthma less than 5 years and were receiving regular asthma controllers. They did not have any symptom of fever, respiratory infection or acute exacerbation when performing MCCT. These children were divided into 4 season groups according to the date of MCCT done and the season classification was defined by Central Weather Bureau, Taiwan. Subgroup analysis included gender, age, and atopy level were compared for the seasonal difference.

Results: The prevalence of methacholine hyper-responsiveness was 70.7% (n = 195) while children with older age and higher IgE are significantly sensitive to methacholine (P = .019, <0.005, respectively). In children with body weight above 97th percentile, the prevalence of MCCT was 58.5%, which is significantly lower than the average (P = .049). There was no significant difference of AHR prevalence among seasons (64.7%, 71.2%, 66.7%, 80%, from spring to winter, P = .48). The percentage of borderline, mild, and moderate severity of MCCT were almost equally distributed; even in different seasons. In the subgroup analysis, there was no significant seasonal variation of MCCT among gender or age groups. Only children with higher IgE level (≥75th percentile) are more sensitive to methacholine in summer season (88.6%, P value = .016).

Conclusions: More than 70% of asthmatic children in Taiwan have airway hyper-responsiveness and the prevalence did not change among seasons. Children with high IgE level may be more sensitive to methacholine in summer season.

1162 | Relation between atopy and positive bronchoprovocative methacholine challenge testing (BPT) in suspected asthma patients

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Introduction: The aim of this study was to present the relationship between atopy and the positive outcome of bronchoprovocative methacholine challenge testing (BPT) in 282 patients suspected of having asthma—tested between 2012 and 2015 in the Outpatient Centre for Respiratory Diseases in Zagreb.

Objectives: Skin prick test (SPT), radioallergosorbent test (RAST), spirometry with bronchodilator reversibility testing (BDT) with salbutamol and bronchoprovocative methacholine challenge testing (BPT) were performed in all patients. Atopy was defined as at least one positive reaction in skin prick test to an inhalatory allergen, confirmed with positive radioallergosorbent test (RAST). An increase of 12% and 200 mL in either FEV_1 or FVC after salbutamol were considered as a positive bronchodilator reversibility test. The methacholine test was considered positive at $PC_{20}FEV1 < 8$ mg methacholine.

Results: Out of 282 patients (mean age 37 ± 13), 100 were male (35.5%), the number of smokers was 33 (11.7%). Atopic diathesis was found in 117 patients (41.5%) and was not confirmed in 165 patients (58.5%). In 117 cases of suspected asthma with atopy, 23 patients (19.7%) were found positive bronchodilator reversibility testing (BDT) and 94 patients (80.3%) were found negative. Out of 165 cases (58.5%) of suspected asthma without atopy, in 27 patients (16.4%) BDT was positive and in 138 patients (83.6%) was negative. Out of 117 subjects with atopy and clinical signs and symptoms of suspected asthma, 72 patients (61.5%) were found positive bronchoprovocative methacholine challenge tests (BPT) and 45 patients (38.5%) were found negative. In 165 cases of suspected asthma without atopy, 70 patients (42.4%) were found positive BPT and 95 patients (57.6%) were found negative. BPT was significantly more frequently positive in atopic patients (X^2 = 0.02).

Conclusions: Our results suggest that positive atopy test (skin prick test and RAST) and positive BPT are related in suspected asthma patients. This finding may suggests that atopic diathesis is predictive factor for asthma, and should strongly encourage further diagnostic testing in suspected asthma patients.

1163 | Prevalence change of asthma and allergic diseases by using claim data from national health insurance service in Korea: 2004-2013

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Introduction: Asthma, allergic rhinitis, and atopic dermatitis are very common in Korea. There are many reports to show the epidemiology and risk factors of allergic diseases. It is available to analyze the National Health Insurance Service Data.

Objectives: To show the prevalence change during recent decade, I designed this study. Medical claim data during 2004-2013 from the Korea National Health Insurance Service were used. These data were classified as kinds of allergic disease, age, sex, and patients type.

Results: The prevalence of allergic rhinitis is increasing (Figure 1). But the prevalence of asthma and atopic disease is not. The cost of allergic rhinitis is increasing (Figure 2), but the cost of asthma and atopic dermatitis is not. The cost of asthma in adult over 18 years old is increasing, but in children under 19 years old is not. The cost of asthma in inpatients is increasing, but in outpatients is not. The prevalence of asthma in boy was higher than in girl, but in women over 50 years old was higher than in men. The prevalence of severe asthma is increasing. The prevalence of severe asthma in boy was higher than in girl, but in women over 50 years old was higher than in men.

Conclusions: The big data (Korea National Health Insurance Service) is good to find out and evaluate the epidemiological characteristics of allergic diseases in Korea.

1164 | Prevalence of asthma in patients with psoriasis

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Introduction: 1236 psoriatic patients (669/54.13% men and 567/45.87% women) were admitted to the Dermatology outpatient clinic during 2004-2012.

Psoriasis was diagnosed based on clinical and histological criteria. All medical data were recorded: age, gender, duration of psoriasis, age of onset of psoriasis, and severity of psoriasis (using PASI- the psoriasis area and severity index). Asthma was diagnosed at Pneumology Department.

Objectives: The aim of the study was to investigate the prevalence of asthma in patients diagnosed with psoriasis.

Results: Among 1236 patients diagnosed with psoriasis only 11 (3 men and 8 women) were diagnosed and treated for asthma at the moment of dermatological examination. Asthma was associated with psoriasis in patients under the age of 20 in 2 cases; 4 cases of asthma were recorded in adults aged 30-50.

Conclusions: The relationship between psoriasis and asthma is controversial. Present study failed to prove a high prevalence of asthma in patients diagnosed with psoriasis regardless the age or gender of patients.

Gender	Nr. cases of psoriasis	Nr. cases of psoriasis associated with asthma
Male	669	3
Female	567	8
Total	1236	11

1165 | Severe asthma profile in Madrid, Spain

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Case report

Introduction: Severe asthma is defined as asthma that requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic corticosteroids to prevent it from becoming "uncontrolled" or that remains "uncontrolled" despite this therapy.

These patients present a special challenge because of the extensive diagnostic evaluation that they need and their high consumption of health-care resources.

Objectives: The aim of this study is to describe the epidemiological features, comorbidities, professional and sensitization profile of patients with severe asthma diagnosis.

Materials and methods: We conducted a retrospective descriptive study using data collected in the Allergy unit of Infanta Leonor Hospital (Madrid, Spain). 84 patients (≥18 years) with severe asthma were included. Skin prick test was performed with the most common aeroallergens of our environment.

Results: In this population aged 29-79, 89% were female, had a medium age of onset of 15.9 years, 57% were non smokers and 87% were born in Spain.

The vast majority were patients without atopic dermatitis, urticaria or angioedema. 31% and 20% had drug and food allergy respectively.

Professional profile was not clearly established but mostly were cleaners.

Regarding comorbidities, 83% had rhinitis (73% perennial rhinitis), 23% nasal polyposis, 30% gastroesophageal reflux disease, 5% obstructive

apnea syndrome and 19% had psychiatric disorders. Forty-two percent of patients were overweight and 25% were obese.

All of this population were atopic, and 82% were polysensitized to aeroallergens.

Conclusion: Our severe asthma profile is a medium age overweight female with earlier age at onset, perennial rhinitis and polysensitized. No association with atopic dermatitis, urticaria/angioedema, drug and food allergy was observed.

1166 | Body mass index and risk of asthma and asthma-like symptoms in childhood

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Introduction: A positive association between body mass index (BMI) and asthma has been suggested. Several theories to explain the complex association between overweight/obesity and asthma include an impact of genetic/epigenetic factors, environmental factors (diet, physical activity), mechanical factors, and immunologic mechanisms.

Objectives: The aim of the study was to examine the relationship between high BMI and asthma in The Republic of Macedonia as a developing country with low prevalence rates of obesity and asthma. Parental-reported data obtained through a survey of 2310 children aged 5-15 years from randomly selected schools in Skopje, the capital of Macedonia, in 2015/2016 was used. BMI of each child was calculated using parental-reported weight and height as weight (kg)/height $(m)^2$. The international cut-off point for BMI defined to pass through 25 kg/m^2 at age 18 for males and females aged 2-18 years, was used to define high BMI (overweight/obesity). The association between high BMI and current asthma-like symptoms, and ever-diagnosed asthma was investigated after adjustments for potential confounders (age, sex, diet, TV-watching time, physical activity, tobacco smoke exposure at home, maternal education level) using multiple logistic regression.

Results: The prevalence of high BMI was 24.1%. Current wheeze was documented in 6.5% of children, sleep-disturbing wheeze in 3.6%, exercise-induced wheeze in 1.7%, dry night cough apart from a cold in 12.2%, and diagnosed asthma in 2.3%. High BMI significantly increased the risk of current wheeze (aOR: 1.72; 1.16-2.55; $P < .01$), sleep-disturbing wheeze (aOR: 1.82; 1.09-3.02; $P = .02$), exercise-induced wheeze (aOR: 2.11; 1.03-4.35; $P = .04$), and asthma (aOR: 1.97; 1.04-3.76; $P = .04$).

Conclusions: These findings suggest a positive association of BMI with current asthma-like symptoms and asthma, thus further supporting the overweight hypothesis in asthma. Healthy diet and regular physical activity should be strongly recommended in children to avoid overweight/obesity and thus to contribute in asthma prevention.

1168 | Birth decade affects the sensitization pattern and asthma-risk in Finnish adult population

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Introduction: The increased prevalence of asthma and allergic diseases is a major public health problem worldwide. The prevalence of adult asthma has increased during the past decades and is around 9% in Northern Europe. Atopy, family history, smoking and exposure to inhaled irritants are known risk factors of asthma. In Finland, sensitization rates to birch pollen and cat have increased during the past 10 years. The risk factors of asthma not only diverge between different environments, populations and age groups, but they are also affected by time of living. We used previous population-based case-control data (N = 523) from Finnish adult asthma patients with one or two matched controls. Asthma was diagnosed based on a typical history of asthmatic symptoms and lung function tests. Allergic sensitization was determined by skin prick test (SPT) to 17 aeroallergens. Information on demographics was obtained by a questionnaire.

Objectives: We have previously shown that a large number of sensitizations to several types of allergens distinguishes subjects with adult-onset asthma in Finland. The aim was to analyze how age affects sensitization and asthma-risk.

Results: Sensitization to more than one allergen type and the number of positive SPT reactions associated with younger age and asthma. Atopic subjects aged 65 or over were characterized by sensitization to only 1-2 allergens, with very few animal danders and without an association with asthma.

Conclusions: Multiple sensitizations and animal dander sensitization might characterize Finnish asthmatic adults aged under 56.

Cohort studies are needed to understand timing of host-environmental interactions behind this.

1171 | The impact of swimming pool attendance on schoolchildren allergic and respiratory inflammation

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Introduction: Swimming is not only one of the most practiced sports worldwide, but is also a frequently recommended by physicians. However, this belief has been questioned over the last decade as some studies suggest that swimming pool attendance and consequent exposure to disinfection by-products exposure may be partly responsible for enhanced incidence of childhood asthma and allergy.

Objectives: The aim of this study was to evaluate the influence of swimming pool attendance on the inflammatory response and asthma prevalence of schoolchildren.

Results: To achieve these objectives, a cross-sectional survey of 858 children (7-12 years old), attending 20 primary schools in Porto, Portugal, was conducted. Skin-prick-tests to aeroallergens, lung function (spirometry with bronchodilation), exhaled nitric oxide levels (eNO), exhaled breath condensate analysis (pH, conductivity, Na^+, K^+) and pupillometry were performed. Subjects were defined as "current swimmers" (CS) if they attended an indoor swimming pool at least once per week in the past six months. If they swam in the past (over six months) but ceased the activity, they were regarded as "past swimmers" (PS). Otherwise, if the children never swam or swam less than once per week, they were classified as "non-swimmers" (NS). Asthma was defined in accordance with four different criteria, as reported in Table 1. Since non-Gaussian distributions were observed, non-parametric tests were used to analyse the data. A total of 205, 228 and 342 children were classified as CS, PS and NS, respectively. The remaining 83 children did not answer the question. There were no significant differences in the prevalence of asthma (for any of the 4 definitions), atopy and baseline lung function variables among the three groups. Median eNO levels were significantly higher in CS when compared to NS, and, FEV1 reversibility after bronchodilation was significantly higher in CS when compared to PS and NS. CS also had a significantly lower pupillary maximum constriction velocity (MCV) that PS and NS. There were no differences in the exhaled breath condensate variables between groups.

	Current swimmers	Past swimmers	Non-swimmers	*P*
N (males)	205 (99)	228 (115)	342 (175)	—
Age (years, mean ± SD)	9 ± 1	9 ± 1	9 ± 1	.011
Weight (kg)	30.9 (26.6-36.9)	32.1 (28.2-37.8)	30.8 (26.9-37.3)	.048
Height (cm)	135 (130-139)	136 (131-141)	136 (131-141)	.196
BMI (kg/m^2)	16.9 (15.4-19.4)	17.5 (15.7-19.8)	16.7 (15.4-19.6)	.099
Atopy (n, %)	32.8%	39.5%	34.2%	.302*
Lung function				
FEV_1 (L)	1.73 (1.58-1.95)	1.78 (1.60-1.99)	1.74 (1.55-1.92)	.081
FVC (L)	1.88 (1.71-2.15)	1.91 (1.71-2.18)	1.88 (166-2.10)	.125
FEF_{25-75} (L/s)	2.23 (1.97-2.71)	2.36 (1.93-2.71)	2.27 (1.91-2.59)	.423
FEV_1/FVC (%)	92.8 (89.1-96.1)	92.5 (89.0-96.6)	92.7 (88.8-96.4)	.998
FEV_1 reversibility (mL)	70 (20-130)	60 (10-120)	60 (-10-110)	.028
FVC reversibility (mL)	40 (-30-100)	30 (-30-80)	20 (-40-90)	.219
Exhaled NO (ppb)	12 (7-20)	11 (6-20)	10 (5-19)	.086
Asthma[¥]				
Clinical criteria (n, %)	11.7%	8.3%	9.4%	.459*
Functional criteria (n, %)	6.3%	7.0%	6.4%	.957*
Treated asthma (n, %)	6.3%	4.0%	6.1%	.441*
Ever asthma (n, %)	7.3%	4.8%	7.3%	.438*
Otitis (n, %)	27.0%	21.0%	32.4%	.043*
Eczema (n, %)	66.7%	62.9%	54.4%	.465*
Allergic rhinitis (n, %)	33.3%	33.8%	31.1%	.907*

(Continues)

TABLE (Continued)

	Current swimmers	Past swimmers	Non-swimmers	*P*
EBC parameters				
pH	6.2 (5.8-6.8)	6.5 (6.0-7.8)	6.5 (6.0-7.5)	.223
Conductivity ($\mu S/cm^3$)	94 (69-135)	109 (54-380)	100 (68-182)	.822
Na^+ (ppm)	38 (30-44)	39 (24-46)	41 (31-48)	.535
K^+ (ppm)	10 (4-35)	14 (6-74)	10 (4-51)	.206
Pupillometry				
Maximum diameter (mm)	5.2 (4.6-5.8)	5.3 (4.7-5.9)	5.4 (4.8-5.9)	.295
Minimum diameter (mm)	3.3 (3.0-3.8)	3.4 (2.9-3.8)	3.4 (3.0-3.8)	.449
ACV (mm/s)	4.0 (3.5-4.3)	4.0 (3.6-4.5)	4.1 (3.6-4.5)	.068
MCV (mm/s)	5.2 (4.6-5.8)	5.4 (4.7-6.0)	5.4 (4.9-5.9)	.019
ADV (mm/s)	1.2 (1.0-1.3)	1.1 (0.9-1.4)	1.2 (1.0-1.4)	.417

Data reported as median (25-75%) unless otherwise stated. BMI: body mass index; FEV_1: forced expiratory volume in the first second of FVC; FVC: forced vital capacity; FEF_{25-75}: forced expiratory flow middle portion of FVC; EBC: exhaled breath condensate; ACV: average constriction velocity; MCV: maximum conscription velocity; ADV: average dilation velocity. The *P* values signalling differences between the three groups were calculated using the Kruskal-Wallis test for non-parametric variables, with the exception of the cases marked with (*) which were calculated using qui-square tests. ¥The following operational asthma definitions were adopted: (i) Clinical criteria—at least a 12% increase in FEV1 after bronchodilation and over 200 mL and/or asthma diagnosed by a physician with reported symptoms (wheezing, dyspnoea or dry cough) occurring in the past 12 months; (ii) Functional criteria—at least a 12% increase in FEV1 after bronchodilation and over 200 mL; (iii) Treated asthma criteria—asthma diagnosed by a physician and currently under inhaled corticosteroid treatment; and iv) Ever asthma—asthma diagnosed by a physician.

Conclusions: Swimming pool attendance was not significantly associated with increased prevalence of asthma or atopy in schoolchildren. Although an impact on airway reversibility, eNO levels and autonomic nervous function was observed, no clinical implications were associated with swimming practice.

1172 | Is there a link between exercise-induced bronchospasm and gastroesophageal reflux in asthmatic children?

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Introduction: Physical activity is known to cause gastro-oesophageal reflux (GER), and GER can exacerbate asthma symptoms. Exercise-induced bronchospasm (EIB) is a frequent finding in young athletes that may impair training and performance.

Objectives: We wished to assess the interaction between asthma, gastro-oesophageal reflux disease (GERD) and exercise based on multichannel intraluminal impedance (MII)/pH recording. Thirty children (16 boys, mean age 14.2 ± 2.3 years) with partially controlled or uncontrolled bronchial asthma were enrolled and 48-h MII/pH recording undertaken. An exercise challenge test (ECT) was done after the first 24 h of MII/pH recording. Data before and after the ECT were analysed separately. Usual asthma treatment was continued throughout the study.

Results: Acid GER was diagnosed in 7 (23.3%) children based on pH recording and in 14 patients (46.6%) based on MII/pH recording. Acid and non-acid GER were found in 17 (56.6%) children based on MII/pH recording. The ECT was positive in 6 children. MII/pH recording during the ECT revealed that physical effort increased the number of reflux episodes ($P = .006$). In the GER-positive group after the ECT, the mean acid clearance time and longest episode of reflux were significantly higher than before the ECT ($P = .019$, $P = .001$; respectively).

Conclusions: EIB is not more frequent in asthmatic children with GERD and is not related to GER episodes. Short-duration intensive exercise increases GER, especially in a group of patients with pathological GER.

TUESDAY, 20 JUNE 2017
TPS 40
RHINITIS AND RHINOSINUSITIS

1173 | Profile of patients with persistent allergic rhinitis prescribed MP-AzeFlu®* in routine clinical practice in the Austria

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Introduction: Many allergic rhinitis (AR) patients visiting their doctor have moderate-to-severe persistent disease.

Objectives: (i) To characterize patients with persistent AR (PER) prescribed Meda Pharma's AzeFlu (MP-AzeFlu) (a novel formulation of azelastine hydrochloride, fluticasone propionate and excipients in a single spray) in real-life in Austria and (ii) to quantify the personal symptomatic burden of PER in Austria prior to MP-AzeFlu prescription. This study had a prospective, observational design and included 214 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to label. Information was gathered on patient demographics, AR phenotype, allergen sensitization, symptomatology, previous AR treatments in the last year (prior to MP-AzeFlu prescription) and reason for MP-AzeFlu prescription.

Results: Classified traditionally, there was a fairly evenly split between patients suffering from both seasonal AR (SAR) and perennial AR (PAR) (n = 113; 52.8%) and those with PAR alone (n = 101; 47.2%). Sensitization to house dust mite predominated (n = 163; 76.2%), followed by animal dander (cat: 19.2%; dog: 7.9%; other pet: 2.8%). Prior to MP-AzeFlu prescription patients reported troublesome symptoms (n = 132; 61.7%), sleep disturbance (n = 112; 52.3%), impairment of daily activities (n = 105; 49.1%), and impairment of school/work (n = 73; 34.1%). Congestion was considered the most bothersome symptom by most patients (n = 115; 53.7%). The most frequent reason for MP-AzeFlu prescription was that other therapies were not sufficient in the past (n = 127; 59.3%) or not sufficient to treat acute symptoms (n = 51; 23.8%). Most of these PER patients were previously treated with oral antihistamines (n = 118; 55.1%), intranasal corticosteroids (n = 97; 45.3%) or intranasal antihistamines (n = 71; 33.2%). 55.1% (n = 118) of patients reported using ≥2 AR therapies in the past year, but 15.4% (n = 33) reported using no AR therapy at all. 15.0% of patients (n = 32) reporting currently undergoing allergen specific immunotherapy (AIT), while 10.7% (n = 23) had had an AIT course in the past.

Conclusions: Many patients in Austria live with uncontrolled persistent AR despite treatment with mono- and multiple therapies. A more effective treatment option, like MP-AzeFlu, should improve AR control and reduce costs associated with its management.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies

1174 | Profile of patients with uncontrolled allergic rhinitis prescribed mp-azeflu®* in routine UK clinical practice

Scadding G[1]; Price D[2]; El-Shanawany T[3]; Ahmed S[4]; Ray J[5]; Sargur R[6]; Kumar N[7]
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Introduction: One in 4 individuals in the United Kingdom has allergic rhinitis (AR), yet this disease continues to be under-estimated, both in terms of its impact on individuals and their families, as well as its cost to the economy.

Objectives: This multicentre, prospective, non-interventional study enrolled patients (n = 193) with moderate-to-severe AR and acute symptoms who were eligible to receive treatment with Meda Pharma's AzeFlu (MP-AzeFlu) (a novel formulation of azelastine hydrochloride, fluticasone propionate and excipients in a single spray) according to its licensed indications. Information was gathered on patient demographics, AR history and symptom severity, symptomatology and previous AR treatments in the last calendar year (prior to MP-AzeFlu prescription). Physicians also recorded number of previous AR visits, specific reasons for these visits and their reason for prescribing MP-AzeFlu. The aims of this study were (i) to characterise the type of patient prescribed MP-AzeFlu in real-life in the UK and physicians' reasons for prescribing it and (ii) to quantify the personal and societal burden of AR in the UK prior to MP-AzeFlu prescription.

Results: Most patients had seasonal AR (SAR) either alone (10.4%) or in combination with perennial AR (PAR; 35.2%), but many had AR of unknown origin (35.8%) and 18.6% had PAR alone. The average length of time with AR was 8.5 years (standard deviation (SD) 9.4). Patients considered suitable for MP-AzeFlu prescription reported troublesome symptoms (78.2%) and sleep disturbance (64.8%), with congestion considered the most bothersome (54.4%) and ocular symptoms reported by 68.4% of patients. The most frequent reason for MP-AzeFlu prescription was that other therapies were insufficient in the past (78.8%) or not sufficient to treat acute symptoms (16.1%). 79.3% of patients reported using ≥2 AR therapies in the past year. An average of 1.6 (standard deviation (SD) 1.9) doctor visits due to AR were reported by these patients.

Conclusions: Many patients in the UK live with uncontrolled disease despite treatment with mono- and multiple therapies and repeat doctor visits. A more effective treatment option, like MP-

AzeFlu, should improve AR control, reduce repeat doctor visits and costs associated with its management, and reduce the number of patients requiring immunotherapy.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies

1175 | Work productivity in rhinitis using cell phones: The MASK study

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Introduction: Uncontrolled allergic and non-allergic rhinitis have a major impact on work productivity, measured by the Work Productivity and Activity Impairment Allergic Specific Questionnaire (WPAI:AS). However, to date, studies have collected weekly data. The WPAI-AS has recently been incorporated into a MACVIA ARIA app called *Allergy Diary* in 6 European countries. The app also incorporates several visual analogue scales (VAS) permitting daily assessment of work productivity (work VAS), global symptoms as well as nasal, ocular and asthma symptoms in 15 EU countries.

Objectives: All consecutive users with allergic rhinitis (AR) from June 1, 2016 to October 31, 2016 were included in the study. VAS scores for global, nasal, ocular, asthma and work were collected. Global VAS calculated was nasal VAS + ocular VAS/2. For the WPAI-AS The percentage of impairment while working due to allergy and the percentage of overall work impairment due to allergy were used. Statistical analysis was based on descriptive elements (medians, percentile), correlation analysis and used chi-square tests. The primary aim of this cross-sectional study was to assess (i) the impact of uncontrolled AR on work productivity (all assessed by VAS) and (ii) the correlation between WPAI:AS and the work VAS.

Results: 5789 days of VAS scores were collected. Three quarters of those with uncontrolled AR, were poorly productive at work compared to just 2.0% of users with well controlled AR (Table). There was a highly significant correlation ($P < .001$) between work VAS and all VAS for AR control. WPAI:AS was assessed in 144 users. There was a significant correlation between WPAI:AS and W-VAS (0.52, $P < .0001$) and for WPAI:AS and global VAS (calculated) (0.57, $P < .0001$).

Conclusions: The *Allergy Diary* represents a suitable tool to assess the negative impact of uncontrolled AR on work productivity and is unique as it can provide daily data, in a large sample and across countries. The work VAS measured daily correlates well with the 7-day reflective WPAI:AS and should be further validated to confirm its applicability in real-life settings.

1176 | Profile of patients with persistent allergic rhinitis prescribed mp-azeflu®* in routine clinical practice in the Ireland

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Introduction: Many allergic rhinitis (AR) patients visiting their doctor have persistent AR (PER) and uncontrolled symptoms.

Objectives: To (i) characterize the type of PER patient prescribed Meda Pharma's AzeFlu (MP-AzeFlu) (a novel formulation of azelastine hydrochloride, fluticasone propionate and excipients in a single spray) in real-life and (ii) quantify the personal symptomatic burden of PER prior to MP-AzeFlu use. The study had a prospective, observational design and included 53 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to label. Information was gathered on patient demographics, AR phenotype, allergen sensitization, symptomatology, previous AR treatments (last year prior to MP-AzeFlu prescription), and reasons for prescription.

	Work VAS						
		<20 (fully productive)		20-50 (partly productive)		>50 (poorly productive)	Total
Global VAS for AR control* (calculated)	<20 Well controlled	3269	84.5%	516	13.3%	82	2.0%	3867
		94.8%		35%		9.2%	
	20-50 Partly controlled	168	16.3%	690	67.1%	170	16.6%	1028
		5.0%		57.7%		19.0%	
	>50 Uncontrolled	12	1.3%	268	18.6%	643	74.6%	923
		0.2%		18.2%		71.8%	
Total		3449		1474		895		5818

*Global VAS could be "unknown", so columns and rows may not add up to 100%.

Results: Patients were fairly evenly split between those that had perennial AR (PAR) alone (n = 24; 45.3%) and those with both seasonal AR (SAR) and PAR (n = 29; 54.7%). Many patients were sensitized to animal dander (dog: 28.3%; cat: 26.4%; other pet: 5.7%) and HDM (54.7%). However, the majority of patients (73.6%) also reported sensitization to 'other' allergens. At least 26 patients (n = 49.1%) were poly-sensitized. Prior to MP-AzeFlu prescription daily activities were impaired in almost all patients (N = 51, 96.2%); school/work was impaired in 49 patients (92.5%), 47 patients (88.7%) had bothersome symptoms and 41 (77.4%) reported sleep disturbance. Congestion was considered the most bothersome symptom by most patients (n = 29; 54.7%). The most frequent reason for MP-AzeFlu prescription was that other therapies were not sufficient in the past (n = 44; 83.0%) or not sufficient to treat symptoms (n = 10; 18.9%). Most of these PER patients were previously treated with oral antihistamines (n = 48; 90.6%), intranasal anti-histamines (n = 11; 20.8%) or intranasal decongestants (n = 9; 17.0%). Only 9.4% (n = 5) of patients had previously received an intranasal corticosteroid. Seventeen patients (32.1%) reported using ≥2 AR therapies in the past year. The majority of the patients (N = 47; 88.7%) had not undergone immunotherapy.

Conclusions: Many patients in Ireland live with uncontrolled persistent AR despite treatment. A more effective treatment option, like MP-AzeFlu, should improve AR control, reduce costs associated with its management, and reduce the number of patients requiring immunotherapy.

*MP-AzeFlu, a registered trademark of Meda AB, is marketed in the U.S. as Dymista®, a registered trademark of Meda Pharma Inc., both Mylan Companies

1177 | Profile of patients with persistent allergic rhinitis prescribed MP-AzeFlu®* in routine clinical practice in the Sweden

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Introduction: Many allergic rhinitis (AR) patients visiting their doctor have moderate-to-severe persistent disease.

Objectives: The aims of this study were (i) to characterize the type of patient with persistent allergic rhinitis (PER) prescribed Meda Pharma's AzeFlu (MP-AzeFlu) (a novel formulation of azelastine hydrochloride, fluticasone propionate and excipients in a single spray) in real-life in Sweden and physicians' reasons for prescribing it and (ii) to quantify the personal symptomatic burden of PER in Sweden prior to MP-AzeFlu prescription. The study had a prospective, observational design and included 161 adults/adolescents with moderate/severe PER for whom MP-AzeFlu was prescribed according to summary of product characteristics. Information was gathered on patient demographics, AR phenotype, allergen sensitization, symptomatology and previous AR treatments in the last calendar year (prior to MP-AzeFlu prescription). Physicians also recorded their reason for prescribing MP-AzeFlu.

Results: When using the traditional classification system, most patients had both seasonal AR (SAR) and perennial AR (PAR) (n = 112; 69.6%), with 30.4% (n = 49) having PAR alone. Sensitization to animal dander predominated (cat: 59.0%; dog: 51.6%; other pet: 22.4%), followed by house dust mite (42.9%) and mould (10.6%); At least 108 patients (67.1%) were polysensitized. Prior to MP-AzeFlu prescription patients reported troublesome symptoms (n = 89; 55.3%), impairment of daily activities and sleep disturbance (both n = 82; 50.9%), and impairment of school work (n = 55; 34.2%). Congestion was considered the most bothersome symptom (n = 110; 68.3%). The most common reason for MP-AzeFlu prescription was that other therapies were not sufficient in the past (n = 128; 79.5%) or not sufficient to treat acute symptoms (n = 26; 16.1%). The vast majority of PER patients were previously treated with intranasal corticosteroids (n = 134; 83.2%) or oral anti-histamines (n = 108; 67.1%), with 73.9% (n = 119) reporting the use of ≥2 AR therapies in the past year.

Conclusions: Many patients in Sweden live with uncontrolled persistent disease despite treatment with mono- and multiple therapies. A more effective treatment option, like MP-AzeFlu, should improve AR control, reduce costs associated with its management, and reduce the number of patients requiring immunotherapy.

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1178 | Burden of allergic rhinitis: Australia vs UK

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Introduction: Allergic rhinitis (AR) affects approximately 500 million individuals around the world and is increasing in prevalence. Often trivialised as a nuisance disease, its burden has been systematically under-estimated.

Objectives: The aim of this survey was to understand the burden of AR in Australia, both from an individual and societal perspective, and to compare it to that in the UK. 1151 adults with a self-reported diagnosis of AR were recruited across Australia via a patient panel to complete an online survey in August 2015. A similar survey was conducted in the UK in 1000 SAR patients in June-July 2011. These surveys included questions on type of AR and its severity, medication utilisation, GP services, absenteeism and presenteeism. Descriptive statistics were used to summarise results.

Results: Most Australian AR patients reported having seasonal AR, either alone (n = 376; 32.7%) or in combination with perennial AR (n = 616; 53.5%), and rated their disease as either moderate (n = 455, 39.5%) or severe (n = 610, 53.0%), predominantly. Patients visited their GP due to AR symptoms on average 2.9 times/year, with 1.1 visits due to dissatisfaction with current treatment. The GP consultation rate was lower in the UK at 1.61 times/year for those with moderate/severe SAR; due to dissatisfaction with therapy in 35.4% of cases. Rates of poly-pharmacy were similar in Australia (n = 810; 79.7%) and the UK (n = 506; 70.5%), with intranasal corticosteroids and oral anti-histamines ± eye drops the most common combination used. In both countries this co-medication behaviour was driven by the need for better and faster nasal and ocular symptom relief. However, in Australia only 16.9% of patients (n = 137) were completely satisfied with their multi-therapy regimen. Patients in both countries continued to experience high nasal (rTNSS UK: 6.4/12; Aust: 5.0/12) and ocular (rTOSS UK: 4.3/9; Aust: 3.4/9) symptom burden and reported an AR-specific absenteeism rate of 4.1 days/year in the UK and 3.9 days/year in Australia. Productivity was negatively impacted due to AR on 37.7 day/year in the UK and by 31.3 days/year in Australia.

Conclusions: The symptomatic and socioeconomic burden of AR is high in both the UK and Australia. Clearly, more effective AR treatments are needed to provide better symptom relief and, by reducing indirect costs associated with absenteeism and presenteeism, provide a cost saving to both the UK and Australian economies.

1179 | Characterization of Australian allergic rhinitis patients: Results from a patient survey

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Introduction: By conservative estimates allergic rhinitis (AR) affects about 15% of the population of Australia, or approximately 3.6 million individuals. The highest prevalence is found in those aged 25-44 years, where any impact on work productivity will be felt most. Like other countries, the socioeconomic burden of AR in Australia is high. AR epidemiological data specific to Australia is scarce.

Objectives: The aim of this survey was to characterize a typical Australian AR patient. 1151 adults with a self-reported diagnosis of AR were recruited across Australia via a patient panel to complete an online survey in August 2015. The survey included questions on allergen and irritant sensitization, type of AR (i.e. seasonal AR (SAR)/perennial AR (PAR); intermittent/persistent) and disease severity (self-reported). Descriptive statistics were used to summarize results.

Results: The most common patient-reported sensitizing allergens reported were grass pollen (n = 815; 70.5%), followed by tree pollen (n = 695; 60.4%) and animal dander (n = 470; 40.8%). 842 respondents (73.2%) also reported a sensitivity to irritants (indicative of non-allergic disease and nasal hyperreactivity), most notably to perfume/deodorants/hairspray (n = 671; 73.8%), smoke (n = 554; 65.8%) and cold air/air conditioning (n = 417; 49.5%), with 44.7% (n = 376) reporting that these irritants bothered them just as much as allergens. The greatest number of individuals had both SAR and PAR (n = 616; 53.5%), 32.7% (n = 376) had SAR alone and 13.8% (n = 159) had PAR alone. There was a slight preponderance of intermittent (n = 683; 59.3%) over persistent disease (n = 468; 40.7%). The vast majority of respondents classified their AR as moderate or severe (n = 950; 82.5%); A small proportion of respondents considered that their AR was of mild severity (n = 86; 7.5%) with 10.0% (n = 115) reporting very severe disease.

Conclusions: Australian AR patients are frequently poly-sensitized. Most experience symptoms all year around (i.e. SAR & PAR) and have moderate/severe disease. The prevalence of mixed rhinitis (i.e. allergic and non-allergic) appears high, with many patients reporting sensitization to both allergen and irritant triggers.

1180 | State of allergic rhinitis control and impact on asthma in Australia: Results from a patient survey

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Introduction: A revolution is currently on-going in the field of allergic rhinitis (AR). Control of disease rather than reduction in symptom severity is at the heart of this revolution. A simple visual analogue scale (VAS) has been endorsed by Allergic Rhinitis and its Impact on Asthma (ARIA) as the new language of AR control. This VAS is now incorporated into an updated ARIA guideline, called the AR clinical decision support system (CDSS), and a cut-off of 5/10 cm used to define control and guide treatment decisions.

Objectives: 1151 adults with a self-reported diagnosis of AR were recruited across Australia via a patient panel to complete an online survey in August 2015. The survey included questions on ARIA defined-AR control. Descriptive statistics were used to summarise results. The aim was to assess the state of AR control and impact on asthma in Australia.

Results: Gaining control of AR symptoms was considered 'very' or 'moderately' important for 94.5% (n = 1088) of patients. However, on the day of the survey, of the 621 (54%) patients who were experiencing symptoms, 46.9% (n = 291) had a VAS score ≥5/10 cm, the ARIA-defined cut-off for uncontrolled disease. Of those who had taken medication in the last 24 hours, 51.6% (n = 205) still had uncontrolled disease. Similarly, when the 88.3% (n = 1016) of

patients who reported using AR therapy to treat their symptoms (79.7% (n = 810) using multiple therapies) were asked to rate their symptoms when on medication, 28.1% (n = 286) of these patients reported a VAS score ≥5/10 cm. Poor control of AR was also associated with poor control of asthma in co-morbid patients (n = 492). 35.5% (n = 165) of co-morbid patients who failed to take their AR medication reported the need to increase their asthma reliever medication, 11.8% (n = 58) needed to increase their preventer medication and 15.7% (n = 77) needed to increase both.

Conclusions: Many Australian patients with AR have uncontrolled disease, despite treatment with mono- and multi-therapy regimens. A more effective AR therapy is needed which provides rapid and sustained AR control.

1181 | Mp-AzeFlu* has superior effect on the transactivation of anti-inflammatory genes than fluticasone propionate and azelastine alone in nasal mucosa and polyp fibroblasts

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Introduction: MP-AzeFlu*, comprising intranasal azelastine hydrochloride (AZE), fluticasone propionate (FP) and a novel formulation, in a single device has demonstrated superior clinical effects in allergic rhinitis and chronic rhinitis compared to these drugs in monotherapy. MP-AzeFlu* has also previously shown significantly greater anti-inflammatory potency than FP and AZE, as evidenced by a greater inhibition of both eosinophil survival and release of pro-inflammatory cytokines from nasal mucosa epithelial cells.

Objectives: To compare the effect of MP-AzeFlu*, AZE and FP on the trans-activation of anti-inflammatory genes in in vitro cultured fibroblasts from control nasal mucosa (NM) and from nasal polyps (NP), taken from patients with chronic rhinosinusitis with NP (CRSwNP). NM and NP fibroblast cultures (n = 6 each) were incubated with serial dilutions of MP-AzeFlu* ($1:10^2$ to $1:10^4$) or equivalent dilutions of FP ($7.3x10^{-6}$M to 10^{-8}M) or AZE ($2.4x10^{-5}$M to 10^{-7}M) for 2 and 6 h. Glucocorticoid-induced leucine zipper (GILZ) and mitogen-activated protein kinase phosphatase-1 (MKP-1) gene expression was analysed by RT-PCR. Results are expressed as fold-increase over untreated cells (mean ± SEM).

Results: MP-AzeFlu* and FP markedly increased GILZ and MKP-1 gene expression in NM and NP fibroblasts at all tested dilutions and times (all $P < .05$). AZE also increased target gene expression but only at the $1:10^2$ dilution ($P < .05$). MP-AzeFlu* ($1:10^2$) induced significantly greater GILZ gene expression than either FP or AZE and significantly greater MKP-1 expression than AZE (Table).

Conclusions: The superior clinical effect of MP-AzeFlu* compared to corticosteroid or antihistamine monotherapy may occur through a stronger induction of the anti-inflammatory genes GILZ and MKP-1. Our findings reveal the molecular basis for the therapeutic benefit of MP-AzeFlu* in rhinitis and its potential benefit in CRSwNP.

This study was sponsored by a research grant form MEDA Pharma.

*Dymista

	NM fibroblasts		NP fibroblasts	
	2 h	6 h	2 h	6 h
	GILZ			
MP-AzeFlu	11.2 ± 1.1	36.5 ± 7.9	14.7 ± 4.5	31.4 ± 9.2
FP	9.4 ± 1.3[a]	19.8 ± 2.4[a]	13.9 ± 3.8	15.3 ± 4.5[a]
AZE	1.8 ± 0.1[a]	7.9 ± 2.8[a]	2.5 ± 0.8†	2.8 ± 0.9[a]
	MKP-1			
MP-AzeFlu	6.5 ± 1.4	5.4 ± 1.7	7.2 ± 2.1	6.2 ± 2.4
FP	5.4 ± 0.6	4.7 ± 1.0	5.7 ± 1.5	4.8 ± 1.6
AZE	2.1 ± 0.3[a]	1.8 ± 0.6[a]	2.9 ± 1.0[a]	1.9 ± 1.3[a]

[a]$P < .05$ vs MP-AzeFlu*

1183 | Autonomic function in adults with allergic rhinitis and its association with disease severity and duration

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Introduction: The association between allergic rhinitis (AR) and the autonomic nervous system (ANS) has recently received substantial attention. However, no studies have assessed how the HRV parameters are associated with duration and disease severity in AR.

Objectives: Using heart rate variability (HRV), we compared difference of autonomic conditions among subjects with AR of various durations and severities, as well as in healthy controls.

Results: We divided subjects with AR into subgroups based on duration and severity. Next, we measured HRV and the results were compared among subgroups and healthy controls. High frequency (HF) and normalized high frequency (NHF) were significantly higher in the intermittent group than in the control group, while normalized low frequency (NLF) and the ratio of absolute LF to HF power (LF/HF) were significantly lower in the intermittent group than in the control group. Furthermore, NLF was significantly higher in the persistent group than in the intermittent group. HF and NHF were significantly higher in the mild group than in the control group, while NLF and LF/HF were significantly lower in the mild group than in the control group. The total nasal symptom and itchy nose scores were negatively correlated with NHF.

Conclusions: Our results indicate that patients with intermittent and mild AR show hypervagal activity and hyposympathetic activity, and the predominance lessens in AR patients with more persistent

and severe symptoms. Further investigation of the mechanisms underlying the relationship between autonomic function and persistent and severe AR is needed.

1185 | Chronic rhinosinusitis with unilateral nasal polyps in Chinese patients—clinical and histopathological characteristics

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Introduction: Chronic rhinosinusitis with nasal polyps (CRSwNP) is commonly reported in patients with bilateral polyps (BNP), where CRS with unilateral polyps (UNP) is rarely reported with little known epidemiology and pathophysiology.

Objectives: In this study, we evaluated the differences of UNP and BNP in clinical characteristics, in particular the involvement of sinus diseases (by CT score) and the histopathological features of epithelial remodeling and inflammatory cell infiltrations (including eosinophils, neutrophils, macrophages, CD4+ and CD8+ T cell), in a cohort of Chinese patients.

Results: The presence of clinical symptoms in UNP patients (i.e. nasal congestion, anterior or posterior nasal drip, reduced smell) were significantly ($P < .05$) less common with a shorter mean duration in UNP (3.8 years, $P < .001$) than BNP (7.2 years). There was a lower Lund-Mackay CT score in UNP (6.1 ± 3.1, $P < .01$) than BNP (8.6 ± 3.3). Posterior ethmoiditis, frontal sinusitis, and sphenoid sinusitis were less common in UNP than BNP, especially when NP was graded in 1 or 2. Epithelial hyperplasia and goblet cell hyperplasia were more severe ($P = .01$ and $P = .03$, respectively) in BNP than UNP. There were significant ($P < .001$) differences in number of patients with eosinophilic NPs (exceeded 10% of the total number of inflammatory cells) between UNP (n = 45, 33.1%) and BNP (n = 80, 55.2%), as well as other cell types such as macrophage and $CD8^+$ cells.

Conclusions: CRS with unilateral polyps is not a rare disease, but with less severity in clinical symptoms, less extends of sinus involvement, and different histopathological features as compared to CRS with bilateral polyps.

1186 | Th17 inflammation may be associated with refractoriness of non-eosinophilic nasal polyps

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Introduction: Refractory chronic rhinosinusitis with nasal polyp (CRSwNP) requires continuous medical therapy and repeated surgery. The pathophysiology of refractoriness in CRSwNP is not clear and efforts to investigate the mechanisms are underway.

Objectives: We sought to identify the differences in cytokine expression between primary and revision CRSwNPs.

Results: 7 control subjects, 20 primary CRS (9 ENP and 11 NENP) and 86 revision CRSwNP (30 ENP and 56 NENP) patients were enrolled. Control subjects and CRSwNP patients underwent surgery and tissues were collected. Cytokines were analyzed including IL-5, IL-13, eotaxin 1, eotaxin 2, periostin, myeloperoxidase (MPO), TGF-β, IFN-γ, IL-6, IL-8, IL-17A, IL-22, IL-23, eosinophilic cationic protein (ECP), and total IgE. Nasal polyps (NPs) were divided into two groups (eosinophilic NP: ENP, non-eosinophilic NP: NENP) in accordance with tissue eosinophilia. Age of revision CRSwNP was younger than control and primary CRS ($P < .001$). Lund-Kennedy score was higher in revision ENP than primary ENP ($P = .001$). Th2 cytokines revealed no significant differences between primary and revision CRSwNPs and slightly decreased in revision NENP group. Neutrophils-associated inflammatory mediators such as MPO, IL-8, IL-17A were elevated in revision CRSwNP especially in revision NENP than primary and control.

Conclusions: Th17 inflammation may play a role in the development of refractoriness in CRSwNP especially in NENP.

1187 | To explore the incidence of chronic sinusitis and analysis of related factors in Northeast China

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Introduction: Chronic rhinosinusitis is inflammatory diseases of nasal cavity and sinus, the occurrence of which is considered to relate to cilia-cleaning transport function, sinus patency of the anatomical structure, health condition of nasal cavity, systemic anti-infection ability.

Objectives: The main purpose of this epidemiological study is to get the prevalence of chronic sinusitis among residents in

Changchun of Northeast China. To analyze its relationship with life style, occupation exposure, environmental factors and other related diseases, eventually to provide scientific basis for effective prevention of chronic sinusitis.

Results: Using a screening questionnaire, we found 148 patients with CRS from 1500 qualified survey, and the overall prevalence of CRS was 9.87%. There was no difference about incidence between male and female, different BMI, marital status, nationality, habitat and education level ($P > .05$). The prevalence of CRS in different age groups, household incomes per capita and different vocational had significant difference ($P < .05$). In the aspect of living environment, there was no difference about smoking, alcohol drinking ($P > .05$), but there was a significant difference in air pollution, physical exercises, keeping pets, insomnia and exposure to dust or harmful gases ($P < .05$). Allergic rhinitis, asthma, chronic obstructive pulmonary disease, gastro esophageal reflux, aspirin exacerbated respiratory disease have higher correlation with CRS ($P < .05$).

Conclusions: The incidence rate of CRS was 9.87% in Changchun of northeast China. To improve the living environment and improve the level of education will reduce the incidence rate of CRS. Allergic disease associated with CRS.

1188 | Histopathologic study of the mucosa tissue remodeling and the bone in chronic rhinosinusitis

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Introduction: Chronic rhinosinusitis (CRS) is a common disease, which can be divided into acute and chronic processes. CRS is caused by various reasons, such as multiple infection, allergy, mucociliary function injury (congenital or acquired), immunodeficiency (congenital or acquired), nasal structural abnormalities, and so on. The multiplicity of the etiology of CRS, determine its pathological mechanism of complex, resulting in a great challenge to the clinical treatment.

Objectives: To study ethmoid bone histopathology of CRS patients in chronic rhinosinusitis tumorigenesis and influence factors. We study the correlation with different clinical type, CT values, the length of the course, operation history and pathological changes through statistical analysis of the experiment.

Results: We classed the ethmoid pathological changes by the Biedlingmaier JF classification in part 1. At the same time, according to the different pathological grading, compared of correlation of different clinical type, CT values, the length of the course, operation history and ethmoid bone pathology. Sixty cases of CRS patients with different clinical type, ethmoid CT values, disease duration, operation history and ethmoid bone and pathological grading were statistically significant difference ($P < .01$).

Conclusions: CRS ethmoid bone pathological morphological change in different degree, there is a significant correlation with the clinical type, ethmoid CT values, disease course and operation history.

1189 | Suppression of neuropeptide production by quercetin in allergic rhinitis model rats

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Introduction: Quercetin, a dietary flavonoid found in many fruits, red wine and onion, among others, has been reported to have potent anti-oxidant, anti-viral and anti-cancer effects. Although quercetin is also reported to have anti-inflammatory and anti-allergic effects, the precise mechanisms by which quercetin favorably modify the clinical conditions of allergic diseases such as allergic rhinitis (AR). The present study was designed to examine the influence of quercetin on the development of AR by using AR model rats.

Objectives: Sprague-Dawley (SD) rats were sensitized with toluene 2,4-diisocyanate (TDI) by intranasal instillation of a 10% TDI in ethyl acetate in a volume of 5 μL once a day for 5 consecutive days. This sensitization procedure was repeated after a 2-day interval. After 5 days of the second sensitization, rats were treated with various doses of quercetin once a day for 2-7 days. Nasal allergy-like symptoms, which were induced by bilateral application of 5 μL of 10% TDI in ethyl acetate, were assessed by counting sneezing and nasal rubbing behaviors for 10 minutes just after TDI nasal challenge. The levels of substance P (SP), calcitonin gene-related peptide (CGRP) and nerve growth factor (NGF) in nasal lavage fluids obtained 6 h after TDI nasal challenge was examined by ELISA.

Results: Oral administration of quercetin for 5 and 7 days, but not 2 and 3 days, could inhibit sneezing and nasal rubbing movements, which were increased by TDI nasal challenge. The minimum dose that caused significant inhibition was 25 mg/kg. Oral administration of quercetin at more than 25 mg/kg for 5 days significantly inhibited the increase in SP, CGRP and NGF contents in nasal lavage fluids induced by TDI nasal challenge.

Conclusions: The present results strongly suggested that quercetin will be a good candidate for the supplement on the management and treatment of allergic diseases, especially AR.

TUESDAY, 20 JUNE 2017
TPS 41
BIOMARKERS IN ASTHMA

1191 | A novel automated immunoassay for measurement of eosinophil derived neurotoxin in serum and urine

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Introduction: Eosinophil Derived Neurotoxin (EDN) is an eosinophil granule protein that is released during eosinophil activation. EDN has been suggested to be implicated in the pathophysiology of asthma and to be a biomarker for asthma diagnosis.

Objectives: Here we present a novel automated immunofluorescence research assay for measurement of EDN and its potential use in diagnosis of asthmatic children.

Results: A research assay was developed based on the ImmunoCAP platform. A pair of complementary monoclonal antibodies was used where the capture mAb was covalently coupled to the solid phase and the detection mAb was labelled with the enzyme β-galactosidase. Commercially available EDN was used for calibrators. The measuring range of the assay was 2-200 μg/L. Three serum samples and three urine samples with different EDN concentrations were used to evaluate precision, linearity, recovery and specificity (serum only) of the assay. Time and temperature dependency of serum sample preparation was investigated using 10 healthy blood donors. Serum samples were allowed to clot for 1 hour or 5 hours at 20°C or 24°C. Asthmatic children aged 6-18 years (n = 164, median 10 years), were analyzed for serum EDN, exhaled nitric oxide (FeNO) and eosinophil fraction (EOS%). Healthy children aged 4-17 years (n = 42, median 9 years), were analyzed for serum EDN only.

Inter- and intra-assay coefficients of variation for serum and urine were below 2.5% and 3.7%, respectively. Dilution linearity was observed down to a 1/500 dilution (ratios obtained/expected ranging from 88%-109%) and recovery was within 87.5%-107% for both urine and serum. No cross-reactivity was observed with ECP, MPO or cathepsin. The limit of quantification was 2 μg/L. Increased clotting time and temperature resulted in increased measured EDN concentrations, giving a maximum average increase of 27%. The EDN serum concentration was significantly higher in the asthma group (mean 77.7 μg/L; 95% CI: 68.4-86.9 μg/L) compared to the healthy control group (mean 17.4 μg/L; 95% CI: 13.7-21.2 μg/L) ($P > .0001$). The EDN concentration correlated with EOS% ($r = 0.81$) but only weakly with FeNO ($r = 0.39$).

Conclusions: We have developed an ImmunoCAP based immunoassay for measurement of EDN with high technical performance and ability to distinguish between asthmatic and healthy children.

1192 | Increased sputum thymus and activation-regulated chemokine levels in children with asthma, not with eosinophilic bronchitis

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Introduction: Thymus and activation-regulated chemokine (TARC), a member of the CC chemokine family, plays a crucial role in Th2-specific inflammation. Elevated serum TARC levels have been described in atopic dermatitis and are suggested as a useful clinical biomarker. TARC has also been studied in asthma, eosinophilic pneumonia, and allergic bronchopulmonary aspergillosis.

Objectives: We aimed to determine the concentration of sputum TARC in children with asthma and eosinophilic bronchitis (EB) and its relation with eosinophilic inflammation, pulmonary function, and bronchial hyper-responsiveness.

Results: In total, 90 children with asthma, 38 with EB, and 45 control subjects were enrolled.. TARC levels were measured in sputum supernatants using an ELISA. Sputum TARC levels were significantly higher in children with asthma than in either children with EB ($P = .004$) or the control subjects ($P = .014$). Among patients with asthma, sputum TARC concentration was higher in children with sputum eosinophilia than in those without sputum eosinophilia ($P = .035$). Sputum TARC levels were positively correlated with eosinophil counts in sputum ($r = .210$, $P = .047$), serum total IgE levels ($r = .224$, $P = .041$), exhaled fractional nitric oxide ($r = .265$, $P = .028$), and bronchodilator response ($r = .311$, $P = .038$). Negative significant correlations were found between sputum TARC and FEV1/FVC ($r = -.326$, $P = .002$) or PC_{20} ($r = -.454$, $P < .001$).

Conclusions: Elevated TARC levels in sputum were detected in children with asthma but not in children with EB. Sputum TARC could be a supportive marker for discrimination of asthma from EB in children showing characteristics of eosinophilic airway inflammation.

1193 | A study of relationships between the regulatory T cells and asthma

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Introduction: Asthma is a chronic inflammatory disease involving cells such as eosinophils, mast cells, T lymphocytes and their cellular elements. $CD4^+$T lymphocytes (Th), including subsets of Th1, Th2, regulatory T cells (Treg),etc., play a critical role. The hypothesis of Th1/Th2 imbalance contributing to induction of asthma has been challenged recently, suggesting that pathogenesis is more complex. The subset of Treg represents strong suppressive properties to effector T cells through secreting immunosuppressive cytokines such as IL-10 and TGF-β, or through contact inhibition. The research on relationships between Treg and asthma is still on the first stage.

Objectives: To investigate relationships between Treg and asthma with evaluation of plasma IL-10 and TGF-β1 levels of asthmatics, IL-10 and TGF-β1 levels produced by peripheral blood mononuclear cells (PBMC) and expression of transcription factors FOXP3 after activation by Dermatophagoides farinae (Df), and intracellular IL-10 and TGF-β1 levels of $CD3^+CD4^+$ T cells activated by Df.

Results: (i) Plasma IL-10 level in asthmatics was significantly lower than that in healthy (t = 2.3037, P = .0256). Plasma TGF-β1 levels in asthmatics had no significant difference with the healthy (t = 0.9319, P = .3548). After activation by Df, IL-10 produced by PBMC in asthmatics was much lower compared with healthy (t = 3.0988, P = .0033). TGF-β1 produced by PBMC in asthmatics had no significant difference with healthy (t = 1.0871, P = .2828). (ii) The amounts of $CD3^+CD4^+IL\text{-}10^+$ and $CD3^+CD4^+TGF\text{-}\beta1^+$ T cells were close to zero in unactivated blood of both asthmatics and healthy. After activated by Df, the proportions of $CD3^+$ $CD4^+$, $CD3^+CD4^+TGF\text{-}\beta1^+$ and $CD3^+CD4^+IL\text{-}10^+TGF\text{-}\beta1^+$ T cells in asthmatics had no significant difference with healthy (t = 0.1891, 1.1889 and 1.5748 respectively, P = .8510, 0.2425 and 0.1254 respectively). The proportion of $CD3^+CD4^+IL\text{-}10^+$ T cells in asthmatics was significantly lower than that in healthy (t = 2.1613, P = .0370). (iii) There were expression of the transcription factor FOXP3 of PBMC in both asthmatics and healthy with no significant difference (t = 0.7768, P = .4421). After activation by Df, expression level of FOXP3 by PBMC was significantly lower in asthmatics than that in healthy (t = 2.0779, P = .0458).

Conclusions: It is supposed that there was a secretion defect of Treg cytokines in allergic bronchial asthmatics, as well as an insufficient expression of FoxP3 in PBMC. Treg deficiency may be a key factor to asthma.

Table 1 IL-10 and TGF-β levels in plasma and upper liquids of incubated PBMCs of asthmatics and healthy (± s)

	IL-10 (ng/L)		TGF-β1 (μg/L)	
	Plasma	incubated liquids	plasma	incubated liquids
Asthmatic	11.4 ± 7.6	39.7 ± 154.4	13.9 ± 11.4	0.1 ± 0.7
Healthy	17.6 ± 13.3	176.3 ± 104.7	16.5 ± 12.0	0.4 ± 0.9
t	2.3037	3.0988	0.9319	1.0871
P	.0256	.0033	.3548	.2828

Table 2 Influence of Df stimulation to $CD4^+$ T cells and subsets proportions in peripheral blood of asthmatics and healthy (±s, %)

	$CD4^+T$	$CD4^+IL\text{-}10^+$	$CD4^+TGF\text{-}\beta1^+$	$CD4^+IL\text{-}10^+$ $TGF\text{-}\beta1^+$
Asthmatic	3.3 ± 5.6	1.2 ± 1.2	1.5 ± 2.8	1.2 ± 2.1
Healthy	3.0 ± 3.1	2.4 ± 1.5	0.8 ± 1.2	0.5 ± 0.7
t	0.1891	2.1613	1.1889	1.5748
P	.8510	.0370	.2425	.1254

Table 3 comparison of FOXP3 expression by PBMC of asthmatics and healthy before and after Df stimulation (±s)

	Un-stimulated	Df-stimulated
Asthmatic	0.27 ± 0.36	0.11 ± 0.32
Healthy	0.35 ± 0.27	0.43 ± 0.66
t	0.7768	2.0779
P	.4421	.0458

1195 | Usefulness of exhaled nitric oxide to predict airway hyperresponsiveness in adults with asthmatic symptoms

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Introduction: The relationship between airway hyperresponsiveness (AHR) and airway inflammation remains controversial.

Objectives: The aim of this study was to determine whether fractional exhaled nitric oxide (FeNO), in the context of induced sputum eosinophil count (ISE), is associated with AHR. Retrospective data from adult patients who complained dyspnea and/or cough at single tertiary center was analyzed. AHR was assessed as the dose of methacholine causing 20% decrease of FEV_1. FeNO levels were classified into three groups (FeNO < 25 ppb (Group A), 25 ≤ FeNO < 50 ppb (Group B), FeNO ≥ 50 ppb (Group C)). The cutoff value for increased ISE was 3%.

Results: Two hundred and eighty-eight patients (women 152 (52.8%), mean age 49.0 years) were included in this study. The incidence of AHR was significantly higher among patients with elevated FeNO (9.6% (13/136) in Group A; 24.6% (17/69) in Group B; 65.1%

(54/83) in Group C, $P < .001$). In Group C, AHR was frequently observed even in the absence of increased ISE.

Conclusions: Our results shows that FeNO is a useful biologic marker to predict AHR in patients with asthmatic symptoms. High FeNO may play an independent role in the development of AHR.

1196 | Fractional exhaled nitric oxide (FeNO) in the screening and diagnosis work-up of occupational asthma

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Introduction: In 2010, the EAACI Task Force on "Non-invasive methods for assessment of airways inflammation in occupational settings" stated that studies on the use of FeNO in the investigation of occupational asthma (OA) have yielded inconsistent results and that several confounding factors impacted their results.

Objectives: We propose a review of the evidence on the use of FeNO in the screening and investigation of OA published since the last position paper, highlighting recent advancements. Using PubMed, a review of the current literature from 1992 to December 2016.

Results: Levels of FeNO have been measured in several populations of workers exposed to high- and low-molecular weight agents for screening or diagnosis purposes. In screening studies of cohorts exposed to HMW agents, an increase of FeNO over time has been associated with the development of bronchial hyperresponsiveness. When used in the investigation of OA, increased levels of FeNO after exposure to the offending agent showed high positive predictive values for positive SIC to HMW agents. Subjects with high specific IgE to their workplace allergens tended to present higher levels of FeNO. With the exception of isocyanates, increases in FeNO levels have been inconsistently reported after positive SIC to LMW agents. In isocyanate studies, positive SIC were associated with an increase in FeNO levels after exposure. In subjects with specific IgE antibodies to HDI, a dose-dependent relationship has been suggested between increasing exposure and FeNO levels. Cluster analyses of patients exposed to various HMW and LMW agents have documented significant increases of FeNO in clusters of patients with OA to HMW agents, but not LMW.

Conclusions: Recent studies have provided useful information for improving the interpretation of FeNO in the screening and investigation of OA. Future studies are still needed to precise the role FeNO in the screening, investigation, and management of occupational asthma.

1197 | Variable inflammatory responses in the airways of patients with aspirin-exacerbated respiratory disease

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Introduction: Aspirin-exacerbated respiratory disease (AERD) is a well defined clinical asthma phenotype characterized by the presence of asthma, chronic rhinosinusitis (CRS), nasal polyps, and hypersensitivity reactions precipitated by aspirin and other cyclooxygenase one inhibitors. However, pathogenesis of the disease is not entirely recognized.

Objectives: To investigate airway inflammatory endotypes and their clinical significance in AERD patients.

Methods: Bronchoalveolar lavage (BALF), nasal lavage (NL), and blood cell differential, together with periostin levels in serum and upper and lower airway samples were measured in 16 AERD patients and 11 aspirin tolerant asthmatics (ATA).

Results: Asthma severity, lung function and steroid treatment were comparable in AERD and ATA patients. AERD group showed increased prevalence of CRS (100%) and nasal polyps (75%) as compared to ATA (36% and 27%, respectively, $P > .01$). Eosinophilic endotype (i.e. >2% eosinophils in BALF) was present in 56% patients with AERD (pauci-granulocytic in 25%, neutrophilic in 19%), and was significantly ($P > .05$) more frequent as compared to ATA patients (eosinophilic in 9%, pauci-granulocytic in 45.5%, neutrophilic in 45.5%). NL eosinophilia (i.e. >10% eosinophils) was significantly higher ($P > .05$) in AERD (31%) than in ATA (9%) patients. This was paralleled by significantly higher periostin levels in serum, NL, and BALF in the former group, which correlated well with CRS. There was a correlation between eosinophilia in NL vs BALF ($R = 0.79$, $P > .01$), NL vs blood ($R = 0.5$, $P > .05$), but not between eosinophilia between BALF vs blood ($R = 0.23$, $P > .05$). NL eosinophilia had superior accuracy (87%) in confirming eosinophilic endotype of AERD as compared to blood eosinophilia (71%) or periostin measurements in serum (69%) and NL (69%). Eosinophilic and non-eosinophilic AERD asthma had similar clinical characteristics, except for a trend towards earlier onset, less severe disease, and less frequent steroid use in case of eosinophilic endotype.

Conclusions: Eosinophilic airway inflammation is more frequent in patients with AERD as compared to ATA. Upper airway eosinophilia, measured in nasal lavage, could be recognized as a surrogate marker of eosinophilic inflammation in the lower airways.

1198 | Eosinophilic cationic protein (ECP) in the clinical work-up of chronic cough

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Introduction: Chronic cough is a common symptom that is generally investigated in the clinical setting by empirical treatment together with laboratory investigations. The purpose of the present study was to investigate the value of testing eosinophilic cationic protein (ECP) serum levels to confirm or rule out suspected pathologies such as Chronic Obstructive Pulmonary Disease (COPD), Post Nasal Drip Syndrome (PNDS), Gastroesophageal Reflux Disease (GERD) and asthma related syndromes.

Objectives: Eighty-two patients (40 females; median age 61 ± 1.9 years) with unexplained chronic cough were evaluated in this study. No subject had received any anti-inflammatory treatment before clinical evaluation, and none were active smokers. ECP was measured with a commercially available fluoroenzyme immunoassay and results were expressed as μg/L.

Results: The mean ECP level was significantly higher in asthmatic and atopic cough. The analysis of variance showed that mean ECP was different among diagnosis categories ($P = .0018$).

Conclusions: ECP measurement is a useful parameter for differentiating asthmatic conditions from other chronic disorders in the clinical work-up for chronic cough.

1199 | Simultaneously elevated exhaled nitric oxide and blood eosinophils in children with atopic asthma

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Introduction: Increased fraction of exhaled nitric oxide (FeNO) and blood eosinophils (B-Eos), as markers of local and systemic eosinophilic inflammation, are observed in asthmatic children with monosensitisation and polysensitisation for aeroallergens. A normal FeNO value is in children of 5-12 years old <20 ppb and in children of 12-18 years old <25 ppb; a normal B-Eos count is <400 cells/mmc.

Objectives: To assess the correlation between FeNO value and B-Eos count in asthmatic children monosensitised and polysensitised for aeroallergens. A prospective study was conducted in "Dr. Victor Gomoiu" Children's Hospital from January 2016 till February 2017. This study included 73 children aged 5 to 18 diagnosed with atopic asthma monosensitised and polysensitised for aeroallergens. In each patient FeNO was measured using chemiluminescence analyser (NIOX MINO).

Results: 36 of the patients were monosensitised; out of these 19 had normal of FeNO value and 17 had increased FeNO value; 21 had normal B-Eos count and 15 had increased B-Eos count; 37 patients were polysensitised; out of these 17 had normal FeNO value and 20 had increased FeNO value; 10 were with normal B-Eos value and 27 with increased B-Eos value. Using Pearson Chi Square test to evaluate the correlation between FeNO value and mono or polysensitisation in asthmatic children we have obtained a P value >.05 (statistically insignificant). Using Pearson Chi Square test to evaluate the correlation between B-Eos count and mono or polysensitisation in asthmatic children we have obtained a P value <.05 (statistically significant).

Conclusions: Our study suggests that asthmatic children with polysensitisation for aeroallergens, in contrast with those with monosensitisation, have a higher risk of eosinophilic systemic inflammation. There is no difference between them regarding the lower airway inflammation reflected in FeNO value.

1200 | Increased frequency of CD56- CD16+/- NK cells in exacerbated asthma respiratory disease—A suggestive role as biomarker

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Introduction: Asthma is a complex of diseases or phenotypes associated with several pathogenic mechanisms. Patients with allergic asthma show a characteristic Th2 airway inflammation. Aspirin exacerbate respiratory disease (AERD), is not a typical Th2-asthma phenotype but an anaphylactoid response not Ig-E mediated. No specific biomarker for AERD and diagnostic test are available. Exist Th2-independent mechanism that explains asthma development, NK cells contribute to the Th1/Th2 checks and balance in this disease. Based on the CD56 and CD16 surface markers NK cells can be divided in subsets with different cytotoxicity and cytokine production. Variation of specific subpopulations of NK cells have been found in allergic asthma where they are

considered as regulator of Th1 response. We evaluate the frequency of NK cell phenotypes in 42 non-asthmatic subjects (NA), 51 patients with aspirin tolerant asthma (ATA), and 42 patients with AERD.

Objectives: To compare the patterns of NK cells subpopulations between two contrasting asthma phenotypes, AERD and ATA.

Results: NK cells showed higher frequency of $CD56^{brigh}$ and lower frequency of $CD56^{dim}$ in patients with AERD. The highest frequencies of CD56- NK cells were found in all patients with AERD. Frequency difference analysis of this NK subset between AERD and ATA was AUC = 1, sensitivity and specificity near 100%, cutoff of 15.6%; and between ATA and AU was AUC = 0.89, cutoff of 6.5%; 86.5% sensitivity and 77.5% specificity. AERD patients with highest CD56- frequencies had more hospitalization events by asthmatic crisis and higher prevalence of respiratory viral infections.

Conclusions: CD56- NK cell phenotype is suggestive as useful asthma biomarker, particularly of AERD disease. The expansion of this aberrant NK cell subset suggests a notable implication of innate immunity and a poor anti-viral response in some asthma phenotypes.

TUESDAY, 20 JUNE 2017

TPS 42

A NEW MULTIPLEX TEST FOR SPECIFIC IGE

1201 | Multiplex IgE diagnostic test: IgE sensitization to furry animal dissected by allergenic molecules and extracts

Alessandri C[1]; Zennaro D[1]; Rafaiani C[1]; Ferrara R[1]; Bernardi ML[1]; Ciancamerla M[1]; Giangrieco I[2]; Tuppo L[2]; Tamburrini M[2]; Ciardiello MA[2]; Mari A[1]

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Introduction: Exposure to animal allergens is a risk factor for the sensitization and symptoms. The risk of unpredictable symptoms is higher when the patient does not know her/his sensitization and for instance go for buying a pet or begins a job with high exposure to animal shedding. The test is a new multiplex test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, coupled to chemically activated nano-particles.

Objectives: To investigate profiles of animal epithelia sensitization by means of allergenic molecules and extracts immobilized on the multiplex test.

Results: The tested allergenic preparations, all spotted on the multiplex array, were eight epithelia extracts (dog, guinea pig, hamster, horse, cat, mouse, rabbit, rat), seven genuine allergenic proteins (Can f 1, Can f 2, Can f 5, Equ c 1, Fel d 1, Mus m 1, Rat n 1). Out of the 1751 routinely tested patients 568 (32.44%) turned out to be sensitized to at least one of the 15 tested allergenic preparation. The most recognized extract was cat epithelium with 57% sensitization prevalence. The least recognized extract is horse epithelium with 1.4% sensitization prevalence. The most recognized protein is Fel d 1 with 63% sensitization prevalence. The least recognized proteins are Mus m 1 and Rat n 1 with 0.4% sensitization prevalence each. It is worth noting that around 5% of the 568 patients are also sensitized to serum albumins (Bos d 6, Can f 3, Equ c 3, Fel d 2, Mus m 4, Ory c 6, Rat n 4, Sus s 1) with several different patterns of IgE recognition.

Conclusions: The present study results confirm differences in sensitization towards different animal epithelia. Allergy testing using single species markers, serum albumin and epithelium extracts when molecules are not available yet, might help in decision making in the need for choosing future non risky exposures to furry animals. The sensitization to serum albumin creates a cluster of IgE co-reactivity that must be clinically interpreted in the light of the inhalation of the unprocessed allergen. The use of homologous lipocalin, showing divergent IgE binding in routinely tested patients, might help in understanding the IgE epitope distribution in this group of allergens.

1202 | Multiplex IgE diagnostic test: house dust mite sensitization dissected using six allergenic molecule groups

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Introduction: Dermatophagoides pteronyssinus, Dermatophagoides farinae, Euroglyphus Maynei, Blomia tropicalis are house dust mites (HDM), representing the main sources of indoor allergens, with concentration highly dependent upon the domestic environmental conditions and external climate. 37 proteins from HDM's described as allergens.

Objectives: To define the sensitization patterns to HDM allergens and extract available in the test in a population of 1751 patients, tested for routine allergy diagnosis.

Results: Der f 1, Der f 2, Der p 1, Der p 2, Der p 7, Der p 9, Der p 10, Der p 23, Eur m 2 and Blomia tropicalis extract were available for testing in a nanobead-based IVD test for specific IgE detection bearing 122 molecular allergens and 122 allergenic extracts, all coupled to chemically activated nanoparticles. Out of the 1751 analyzed patients 641 (36.61%) turned out to be sensitized to at least one HDM protein. The sensitization prevalence of each allergen was as follows: Der p 2 88%, Der f 2 85%, Eur m 2 52%, Der p 23 48%, Der p 1 44%, Der f 1 37%, Der p 7 24%, Der p 9 7%, Blo t extract 13%. Pattern of sensitization and specific IgE concentration were different, resulting in different patient clustering. Analyzing the data by patients' age, all proteins behave quite similarly, with sensitization peaks in the second and third decades of life.

Conclusions: Although the proteolytic activity of mite group one allergens is claimed as a cause of the high prevalence of HDM sensitization, Der p 1 and Der f 1 do not represent the most common sensitization in mite allergic patients. This evidence is further supported by the low sensitization prevalence to Der p 9, another proteases. Group Der p 2 and Der p 23, whose biological function is almost unknown, represent the most common sensitizers. From a therapeutic perspective and considering the need of a personalized medicine, knowledge about single patient IgE profile leads to the selection of the most suitable extract for immunotherapy. This implies that the allergy investigation should be carried out in the most extensive and comprehensive manner starting with mite allergy representing one of the most common allergy worldwide. The test is the newest in vitro test for specific IgE detection, including molecules and extracts, actually allowing to test the patients' responses to the broadest spectrum of available HDM allergens in the routine setting.

1203 | Multiplex IgE diagnostic test: the broad view on IgE reactivity to seeds, legumes, nuts, and cereals

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Introduction: A seed is a reproductive structure that possesses embryonic plant, stored material, and a protective coat. Its content of proteins belonging to different allergenic families is high with possible but not sure phenomena of cross-reactivity. Several seeds have been increasingly added in human diet with consequent risk of hypersensitivity reactions that are often severe. The test is a new nanobead-based IVD test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, coupled to chemically activated nano-particles.

Objectives: To investigate profiles of seeds sensitization by means of test. The tested allergenic preparations, all spotted on the chip, were 28 allergenic extracts (almond, amaranth, barley, bean, brazil nut, buckwheat, cashew, chestnut, carob, corn, chickpea, hazelnut, kamut, kiwi, lentil, linseed, lupine, peanuts, pine nut, pistachio, quinoa, rice, sesame, soy, tomato seed, walnut, wheat, white mustard) and 23 allergenic proteins (Act d 10, Ana o 3, Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h Agglutinin, Cor a 8, Cor a 9, Cor a 14, Gly m1, Gly m Agglutinin, Gly m TI, Jug r 2, Jug r 3), along with markers for IgE-CCD reactivity and plant allergens belonging to other groups.

Results: Out of the 1751 routinely tested patients 519 (29.64%) turned out to be sensitized to at least one allergenic preparation. The most recognized extract are buckwheat and carob with 50% and 49% sensitization prevalence respectively. The least recognized extract is soy with 0.8% sensitization prevalence. The most recognized protein is Jug r 3 with 19.5% sensitization prevalence. The least recognized proteins are Jug r 2 and Gly m 1 with 0.2% sensitization prevalence. It is worth noting that within the 519 patients sensitized to at least one allergenic preparation 19% were sensitized to Bet v 1-like protein, 18% to profilins, 33% to CCD, 33% to LTP. The cluster analysis shows several patterns of sensitization considering molecules and extracts together.

Conclusions: The results confirm differences in sensitization towards different allergenic sources from seeds and seeds allergenic proteins regardless if they are consumed as such or processed. Filtering the sensitization results by positive tests, taking into account the chance of co-sensitization to panallergens and CCD, the decision making on which seeds have to be excluded from the diet becomes easier with the Multiplex IgE test.

1204 | A digital reporting system an exclusive online free tool for allergy test visualization dedicated to patients and accessible by allergists

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Introduction: Nowadays IgE to an increasing number of different allergens can be detected simultaneously by means of micro and nano technologies providing the patient with an extensive and detailed sensitization profile. Sometimes such a big amount of available information is claimed to be confusing. A new nanobead-based IVD test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, is supported by a specific reporting system aimed at simplifying the test result interpretation.

Objectives: To illustrate how the CAAM Digital Reporting System (CDRS) runs and how both the patient and the allergist can be assisted in the interpretation of the multiplex test results.

Results: CDRS is an Internet-based dynamic visualization system of the patient's allergy test results showing data, graphs, images and comments as they are real time generated in the platform and in its modules, InterAll and ReTiME. CDRS uses the single patient's generic demographic and diagnostic data, the aggregated data of all patients and the Allergome data on molecular allergens and allergenic sources. CDRS provides real-time the information needed to better understand the test results. Comments to each allergen in a multiplex isle test, regularly updated on the basis of the scientific literature and the CAAM's expert opinion, is provided by CDRS to all test performed and uploaded in the system. Users access the test comments as they are available even if the test has been done earlier than the last comment release. CDRS is easily and available free of charge on own mobile devices or personal computer. CDRS PRO, the sister tool addressing professional needs, gives access to a gallery of information, news, and educational tools along with the chance to have patients connected to the specialist. CDRS and CDRS PRO are developed in several different languages allowing the easy access to explanations for natives and foreigners in any given country.

Conclusions: The widest possible knowledge of the patient's sensitization profiles is a fundamental piece of information for the allergist focused to identify and provide the most appropriate solutions to the patient's allergy problems. The digital reporting system multiplex isle is a unique and exclusive tool for providing the most up-to-date info and data using modern ICT, making the results easy to understand to both the patient and the allergist.

1205 | Multiplex IgE diagnostic test: the most comprehensive view on IgE sensitization to vegetables, fruits and seeds due to lipid transfer proteins

Alessandri C[1]; Giangrieco I[2]; Tuppo L[2]; Ferrara R[1]; Zennaro D[1]; Bernardi ML[1]; Rafaiani C[1]; Ciancamerla M[1]; Tamburrini M[2]; Ciardiello MA[2]; Mari A[1]

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Introduction: The plant LTP family consists of ubiquitous proteins typically involved in defense mechanisms against the attack of bacteria, fungi and viruses. They constitute an important cause of allergic sensitization in the Mediterranean area. A new nanobead-based IVD test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, all coupled to chemically activated nano-particles. Eight LTP purified from kiwi, hazelnut, pomegranate, peach, walnut, corn, tomato and wheat are immobilized together with 25 extracts from plant-derived foods bearing, along with other allergens, their LTP.

Objectives: To describe the LTP sensitization in a population of 1751 patients by using molecules and extracts.

Results: Out of the 1751 routinely tested patients 208 (11.88%) turned out to be sensitized to at least one LTP. The sensitization prevalence of each specific LTP within the 208 patients was detected as follows: Pru p 3 94%, Jug r 3 49%, Cor a 8 30%, Zea m 14 30%, Pun g 1 23%, Act d 10 21%, Tri a 7k-LTP 3%, Sola l 6 2%. Pru p 3 reaches 100% prevalence in pediatric patients between 0 to 10 years old population. The 6% Pru p 3 negative subjects turned out to be mono-sensitized to one of the other tested LTP. The availability of extracts from many other vegetables, fruits and seeds allowed the definition of the sensitization to a broader number of relevant LTP. An IgE reactivity was detected to allergenic sources whose content in LTP is still unknown. A different IgE reactivity has been recorded for the 9 k-LTP and the 7 k-LTP. Patients recognizing the latter group have a broader recognition pattern and higher IgE levels.

Conclusions: The specific advantage of a MULTIPLEX isle test relies on the chance of testing patients to a broader panel of LTP as well as to a large number of extracts, complementing the results on the single allergenic molecules.

The availability of the MULTIPLEX test of allergens belonging to the Bet v 1-like proteins, Profilins, CCD markers and Anti-Microbial Peptide groups allows to greatly improve the patient sensitization profiling. The use of extracts to consumed food or newly introduced ones increases our knowledge on allergens.

1206 | Multiplex method for IgE determination: a report of six severe 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 evaluate the multiplex method for specific IgE determination in six peach-allergic patients from Marseille (Southern France) unresolved by previous molecular work-up.

Methods: Skin prick tests with native peach (peel and pulp). Singleplex determination of specific IgE to peach extract, rPru p 1, rPru p 3, rPru p 4, nPru p 1, nPru p 3, nPru p 4. Multiplex specific IgE assays. Basophil activation test with peach extract (Bühlmann).

Results: The six patients (mean age 34 years, range 16-50; 2 males) had a history of peach-induced anaphylaxis. Skin prick tests with native peach were positive in all six patients. Specific IgE to peach were demonstrated in five patients, but were undetectable to Pru p 1, Pru p 3, and Pru p 4 (recombinant and purified allergens). ISAC microarrays were performed and did not evidence any relevant sensitization. Basophil activation tests were positive to peach extract in all patients. The assays evidenced specific IgE to peach in three patients (3 peel, 1 pulp) and to Pru p 7 (peamaclein) in five patients. One of these patients also displayed sensitization to Pun g 7, the pomegranate homolog of peamaclein.

Comparison of the multiplex assays showed concordance for Cup a 1- sensitization in all six patients, and Ole e 1—sensitization in four patients. Overall agreement between the two methods was good, although some discordant results were noted for Cry j1, Phl p 5, Phl p 6, and Phl p 7.

Conclusions: The multiplex assay evidenced Pru p 7 sensitization in 5 out of 6 peach-allergic patients from Southern France with unresolved molecular diagnostics. Comparison of multiplex and singleplex platforms showed an overall good agreement. In conclusion, the new multiplex provides a mixed panel of allergenic extracts and molecules, some of which are uniquely available through this method and therefore bring important update to currently available diagnostic tools in molecular allergy.

1207 | Multiplex IgE diagnostic test performances compared to singleplex

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Introduction: Laboratory allergy testing systems for IgE detection are evaluated for standard parameters and performances. Multiplex is the new generation of multiplex IgE detection systems based on allergen preparations coupled on nano-beads using molecules and extracts. The best way to understand the performances of a new system is to compare with others.

Objectives: To report the comparative evaluation of the multiplex IgE test versus the most used singleplex IgE testing systems.

Results: The evaluation of the IgE binding was obtained by using an Allergen IgE (BL-IgE), a standard polyclonal commercial product. BL-IgE is supplied after being tested on the 3 IgE testing systems. IgE mean values and ranges are provided. The product data sheet shows IgE values for 15 allergen extracts. 12 were used: Alt a, Ara h, Art v, Asp f, Bet v, Bos d, Can f, Der p, Equ c, Fel d, Gal d, Phl p. BL-IgE was tested on 22 consecutive multiplex batches, and extract to extract comparison was performed when the same was available on FABER. FABER IgE, expressed as arbitrary units (FIU) gave the following results: Ara h, overlapping with CAP-IMM-HYT; Art v, slightly below CAP, overlapping with IMM, above the HYT; Bet v, slightly below CAP-IMM; Bos d, above CAP-IMM-HYT; Can f, slightly below CAP-IMM, overlapping with HYT; Fel d, reproducible but below the three systems; Gal d, below IMM, overlapping with CAP-HYT; Phl p, overlapping with CAP-IMM. Alt a 1 performed better than CAP-HYT, overlapping with IMM. The 6 Der p FABER allergens gave overlapping results with the 3. Although reproducible results were record with Equ c FABER extract, average values always fell below the range of the three systems. Asp f values were hardly reproducible and always below the three systems, but the use of a similar extract, Asp n, and the Asp r 1 allergen supported the Asp f IgE detection. A plus value of our study was to disclose IgE binding to allergens not declared in the BL-IgE data sheet (e.g. Cup a 1, Pru p 3), mostly all the molecule detected specificities (e.g. mite allergens) and all the IgE co-recognized preparations (e.g. eggs).

Conclusions: The three systems having different reference standards do not overlap each other. FABER IgE measurements performs very well with most allergens, but improving the quality of some extracts will lead to better FABER performances. The multiplex IgE detection is useful to disclose unknown sensitizations.

1208 | Evaluation of a multiplexed biochip (friendly allergen nano-bead array) in different clinical contexts

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Introduction: A new IgE multiplexed biochip including molecular allergens and extracts was recently developed.

Objectives: The usefulness of this biochip was assessed on well characterized patients chosen by a group of allergists and biologists with a good experience on molecular allergy.

Results: Twelve sera from adults (n = 5) and children (n = 7) suffering from food and respiratory allergies (n = 8), not clearly explained anaphylaxis (n = 2), severe atopic dermatitis (n = 1), eosinophilic esophagitis (n = 1) and chronic urticaria (n = 1) were included. Clinical history, skin prick tests, and results of specific IgE already performed by singleplex Bichat hospital (Paris) and Lyon-Sud hospital (Hospices Civils de Lyon) were collected for each patient. All patients or their parents for children gave a written informed consent. Sera were tested by multiplex biochip based nano-bead array technology including 244 allergens (122 molecular allergens, and 122 extracts) in the molecular allergy lab (CAAM, Roma).

Data from the multiplex biochip confirmed the sensitization to common food and aeroallergens such as dog, cat, grass and birch pollens, house dust mites and molds (*Alternaria*). A good sensitivity was observed for IgE to nuts particularly to 11S globulins, 2 S globulins and LTP. In accordance to clinical history and skin tests, IgE to several extracts of legumes (lentils, chickpeas), fish allergens (sole, sardine, cod) and molecular allergens could be detected. For three patients, unexpected sensitizations to alpha-Gal and human lactoferrin were observed. A frequent unexpected positivity to amaranth (n = 6) was observed without sensitization to profilin (n = 4). An unexpected sensitization to tropomyosin was also highlighted. Furthermore, the carbohydrates determinants displayed by several raw extracts seem to be frequently positive (n = 7). This new test failed to clarify the unexplained anaphylaxis here. The results reports need to be improved for a better interpretation of the results.

Conclusions: This preliminary study suggest that the biochip could be a helpful tool to explore polysensitized patients. More patients need to be studied to better evaluate the place of this new biochip in allergy diagnosis.

1209 | Comparing IgE reactivity distribution between Iranian and Italian allergic patients using a multiplex IgE diagnostic test

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Introduction: IgE-mediated Allergic diseases are increasingly common worldwide affecting population often exposed to different allergenic sources. In fact, environmental exposure to allergens might be different from one geographic area to another, sometime closer (regions of the same Country) sometime not (distant countries with very different climates. To compare prevalence of IgE sensitization between regions investigational tools must be standardized in terms of used and kind of reagents. The use of broad panels of allergens could ease the study design. Multiplexed IgE detection system might be suitable for the purpose. The multiplex test for IgE detection bearing 244 allergens, both molecules (122) and extracts (122), is the most advanced tool for this purpose.

Objectives: We aimed to perform a pilot study comparing IgE sensitization in two Countries with quite different environment allergen exposure.

Results: A multiplex Assay version has been used to perform IgE detection. Serum samples were all tested in a single lab. The two group of 62 patients each were age and gender matched. Der f 2 and Der p 2 mite allergens were IgE recognized with a slightly non statistically different prevalence. A higher difference in prevalence, higher in Italians, was detected for Der p 23 and Der p 7, whereas Der p 1, Der f 1, and Der p 9 reactivity had a lower prevalence in Iranians. The same behavior was not recorded for grass allergens where the groups had almost the same prevalence but the molecule profiles where differing as group 2, 5, 6 were 3-4 time fold less positive in the Iranian group. Genuine markers of some pollen species exposure, like Par j 2, showed positive vs negative prevalence in Italian vs Iranians, whereas IgE results for Ole e 1 were higher in Iranians. Number of Cup a 1 and Art v 1 positive subjects had almost an identical prevalence, whereas profilin sensitization was higher in Iranians, as well as CCD one. Few Bet v 1 positive subjects and to homologs were recorder in both Countries, whereas LTP sensitization was almost absent in Iranians.

Conclusions: IgE detection by means of the multiplex test preliminary discloses differences between allergics living in different Countries. Due to the small number of observations, unwanted biases could be introduced in the patient selection from the two Countries, thus, to draw conclusions, the study using the same multiplex tool on larger cohorts should be performed.

1210 | A multiplex diagnostic test: exploring IgE sensitization to tropomyosins and related sea foods and arthropods

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Introduction: Tropomyosins are allergenic proteins present in invertebrate muscle and non-muscle cells, involved in muscle contraction together with actin and myosin. A great number of allergenic tropomyosins have already been described in invertebrate (crustaceans, molluscs, snails, mites, insects) whose IgE cross-reactivity is related to the high structural similarity in amino acid sequences. The test is a new nanobead-based IVD test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, all coupled to chemically activated nano-particles.

Objectives: To analyze the sensitization profiles of tropomyosin sensitized patients by means of the multiplex test, considering allergenic molecules and extracts from crustaceans and mollusks.

Results: The tested allergenic preparations, all immobilized on the chip, were 10 invertebrate extracts (Anisakis pegreffi, Anisakis simplex, calamari, clam, German and American cockroach, mussel, octopus, shrimp, snail), and seven tropomyosins (Ani s 3, Der p 10, Hel a s 1, Lit v 1, Per a 7, Uro du 1, Ven ga 1). Out of the 1751 analyzed patients 115 (6.58%) turned out to be sensitized to at least one of the 17 tested allergenic preparations. The most recognized extract was clam with 36% prevalence, the least recognized is American cockroach with 5% prevalence. The most recognized tropomyosin is Ven ga 1 with 29% prevalence, the least recognized is Hel as 1 with 20% prevalence. The patients recognizing at least one of the seven tropomyosins are 49, 33% of them having IgE to all seven tropomyosins, 16% of them recognizing one only.

Conclusions: The study results confirm differences in sensitization patterns toward the tested invertebrates extracts and tropomyosins. The single patient defined IgE profile, supported by clinical data and oral food challenge if needed, might lead to a better selection of which of the involved foods should be excluded from the diet. Anyhow, highly similar tropomyosins seems to behave in a patient-related manner. Food and non-food extracts from allergenic sources with known or still unknown tropomyosins help to broad the IgE profile definition. Testing extracts from vertebrate species and fishes seems not to bring evidence of any IgE cross-reactivity.

1211 | FABER IgE diagnostic test: a useful help in understanding IgE sensitization to fishes

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Introduction: Parvalbumin is an allergenic protein from fish white muscle responsible for more than 95% of food allergies induced by fish. The content of parvalbumin is higher in bottom dwelling fish species such as cod and solea whereas is lower in the active fishes (rich in dark muscle) such as tuna, sardine, salmon. The parvalbumin content also depends on muscle parts: higher levels in rostral part than in caudal part. Parvalbumin sequences from different species are homologous but not identical. FABER test is a new nanobead-based IVD test for specific IgE detection using 122 molecular allergens and 122 allergenic extracts, all coupled to chemically activated nano-particles. The array contains Mer mr 1 parvalbumin from European hake along with five allergenic extracts from Atlantic cod (Gad m), Atlantic salmon (Sal s), Sardine (Sar m), Common sole (Sol so) and Yellowfin tuna (Thu a).

Objectives: To investigate the IgE profiles of fish sensitized patients.

Results: Out of 1751 routinely tested patients, 47 (2.68%) turned out to be sensitized to at least one fish allergenic preparation. The sensitization prevalence of each specific fish extract within the 47 patients was as follows: Sardine 66%, Sole 62%, Cod 34%, Salmon 26%, Tuna 19%. The sensitization prevalence of Mer mr 1 was detected 43%. It is worth noting that 25 out of the 47 patients were monosensitized, with sensitization concentrated exclusively on Sardine extract, Sole Extract and Mer mr 1 parvalbumin. Co-reactivity to most or all fish extracts was always present when IgE levels were detected high or very high. Few single fish species isolated sensitization have been detected.

Conclusions: The presence on the FABER test of several fish extracts together with Mer mr 1 parvalbumin allows to improve the patient's sensitization interpretation. The specific advantage of FABER relies on the chance of testing patients to a broad panel of fish extracts complementing the results on the single allergenic protein, thus non missing any non-parvalbumin IgE reactivity. Interpreting the sensitization profiles with an accurate patient's history combined with specific oral food challenges could provide improvement to the allergic patient's diet.

1212 | Faber IgE test: A standard multiplex diagnostic tool to explore allergic sensitization across Northern, Central and Southern areas in Italy

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Introduction: IgE-mediated diseases are the most common allergic diseases worldwide. Precision medicine includes stratification of patients also according to their geographical distribution. The allergenic sources vary from one geographic area to another. The use of a broad panel of allergens facilitates the study design to comparatively investigate different areas. The FABER test for IgE detection bearing 244 allergens, both molecules (122) and extracts (122), is the most advanced tool for this purpose including inhalant and food allergens.

Objectives: The aim of this pilot study is to investigate the allergic sensitization prevalence in three groups of Italian patients living in Piedmont (North-western area, PM), Latium (Central area, LZ) and Apulia (South-eastern area, PG). FABER 244 version has been used to detect specific IgE. Serum samples were all tested in a single lab for the routine diagnostic workup. The three groups of 122 (PM), 122 (LZ) and 100 (PG) patients were matched for both age (0.1-79 yo, average: 33 yo) and gender distribution (F/M = 1.25:1).

Results: The three groups behave differently in terms of the overall number of IgE recognized allergens: the average number was 22 for PM, 20 for LZ, and 14 for PG. The sensitization for all dust mite allergens appears to be homogeneous in the three groups with the highest values in LZ for Der p 2 (47%) and the lowest in PG for Der p 9 (2.5%). Der p 23 showed marked differences in prevalence between LZ (31%) versus PG (22%) and PM (18%). Grass, Fagales, Parietaria, Olive and Cypress pollen marker allergens were as follows: Bet v 1 (PM 28%, LZ 9%, PG 2%), Par j 2 (PM 11%, LZ 16%, PG 18%), Ole e 1 (PM 25%, LZ 20%, PG 17%), Cup a 1 (PM 25%, LZ 38%, PG 37%), Phl p 1 (PM 50%, LZ 37%, PG 22%), Phl p 5 (PM 36%, LZ 29%, PG 5%), and Amb a 1 (PM 4%, LZ 1.6%, PG 0%). The LTP sensitization was recorded higher in LZ (20%) compared to PG (17%) and PM (16%). Other allergen sensitizations were: Tropomyosin (PM 4%, LZ 3%, PG 3%); Profilin (PM 18%, LZ 8%, PG 1%); Parvalbumin (PM 2.5%, LZ 1%, PG 2%).

Conclusions: IgE detection by means of the FABER multiplex test might allow to precisely detect sensitization prevalence to inhalant and food allergens using data from the routine diagnosis. FABER testing preliminary discloses differences and similarities among different Italian regions having quite different climates. To draw any conclusion the study using the same FABER multiplex tool on larger cohorts of patients will be performed.

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RESPIRATORY PEDIATRIC ALLERGY

1213 | Identification of pediatric asthma phenotypes in daily practice

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Introduction: Asthma in childhood is a heterogeneous disease. Currently many different asthma phenotypes are described. However, pediatric asthma phenotypes using easy to get clinical parameters in a broad population of patients in a daily practice are lacking.

Objectives: The aim of this study was to investigate specific asthma phenotypes in children based on the presence and impact of (atopic) co-morbidities: food allergy, eczema, allergic rhinitis and recurrent respiratory infections.

Methods: In this cross-sectional study, the Electronic Portal (EP), was used. The EP is a web-based application with prospectively collected self-reported data in children referred for respiratory and atopic symptoms, both in primary-, second- and third line health care. Large amount of data on patient determinants and outcomes are available. Asthma was defined as (at least 2 out of 3 criteria fulfilled): a doctor's diagnosis (a), prescription of daily asthma medication in the last 12 months (b) or at least one episode of wheeze in the last 12 months (c).

Results: Until now, 9399 children were invited for the EP, a total of 5618 children (60%) did log in and 4877 (52%) completed the baseline questionnaire and gave consent for data usage for research purposes. Thirty-eight percent of children (n = 1840) were considered to have asthma. In these children (mean age 7.7 years SD 4.4; 61% male), symptoms of asthma during the last 12 months were reported in 1727 children (94%) and 1603 children (87%) used inhaled asthma medication in the last 3 months. Eczema, allergic rhinitis and recurrent infections were self-reported in respectively 1233 (67%), 693 (38%) and 700 (38%) children. Self-reported food allergy was reported in 846 children (46%)of which 545 (64%) were diagnosed by a physician (n = 406 pediatrician, n = , n = 97 GP, n = 41 other). An allergic reaction to food during the last year was reported by 380 children (45%). Majority of children described one (n = 582) or two (n = 545) atopic or respiratory comorbidities. No comorbidities were reported in 263 children (14.3%), while in 80 children (4.3%) all four comorbidities were described.

Conclusions: Our preliminary data show that atopic comorbidities and recurrent infections are common in children with asthma. Further analysis will highlight impact of these comorbidities on asthma related outcome measures.

1214 | Clinical state during last one year treatment and examination before remission about asthmatic children in long-term remission cases

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Introduction: We reported the characteristics and clinical usefulness of airway hyperresponsiveness examination about asthmatic children at EAACI 2014, EAACI 2015 and EAACI 2016 congress. Last year I reported annual change about remission cases during 5 years.

This time I studied clinical state (background, treatment, examinations) during last one year before remission. Then I tried to discuss about the clinical indicator when we will quit the treatment for leading long-term remission.

Objectives: Remission cases (no symptom and no therapy) for 5 years of asthmatic children were studied.

Clinical background and treatment (drugs) was studied during last one year before remission. Acetylcholine inhalation test by standard method was performed, and respiratory threshold of acetylcholine (RT-Ach) was obtained. FEV1%, and serum IgE also examined. These data were compared before remission with after one.

Results: Mean age of 25 cases at one year before remission was 11.3 years old. Male to female ratio was 1.2.

Severity of asthma was all mild type, and number of attack was 1-5 times in the year. There was no admitted case during this study.

The long-term therapeutic drugs were leukotriene receptor antagonist (Anti LT) in 15 cases, inhaled corticosteroids (ICS) in five cases, but five cases had no treatment for the control.

Geometric mean of RT-Ach (after then, before and after remission) was 3200 μg/mL and 3700 μg/mL. The mean FEV1% was 85% and 90%. Geometric mean of serum IgE level was 370 IU/L and 420 IU/L .

Complicated cases of atopic dermatitis decreased after remission, but the incidence of allergic rhinitis did not change.

Conclusions: Characteristics of asthmatic children during last one year before remission were mild type, had only several times of small attack, and the treatment was mainly Anti LT. FEV1% was within normal range, and serum IgE level did not change after remission. RT-Ach had the tendency to improve after remission. These data suggest that airway hyperresponsiveness examination is one of the indicators for quitting treatment.

1215 | Airway diseases education and expertise (ADEX) in pediatrics: The success so far in India

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Introduction: Asthma and allergic rhinitis represent spectrum of united airway disease (UAD) and common cause for sleep disordered breathing. Educating primary-care physicians in developing countries with high disease burden is essential.

Objectives: A panel from Pediatric Allergy Association of India and Indian Academy of Pediatrics on Airway Diseases Education and Expertise (ADEX) was formed to prepare a comprehensive module on understanding, diagnosing and managing UAD incorporating global knowledge as well as adapting to local socioeconomic factors. Extensive literature search with 584 abstracts and 49 full texts was done with multiple panel discussions.

Results: ADEX module reviewed by international experts has been cascaded to over 3000 child-care physicians in India. ADEX module comprises four sections: pathophysiology linking airway allergies, clinical features and co-morbidities, role of diagnostic tests and management. Panel suggested that good clinical history and physical examination is cornerstone for diagnosis. Goals of management include symptom relief, preventing disease progression, good lung function and ability to perform daily activities. The practical five point approach recommended is: ILL (what makes you ill –triggers and environment control), HELL (what makes it worse-aggravators, consider asthma phenotypes—exercise, allergen, virus and obesity), PILL (appropriate medications and dosing—least sedating second generation antihistamines, ICS/INS with low systemic availability Mometasone or Fluticasone, ICS + LABA preferred in children >5 yr uncontrolled on ICS monotherapy, INS +Montelukast in allergic rhinitis predominant, ICS +Montelukast in asthma predominant preferred, immunotherapy for definite unavoidable specific allergen exposure in patients unresponsive to maximum pharmacotherapy with FEV1 >65%. SLIT preferred over SCIT for better safety), SKILL (individualizing device, regular assessment of technique, patient education) and WELL (maintain wellness with regular monthly monitoring of upper and lower respiratory score to achieve good control then 3 monthly).

Conclusions: Scientific progress in airway allergy management involves practitioners, academicians, researchers and pharmaceuticals. The doctors found ADEX module to be extremely useful for understanding, diagnosing and managing airway allergy. The module is regularly updated and is being continually used by as well as being further cascaded to primary child care practitioners in India.

1216 | Prevalence of psychogenic disorders of breathing in children with bronchial asthma. Ukraine

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Introduction: In Vinnitsa region registered 624 135 children. Bronchial asthma was registered in 1472 children, 917 boys and 555 girls. The percentage of boys and girls is 62.29% and 37.7%, respectively. The average age of the boys was 7.43 years, girls—8.36. Mild asthma was diagnosed in 50% (737), moderate—38.3% (565) and severe—11.5% (169).

Objectives: The main purpose of our study was to investigate the prevalence of psychogenic disorders of breathing in children with asthma. Use the following additional.

Methods: spirometry test with exercise and test of reversibility with β_2- short-acting agonist, peak flow and performance evaluation of placebo therapy.

Results: It was established that 2.9% (5) children with severe asthma was diagnosed accompanying hyperventilation syndrome, of which girls accounted for the largest number (4). None of the patients diagnosed with asthma not associated psychogenic cough.

Conclusions: The combination of hyperventilation syndrome and psychogenic cough in 1.15% (17) simulated severe asthma in children. Vocal cord dysfunction was the cause of misdiagnosis in 4.2% (7) of the patients with severe and 1.6% (9) with an average degree of severity asthma. Psychogenic cough in 2.0% (15) were the causes of misdiagnosis mild asthma. The average time to establish the true diagnosis was psychogenic cough to 4.2 $\pm$ 1.1 months, hyperventilation syndrome—3.4 $\pm$ 1.3 months, combination of the hyperventilation syndrome and psychogenic cough—1.3 $\pm$ 0.2 months. Overall, among children, we observed with asthma found 9.3% (48) with a false diagnosis due to psychogenic respiratory disorders.

1217 | Childhood asthma analysis from the Korea national health insurance claims database

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Introduction: Asthma incidence is increasing, but reports on incidence rate of childhood asthma in Korea were relatively rare.

Objectives: The aim of this study is to estimate the prevalence of childhood asthma and investigate trend of asthma-related treatment and its costs.

We analyzed the insurance claims records from the Korea National Health Insurance claims database from January 2010 to December 2014. Subjects were limited to children (< 19 yr) with asthma based on ICD-10 diagnostic codes.

Results: The mean prevalence of asthma in children under 19 year-old was 14.3% over 5 years and increased from 11.2% in 2010 to 16.5% in 2014. By age, the prevalence of asthma was 41.7% for 1 year-old and 2.3% for 18 year-old. Each asthma patient (<19 year-old) had mean 6.2 outpatient visits over 5 years, 7.7 visits for 1 year-old and 2.3 for 18 year-old children. The yearly cost per person in outpatient clinic decreased from 165 500 won in 2011 to 127 640 won in 2014, while that of hospitalization for asthma patients were not different. The frequency of outpatient visit per person was constant over 5 years. Each asthmatic patient had mean 1.49 emergency room visits and mean 0.11 admissions per year to treat asthma. About 2% of children (≥5 year-old) with asthma performed the pulmonary function tests.

Conclusions: The prevalence of asthma in children under 19 year-old gradually increased year over year and was lower at increasing age. Frequency of hospital visit for asthma was not different over 5 years. The expenditure for treating asthma decreased in recent 5 years.

1218 | Pre-clinical diagnosis of formation of asthma in children with allergic rhinitis

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Introduction: Bronchial asthma and allergic rhinitis are multifactorial diseases. However it is not possible to solve the problem to date on revealing pre-clinical diagnosis of formation of asthma in children.

Objectives: The research objective was pre-clinical diagnostics of formation of asthma in children suffering from persistent allergic rhinitis.

Results: We observed 105 children aged 6-18 years, divided into three groups: the first one—children with persistent allergic rhinitis (PAR) of medium severity in the acute period (35 persons); The second one—children with PAR of medium severity in the period of exacerbation and mild persistent bronchial asthma (40 persons); the third one—children with mild persistent BA (30 persons). The gender analysis proved that there were 65.4% of boys (70 persons) and 34.6% of girls (35 persons) among the examined children.

Amongst most of the patients suffering BA and AP there was marked sensitization to house dust, delay of appointment of anti-inflammatory therapy of AP up till 5 years of age and disease duration more than 5 years. We have conducted analysis of cytological spectrum, level of eosinophil in peripheral blood and total IgE in the serum. It was revealed that in patients with a combination of BA and AP, the allergic process was more apparent when compared with children with only AP or BA only. Thus, the total IgE level in serum was 1.8 times higher and indices of the serum IgE more than 300 ME/has been met 2.7 times more in children group with combination of BA and AP compared to patients with only AP. The high rates of peripheral blood eosinophils (more than 10%) had approximately observed about three times more in children with a combination of BA and AP compared to patients with only the AP, and only with BA.

Conclusions: The high values of nasal content eosinophils (over 10%) in children of the 2nd group were two times higher than in patients from the 1st group and 2.6 times higher in the 3rd group patients. Thus, the data received by us are informative diagnostic risk factors for the formation of asthma in children with rhinitis.

1219 | Acute respiratory failure in pediatric patients with bronchiolitis: series of 2 years in a pediatric intensive care unit (PICU)

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Introduction: Bronchiolitis is a common acute inflammatory injury of the bronchioles that is usually caused by a viral infection and affects children under the age of two. It's often a mild illness but some children develop severe bronchiolitis.

Objectives: The objective of this study is to characterize the severe bronchiolitis cases admitted to PICU, understand risk factors that led to hospitalization, patient characteristics, morbidity and mortality associated factors. Retrospective analysis of clinical records of patients admitted to the PICU over two years for acute respiratory failure with the primary diagnosis of bronchiolitis. The variables analyzed were: sex, age, prematurity, breastfeeding, family atopy, duration of hospitalization, respiratory virus testing, mechanical ventilation, therapeutics and complications.

Results: Twenty one patients were included, F/M = 1/3. The average age was 2 months old, 4 were born prematurely, 8 were breastfed and 6 had family atopy. The average hospital stay was 6 days. VSR was found in respiratory virus testing of 14 patients. Three children required invasive mechanical ventilation. Only 4 patients had not antibiotherapy. Complications recorded were: 1 pneumothorax, 2 atelectasis, 1 sepsis, 1 tachycardia, 1 nosocomial pneumonia and 1 death.

Conclusions: Viral bronchiolitis is usually associated with favorable outcome however it is important to understand risk factors and more effective ways of managing the severe form of this disease.

1220 | Pediatric Asthma E-care: a smart tool for improving asthma controlled in children

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Introduction: Samitivej Children's Hospital (SMCH) provides Childhood Asthma Clinical Care Program (SMCH-CCP-Asthma) with a multidisciplinary team including pediatric allergists/pulmonologists, nurses, pharmacists and physical therapists. In 2014, there were 119 asthmatic children in our SMCH-CCP-Asthma, 65 of them (54.6%) were lost to follow-up, and 41 had asthma exacerbation and needed hospitalization. From telephone survey, we found 2 common reasons: unavailable times of parents taking patients to follow-up at clinic, and tight-schedule of patients for tutorial school. Most of them had clinical asthma controlled at home during appointment times, so they just believed that no need to follow-up visit was fine.

Objectives: We developed a tool, Pediatric Asthma E-care, using informative technology in assisting communication between patients-family and SMCH-CCP-Asthma, which help to assess clinical asthma controlled in patients, adjust controlled medication, and alarm need for emergency visit when asthma exacerbation. This tool aims to prevent unscheduled visit to emergency room or hospitalization from asthma exacerbation. We collected the following outcomes: (1) rate of asthma exacerbation, (2) hospitalization from asthma exacerbation, (3) scheduled visit and follow-up rate, and (4) patients-family satisfaction with SMCH-CCP-Asthma. Data were collected monthly and were analyzed for percentage change quarterly, and for monitoring any problem.

Results: From launching this tool in August 2015; the outcomes were collected from the third quarter (Q3) of 2015 to the first quarter (Q1) of 2016. We found rate of asthma exacerbation dropped from 54.1% in Q1/2015 to 49.2% in Q1/2016, hospitalization from asthma exacerbation dropped from 13.0% in Q1/2015 to 12.5% in Q1/2016, scheduled visit and regularly follow-up of asthmatic children by Pediatric Asthma E-care system from 50.6% in Q1/2015 to 61.1% in Q1/2016, and perception surveys of patients-family with SMCH-CCP-Asthma for overall program evaluation was increased from 4.63 in Q1/2015 to 4.67 in Q4/2015, and adopting information of program was increased from 8.95 in Q1/2015 to 9.35 in Q4/2015.

Conclusions: Pediatric Asthma E-care is a tool for easily assessing clinical asthma controlled, initiating asthma action plan for self management or taking more action if clinically unresponsive to initial treatment. The clinical service improvement using the tool with informative technology will assist adherence of patients with asthma.

1221 | Allergic bronchopulmonary aspergillosis misdiagnosed as recurrent pneumonia in a child: a case report

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Case Report

Introduction: Allergic bronchopulmonary aspergillosis (ABPA) is an allergic lung disease usually caused by *Aspergillus fumigatus*, which characterized by wheeze, productive cough and pulmonary infiltrates associated with a decline in lung function. The prevalence of ABPA is estimated to be approximately 1–2% in adult patients with asthma and 2–15% in patients with cystic fibrosis (CF). In children, the incidence of ABPA is unknown. Here we report the case of a 13-year-old girl with ABPA who presented with recurrent pneumonia.

Case Report: A 13 year old girl referred to our hospital with a 15 months history of productive cough and 4 months of intermittent wheezing. Fifteen months ago, she complained of cough and occasionally cough up purulent sputum, then she was admitted to local hospital, her chest X ray showed opacities, she was diagnosed pneumonia and treated with cephalosporin for 8 days and discharged after cough improving. However, she still suffered from intermittent cough after discharge,and symptoms were aggravated after exercise or cold. Nine months ago, her suffered productive cough and increased thick sputum, combined with fever, she was admitted to the local hospital again, the routine blood test showed WBC 6.53×10^9/L, N 43.2%, L 40.6%, E 7.7%, CRP 6 mg/L, her chest X ray still showed opacities, and she treated as pneumonia using azithromycin and cephalosporin, her symptoms slightly improved. Eight months ago, her symptoms were exacerbated after cold, and purulent sputum occasionally contained brown particle, the routine blood test showed WBC 7.59×10^9/L, N 55.3%, L 36.5%, E 3.6%, CRP 0.5 mg/L, her chest X ray showed multiple opacities in left lung, she was diagnosed mycoplasmal pneumonia and received treatment by azithromycin (3 courses), her symptoms had slight remission. Four months ago, her experienced wheezing, short of breath and chest tightness when she travelled abroad, the symptoms relieved after oral glucocorticoid and in the following months she often felt short of breath especially after exercise and gradually exercise intolerance. One months ago, her symptoms got worse after upper airway infection, she presented productive cough, wheezing and expectorated an amount of brown black sputum, and referred to local hospital, the routine blood test showed WBC 10.06×10^9/L, N 60.2%, L23.3%, E 10.51%, CRP 6.9 mg/L, Total IgE >3000 IU/mL, pulmonary function test showed mild restrictive ventilatory functional disturbance (FEV1: forced expiratory volume in one second 67.3% predicted), bronchial dilation test (+), chest X ray showed right upper lung opacities, she was still treated as pneumonia and received cephalosporin with no obvious improvement. Then she referred to our hospital, further investigation was done and the laboratory results were as follows:

total immunoglobulin E and serum IgE were both detected using ImmunoCAP system (Phadia, Uppsala, Sweden). total IgE was 25180 kU/L (positive,>60KU/L), *Aspergillus*-specific IgE was 34.7 kUA/L (positive, >0.35 kUA/L). other positive allergens included: dust mite, chest high-resolution computed tomography (HRCT) showed infiltration、central bronchiectasis and high-attenuation mucus in the left lower lobe and lingula. On bronchoscopy a large amount of purulent material and brownish sputum plugs within the posterior and anterior segment of the right upper lobe、anterior basal segment of right lower lobe and lingual segment airways were seen. (Figure) Bronchiectasis was seen in anterior segment of right upper lobe and anterior basal segment of right lower lobe. *Aspergillus fumigatus* were cultured from bronchoalveolar lavage (BAL) and sputum. Tests for other possible pathogens including: cultures and/or stains of blood and sputum for viruses, mycoplasma pneumoniae,fungi (G and GM test), bacteria were negative. All autoimmune antibodies (ANAs, ENA, dsDNA, ANCA)were negative. The diagnosis of ABPA was considered. Corticosteroid (prednisone 0.5 mg/kg/day) plus itraconazole (200 mg, twice a day) was initiated. The girl responded well to the therapy. Two weeks later, she was free of symptoms. Lung function nearly improved to normal. One month later, her condition stabilized. Peripheral eosinophil percentage and IgE decreased to 1% and 404 IU/L, respectively. Chest CT showed improvement in pulmonary infiltration.

Conclusion: The present case emphasizes the importance of considering the diagnosis of ABPA in children with uncontrolled pneumonia, hypereosinophilia, and bronchiectasis. Early diagnosis and initiation of systemic corticosteroids are essential to prevent irreversible damage.

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FUNCTIONAL GENOMICS AND PROTEOMICS

1222 | Mite allergoid immunotherapy: allergome content and immunoreactivity defines effective platform for SCIT

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Introduction: *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* cause the symptoms of asthma and allergic disease in the vast majority of patients sensitized against house dust mites.

Allergen-specific immunotherapy using modified mite allergens adsorbed on tyrosine has been shown to exhibit clinical efficacy with enhancement in safety profile compared to native allergens. Manufacture of the vaccine is based on extraction of whole mite culture to ensure presence of major and minor allergens from faeces and bodies in the final vaccine formulation. The objectives of this study were to assess allergen preservation following the modification process and immunoreactivity of major mite allergens of group 1 and 2.

Objectives: Whole mite culture was extracted as 1.2% v/w in glycerinated medium, diafiltered to remove impurities and modified with 10% glutaraldehyde. Mass spectrometry analysis of native mite extract vs. modified extract was performed across the molecular weight range 2-250 kDa to identify major and minor allergens present in the product. An ELISA platform was employed to determine absolute content of Der f 1 before and after modification. SDS-PAGE and Western blotting were used to confirm retention of immunoreactivity for major mite allergens from group 1 and 2 in the modified product.

Results: Detailed molecular fingerprinting of native vs. modified mite allergomes revealed the presence of an extensive range of mite allergens from faeces and whole bodies, including major allergens of group 1 and 2. In comparison with the native mite formulation, the modified formulation showed a consistent increase in the relevant molecular weight, confirmation in the sequence coverage and identification of various isoforms between group 1 and group 2 allergens. Allergen content analysis revealed a significant proportion of total protein content being quantified as group 1 major allergens. Immunoblot with monoclonal antibodies against group 1 and group 2 allergens from native and modified formulations confirmed immunoreactivity of these allergens in both cases.

Conclusions: Mass spectrometry analysis has shown a high degree of preservation of major and minor allergens representative of mite bodies and faeces in a modified vaccine formulation. The major group 1 allergen content was determined in native and modified formulations and immunoreactivity of modified group 1 and 2 allergens was confirmed.

1223 | Impact of bacteria bifidobacterium bifidum and bacterial components on gene expression of immune response cells

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Introduction: An integrated model of immune cell function and response to microorganisms is required to assess interactions of bacteria and bacterial components with immune cell receptors and intracellular activation pathways. The microorganism *Bifidobacterium Bifidum* and its components were assessed for immune signaling activation.

Objectives: Inactivated cells from the probiotic bacteria Bifidobacteria along with cell walls were used to assess activation and growth of peripheral blood mononuclear (PBM) cells and dendritic cells. Gene expression in PBM was assessed under the influence of *E. coli* Lipopolysaccharide (LPS) and Bifidobacteria (n = 9) and their cell walls (n = 9). Total RNA was isolated by Tri-Reagent. cDNA was synthesized using Superscript cDNA Synthesis Kit (Invitrogen, CA). Hybridization of labeled cDNA was carried out on a biochip Arrayit Dendritic & Antigen Presenting Cell Pathways Microarrays and scanned to Innoscan 700 (Carbon, France). For statistical analysis Expander 6 and Statistica 10.0 were used. The differences were considered as statistically significant at the level $P < .05$ for the *t*-test.

Results: The study analyzed the expression of 96 genes most significant for the immune system. Bifidobacteria and their component cell walls during interaction with the immune system cells caused increased expression of genes including those for CCL13, IFNG, IFNGR1, IL8RA, CDC42, CD1c, CD1a, and ILR8.

Conclusions: Bacterial components including cell walls and inactivated microorganisms have a stimulating effect on immune cells inducing maturation and activation. Evaluation of immune cell gene expression provides new information about the differential response to various immune activators including the potential for specific effects such as tolerance, allergy, or activation of cellular and/or humoral immune responses.

1225 | IL-33 and its soluble receptor sSt2 in lower airways of seasonal allergic rhinitis patients

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Introduction: Interleukin-33 (IL-33) is an epithelial 'alarmin' inducing a Th2-type reaction in response to external stimuli such as viral infections, airway irritants and allergens via innate helper cells type 2 stimulation. It is implicated in airway inflammation and airway hyperresponsiveness in allergic rhinitis and asthma and has been measured in supernatants of sputum from asthmatic children and sera from asthmatic adults. Soluble receptor of IL-33 (sST2) attenuates this inflammatory response by acting as a decoy receptor that prevents the interaction of IL-33 with its membrane receptor. To date, there are no data concerning IL-33 and sST2 levels on samples of adult patients suffering from allergic rhinitis.

Objectives: We evaluated the presence of IL-33 and its receptor sST2 via ELISA measurements in sputum supernatants from seasonal allergic rhinitis patients without concomitant asthma, during and out of the pollen season.

Results: IL-33 and sST2 levels were investigated in sputum supernatants of 20 seasonal allergic rhinitis patients by the Quantikine® (IL-33Q, sST2Q), and Luminex High Sensitivity® (IL-33HS) immunoassays (all R&D Systems Abingdon UK), and were compared to 12 non- allergic and non-asthmatic controls. For IL-33, mean levels were 6.85 pg/mL [0-37.7, $P = .041$] and 9 pg/mL [0-53, $P = .22$] with the High Sensitivity® method and Quantikine ® kit respectively, compared to 0 pg/mL for the healthy controls. For sST2 mean levels were 9 pg/mL [0-53], compared to 10 pg/mL [0-202] for the healthy controls ($P = .243$). There was no difference between mean levels of either IL-33 or sST2 for in and out of the pollen season measurements (IL-33HS $P = .917$; IL-33Q $P = .703$; sST2Q $P = .597$).

Conclusions: This study shows that IL-33 is higher, and best detectable by the Luminex High Sensitivity kit in human supernatants of sputa of patients with seasonal allergic rhinitis, compared to controls. The presence of this 'alarmin' in the lower airways of allergic patients without asthma, could indicate a latent epithelial activation, supporting the 'one airway, one disease' concept. The similar levels of sST2 in both populations despite high IL-33 levels in allergic rhinitis, suggest a defect in sST2 regulatory mechanism.

Data also disclosed a perennial presence of IL-33 in lower airways of patients with seasonal allergic rhinitis, suggesting that epithelial activation is a permanent feature of atopy.

1226 | Evaluation of the seasonal and immunotherapy-related alterations in nasal epithelial transcriptome in subjects with birch pollen allergic rhinitis

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Introduction: Birch pollen allergic rhinitis (AR) is common in Europe. We and other groups have previously shown nasal epithelial alterations in transcriptome during airborne allergen exposure.

Objectives: This prospective controlled follow-up study aimed at evaluating the seasonal and immunotherapy-related alterations in nasal epithelial transcriptome in subjects with or without birch pollen AR.

Results: We performed RNA sequencing of the transcriptome of 44 nasal epithelial samples of 11 adult nonsmoking subjects with/without AR. The sampling was performed 4 times in each subject in 2011-12. Half of the AR patients started subcutaneous birch pollen immunotherapy during the second year. AR was diagnosed based on a typical history, skin prick test, and allergen specific IgE antibodies. We have found a total number of 19808 protein coding genes, amongst them 6633 were up-regulated and 5127 were down regulated. Moreover, immunity related pathways were identified in differentially expressed genes. We also observed variations in biological processes of IL-2 and cytokines production, regulation of lymphocyte and leukocyte differentiation. The patients showed a down regulation of pathways during immunotherapy. The down regulated pathways include adhesion and diaphysis of granulocytes, Monocytes and cell surface molecules and B lymphocytes cell surface.

Conclusions: Compared to controls, natural birch pollen exposure and immunotherapy seems to alter regulation of immunity related functions and pathways. We will further analyze this cohort to find genome-based key-factors and pathways associating with birch pollen AR and the effects of immunotherapy, in order to find novel molecules with prognostic or therapeutic potential. More research with larger number of samples from different populations is needed.

1227 | Polymorphisms in complement lectin pathway serine proteases genes are associated with ischemic stroke

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Introduction: Complement lectin pathway plays a crucial role in the pathogenesis of ischemic stroke (IS). Mannan-binding lectin-associated serine proteases (MASP)-1 and MASP-2 play an initial role in

the activation of complement lectin pathway. Thus, MASP-2 autoactivates and cleaves complement C4 and C2 components to make a C3 convertase, C4b2a, while MASP-1 aids MASP-2 convertase generation by auxiliary C2 cleavage.

Objectives: The aim of current study was to clarify the role of complement lectin pathway Mannan-binding lectin-associated serine proteases, MASP-1 and MASP-2 in ischemic stroke by investigating the potential association of the single nucleotide polymorphisms in their genes (rs3203210, rs28945070, rs28945073 in *MASP1* gene and rs2273343, rs12711521, rs147270785 in *MASP2* gene) with IS

Results: The genotyping of the 200 ischemic stroke patients and 250 healthy subjects with the method of polymerase chain reaction with sequence-specific primers demonstrated that the rs3203210 polymorphism in *MASP1* gene and the rs147270785 polymorphism in *MASP2* gene are associated with ischemic stroke.

Conclusions: Based upon the data obtained it has been concluded that the minor alleles of these polymorphisms can be considered as risk factors for ischemic stroke at least in Caucasians.

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Table 1. *IL-2* and *IFN-γ* allele and genotype polymorphisms in Iranian patients with CHF and controls

Cytokine	Position	Alleles/ Genotypes	Controls (n = 139) N (%)	Patients (n = 56) N (%)	Odds Ratio (95% CI)	P-value
IL-2	-330	G	110 (39.6)	49 (43.7)	1.19 (0.76-1.85)	.495
		T	168 (60.4)	63 (56.3)		
		GG	8 (5.8)	10 (17.9)	3.56 (1.32-9.57)	.013
		GT	94 (67.6)	29 (51.8)	0.51 (0.27-0.97)	.049
		TT	37 (26.6)	17 (30.3)	1.2 (0.61-2.38)	.600
	+166	G	219 (78.8)	80 (71.4)	0.67 (0.41-1.11)	.145
		T	59 (21.2)	32 (28.6)		
		GG	82 (59)	29 (51.8)	0.75 (0.4-1.39)	.425
		GT	55 (39.6)	22 (39.3)	0.99 (0.52-1.86)	1
		TT	2 (1.4)	5 (9)	6.72 (1.26-35.71)	.022
			N = 138	N = 51		
		A	140 (50.7)	49 (48)	0.89 (0.57-1.41)	.728
		T	136 (49.3)	53 (52)		
IFN-γ	+874	AA	43 (31.2)	12 (23.5)	0.68 (0.32-1.43)	.369
		AT	54 (39.1)	25 (49)	1.5 (0.78-2.86)	.247
		TT	41 (29.7)	14 (27.5)	0.89 (0.44-1.83)	.858

Table 2 *IL-2* haplotype polymorphism in Iranian patients with CHF and controls

Cytokine	Position	Haplotype	Controls (n = 138) N (%)	Patients (n = 56) N (%)	Odds Ratio (95% CI)	P-value
IL-2	-330, +166	GG	107 (38.8)	46 (41.1)	1.1 (0.7-1.72)	.731
		TG	112 (40.6)	34 (30.3)	0.64 (0.4-1.02)	065
		TT	56 (20.3)	29 (25.9)	1.37 (0.82-2.3)	.226
		GT	1 (0.3)	3 (2.7)	7.57 (0.78-73.56)	.074

1229 | Interleukin-2 and interferon-gamma single nucleotide polymorphisms in Iranian patients with chronic heart failure

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Introduction: Cytokines, including interleukin-2 (IL-2) and interferon-gamma (IFN-γ), seem to play role in the pathogenesis of chronic heart failure (CHF). The aim of this study was to investigate the associations of *IL-2* and *IFN-γ* single nucleotide polymorphisms (SNPs) with susceptibility to CHF in Iranian population.

Objectives: Fifty six Iranian patients with CHF were enrolled in this study as the case group and compared with 139 healthy subjects, using polymerase chain reaction with sequence-specific primers method, so as to determine the frequency of alleles, genotypes and haplotypes of *IFN-γ* (A/T at +874) and *IL-2* (G/T at −330 and +166) SNPs.

Results: The GG genotype at *IL-2* −330 in patients with chronic heart failure was significantly overrepresented in comparison with the control group (P = .013). Such a positive genotypic association was also observed for *IL-2* +166/TT (P = .022). Meanwhile, the GT genotype frequency at *IL-2* −330/GT in the patient group was significantly lower than in healthy controls (P = .049).

Conclusions: Certain genotypes in *IL-2* gene were overrepresented in patients with CHF, which could render individuals more susceptible to this disease.

1230 | Identification of two novel CFTR mutations in Iranian patients with cystic fibrosis

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Introduction: Cystic Fibrosis (CF; MIM # 219700), is the most common genetic disorder with an autosomal recessive inheritance among Caucasians. This disease is caused due to mutations occurred in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The *CFTR* gene is accounts for a 190 kb region on the long arm of chromosome 7 and has 27 exons and codes for a glycosylated, 1480-amino acid protein. The CFTR protein functions as a chloride channel in epithelial cells and regulates salt and water current. To date, approximately 1970 mutations have been reported in the *CFTR* gene that are listed in the CFTR mutation database (http://www.genet.sickkids.on.ca/cftr).

Objectives: Aim of this study was to find the possible disease causing mutations in CFTR gene in order to help future life in patient families by genetic counseling, carrier detection and prenatal diagnosis.

A total of 25 Iranian CF patients were enrolled in this study. These patients were from different cities of Iran who were referred into immunology, asthma and allergy research institute (IAARI) and special medical center (SMC). Their CF disease was confirmed by sweat chloride testing (>60 mEq/L). Genomic DNA was extracted from whole blood samples. Mutation analysis of these patients was performed for the *CFTR* gene using specific primers for exons and exon/intron boundaries followed by direct sequencing.

Results: We found 18 different mutations in present investigation. Of these, sixteen mutations are previously reported and two are novel. DeltaF508 was the most common mutation observed in Iranian CF patients included in the study (in seven patients either homozygous or heterozygous). The second abundant mutation, N1303K, were seen in two patients. However, many mutations were present only in one patient. Also one novel nonsense and one delins mutation were found.

Conclusions: As other regions, in Iran deltaF508 is the most common mutation but with less frequency compared to European countries. Other mutations are distributed with the same frequency and are not prevalent.

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1233 | Is the skin prick test sufficient to diagnose vespid venom allergy?

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Introduction: In primary and secondary care, the nature of sensitization to insect venom is mainly assessed by the use of skin prick tests (SPT) for cost and time saving reasons. In contrast to intradermal testing (IDT) several dilutions of insect venom are commercially available for SPTs and can be used without time consuming preparations. The aim of this study is to assess whether the SPT offers an acceptable sensitivity-specificity-profile compared to the generally more sensitive and sophisticated IDT.

Objectives: Until now 51 vespid venom allergic patients from our allergy outpatient clinic were prospectively included. Results of prick tests (dilutions: 10, 100, 300 μg/mL) and intradermal tests (dilutions: 0.01, 0.1, 1.0 μg/mL) with vespid venom were evaluated for the assessment of sensitivity. Results were compared with the outcome of specific IgE testing. In the further course of this study skin test data of another 88 subjects will be collected. Additionally, we plan to include 101 controls not having had previous systemic sting reactions or large local reactions and not being sensitized to insect venom for the assessment of specificity. Results will be compared with data of a previous study, where skin tests were done in 54 subjects with proven clinically irrelevant sensitization to vespid venom.

Results: In the SPT 4 of 51 allergic subjects (8%) were positive at the concentration of 10 μg/mL vespid venom extract, 33/51 (65%) at 100 μg/mL and 45/51 (88%) at 300 μg/mL. 6 of 51 (12%) vespid venom allergic subjects were tested negative in the SPT. However, adding serological testing for sIgE, all those SPT negative subjects were positive for sIgE to vespid venom extract. In the IDT positive results were obtained as follows: 35/51 (67%) at 0.01 μg/mL, 50/51 at 0.1 μg/mL (98%) and 51/51 (100%) at 1 μg/mL. No patient was tested negative with the IDT. In subjects with clinically irrelevant sensitization the IDT was positive in 86% of cases. In contrast, only 38% were positive in SPT.

Conclusions: The IDT proved to be the far more sensitive skin test for the diagnosis of vespid venom allergy. However, when combining the routinely performed serological testing for specific IgE with the SPT, no vespid allergic subject was missed. Considering the broader applicability and also cost-saving properties of the SPT, its use can be recommended for a basic diagnostic workup. In the case of inconclusive results, additional intradermal testing should be performed.

1234 | Inconsistency of the common diagnostic tests to identify the venom to be used for immunotherapy in patients with allergic reactions to vespa crabro

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Introduction: Allergy to the European hornet *Vespa crabro* is less investigated than allergy to *Vespula spp*. and *Polistes spp*, particularly concerning the venom to be used for immunotherapy. The available scant literature suggests, due to the extensive cross-reactivity between *V. crabro* and *Vespula*, that also the latter may be used. We evaluated the data from skin tests and in vitro IgE tests in a group of patients with a clear history of *V. crabro* as the culprit insect.

Objectives: We included in the evaluation data from medical records of 23 patients who were able to identify *Vespa crabro* as the cause of the reaction. Skin tests were performed by an initial prick test followed by intradermal tests (IDT) at concentration of 0.1 mcg/mL and 1 mcg/mL. Specific IgE (sIgE) to both *V. crabro* and *Vespula* spp. were measured by specific IgE Assay. All patients gave their consent to the treatment of data.

Results: sIgE to *Vespula spp*. were detected in all patients and sIgE to *V. crabro* in 19 of 23 patients (82.6%). In 18 of patients with sIgE to both venoms, the values were higher for *Vespula spp* than for *V. crabro*. Skin test were positive to *Vespula spp*. in all patients and were positive to *V. crabro* in 22 of 23 patients (95.6%). In patients with double positivity, 4 patients showed a lower threshold concentration to IDT with *V. crabro* and 4 to IDT with *Vespula spp*.

Conclusions: The common diagnostic methods give inconclusive results in guiding the choice of the venom to be used for immunotherapy in patients who recognize *V. crabro* as the culprit insect. Currently, immunotherapy with *V. crabro* venom should only be indicated in patients with monosensitization or certainty of recognition of the culprit insect. Studies of CAP-inhibition and molecular-based allergy diagnostics are warranted to provide reliable data indicating the correct choice in patients with reaction to *V. crabro* and positive tests also to *Vespula spp*.

1235 | History of large local reaction to hymenoptera stings: outcome of re-stings (preliminary data)

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Introduction: Hymenoptera stings can cause reactions with either toxic or allergic mechanisms and these reactions may largely vary in severity, from local reaction to systemic anaphylaxis. Among the Hymenoptera-induced reactions, the so-called large local reactions (LLR) have been classified as a special aspect for decades, mainly in relation with their possible predictive value for subsequent systemic reactions. The definition of LLR is essentially clinical and empiric. A LLR is defined as a reaction of oedema, erythema and pruritus, with a diameter greater than 10 cm and which peaks at 24–48 hours, and then subsides. Despite the general interest, the literature concerning LLR is overall poor and fragmentary. It is estimated that the risk of developing a systemic reaction after a LLR is relatively low, ranging from 5 to 15%. In a prospective study among 53 patients, only 31 of them (58.3%) were restung by the same type of insect, with an overall number of 59 stings, presenting only LLRs and no SR.

Objectives: The aim of this study is to evaluate the outcome of re-stings in patients with a LLR over a period of five years (2012-2017); in these patients specific immunotherapy with Hymenoptera venom was not necessary. according to current guidelines.

Results: 430 patients were be enrolled in the study up to now. Skin testing (intradermal tests) and specific serum with bee venom, Vespula, vespa crabro (if available) and Polistes spp or Polistes dominulus (if the latter is available or relevant in the geographic area), total IgE and tryptase assay were carried out; sera were collected for future studies. 70 out of 430 patients were re stung. 20 (28.5%) patients experienced a systemic reaction, 26 patients experienced a LLR and 24 patients were negative.

Conclusions: By now our preliminary data show that the risk of developing a systemic reaction after a LLR is superior to the previous data from literature, but these results have to be confirmed by the end of our study

1236 | Is the severity of anaphylactic reaction influenced by the site of hymenoptera sting?

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Introduction: Anaphylaxis is a serious systemic allergic reaction. It is thought to have affected between 1% and 2% of the general population. The potential for developing anaphylaxis after the next sting is quite serious because almost 50% of previously stung patients presented such a reaction At present there is no report in European country on the relationship between site of the sting and the severity of anaphylaxis after hymenoptera venom sting. The most common reasons of anaphylaxis are foods, medications and insect Sting by an hymenoptera insect of a sensitized subject is life-threatening issue.

Objectives: The subject of the retrospective study was a total of 429 patients medical records among the 2674 patients allergic to hymenoptera venom treated in the years 1992-2016. Medical care given to the patients with systemic reaction after hymenoptera insect sting in Silesia, south region of Poland was investigated. Patients were classified according to a kind of insect and site of a sting (head and neck, back and torso, upper limb, lower limb). All included patients completed questionnaire and have completed medical records. All the reactions meeting the criteria for anaphylaxis presented by World Allergy Organization

Results: Among the 429 patients (231 women (54.6%) and 198 men, mean age 40.0 $\pm$ 6.8) the majority have experienced a severe anaphylactic reaction (66%). Anaphylaxis was caused mostly by vespidae—235, honey bee-194.

Most severe anaphylaxis have developed after the sting in head and neck region (59% honey bee and 53% wasp), sting in upper limbs result in less severe symptoms (44% HB, 36% wasp).

sting in upper limbs result in less severe symptoms.

Epinephrine was used only in 13% of anaphylactic patients, but during the last five years (2010-15) epinephrine was administered in 36% patients (statistically significant change $P < .05$). 44 patients were hospitalized (12.6%),

Conclusions: Site of Hymenoptera sting influences the progress and intensity of anaphylactic reactions. Particularly dangerous are stings of head and neck, whereas stings of lower limbs present less severe symptoms.

The use of epinephrine in observed therapeutic interventions need to be improved.

1237 | The severity of hymenoptera sting reactions and the levels of recombinant sFsE and the bat response

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Introduction: No study has assessed if quantitative levels of different immunological factors can discriminate between patients with systemic reactions (SRs) and large local reactions (LLRs) or determine the severity of SRs in Hymenoptera venom allergy.

Objectives: To assess if immunologic factors (levels of sIgE and sIgG antibodies against bee and wasp venoms, sIgE against rApi m1 and rVes v5, the basal tryptase and the BAT with 4 bee and wasp venom concentrations, evaluated as BAT-AUC) differentiate between different reaction groups.

Results: On 107 monosensitized Hymenoptera allergic patients we assessed the above factors. The patients with Mueller I, II, III, and IV reaction severities had significantly ($P < .05$) higher values of recombinant sIgEs than patients with LLRs. However, there were no differences between different Mueller groups. Similarly, the BAT-AUC was significantly higher in patients with Mueller II, III and IV reaction severities when compared to those of the patients with LLRs. Again, the values of the BAT-AUC did not differ significantly between different Mueller groups. The levels of venom sIgEs were higher only in the Mueller II group when compared to the patients with LLRs; the sIgG levels were substantially higher in the Mueller II and III groups when compared to the Mueller I group and to patients with LLRs. The basal tryptase levels were higher in the Mueller IV group when compared to all other groups. There were no other statistically significant differences. Only the BAT-AUC and basal tryptase levels were significantly correlated ($r = .3$; $P = .002$ and $r = .17$; $P = .04$) with the numerically transformed (LLR = 1, Mueller I = 2 . . .) reaction severity groups. When all SR patients across all Mueller reaction grades were combined into a single group, just the recombinant sIgEs and BAT-AUC varied significantly between this group and the patients with LLRs. The significant difference of the two factors was retained, when all the above immunological factors and demographic variables (age, sex) were used as predictors in a penalized log regression analysis (LLR vs. SR).

Conclusions: In Hymenoptera venom allergy, the severity of SRs did not vary significantly with the levels of recombinant sIgEs or the BAT response. However, the BAT response showed a significant trend of higher values with higher numerically transformed reaction severity groups. Both, the BAT response and the recombinant sIgEs were independent statistically significant predictors of SR (SR vs. LLR).

1238 | Severity of sting-induced anaphylaxis in relation to the culprit insect sting: is European hornet (vespa crabro) a risk factor for life-threatening allergic reaction?

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Introduction: Life-threatening reaction in hymenoptera venom allergy has been associated with a number of risk factors including elderly, elevated baseline serum tryptase, concomitant cardiovascular diseases and severity of previous reaction. Also an association between Vespa crabro sting and severe systemic reaction had been detected in the past, however more recent data did not confirm this correlation. The aim of the study was to evaluate the relationship between the severity of sting-induced anaphylaxis and the culprit insect sting.

Objectives: We retrospectively collected data from a total of 490 patients with a history of systemic allergic reaction after hymenoptera sting. On the basis of unequivocal identification of the culprit insect in 106 patients (23%) the stinging insect was Vespa crabro, in 272 (58%) other Vespids (Vespula spp or Polistes dominulus) and in 91 (19%) Apis mellifera.

Results: In patients stung by hornet the rate of life-threatening reactions (IV grade according to the Mueller classification) reached 61.3% and it was significantly higher compare to the prevalence found in honey bee and yellow jacket or paper wasp allergic patients (respectively 43.9% and 44.4%).

Conclusions: Our study data provide evidence, in a large cohort of patients, that Vespa crabro sting represents a risk factor for more severe reaction in patients with hymenoptera venom allergy.

1239 | Prevalence of mastocytosis in hymenoptera venom allergic patients from ciudad real

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Introduction: In the last years systemic mastocytosis (SM) have shown to be closely related to Hymenoptera venom allergy (HVA). Allergists must be aware of this problem as they may be the first specialist to suspect this pathology and begin the appropriate investigations for the final diagnosis.

Objectives: In this communication we present our experience win SM and HVA in the last 8 years.

We performed screening of SM with REMA score in all patients with HVA, patients with score ≥2 where evaluated for bone marrow biopsy (BMB).

We reviewed the clinical data of these patients.

Results: We have found 17 cases of REMA score ≥2, in 182 patients diagnosed of HVA since 2008 (prevalence 9.3%). SM was confirmed by BMB in 10 patients (more results are pending).

The mean age was 51.47 years and 94% were males.

The responsible insect was *Polistes* in 12 patients (70.5%), and *Vespula+Polistes* in 3 patients.

Tryptase mean level was 15.45 mcg/L with normal values (<11.4 mcg/L) in 53% of the patients.

Interestingly, 3 patients who had finished venom immunotherapy years ago, relapsed with grade IV anaphylaxis after field stings.

7 patient tolerated field stings while receiving immunotherapy.

Conclusions: The prevalence of REMA score ≥2 in the patients diagnosed of HVA was 9.3% in our health area.

We would like to emphasize the high rate of normal tryptase in our patients, and the risk of relapse after 5 years of VIT that support the recommendation of lifelong immunotherapy in this group of patients.[querry: 1240 missing]

1241 | Protein identification in apis mellifera crude venom by a shotgun proteomics approach

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Introduction: *Apis mellifera* venom, thanks to the available proteomic and genomic data, is the best characterized hymenoptera venom [1, 2]. The most important honeybee venom (HBV) allergens are phospholipase A_2 (Api m 1), hyaluronidase (Api m 2) and the peptide melittin (Api m 4). Recently, additional allergens of lower abundance have been characterized, such as acid phosphatase (Api m 3), dipeptidyl peptidase IV (Api m 5), protease inhibitor (Api m 6), major royal jelly proteins 8 and 9 (Api m 11.0101 and Api m 11.0201), icarapin (Api m 10) and vitellogenin (Api m 12).

Patients with bee venom allergy display distinct sensitization profiles to a panel of HBV allergens, some of which have been reported to be absent or underrepresented in therapeutic HBV preparations [3]. The shortage of these allergens often leads to the failure of Venom Immunotherapy (VIT).

Objectives: The aim of this work is to characterize allergens in two different *Apis mellifera* extracts: capillary-extracted venom and electro-stimulated venom, using Peptide Mass Fingerprint by Shotgun proteomics technique.

Results: After denaturation with urea/thiourea mix, reduction with dithiothreitol and derivatization with iodoacetamide both the venom extracts are digested with trypsin. The digested samples are then analyzed by HPLC-ESI-MS/MS. The resulting spectra are processed by Mass Spectrometer software which uses different specific algorithms for database matching. This technique allows to unambiguously identify proteins present in the sample.

Both *Apis mellifera* venom contain the major allergens Api m 1, Api m 2 and Api m 4. Moreover in capillary-extracted venom it's possible to identify: Api m 5, Api m 6, Api m 11.0101 and Api m 11.0201, Api m 10 and Api m 12. Api m 10 is also identified in electro-stimulated venom.

Conclusions: These results show that the two *Apis mellifera* venom extracts contain all the relevant allergens for VIT. This confirm the suitability of both the crude extracts to be used as raw material for diagnostic and therapeutic preparations.

1242 | Benefits of venom immunotherapy: how soon can they be expected

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Introduction: Allergic reactions to insect stings are medical emergencies that could be prevented by venom immunotherapy (VIT).

Objectives: We aimed to show the rapidity with which patients experience the benefits of VIT and estimate the number of emergency treatments that are prevented.

We reviewed the medical files of patients who started VIT between 2010 and 2014. We calculated the costs of treatment (according to Slovenian health insurance prices) of the sting reactions, the costs of immunotherapy and estimated the costs of the prevented allergic reactions.

Results: In a cohort of 587 patients (40.9% female, age 47.2 ± 14.4 years) the cost of treatment of the index sting reaction was 180.4 ± 166.8 E. 358 (61.0%) were treated with wasp venom, 229 with honey bee venom. During VIT 303 patients (51.8%) experienced 860 field stings. In 89.5% of patients stings were well tolerated. 8 (7 wasp allergic) patients reported subjective symptoms only, 15 (8 wasp) had Mueller grade I, 8 (4 wasp) Mueller II and 1 (wasp) Mueller III reaction. 113 (19.2%) of VIT treated patients were stung already during the first year of VIT (70 (61.9%) wasp). The expenditure for 5 years of VIT was 2886 E per patient, which corresponded to an average of 16.0 emergency treatments for systemic reactions.

Conclusions: Wasp and honey-bee treated patients were filed stung during VIT with equal frequency. The probability of treatment failure was equal in wasp and honey bee allergic patients. Emergency situations were prevented in a substantial number of venom allergic patients and a beneficial effect was observed already during the first year of VIT.

1243 | The frequency of venom re-stings in field and protectiveness of venom immunotherapy: real life results

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Introduction: Venom immunotherapy is the most effective form of immunotherapy. Prophylaxis from venom anaphylaxis begin in earlier phases of venom immunotherapy (VIT).

Objectives: In this study, we aim to determine the frequency of venom re-stings in field and protectiveness of VIT.

Results: Between 2010 and 2015 years, 97 patient had VIT with maintenance dosage of 100 mcg purified venom vaccines. We contacted to 86 of them. 37 were female and 60 were male. Mean age was 43 (20-72). 41 patients were allergic to apis mellifera, 39 to vespula, 1 to polistes species, 5 to both of apis mellifera and vespula. 55 of 86 patients hadn't any re-sting. 31 of 86 patients had at least 1 re-sting. 22 of them were in maintenance phases of therapy and 9 of them were in building phases when they were restung by their allergic bee type. 4 of 31 (13%) had systemic reactions. Those of 2 were 4th degree and 2 were 3th degree anaphylactic reactions. 3 of 4 were in building phases and 1 was in maintenance phase. Basal tryptase levels were normal in all of 4 patients. The frequency of allergic reactions was 1/22 (4%) in maintenance phase, protectiveness of VIT in maintenance phase was 96%; the frequency of allergic reactions in building phase was 3/9 (30%),and protectiveness in building phase was 70%.

Conclusions: According to our results, protectiveness of VIT is 96% in maintenance and 70% in building phases of VIT. In literature, if these patients don't be treated by immunotherapy, the risk of systemic reaction after re-sting is up to 85%-90%. If venom allergic patients had immunotherapy, allergic reaction risk is decreasing to 5% and lower. Our results show that VIT is protective from the beginning of therapy, especially from early shots of venom vaccines. In our study, 1 bee keeper patient was restung in the second week of VIT,and he hadn't any allergic reaction. In our study, patients with apis mellifera re-sting were reactive in building phases and the patient with vespula re-sting is reactive in maintenance phase. According to our data, this patient was having vespula VIT for 3 years and had 4th degree systemic reaction in maintenance. This result is in contrast with literature, because other studies showed VIT with apis mellifera is less protective than vespula in maintenance period and duration of effectiveness continues less than vespula VIT.

1244 | Allergy to vespa crabro venom: Venom Immunotherapy with vespula vs vespa crabro

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Introduction: Among the *Vespa* genus, it is the *Vespa crabro* (*VC*—European hornet) that predominates in Europe. A recent study conducted in the Mediterranean area showed that the relative risk of developing severe systemic reactions is three times higher from a hornet sting compared to the bee or wasp.

In the case of sensitization to *VC* venom, the European guidelines consider venom immunotherapy (VIT) using only *Vespula* (*VE*) venom sufficient for obtaining adequate protection against an allergic reaction.

However, antigen 5 immunoblotting studies showed that there is a true allergic sensitization to *VC* venom, so this venom should be used in VIT.

For the last few years, *VC* venom has been available for use in diagnosis and in VIT (Anallergo Florence, Italy).

Objectives: In patients stung by *VC* we evaluated the efficacy of VIT with *VC* venom vs VIT with *VE* venom.

Results: Using a retrospective observational design, we collected 1202 records from 303 patients that reported systemic reactions from *VC* stings. The patients were recruited at an outpatient clinic from four Italian Allergic departments (Como, Faenza, Firenze and Rimini). 83 patients were treated with *VE* and 220 with *VC* venom. A subset of 136 patients (45.2%) were re-stung by *VC* during 5 years of VIT (66 with *VC* venom and 70 with VE venom).

Table 1 Allergic reaction results of patients who had VIT, after they were re-stung in field

Venom re-sting (+):31 (36%)				Venom re-sting (-):55 (64%)	Total number of patients: 86
Allergic reactions (-):27 (87%)		Allergic reactions(+):4 (13%)			
Building phase:6 (22%)	Maintenance phase:21 (78%)	Building phase:3 (75%)	Maintenance phase:1 (25%)		

In the group treated with *VC*, 66 patients were re-stung by *VC*: 50 re-stings were negative, 12 were large local reactions (LLR), but 4 were systemic reactions (SR). All of SRs were Muller grade 1. Efficacy of VIT with *VC* was 93.9%.

In the group treated with *VE*, 70 patients were re-stung by *VC*: 51 re-stings were negative, 10 were LLR, but 9 were SR: 5 reactions of Muller 1 grade, 3 reactions of Muller 3 grade and 1 reaction of Muller 4 grade. Efficacy of VIT with *VE* was 87.1.

Conclusions: In patients stung by *VC*, VIT was efficacy either with *VE* venom or with *VC* venom and the results of re-stings confirmed the data reported in the literature. But the fact that field sting SRs of Muller 3 grade and Muller 4 grade were detected only in patients treated with *VE* venom, seems to support the hypothesis that in patients with VC sting systemic reactions, a VIT with *VC* venom might be more adequate.

1245 | Comparison of bee and wasp venom allergic patients treated by venom immunotherapy

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Introduction: Risk factors may play a role in various aspects of Hymenoptera venom allergy, such as the severity of sting reaction and efficacy of venom immunotherapy. Most often discussed factors are patient's age, gender, insect type, elevated baseline serum tryptase, concomitant medication and preexisting cardiovascular and respiratory diseases. The aim of our study was to characterize in detail our bee and wasp venom allergic patients, compare detected characteristic features and thus indentify risk factors in both groups.

Objectives: 80 bee and 65 wasp venom allergic patients treated by venom immunotherapy were included in our study. Every patient filled in a questionnaire and was individually interviewed by a physician. All data—patient's age, gender, grade of reaction (I.-IV.), comorbidities, concomitant medication, character of previous sting reaction, localization of sting, baseline serum tryptase, field re-sting reaction—were collected and statistically processed separately in bee and wasp venom allergic group.

Results: More men (65% vs 46%), more children (21.25% vs 7.7%), lower average age (33.7 vs 44.7 years) and higher number of systemic sting reactions in previous clinical history (23.7% vs 9.2%) were seen in bee venom in contrast to wasp venom allergic patients. Wasp venom allergic patients significantly more frequently reacted by the IV. Mueller's grade (36.9% vs 17.5%), more often suffered from arterial hypertension (24.6% vs 11.25%) and more often were treated by beta-blockers (18.5% vs 5%) than bee venom allergic patients. Significantly more bee venom allergic patients reacted on field re-sting during treatment (16.21% vs 3.3%). We didn't find significant differences in sting localization, in other comorbidities, in other concomitant medication, in previous large local sting reactions, in tryptase levels and in re-sting reactions after treatment between study groups.

Conclusions: Wasp venom allergic patients are older, suffer more often from arterial hypertension, take more often beta-blockers and suffer more often from the most serious sting anaphylaxis in comparison with bee venom allergic patients. Our finding suggests that wasp venom immunotherapy may better prevent anaphylaxis during treatment than bee venom immunotherapy.

1246 | Questionable benefit of the commercially available panel of bee venom components in the diagnosis of bee venom allergy

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Introduction: For many years, only the major allergen rApi-m-1 has been available on the most widely used test platform for routine diagnosis. However, low sensitivity for rApi m 1, ranging from 57%-82%, has been reported. Therefore, it is insufficient to support, or even exclude, a definitive diagnosis of bee venom allergy. Now, there are 5 recombinant allergens available for specific IgE measurement and we aimed to detect sensitivity and specificity of rApi m 1, 2, 3, 5 and 10 in bee venom allergic patients.

Objectives: We included 134 patients solely allergic to bee venom as well as 55 patients allergic to bee and vespid venom to investigate possible differences in the sensitization profile between monosensitization and clinically relevant double sensitization. All patients had a history of systemic sting reactions. Sixty-six patients with a negative history of Hymenoptera venom allergy served as controls. Furthermore, we evaluated if the alternative determination of rApi-m-1 and 2 on an alternative system increased overall sensitivity.

Results: In monosensitized patients, analysis of the whole panel of bee venom allergens still resulted in a lower sensitivity than the combination of rApi-m-1 and 2 on the Immulite (71.6 vs 85.8%).

The results for double-sensitized patients differed substantially: overall sensitivity of the whole panel was markedly higher compared to monosensitized patients (92.7 vs 71.6%). Sensitization rate of rApi-m-5 was more than doubled in double-sensitized patients, while there was no difference for rApi-m-2. Additionally, the sensitization rate to rApi m 1 was 20% higher in double-sensitized patients.

Conclusions: Sensitivity of the commercially available panel of bee venom allergens was still too low, particularly in monosensitized patients. Interestingly, the sensitization rate of rApi m 1 differed markedly between mono- and double-sensitized patients which might explain the differences in reported sensitivities. However, the underlying reason is unclear. Genuine sensitization to rApi m 2 appeared to be irrelevant in terms of cross-reactivity, whereas rApi m 5 was obviously highly cross-reactive to rVes v 3. Since important cross-reactive allergens are still not available, the usefulness of the component resolved diagnosis in the present form is questionable.

1247 | Maintenance specific immunotherapy for hymenoptera venom allergy: what to do if the allergenic extract is suddenly no longer available?

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Introduction: Hymenoptera venom immunotherapy (VIT) is an highly effective treatment for Hymenoptera venom allergy (HVA), that improves the quality of life of affected individuals (1,2). Several allergenic extracts are currently available, with comparable efficacy (1). In early 2016 a shortage of certain non-purified aqueous preparations used for VIT occurred, and in literature there is no clear indication on what to do if the allergenic extract is no longer available (3). Current clinical practice discourages the abrupt switch to a new allergenic extract without an induction phase for safety reasons. According to expert opinion, an ultra-rush induction scheme with a new extract can be performed safely in selected cases, however data on VIT switch protocols are lacking.

Objectives: Patients on maintenance VIT with out-of-stock extracts were clinically assessed for potential discontinuation of VIT. Patients who could not discontinue VIT were switched to retard preparations made by other manufacturers according to specific HVA. Every selected patient signed an informed consent; medical examination and IV access were performed before the administration of the new extract.

The following VIT switch protocol was adopted: patients received 1 mL of extract containing 100 mcg of venom, divided into 3 aliquots (0.35 + 0.35 + 0.30 mL), administered on a 60-minute interval. After a 2-hour follow-up for immediate adverse reaction monitoring, patients received a schedule for subsequent VIT administrations and were instructed to report any potential delayed adverse reactions.

Results: A group of 54 patients (14 females) that experienced a grade III-IV Müller reaction (mean age 59.2 ± 13.6 years) switched to a new allergenic extract. They received a 100 mcg maintenance dose of venom on a mean 9-week interval (range 4-12 wks). Mean duration of VIT maintenance was 145.6 ± 12.1 months. During the VIT switch protocol no immediate or delayed reactions were reported. Successive maintenance phase administrations were uneventful (mean follow-up 24.6 ± 14.7 wks).

Conclusions: The VIT switch protocol was successfully applied, with no adverse reactions reported and no need for an induction phase using lower doses of venom. The use of retard preparations was preferred according to clinical experience (4.5). The VIT switch protocol has proven to be safe, however it has to be performed in a proper environment by an experienced staff.

1248 | Omalizumab in prevention of anaphylaxis due to bee venom immunotherapy

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Introduction: Specific immunotherapy is an established therapeutic option in patients with hymenoptera venom allergy, offering long-term protection from further generalized reactions. Nevertheless, venom immunotherapy (VIT) may be associated with severe systemic reactions which compromise treatment tolerance. In the last years, some case reports appear to demonstrate that pre-medication with anti-IgE antibody, Omalizumab, may be useful to prevent systemic adverse reactions related to VIT. However, this approach is still off label and not standardized, leading to different treatment schedules.

Objectives: We report 3 successful cases of tolerance to bee VIT after initiation of pre and concurrent treatment with Omalizumab. Omalizumab doses were calculated based on weight and total IgE level.

Results: All patients had normal basal tryptase levels and severe systemic reaction during VIT administrations using an antihistamine pre-treatment.

The first case was a 43-year-old female, beekeeper, previously healthy, with a history of a grade II reaction according to Mueller's classification; the second one was a 16-year-old male, son of the first patient, also healthy, who experienced a grade IV reaction according to the same classification; the third case was a 33-year-old male, beekeeper, suffering from hypertension treated with Irbesartan 150 mg daily, with a history of a grade III reaction.

In the first two patients, subcutaneous Omalizumab 450 mg was initiated 1 week before VIT in the first administration and 1 hour before in the subsequent ones, every 4 weeks during 6 months. VIT maintenance dose of 100 μg was tolerated without any severe systemic reactions occurred. However, it was never possible to increase the administration interval for more than 4 weeks.

In the third patient, subcutaneous Omalizumab 300 mg was initiated and maintained every 4 weeks, 1 week before VIT administration,

which is still ongoing. VIT tolerance was also achieved, with no anaphylactic reactions documented so far. We also intend to maintain this protocol for 6 months.

Conclusions: These cases support that Omalizumab may prevent systemic adverse reactions during VIT administrations. However, more studies are needed to establish doses, frequency and duration of treatment.

1249 | Omalizumab in immunotherapy with hymenoptera venom

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Case Report: Introduction: In Europe the prevalence of systemic reactions with hymenoptera sting varies between 0.3% and 7.5%, being higher in beekeepers. Hymenoptera venom immunotherapy (VIT) provides protection in 80%-100% of the cases. Allergic reactions may occur with VIT especially during the initiation with ultra-rush, preventing its progression. Omalizumab can be used in combination with ITV, in order to reduce allergic reactions.

Clinical case: A 53-year-old man, beekeeper in his free time, goes to the emergency room with nasal obstruction, rhinorrhea, dyspnea and facial erythema beginning 10 minutes (min) after a bee sting on the right index finger. At the emergency room, 3 hours after the sting, he was hemodynamically stable, eupneic, without bronchospasm, with nasal obstruction and facial erythema. He was treated with systemic steroids, clemastine, and ranitidine, with improvement. The tryptase was 16.6 μg/L. Immunoallergology workup revealed bee venom specific IgE >100 kUA/L and positive intradermal skin test for bee venom extract at concentration of 0.01 μg/mL. Bee venom ultra-rush was started with pretreatment with clemastine and montelukast but it was interrupted by anaphylactic reaction 30 min after administration of 10 μg of bee venom. He was treat with adrenaline, methylprednisolone and bronchodilators, with improvement. He repeated new ultra-rush with pretreatment with montelukast and antihistamine for 15 days and had a new reaction 30 min after administration of 10 μg of venom: erythema on the face and neck, that regressed after corticosteroid and ranitidine ev. On the same day he repeated the administration of 10 μg, with reappearance of skin complaints and edema of the uvula on observation. He made hydrocortisone, ranitidine and aminocaproic acid ev, with improvement. A new ultra-rush was performed under omalizumab, maintaining antihistamine and daily montelukast. Initially, he did 2 administrations of omalizumab, 7 days and 1 hour before the ultra-rush, with onset of erythema of the face and nasal obstruction. He subsequently performed 4 doses of 300 mg omalizumab with a 15-day interval. On the 7th day he restarted ultra-rush with good tolerance.

Conclusions: Omalizumab has been used in association with IT in the control of allergic reactions with good results. The authors describe a clinical case in which the use of omalizumab successfully allowed the progression of ultra-rush with hymenoptera venom.

1250 | Omalizumab as adjuvant treatment during venom immunotherapy in mast cell disorders

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Case Report: Introduction: Patients with mast cell disorders (MCD) are more likely to present anaphylactic events regarding general population, especially after Hymenoptera stings. Venom immunotherapy (VIT) is indicated in patients in whom an IgE induced mechanism has been demonstrated. VIT has been demonstrated to be a safe and effective treatment, still higher rates of adverse reactions have also been reported. In cases of severe adverse reactions during immunotherapy, the use of omalizumab as an adjunct treatment has been occasionally reported.

Objectives: A 34-year-old man presented with malaise, dizziness and hypotension after the sting of 8 bees. Specific IgE to bee venom was detected (5.8 kU/L out of a total IgE of 73 kU/L) and baseline serum tryptase was 8.2 ng/mL. He started VIT up to a 100mcg maintenance dose every 4 weeks. Within minutes after the seventh dose the patient developed chest tightness, followed by oxygen desaturation and hypotension (60/30 mmHg). With a mast cell disorder (REMA score >2) under suspicion, VIT was temporarily interrupted; new analytic determinations were carried out, the patient started on daily anti-mediator therapy, and omalizumab was initiated previous to new VIT administration.

Results: Component resolved diagnosis (CRD) after the adverse reaction showed the following results: specific IgE to Api m1 0.82 kU/L, Api m2 16.8 kU/L, Api m4 0.00 kU/L and Api m10 0.9 kU/L. The patient began on 800 mg of sodium cromolyn daily, and 300 mg of omalizumab every 4 weeks were initiated two months before resuming VIT—extract containing Api m10, as the previous one-. No adverse reactions have occurred after 2 months of maintenance doses.

Conclusions: Although the mechanisms of action of omalizumab in MCD have not been clearly elucidated yet, it seems to be a valid option for those patients who do not initially tolerate VIT alone and are at higher risk for anaphylaxis. Besides, CRD should be mandatory

in patients with Hymenoptera venom anaphylaxis in order to identify their pattern of sensitization and try to predict adverse reactions.

1251 | Bee venom immunotherapy only tolerated with concurrent treatment with omalizumab

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Case Report: Hymenoptera venom immunotherapy is the established treatment for all individuals who experience anaphylaxis due to hymenoptera venom, despite adverse reactions occur during treatment.

A 50-year-old woman, wife of a beekeeper, presented two severe reactions after bee sting. Allergologic exploration revealed positive intradermal skin test for honey bee venom and increased honey bee-specific IgE level (>100 kUa/L); baseline serum tryptase levels were normal (6.94 μg/L). Bee venom immunotherapy (VIT) was started using a rush protocol, but it had to be stopped after a severe anaphylactic reaction. Then, an ultra-slow protocol with premedication (H1 antihistamines and oral prednisone) was decided to continue immunotherapy, due to the vital risk of being stinged again. It was well tolerated until a 40 mcg dose was reached, when she experienced repeated anaphylactic reactions. Due to this fact, omalizumab treatment was started at 300 mg every 2 weeks, maintaining drug premedication. Once maintenance dose was reached, drug pretreatment was retired, and after three more administrations of bee VIT, omalizumab could be retired as well. Then anaphylactic reactions started again, so bee VIT was stopped and omalizumab newly introduced.

Our observation confirms that concomitant treatment with omalizumab may be an option for patients with allergy to hymenoptera venom who present severe reactions to VIT. However, as in our patient, this protection effect is lost a few weeks after removal of the monoclonal antibody. In this situation, treatment with both omalizumab and VIT should be maintained, but an alternative option might be treatment with omalizumab alone.

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1252 | Allergic contact dermatitis from ophthalmic medications

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Introduction: The skin of the eyelids is particularly susceptible to irritant dermatitis and allergic contact dermatitis, as the extremely thin skin in the eyelids may facilitate allergen penetration.

Objectives: To study contact allergy caused by topical ophthalmic medications in patients with periorbital dermatitis.

Methods: We retrieved allergic reactions to a patch test series consisting of ophthalmic medications and preservatives for the years 2002-2014 at the Helsinki University Central Hospital.

Results: 71 out of 622 tested patients (11.4%) had one or more allergic reactions in the ophthalmic patch test series. 23 of 622 tested patients (3.7%) had an allergic reaction to the antibiotic chloramphenicol. Of 448 patients, 14 (6.1%) had an allergic reaction to the preservative thimerosal. Other common allergens in the test series were anti-glaucoma agents timolol (2.6%), latanoprost (1.6%) and dorzolamide (1.1%), myadriatic agent phenylephrine (1.8%), and the preservative benzalkonium chloride (1.6%).

Conclusions: Patch testing is encouraged in all patients in which periorbital contact dermatitis is suspected in order to identify allergens causing contact dermatitis of the eyelids. Especially in those who are using any kind of ophthalmic medication as e.g. glaucoma drugs.

1253 | Our experience in allergic contact dermatitis: a map of allergens through the body

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Introduction: Lesions of allergic contact dermatitis are usually localized in the skin areas that come in contact with the allergen. The regional factors play an important role in the onset and clinical aspects of the injuries

Objectives: The aim of the study is to evaluate the prevalence of contact sensibilization of the studied patients and to identify the association with the localization of the lesion and the most common allergens in each specific body parts.

Results: We present a retrospective analysis of 577 patients with allergic contact dermatitis, carried out by Allergy Department of Hospital Universitario de Burgos, from 01.01.2015 to 31.12.2015. Patients were studied with European standard patch-testing and specific batteries of allergens according to the possible origin of dermatitis and the occupation of the patient.

Fifty-nine percent of the patients were allergic to at least one allergen. Women presented a higher rate of sensibilization compared to men (69% vs 31%) with a medium age of 46.8 $\pm$ 19 years for both groups. The three more frequent allergens affecting the faces are nickel, Kathon and drugs. Specifically causing lesions on the perioral area are nickel and Kathon. It enhances the fact that Kathon is the first allergen, in frequency, specifically affecting the eye lid. Eye conjunctive is mostly affected by cosmetics of patients, and oral mucosa by nickel. Hands lesions are due to Nickel, Kathon and cobalt chloride. In our patients, nickel, Kathon and drugs are the three main allergens of leg injuries.

Conclusions: Our results are similar to the previously published studies of national level. After this analysis we are able to predict with a better accuracy which allergen is most likely responsible, in our area, for the skin injury studied.

	MUCOSA	EYE CONJUNCTIVA	MUCOSE ORAL	GENITAL	OTHER	HAND	LEG	HIP + KNEE PROSTHESIS	FACE	EYE LID	PERIORAL AREA
Number of patients with suspected allergy	60	13	28	4	3	322	401	4	292	8	9
Number of patients with positive patch test	30	8	16	3	0	204	246	2	152	5	6
% of patients with positive result	50%	62%	57%	75%	0%	63%	61%	50%	52%	63%	67%
1st most prevalent allergen	20	3	13	3		101	67	2	144	2	6
	34%	21%	38%	50%		31%	30%	100%	32%	25%	38%
	NICKEL	COSMETIC PRODUCTS PATIENT	NICKEL	NICKEL		NICKEL	NICKEL	NICKEL	NICKEL	KATHON	NICKEL
2nd most prevalent allergen	6	3				50	30		67	2	2
	10%	21%				15%	14%		15%	25%	13%
	KATHON	COSMETIC PRODUCTS PATIENT				KATHON	KATHON		KATHON	KATHON	KATHON
3rd most prevalent allergen	3					17	19		21		
	5%					5%	9%		5%		
	2-HYDROXYETHYL METHACRYLATE					CLORURO DE COBALTO	DRUGS		COSMETIC PRODUCTS PATIENT		

1254 | Clinicopathological analysis of pigmented contact dermatitis from henna in Korean patients

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Introduction: The henna is a vegetable hair dyes that can be recommended to the patients who are sensitized to oxidative dyes due to their low allergenicity. The incidence of contact dermatitis after henna appears to be extremely rare. Pigmented contact dermatitis, commonly known as Riehl's melanosis, is caused by antigens mostly present in the cosmetics and fragrances. To date, the pigmented contact dermatitis after henna has been reported extremely rare.

Objectives: We sought to analyze the clinical and histopathological features of pigmented contact dermatitis after henna in Korean patients.

Results: Of 11 patients, all (100%) were females with Fitzpatrick skin phototype IV. The mean age was 60.7 years. The hyperpigmentation in the lateral side of face and neck were the most commonly involved site in 8 (72%) patients. The central face was spared in all patients. Xerosis was observed in 5 (45%) patients. Patch test with henna was positive. Histopathology revealed liquefaction degeneration of the epidermal basal layer with pigmentory incontinence in the papillary dermis in all patients. In addition, epidermal atrophy with rete ridge flattening was observed.

Conclusions: Hair dye with henna is associated with pigmented contact dermatitis in Korean. Because it occurs mostly in middle-aged women and requires long-term treatment, careful attention should be paid when hair dyeing in this age group with henna.

1255 | Occupational contact dermatitis: to whom? Due to what?: our experience in 2015

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Introduction: Contact allergy prevalence rates change over different professions according to the exposure to the allergen. Epidemiological facts can be extremely useful to obtain information of the incidence and prevalence of this illness, as well as the impact on public health. It allow us to identify the possible factor risks and etiological agents implied.

Objectives: The aim of our study is t identify sensitization to the most common allergens associated with the most frequent professions in our area. All patients were patch tested with the European baseline series, plus specific batteries according to their occupation. Our observational project, took place from 01-01-2015 to 31-12-2015, in the Department of Allergy of Hospital Universitario de Burgos, between all the patients who were studied for contact dermatitis with diverse batteries of patch-tests.

Results: A total of 371 patients with specified occupations in their clinical history, underwent patch testing
during the period described, 215 had positive patch-tests to different allergens. The three most frequent
occupations in our population is housekeepers, office work (which includes students, teachers, clerks) and retired people. The most frequent allergen in the three most common occupations is nickel, followed by Kathon. In third place, stand out Cobalt
Chloride for house keepers, drugs for jubilee and fragrance mix for office workers. The rate of sensibilization in each professional studied with suspected allergy is over
50% in all the groups (except for office works and carpenters). Manufacturer professionals (maintenance labours, production of products, transport) present the highest rate of sensibilization between all the other groups (91%), to Nickel, Kathon and Carba Mix.

Conclusions: Our study highlights the importance of testing the European Standard Patch-test extended with specific batteries for each professional occupation in order to carry out a complete study of the occupational contact dermatitis of our patients.

Specified profession of 371 patients, of which 215 were positive.					Number	%	Name	Number	%	Name	Number	%	Name
PROFESSION	Total of patients of each profession	Number patients with positive patch test	% of positive patients	Number of elements they are allergic to	1° most prevalence allergen			2° prevalent allergen			3° prevalent allergen		
AGRICULTURE	6	1	17%	4	1	25%	KATHON	1	25%		1	25%	
HOUSEKEEPER	54	36	67%	24	27	36%	NICKEL	14	18%	KATHON	5	7%	COBALT CHLORIDE
ARCHITECT	4	3	75%	7	2	25%	NICKEL	1	13%		1	13%	
FIREMAN	2	1	50%	1	1	100%	KATHON	0	0%		0	0%	
CARPENTER	4	1	25%	2	1	50%	BACITRACIN	1	50%	BACITRACIN	0	0%	
LOCAL TRADE	5	4	80%	8	3	27%	NICKEL	2	18%	KATHON	1	9%	LANOLINE
CONSTRUCTION	5	3	60%	7	2	22%	COBALT CHLORIDE	2	22%	CLORURO DE COBAL TO	1	11%	POTASSIUM DICHROMATE
SPORT	2	1	50%	2	1	50%	NICKEL	1	50%	NITRATO DE PLATA (1%)	0	0%	
MANUFACTURER	11	10	91%	14	7	27%	NICKEL	6	23%	KATHON	2	8%	CARBA MIX
HOSTELERIA	12	7	58%	14	6	30%	NICKEL	2	10%	TWEEN 80	1	5%	TWEEN 80
CHEMICAL INDUSTRY	10	7	70%	13	4	20%	NICKEL	3	15%	COBALT CHLORIDE	3	15%	KATHON
RETIRED	94	52	55%	34	34	30%	NICKEL	16	14%	KATHON	13	12%	DRUGS
NUCLEAR MEDICINE	7	4	57%	6	4	40%	NICKEL	2	20%	KATHON	1	10%	
OFFICE WORK	73	33	45%	26	24	33%	NICKEL	10	14%	KATHON	6	8%	FRAGRANCE MIX
BAKERY	2	1	50%	4	1	25%	COSMETIC PROD. PATIENT	1	25%	NICKEL	1	25%	THIMEROSAL
HAIR DRESSER	19	15	79%	15	14	42%	NICKEL	3	9%		2	6%	
FOOD PREPARATION	24	13	54%	16	10	28%	NICKEL	7	19%	KATHON	2	6%	COSMETIC PRODUCTS PATIENT
HEALTH WORKERS	24	18	75%	15	16	44%	NICKEL	3	8%	COBALT CHLORIDE	3	8%	KATHON

1256 | Utility of scratch test for allergic contact dermatitis caused by Dermabond®

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Case Report: Introduction: Topical skin adhesives such as Dermabond® (Ethicon GmbH, Norderstedt, Germany) are used as alternative to traditional sutures. We report 2 cases of allergic contact dermatitis with negative patch tests, but positive scratch tests with Dermabond®.

Cases: 2 patients, 30 and 28-year-old, without atopy history have presented 24 hours after surgery, where Dermabond® had been used for wound closure, a localised pruritic eczema around the wound.

Three months later, patch testing was performed with the European baseline series, an acrylate series, and with not diluted Dermabond®. The patch tests were applied to the patient's upper back for 2 days. We also performed scratch tests with Dermabond®, and a mixture (1:1) of Dermabond® with povidone iodine (1% aq.), and Dermabond® with chlorhexidine (0.2% aq.), in order to reproduce the conditions of use. Povidone iodine and chlorhexidine were also both tested alone in above-mentioned concentrations. Readings were performed on D2 and D3. In order to rule out irritation causing these results, we performed these tests in 10 healthy volunteers.

Results: Patch tests were negative for both patients.

For patient 1, scratch test with the mixture of Dermabond® and chlorhexidine was positive. Scratch tests with Dermabond® and povidone iodine were both negative.

For patient 2, scratch tests were positive for Dermabond®, Dermabond® with chlorhexidine, and Dermabond® with povidone iodine.

Scratch tests were negative for the 10 healthy volunteers.

Conclusion: Despite the widespread use of Dermabond®, few allergic reactions have been reported. In most cases, patch tests or even open tests were sufficient to show the sensitisation. If patch tests are negative, scratch-tests can be used to show the sensitisation.

We can speculate that this bypassing of the epidermal barrier, which is quite similar to the clinical application for wound closure, allows the penetration of greater amounts of the hapten, causing the clinical response, but may also be due to the creation of a new hapten between 2 molecules.

Negative skin reactivity in 10 healthy volunteers confirmed the absence of irritation with these scratch tests

1258 | Allergic contact dermatitis to temporary black henna tattoo due to sensitization to paraphenylenediamine

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Case Report: Temporary "black henna tattoos" have become increasingly widespread among young adults and teenagers. It contains PPD, other additives (diaminobenzene and diaminotoluene) and heavy metals. Those are used for speed up the drying process and satisfying permanency. PPD is an extreme contact sensitizer and presents in hair dyes and in black henna tattoo. Minimum concentration (2.5%) of PPD in the tattoo leads to sensitization.

A 15-year-old male patient was applied to allergy outpatient clinic with itching, erythema, edema and inflammatory discharge on his right forearm. The parents explained that the symptoms began two days after the temporary tattoo application. One year ago, the patient had experienced the same mild local symptoms after temporary tattoo application. Physical examination of the patient showed that a devil fork shaped, erythematous, edematous area with yellow dry and purulent discharge exists on tattoo application area. The affected area was about 10 cm size around the elbow and extending to forearm and arm and his arm was completely edematous.

The patient was hospitalized with the diagnosis of allergic contact dermatitis and soft tissue infection. Laboratory examination showed that white blood cell count of 10.500/μL; erythrocyte sedimentation rate of 4 mm/hour, C-reactive protein of 0.25 mg/dL. Although the findings did not support infection, the clinical signs were compatible with tissue infection. The patient was treated with intravenous sulbactam-ampicillin, clindamycin, oral antihistamine drugs, and moderate potency topical steroid. Second day of the treatment, systemic steroid was also added to therapy. After the treatment for 5 days, the lesion was healed.

To determine contact sensitizer, atopy patch test (T.R.U.E. Test®) was performed one month after the end of the treatment. A bullous reaction (3+) was observed against to p-phenylenediamine (PPD) at the 48th and 72th hours of evaluation after application. Furthermore, other allergenic materials including caine mix (benzocaine + tetracaine + dibucaine) (1+); black rubber (1+); and bronopol (+1) revealed suspected positive results. The patient was informed regarding the allergenic materials detected in the tests and advised to avoid.

Sensitization to PPD in children may have important consequences especially among teenagers while growing popularity of temporary tattoos. Atopy patch test should be performed to establish the sensitization in patients who have allergic contact dermatitis or impetigo-mimicking dermatitis after henna tattoo exposure.

1260 | A rare cause of contact dermatitis

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Introduction: We present the case of a 28 years old patient, nurse therapist, who makes daily therapeutic massages to patients with spine-disorders. From 6 months she accused dry skin on the hands, than erythematous small posters at fingers, which were subsequently, generalized on hands. Associate she presented also ulcers on the hands. The patient changed the oils for massage, but the symptoms persisted.

Objectives: Results: Following dermatological consultation it was administered local cortisone therapy with improvement, but recurrence of symptoms after interruption of treatment. After allergological consultation allergy skin tests were performed to environmental allergens and food, but did not reveal the presence of atopy. It was performed skin patch testing with European standard kit which revealed after 72 hours erythema, edema and vesicles to methylisothiazolinone.

Conclusions: It was recommended the use of products that do not contain this preservative, local corticosteroids and emollients, with favorable evolution.

1263 | Allergic contact dermatitis in athlete adolescent: Mercaptobenzothiazole and mercapto mix

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Case Report: A 13-year-old male patient was admitted to our clinic for two months, with both hands and feet being pruritic lesions. Physical examination revealed a 4 × 4 cm dry, eczematous and licheniform area in the medial part of the right hand, dryness in the left hand, and lichenification in the right foot toe. System examinations were evaluated as normal. It was learned from the story of the patient that he spent two months of intense sports, playing goalkeeper's gloves while playing soccer, and using rubber slippers during swimming.

The patient was considered contact dermatitis as primary. A patch test was performed with the European Standard Series for differential diagnosis. Mercaptobenzothiazole and mercapto mix were evaluated positively.

Allergic contact dermatitis is a delayed type (Type 4) hypersensitivity reaction that occurs after recurrence of previously encountered and sensitizing substances. In the acute period erythema, edema, vesicle and bulla but in chronic, lichenification, deep itching and fissure formation is seen. Although adults have the most occupational exposure, hobbies, toys and sports equipment may also be associated with this clinic in children. It is the gold standard patch test to make definite diagnosis and to detect allergy.

Through this phenomenon, in the diagnosis of dermatitis in childhood, sports activities, toys, and hobbies should be questioned in terms of possible contact allergen and is intended to highlight the importance of the patch test in the diagnosis.

1264 | Allergic contact hand dermatitis with an unexpected route of sensitization. Case report

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Case Report: Background: Band rubber ligation is one of the most used outpatient treatments for hemorrhoids world-wide, being considered nowadays as a first-line therapy for first- to third-degree internal hemorrhoids. The medical devices used for this procedure are preferably made of stainless steel or a biologically inert plastic whereas elastic rings are usually made of latex rubber, silicone rubber or contractible, elastic polymer.

Case Report: We present the case of a 41-year old female who began to present symptoms of non-occupational relapsing hand eczema reluctant to treatment, starting 3 months later after rubber band ligation applied for internal hemorrhoids in her mid-30s, at the same time associated with erythematous papular, vesicular and occasionally crusted lesions occurring singly on the trunk, generalized pruritus, dry skin. Over the next 7 years, she presented recurrent and frequent hand eczema episodes on both hands, especially after nail polish application by personnel using latex gloves and during home cleaning activities. She was referred by her family physician for allergy evaluation where she underwent skin prick testing (6 mm house dust mites, with negative results including for latex skin prick testing) and epicutaneous patch testing (+++thiuram mix at 72 hours reading) using European standard series.

Among additives to rubber, thiurams are considered as the most important class of contact allergens. A diagnosis of allergic contact hand dermatitis with sensitization to thiuram mix, aggravated by nonspecific irritants was established. In allergic contact dermatitis an

unusual route of sensitization could be represented by previous use of band rubber ligation for internal hemorrhoids treatment.

Conclusions: We describe a case of allergic contact hand dermatitis due to sensitization to rubber bands used for hemorrhoids ligation. The sensitization to thiuram mix may have long-life lasting consequences, due to cross-reactivity to other accelerators making it necessary to recommend proper use of bands and gloves made of a synthetic co-polymer free from thiuram mix (e.g. styrene, butadiene, vinyl, nitrile, polyvinyl chloride, polyvinyl acetate or silicone).

Statement of Consent: Written informed consent was obtained from the patient for publication of this abstract and any accompanying images.

TUESDAY, 20 JUNE 2017
TPS 47
DRUG ALLERGY: CLINICAL ASPECTS AND DIAGNOSIS

1266 | Is gadolinium a safe alternative to iodinated contrast agent allergy?

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Case Report: Introduction: The usage of imaging contrast agents such as gadolinium based contrast agents (GBCAs) or iodinated contrast agents (ICAs) has been gradually increased for last twenty years. GBCAs are used for magnetic resonance imaging (MRI) and considered to be safer than ICA. However, there are few case reports regarding severe allergic reactions against to GBCAs. In this report, we present a patient who had reactions to both iodinated and gadolinium based contrast agents.

Case Report: A 36-year-old female patient underwent an abdominopelvic computerized tomography (CT) for evaluation of abdominal pain and fever four years ago. After receiving ICA, generalized rash, hives and itching had been developed immediately. She had felt distinctly shortness of breath and noticed an abnormal swelling of her tongue. She had been diagnosed with endometrial cancer three years ago. One year later MRI was performed for the routine control of endometrial cancer. Same signs and symptoms had been occurred in a few minutes after receiving GBCA. Prior to another abdominopelvic MRI scan, she was referred to our clinic because of adverse reaction histories to both iodinated and gadolinium contrast agents. Skin tests were performed with gadobenate dimeglumine and gadodiamid. Intradermal tests were positive to 1:10 dilution of two agents. We suggested her MRI procedure should be performed without contrast agent. MRI was performed without GBCA with any adverse reactions. Twenty days later, she was referred to our clinic from cardiology department before elective coronary angiography (CA). Skin tests were performed with Iodixanol and Iomeprol. Skin prick test was positive to Iodixanol and intradermal test was positive to 1:100 dilution of Iomeprol. Therefore, we suggested another procedure instead of elective CA. She had a myocardial scan without adverse reactions.

Discussion: If a patient is referred to allergy and immunology department due to history or suspicious of contrast agent allergy, physicians should consider medical history. The patient should be inquired detail regarding about allergy history with drugs, foods, inhalant allergens especially with ICA or/and GBCA. The patients may have allergies to both ICA and GBCA. Alternative imaging methods or CT and MRI without contrast agents should be recommended. In urgent conditions, allergic patients consider premedication involving both corticosteroid and antihistamine.

1267 | Potentially life-threatening dress—syndrome in a 19 year old male patient

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Case Report: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, potentially life-threatening, drug-induced hypersensitivity reaction that includes skin eruption, hematologic abnormalities (eosinophilia, atypical lymphocytosis), lymphadenopathy and internal organ involvement (liver, kidney, lung). Although the precise pathogenesis of DRESS syndrome is not fully understood, an immunological reaction to a drug or drug metabolites is accepted as the main mechanism.

Nineteen years old boy was admitted to the Allergy Clinic with non-specific morbilliform skin eruption, fever, facial and legs edema. These were followed by other systemic reactions such as cervical, occipital, axillar and inguinal lymphadenopathy, hepato- and splenomegaly. One month ago the patient was diagnosed with epilepsy and began his treatment with Carbamazepine. Eosinophilia, leukocytosis with atypical lymphocytosis, rapid elevation of liver function tests was recorded.

The patient was diagnosed with DRESS syndrome.

High doses of methylprednisolone were prescribed as a main treatment of the disease. Patient condition improved, and lab results normalized after 5 days.

There is still no universal consensus about the definition of DRESS syndrome. Besides, there are numerous cases of adverse drug reactions with skin eruption, systemic symptoms, and visceral involvement, which made difficult the accurate diagnosis and treatment.

Thus, the presentation and discussion of such cases is very important and will contribute for better understanding and better efficacy of diagnosis and treatment.

1268 | Nonimmediate reactions to amoxicillin in infectious mononucleosis: three case reports

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Case Report: Introduction: Although amoxicillin-induced eruption of infectious mononucleosis is a well-known clinical phenomenon, some reactions could be due to a true hypersensitivity reaction. Amoxicillin hypersensitivity is facilitated by generalized immune

stimulations such as those caused by viral infections as Epstein-Barr virus (EBV) or other herpes virus infections.

Methods: We describe three patients with amoxicillin-induced exanthema within infectious mononucleosis who were studied by prick and intradermal tests (amoxicillin, ampicillin, penicillin G, penicilloyl polylysine (PPL) and determinant mixture (DM)) and drug provocation tests with phenoxymethylpenicillin or cefuroxime.

Case 1- A 20-year-old, that developed a pruritic exanthema and fever, two days after starting amoxicillin for a dental infection. She referred another eruption 6 years earlier during the treatment with amoxicillin within infectious mononucleosis.

Case 2- A 20-year-old girl reporting a pruriginous and generalized eruption during an infectious mononucleosis 3 years ago that was initially medicated with amoxicillin.

Case 3- A 26-year-old boy experienced a generalized rash during an infectious mononucleosis that was complicated with hepatitis and autoimmune hemolytic anemia. Before the onset of the eruption he had been treated with amoxicillin for 4 days.

Results: The three patients had strong positive intradermal tests with amoxicillin (20 mg/mL).

The drug provocación tests with phenoxymethylpenicillin in two patients (case 1 and 2) and with cefuroxime in the third case were negative.

Conclusion: We describe true delayed-type allergic reactions to aminopenicillins in patients who suffered an infectious mononucleosis. Latent EBV infections could play a role in the development of nonimmediate hypersensitivity to amoxicillin, so allergologic tests may be performed in these patients.

1269 | Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome and tuberculosis: case report

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Case Report: Background: Drug rash with eosinophilia and systemic symptoms syndrome (DRESS Syndrome) is a severe and life-threatening drug reaction that causes a diverse array of clinical symptoms. It usually appear with a latency of 2 to 8 weeks after introduction of the triggering drug. The diagnosis of DRESS syndrome is mainly clinical and the management is not well supported by strong evidence-based data. The early diagnosis and suspension of the offending drug is strongly recommended in order to avoid complications. We present the case of a 40 years old woman who suffered DRESS syndrome when treated with anti-tuberculosis drugs and Allopurinol for an active pulmonary tuberculosis (TB). She unfortunately died of multi-organ failure after approximately 7 months.

Materials and Methods: The case required several changes of TB drugs until the complete suspension of TB treatment. It needed a multidisciplinary management and analytical controls, different radiological procedures, skin and lung biopsies. We started corticosteroid treatment adding cyclosporin later. The syndrome presented approximately with 8 exacerbations consisting in fever, eosinophilia, maculopapular eruption, facial edema, vomiting, hepatitis and Cytomegalovirus (CMV) activation. After 5 months of hospitalization she sustained pneumonitis and pulmonary fibrosis with a suprainfection by P. Jiroveci.

Results: ALT 1234 U/L; AST 703 U/L; gamma gt 462 U/L; ALP 209 U/L; WBC 18000; 2610 Eosinophils (14.6%), activated lymphocytes mononucleosis-like, skin biopsies: perivascular and interstitial dermatitis with abundant eosinophils, ecography and MRCP: no evidence of Cholecystitis, IgE>5000, Immunological study normal, Negative HLA-B*58:01, no evidence of parasites, CMV seroconversion with viral load 3690 UI/L, Pulmonary CT: fibrosis and groundglass; bronchoalveolar lavage negative Zhiel-Nielsen n; punch pulmonary: positive p. jirovecii

Conclusions: Contrary to expectations, the evolution of TB did not progress under corticosteroid treatment and ciclosporin. We observed that the decreasing Corticosteroid therapy affected the course of the syndrome; We didn't notice clinical benefits by ciclosporin use. we realized we had underrated the importance of preventing suprainfection during a prolonged immunosuppression. By the way The lack of treatment guidelines was the major problem we faced.

1270 | Acute hepatitis due to adverse drug reaction in two young patients – Different mechanisms and clinical approach

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Case Report: Adverse drug reactions (ADRs) represent a matter of concern in medical practice, for both outpatients and hospitalised patients. Drug hypersensitivity reactions (DHRs) comprise 15% of all ADRs, affect about 10% of general population and are mostly unpredictable. Drug allergies are immunologically–mediated DHR, may have immediate or non-immediate onset and variable clinical picture and severity. We report two cases of ADRs in young patients, clinically manifested with acute hepatitis. The first case is a 27 years old woman who came to the clinic for acute generalised exanthema, fever and asthenia since few days. One month ago she started daily anticonvulsant therapy with phenytoin 300 mg and levetiracetam 1000 mg for focal seizures secondary to astrocytoma operated at age of four years. At admission she had generalised pruriginous exanthema and fever, no organomegaly. Laboratory showed significant increase of hepatic enzymes, mainly cholestasis, mild anemia and hypoproteinemia, without eosinophilia. We diagnosed DHR

manifested with acute hepatitis secondary to anticonvulsant therapy, very probably to phenytoin. We stopped both anticonvulsants for few days, we administered systemic corticosteroids and supportive therapy, then we progressively reintroduced levetiracetam low doses, well tolerated. She had favourable clinical evolution, with progressive remission of exanthema and normalisation of liver function after one month. The peculiar feature of this case is monoorganic hepatic manifestation of DHR induced by an anticonvulsant drug, without eosinophilia, which is characteristic of DRESS syndrome. The second case is a 20 years old woman who came for intermittent urticaria and chronic toxocariasis, treated with repeated cures of albendazole since two months. At hospital admission she had marked asthenia, moderate pruritus, but no skin lesions or other relevant changes. Laboratory showed significant increase of hepatic enzymes, mainly cytolysis and mild inflammation. We diagnosed acute toxic hepatitis induced by antiparasitic therapy, associated with chronic intermittent urticaria and chronic Toxocariasis. We stopped all medication, closely monitored diet and liver function. Clinical evolution was progressively good, with complete remission of acute hepatitis after one month. We concluded that early diagnosis of ADRs and correct identification of underlining mechanism, especially in cases with severe organic manifestation, are essential to avoid complications and severe evolution.

1271 | Rituximab hypersensitivity reaction in a child with nephrotic syndrome: a case report

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Case Report: Background: Rituximab is a chimeric monoclonal antibody targeted against the CD20 B-cell antigen. It is used both in oncologic diseases and in steroid and calcineurin-dependent nephrotic syndrome (NS). Although the mechanism of the therapeutic effect remains unknown, the efficacy of this agent seems to be related to B-cell depletion. In several patients, it has been reported the appearance of rituximab antibodies. However, current knowledge on the production and clinical significance of such antibodies in the pediatric population is still quite limited. We report the case of a pediatric patient with NS, who developed a hypersensitivity reaction to rituximab.

Case Report: Rituximab, at a dose of 400 mg, was given as rescue therapy to a 9-year-old boy with steroid-resistant NS treated with oral cyclosporin (70 mg/die). The reaction occurred during the administration of sixth dose of Rituximab. Previous drug administration had been well tolerated. The patient was premedicated with paracetamol/acetaminophen (450 mg), prednisolone (40 mg) and chlorphenamine (10 mg). After administration of 70 mg of Rituximab, the patient had an anaphylactic reaction characterized by generalized urticaria, angioedema, cough and wheezing. Drug administration was stopped and the patient received an intravenous injection of chlorphenamine (10 mg) and steroids (40 mg) and an intramuscular injection of adrenaline (0.3 mg), with progressive improvement. The analysis of histamine and tryptase levels showed an elevation of histamine but not of tryptase (basal histamine 3.29 ng/mL; tryptase: 3.44 μg/L; after reaction: histamine 20.55 ng/mL; tryptase 6 μg/L). The reaction was therefore considered as non IgE-mediated.

Conclusion: This report shows that rituximab may induce non-IgE-mediated reactions after sensitization, with the development of human anti chimeric antibodies (HACA). Further studies are needed to determine the incidence of such antibodies in pediatric patients with NS and their clinical significance.

1272 | Carbamazepine induced dress syndrome: A case report

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Case Report: Introduction: Drug reaction with eosinophilia and systemic symptoms (DRESS)/drug induced hypersensitivity syndrome (DIHS) is characterized with fever, skin rashes, lymphadenopathies, hematologic abnormalities (eosinophilia, atypical lymphocytosis) and organ involvements (mainly liver and renal) 2 to 6 weeks after the use of some drugs. DRESS incidence is not known exactly and changes according to drugs. Anticonvulsants and sulfonamides are the most common offending agents. Herein, a case of DRESS syndrome associated with carbamazepine use was reported.

Case Report: A 59-year-old woman was admitted to the allergy and immunology outpatient clinic with the complaints of widespread pruritic rashes continuing for 2 days. Her medical history revealed that she had been under treatment of a carbamazepine therapy for six weeks because of chronic headache ongoing almost 2 months. Physical examination showed extensive maculopapular rashes on all of the body. Bilateral cervical, axillary and inguinal lymph nodes were detected in pathological dimensions. Other systems were considered normal. Laboratory examination revealed eosinophilia 1300/mm^3, elevations of liver function tests (AST 294 U/L, ALT 559 U/L), cholestatic enzymes (GGT 1008 U/L, ALP 430 U/L), LDH 631 U/L and acute phase reactants (C-reactive protein 67.4 mg/L, erythrocyte sedimentation rate (ESR) 45 mm/h). The patient was diagnosed as DRESS syndrome caused by carbamazepine therapy on the basis of clinical appearance and laboratory tests. Pulse oral steroid and oral antihistamine were initiated as antiallergic therapy. After the third day of treatment the patient's fever, liver and cholestatic enzymes, skin rashes and complaints of itching began to decrease gradually. Three

weeks later the patient showed full recovery both in clinical status and laboratory tests.

Discussion: DRESS syndrome is a severe life threatening drug reaction with eosinophilia and systemic symptoms. Mortality rate is approximately 10% and is primarily associated with systemic organ involvement. Early diagnosis and early discontinuation of the suspected drug will contribute to a reduction of mortality and morbidity in these patients. Our patient was diagnosed as DRESS at the second day of the complaints related to skin and recovered completely 21 days later. DRESS exhibits a broad range of clinical manifestations with its laboratory abnormalities. Despite a variable clinical status, DRESS can be managed successfully with a careful systemic approach.

1273 | Infusional fever cause by piperacillin-tazobactam and meropenem, report of a case

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Case Report: Introduction: The drug fever is one that coincides temporarily with the administration of a drug in the absence of other causes or conditions that justify it. It is usually misdiagnosed due to its lack of knowledge and frequent association with infection, which may be due to an hypersensitivity mechanism.

Case Description: A 37-year-old male, without allergic or pathological antecedents of interest, entered scheduled hemicolectomy surgery for colon adenocarcinoma. It starts prophylactic antibiotic with Amoxicillin-Clavulanic 1 g every 8 hours presenting from the sixth day temperature of 38°C. They request abdominal Tc which reports laminar collection at the mesogastrium level, thus increasing antibiotic spectrum with Piperacillin-Tazobactam 4 g every 8 hours, referring fever. At day 18 of treatment, T: 39°C, HR: 78 lpm, TA: 95/60, associated with intense myalgias on the posterior aspect of forearms and thighs, which started during the infusion of this drug, improving after Metamizol. Blood cultures are taken, catheter culture, general analytical with acute phase reactants. The next day, during the infusion of the antibiotic reappears the described clinical with greater intensity yielding again with analgesics. In the results of the requested tests, we highlight: blood culture and MAKI culture: sterile, frank leukopenia, neutropenia, mild transaminase increase, PCR: 99.8 mg/L, troponins: 0.0. CK: 37 U/L. Suspension is withdrawn by transmitting the fever within 48 hours and substantially improving the altered analytical parameters. Meropenem is given 1 g and Vancomycin 500 mg every 8 hours. On the seventh day of treatment, it starts again with T: 37.7°C during the infusion of these antibiotics accompanied by myalgias and arthralgias, of progressive intensity until requiring analgesics. The low-grade fevers persist for 24 more hours; it is requested complement that is in normal limits and analytical general anodyne. Antibiotic regimen is discontinued and they change to Metronidazole 500 mg every 8 hours and Ciprofloxacin 200 mg every 12 hours culminating an additional week of antibiotic without presenting new incidents.

Materials and Methods: Total IgE: 228, CAPS Penicillin G: 0.01, Penicillin V: 0.02, Amoxicillin 0.03 and Ampicillin: 0.05

Prick and ID skin tests against PPL, MDM, PENI G, Amoxicillin, Piperacillin -Tazobactam, Meropenem and Vancomycin, with immediate and late reading at 48 hours: NEGATIVES.

Controlled provocation with Vancomycin 500 mg IV: Negative. No fever or other companions 48 hours later.

Epicutaneous tests with Piperacillin-Tazobactam, Meropenem and Vancomycin with reading at 48 and 96 hours: negative.

Conclusions: We report the case of a patient who presented fever and neutropenia associated with the administration of Piperacillin-Tazobactam and fever with the administration of Meropenem. Fever is documented as a mechanism of hypersensitivity to the administration of Antineoplastics although it is rarely described in beta-lactam antibiotics and in particular with 2 of them with little cross-reactivity More cases would be needed to establish the mechanism of hypersensitivity of these febrile cases associated with the administration of such antibiotics.

Bibliography:

* Patel RA, Gallagher JC. Drug fever. Pharmacotherapy. 2010;30 (1):57-69.

* R. Madrigal, Desensitizing Oxaliplatin-Induced Fever: A Case Report. J Investig Allergol Clin Inmunol 2013.

* W. Pichler and O. Hausmann, Classification of Drug Hypersensitivity into Allergic, p-i, and Pseudo-Allergic Forms, Allergy Immunol 2016;171:166-179

* T. Linares, Drug Fever Caused by Piperacillin-Tazobactam. J Investig Allergol Clin Inmunol 2011.

* Swe T, et al. Drug fever induced by piperacillin/tazobactam in an elderly patient with underlying human immunodeficiency virus (HIV) infection, BMJ Case Rep 2016.

1274 | Serum sickness-like reaction due to amoxicillin/clavulanic acid in two children

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Case Report: This report describes two patients who developed Serum sickness-like reaction (SSRL) after receiving amoxicillin/clavulanic acid. SSLR is an uncommon immunological condition and

SSRL due to amoxicillin/clavulanic acid is rarely reported in literature.

Case 1: A 7-year-old female child who presented with acute-onset polyarthralgia, maculopapular rash of arms, face and chest, fever to 38°C that appeared 6 days after starting amoxicillin/clavulanic acid therapy for the treatment of acute tonsillopharyngitis was admitted. The patient's history revealed that she had developed polyarthralgia, 38°C fever and maculopapular rash on face, body and arms on the seventh day of amoxicillin clavulanate therapy for the treatment of acute tonsillopharyngitis one year ago

Case 2: A 4-year-old male child was admitted to the emergency department because of rash and arthritis. He had a history of using amoxicillin clavulanic acid for his acute tonsillopharyngitis for 5 days. Two days after amoxicillin clavulanic acid withdrawal, his complaints began. In his medical history, he has presented acute-onset polyarthralgia, maculopapular rash of trunk, face and extremities, fever to 38°C that appeared 10 days after starting amoxicillin/clavulanic acid therapy for the treatment of acute tonsillopharyngitis two years ago.

SSLR is a rare immunological condition characterized by fever, pruritus, urticaria, and arthralgia that usually begin 1–3 weeks after drug exposure.

Although both patients had a history of SSRL that developed after amoxicillin/clavulanic acid therapy, both were given the same drug again and the same reaction repeated. Thus, it is important to assess the association between drug use in the past and the reaction before prescribing drug to patients. Two cases were presented for paying attention in terms of SSLR development during amoxicillin clavulanic acid use.

1275 | NSAIDs non chemically related induced urticaria

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Introduction: Patients suffering from NSAID-induced urticaria/angioedema have been classified in different categories, including single reactors, multiple reactors, and multiple reactors with underlying chronic urticaria. In patients with urticaria induced by distinct NSAIDs cross-reactions occurred mainly among COX-1-inhibiting drug or cross-reactions are induced by other chemically related.

We present a case of a woman who reacted with two non-structurally related NSAIDS (metamizol and ibuprofen) and tolerated another chemically related (dexketoprofen).

Objectives: A 40 years old woman, with no history of underlying urticaria, presented immediately after the intake of ibuprofen, metamizol and paracetamol an universal maculopapular itchy rash. It lasted 3 hours without any treatment.

The patient tolerates dexketoprofen.

Skin tests with metamizol, ibuprofen, dexketoprofen and etoricoxib were performed. Single-blind placebo control oral challenge (SBPCOC) with ibuprofen, dexketoprofen and etoricoxib was carried out.

Results: Skin tests: Intradermal (ID) test with metamizol were positive. ID test with ibuprofen, dexketoprofen and etoricoxib were negative.

SBPCOC with ibuprofen:: 1st day: doses of 50, 100 and 250 mg every 30 minutes with a 120 minutes observation period was positive. Maculopapular itchy rash affecting face and forearms.

SBPCOC with dexketoprofen: doses of 6.25, 6.25 and 12.5 every 30 minutes with a 120 minutes- observation period: negative.

SBPCOC with etoricoxib: doses of 30 mg every 60 minutes and 120 minutes after observation: negative.

Conclusions: Our patient presented urticaria after the intake of two non-structurally related NSAIDS (ibuprofen and metamizol) with tolerance to other chemically related (dexketoprofen).

1276 | Immediate hypersensitivity to oral dimethyl fumarate (tecfidera®): A new desensitization protocol

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Introduction: Dimethyl fumarate (DMF) is one of the new oral drugs available for the treatment of multiple sclerosis (MS). Although DMF has been used as an oral drug since 2013, to our knowledge, no immediate hypersensitivity reactions associated to its administration have been reported, so far. Here, we describe a case of a woman with MS, treated with oral DMF, who complained about immediate hypersensitivity symptoms.

Objectives: To assess the efficacy and safety of an *ad hoc* desensitization procedure, in order to prevent discontinuation of treatment.

Results: A 57-year-old woman, affected by relapsing-remitting MS, previously treated with interferon β-1a, commenced an oral treatment course with DMF (240 mg b.i.d). One month after the beginning of treatment, the patient experienced an immediate drug-related hypersensitivity skin reaction, characterized by rapid onset of urticaria with confluent wheels and itching within minutes from drug intake, suggesting a causative role for DMF. The immediate nature of the reaction was confirmed by a lymphocyte proliferation test (LPT), which proved negative. Thus, skin prick tests and intradermal tests were also performed but proved negative.

Considering the good clinical response to DMF, we decided to desensitize the patient. To this purpose we used the dose-escalating scheme reported in the Table. The patient developed very mild

urticarial reactions for the first 5 days of the desensitization protocol. Afterwards, no more reactions were observed. The desensitization schedule was implemented for 40 days. Afterward, the patient was able to tolerate the therapeutic dose (480 mg/die).

Conclusions: DMF can be responsible for immediate hypersensitivity drug reactions. Given the increase in the use of this drug for MS, it is important to underline that desensitization can be carried out as a safe and effective method, in order to avoid discontinuation of treatment.

Table 1. Oral desensitization schedule for to DMF*. Dose number Time (min) day 1 to 40 Dose (mg): day 1 to 30 Dose (mg): day 31 to 40 Time (hour) day 41 on Dose (mg): day 41 on 1 0 1 2 0 120 2 30 3 6 1 120 3 60 6 12 12 120 4 90 10 20 13 120 5 120 20 40 6 150 40 80 7 180 50 100 8 210 50 100 9 240 60 120 Total dose: 240 mg Total dose: 480 mg Total dose: 480 mg * Inspired by Castells MC, et al. J Allergy Clin Immunol. 2008; 122:574-80.

1277 | Usefulness of histamine and tryptase in allergic reaction during surgery

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Case Report: Background: This is the case of a 23 years old woman with a previous history of ictus (MRI findings of ischemia in middle cerebral artery area), suspected metal allergy, smoker (10 cigarettes per day), with patent foramen *ovale* (PFO). She underwent PFO closure on cardiopulmonary bypass (CPB) in right minithoracotomy access. After induction of general anesthesia (propofol 100 mg, fentanyl 200 mcg, succinylcholine 75 mg, cisatracurium 14 mg), she developed three wheals on forehead, neck and chest so, after aspiration blood samples for tryptase and histamine dosing, she received antihistaminic and steroids as treatment of allergic reaction. On CPB (maintenance of general anesthesia, with continuous infusion of propofol and fentanyl and a single bolus of cisatracurium), she had severe hypotension treated with fluids resuscitation, vasopressors, epinephrine and again steroids (after a second blood sampling), with adequate control of perfusion pressure. At the end of the surgery, the patient was hemodynamically stable with low inotropic and vasopressor support, with no signs of bronchial obstruction, so she was extubated successfully and accompanied to ICU.

Method: Serum tryptase and plasma histamine were measured by a fluoroenzyme immunoassay (ImmunoCAP; ThermoFisher, Uppsala, Sweden) according to the manufacturer's instructions.

Results: The value of histamine release at the induction was 17.7 ng/mL and tryptase serum level was 3.4ug/L and after 24 hours respect 0.82 and 1.91

Conclusion: These markers can be both easily measured, ant they are useful for confirm or not the IgE mediated allergic nature of a reaction in the real-life setting of drug allergy. In this case we demonstrated that mast cells have not implicated in reaction for not increasing of tryptase. The clinical presentation does not allow to distinguish the experience allergic forms from non-allergic. These biological results are useful in case of new surgery, to allow an accurate and safer diagnostic approach

1278 | "Baboon syndrome" in relation to the intake of lysine carbocysteinate

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Case Report: Introduction: Lysine carbocysteinate is an S-acetylated derivative of the natural cysteine amino acid. It produces a decrease in the viscosity of the bronchial secretions, so it facilitates expectoration. Using as mucolytic or expectorant

Baboon syndrome is a systemic contact dermatitis characterized by a pruritic, maculopapular eruption, converging on the gluteal area and major flexures, occurring several hours later and up to several days after oral, inhaled, parenteral or by contact with a drug or other agent. The distribution of lesions is pathognomonic although pathogenesis is unknown.

Clinical case: A 68-year-old male, with no prior history of allergy, consulted with his physician for catarrhal disease, treated with lysine carbocysteinate 2.7 g sachets every 24 hours, presenting at 12 hours after the fourth dose, pruritic erythema which included glutes and inguinal folds, has no other symptoms or other lesions. The same day he met his doctor who applied IM corticosteroid, without presenting any clinical improvement so that 5 days later he returned to consult, treating with antihistamine for a week, presenting progressive improvement during the next 7 days.

Materials and Methods: A single blind oral challenge was performed. Patient received lysine carbocysteinate in 2.7 g sachets, every 24 hours for 2 days. 22 hours after the last dose, symptoms reappeared whit pruritus and marked erythema in the gluteal area and inguinal folds, without others symptoms (See image). Being treated with corticoids and antihistamines, presenting improvement in the following 48 hours.

Conclusions: The late reaction with lysine carbocysteinate was checked with the typical lesion of "Baboon syndrome".

This is the first documented case of "Baboon syndrome" produced by lysine carbocysteinate.

1279 | Severe ibuprofen hypersensitivity – case report

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Case Report: Introduction: NSAID is the most frequent drug group involved in hypersensitivity reactions; these can be due to Cox-1 inhibition or an immunological mediated reaction, whether immediate (IgE dependent) or non immediate (T-cell dependent). Case Report

We present the case of a 47 years old female. She was medicated with amoxicillin and clavulanic acid for 8 days for sore throat with fever, asthenia and myalgia. She got apyretic but she still had sore throat, asthenia and myalgia and was therefore prescribed with another antibiotic for another 8 days, maintaining some asthenia and myalgia. During all this time she was taking ibuprofen 600 mg SOS to pain and fever. In February she starts with an erythematous/violaceous non pruriginous rash with fixed lesions that started in the thighs but then generalized throughout the integument. She went to the emergency room and was admitted to the infectious diseases ward. It was performed blood cells count, biochemical analysis, urinalysis, serologic tests that showed leukopenia and abnormal liver enzymes. She was medicated with systemic corticosteroids with resolution of the symptoms within weeks. She was referred to de Allergy Outpatient Department. We performed lymphocyte transformation test to ibuprofen that was positive, and instructed the patient to avoid this drug group. She refused any other diagnostic test.

Conclusion: In this case we report a severe reaction to ibuprofen, luckily not the most common reaction to this drug, and the importance of the lymphocyte transformation test in the diagnosis.

1280 | Continuation of treatment with etanercept despite drug hypersensitivity

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Case report: Introduction: Biological drugs can cause hypersensitivity reactions, including allergic reactions, while modulating the immune system. Aim of our study is to present the case of adult patient with drug hypersensitivity syndrome (DHS) induced by etanercept.

Case presentation: A 43 years old female with more than 15 years history of rheumatoid arthritis (RA) was referred to Vilnius University Hospital "Santariskiu Klinikos" for allergologist and clinical immunologist consultation. Previously patient was treated with tocilizumab, which was discontinued due to facial swelling. In February of 2016 once per week intramuscularly Enbrel (etanercept) was prescribed. A pruritic erythematous solid skin infiltrate appeared after the 4th injection of the drug and persisted for 2 weeks. Same, but more severe rash was observed after the 5th injection. Treatment was stopped. Skin biopsy confirmed drug induced urticarial skin hypersensitivity reaction. Intradermal test with Enbrel (1/10) was positive, as well as patch test with nickel (3+) and thimerosal (2+). Diagnosis of DHS induced by etanercept was made. Whereas the drug was vital for the treatment of RA and allergic reaction was not severe, etanercept was continued to use in addition with local treatment of corticosteroid ointment and antihistamines, also under every three months allergist supervision.

Conclusion: True hypersensitivity to etanercept was confirmed. Despite local hypersensitivity reactions, treatment was continued successfully.

1281 | Sonovue® (sulfur hexafluoride), immediate hypersensitivity reaction in echocardiography

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Case Report: Background: SonoVue® is a new generation radiologic contrast agent, composed by a suspension of phospholipid-stabilized sulfur hexafluoride. It is used to improve the echogenicity and the endocardial border delineation during echocardiography and further applications. It belongs to a new generation of contrast with a real good safety profile, and there are very few published cases reporting adverse reaction to this agent.

Case Report: We report a case of a 22-year old man with history of hypertrophic cardiomyopathy (carrier of TNNT2 mutation) and an abnormal electrocardiogram. A contrast-enhanced echocardiography with SonoVue® was realized. Within a few seconds after a SonoVue® intravenous bolus injection (not previously used in this patient), he developed nausea, vomiting, a skin reaction with pruritic and isolated hives in chest, back, abdomen, upper and lower limbs without other symptoms. He improved in 20 minutes after intravenous injection of 20 mg of methylprednisolone and an antihistamine.

Methods and Results: Allergologic study was performed, once the informed consent form had been signed. Basophil Activation Test (BAT) was negative to SonoVue®. Skin prick and intradermal tests were performed. Prick test with undiluted (5 mg/mL) solution was negative. Intradermal tests with a 1/100, 1/10 dilution and undiluted were also negatives.

However 40 minutes after the undiluted intradermal test the patient developed few hives in the outside of the elbow and the back of left hand. He progressively improved without treatment. We considered that the allergologic study was positive due to the reproducibility of clinical reaction after intradermal skin test.

Conclusion: We present a case of immediate hypersensitivity reaction to SonoVue®.

According the results obtained (negatives skin tests and BAT) and making reference to the few literature published and also because was the first administration of SonoVue® in this patient, we consider that this is not a IgE- mediated hypersensitivity reaction to SonoVue®.

As an alternative radiologic test for the medical follow-up of this patient his cardiologist decided to realize a cardiographic NMR.

1283 | Dress syndrome caused by anti-tuberculosis drugs in a child

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Case Report: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) is sever, life-threatening drug reaction with long latency period. This syndrome is characterized by cutaneous rush, fever, lymphadenopathy, hematological findings (eosinophilia, leukocytosis, etc.) and visceral involvement (hepatic, renal and lung involvement). The mortality of DRESS syndrome is estimated to be around 10%.

We report a case of DRESS syndrome caused by anti-tuberculosis drugs (streptomycin and isoniazid). Our patient was 13 years old boy with rhombencephalitis. Three weeks after starting therapy with meropenem, vancomycin, isoniazid, rifampicin, pyrazinamide and streptomycin he developed fever (39.8°C), cutaneous rush, leukocytosis (21.4 x 10) with eosinophilia (13%) and atypical lymphocytosis (10%), hepatitis (AST 166 U/l, ALT 287 U/l) with lymphadenopathy at the hepatic hilum and pleural effusion. Immediately after appearing symptoms we stopped above mentioned therapy. We gave corticosteroides with supportive and symptomatic therapy and after twenty days all symptoms disappeared.

After 3 months we performed allergy work-up (patch tests and if the patch tests were negative we performed intradermal tests with delayed reading). Patch tests were positive to streptomycin and isoniazid. Patch tests and intradermal tests with delayed reading for other drugs were negative. We did not performed lymphocyte transformation test.

We concluded that DRESS syndrome was caused by isoniazid and streptomycin. This is the first described case that isoniazid and streptomycin caused DRESS syndrome in child.

TUESDAY, 20 JUNE 2017
TPS 48
DRUG ALLERGY: DIAGNOSIS

1284 | Differential features between DRESS syndrome and angioimmunoblastic T cell lymphoma

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Introduction: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, a severe adverse drug-induced reaction, is characterized by skin rash, blood eosinophilia and systemic organ involvements including lymphadenopathy. The estimated incidence ranges from 1 in 1000 to 1 in 10 000 drug exposures. However, similar manifestations may be found in patient with angioimmunoblastic T cell lymphoma (AITL). It should be needed to exclude a possibility of AITL in suspicious cases of DRESS syndrome manifested with lymphadenopathy, because AITL is an aggressive form of lymphoma.

Objectives: We are aiming to look at differential features between DRESS syndrome and angioimmunoblastic T cell lymphoma.

Results: There were no differences in the degree of fever and the blood levels of leukocytes, lymphocytes, eosinophils, platelets, C-reactive protein, ferritin, beta2-microglobulin and lactic dehydrogenase between AITL and DRESS syndrome groups. RegiSCAR scores did not differ between the two groups. However, blood levels of alanine aminotransferase ($P < .05$) and creatinine ($P < .05$) were lower and higher in patients with AITL compared to DRESS syndrome, respectively. Naranjo scores were lower in patients with AITL than in those with DRESS syndrome ($P < .001$).

Conclusions: In patients with suspected DRESS syndrome accompanying lymphadenopathy, low causality probability score and renal dysfunction may suggest the diagnosis of AITL rather than DRESS syndrome. Under such a situation, lymph node biopsy should be performed earlier to exclude the possibility of AITL.

1285 | Anaphylaxis thiocolchicoside: two new cases

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Introduction: Allergic reaction to thiocolchicoside is a rare condition. Two new cases of secondary systemic reaction to i.m thiocolchicoside are presented below.

C.G, a 62 years old female was treated for low back pain with piroxicam and thiocolchicoside. After a few minutes she presented anaphylaxis (Grade III Ring and Messmer). She was treated with methylprednisolone sodium hemisuccinate, chlorphenamine maleate, oxygen and ranitidine and then released after a few hours. Subsequently she has tolerated paracetamol.

M.A., a 67 years old male was treated for bone and joint pain with thiocolchicoside and diclofenac. After a few minutes he presented anaphylaxis (Grade III Ring and Messmer). He was treated with adrenaline, corticosteroids and anti-histamines. Then, ECG changes and increased level of Troponin I were detected in the Emergency Room (Kounis syndrome). Subsequently he tolerated paracetamol and codeine. In clinical history he experienced an episode of facial angioedema after thiocolchicoside injection years before.

Objectives: Patients were subjected to skin tests with thiocolchicoside 2 mg/mL: skin prick test (SPT) with 1:10 (0.2 mg/mL) and I.D. with 1: 10 000 dilution (0.0002 mg/mL). Then they were tested respectively for piroxicam and diclofenac: SPT with 1/10 dilution and I.D. from 1/10 000 to 1/10. We also tested 10 healthy people as negative controls.

Results: Both patients resulted positive to SPT and ID with thiocolchicoside and negative, respectively, to piroxicam and diclofenac. Then, they were subsequently subjected to tolerance test (TT), respectively, with piroxicam and diclofenac: C.G without reaction; M.A. experienced a diffuse erythema and urticaria after 0.15 mg i.m. diclofenac injection. Serum tryptase was measured in acute phase (17.4) and at baseline (5.5). Then a TT for meloxicam was performed without reactions.

Conclusions: In case of severe systemic reaction all efforts must be aimed at seeking an IgE-mediated reaction to the drugs involved. So we performed skin tests also for drugs, such as NSAIDs, for which we generally consider a different underlying pathogenetic mechanism. Furthermore drugs of less allergological interest, such as thiocolchicoside, should also be assessed. These two cases of anaphylaxis to thiocolchicoside can be added to the few described in literature.

1286 | Anaphylactic reaction due to an excipient included in an injectable corticosteroid formulation

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Case Report: Introduction: Carboxymethyl cellulose or carmellose is a hydrophilic derivative of cellulose used as excipient in injectable and oral drugs, as active principle in bulk-forming laxatives and as an

additive in food products (E-466). It is also used as lubricant *eye drops*.

Case Report: A 48-year-old male with a poorly controlled severe allergic asthma, severe atopic dermatitis and gastroesophageal reflux, presented a chronic low back pain secondary to L4-L5 radiculopathy. Infiltration with mepivacaine and a commercial preparation of triamcinolone (triamcinolone acetonide, polysorbate 80, carmellose) was recommended, presenting an anaphylactic shock 90 minutes after first dose. Treatment in emergency room and hospitalization was required, developing a delayed reactivation with generalized cutaneous erythema 24 hours later. Serum tryptase level was 40 μg/L within minutes of anaphylaxis and the level gradually reverted to normal (8 μg/L) over the next 24 hours.

Material and Methods: Skin prick-test with the commercial preparation, polysorbate, carmellose (lubricant *eye drops)*, latex and mepivacaine were done. Subsequently were performed prick and intradermal-test with several corticosteroids (hydroxycortisone, methylprednisolone, betamethasone, paramethasone, prednisone, dexamethasone, mometasone, fluticasone, deflazacort and beclometasone).

Finally, oral challenge-test with prednisolone and deflazacort as well as intramuscular challenge-test with mepivacaine and betamethasone were also made.

Results

Prick-tests were strongly positive with both commercial preparation of triamcinolone and carmellose, but negative with polysorbate, latex and mepivacaine. All skin tests performed with other corticosteroids showed negative results. Challenge-tests were also negative.

Conclusions: We present a patient with anaphylactic shock after the administration of a commercial preparation of triamcinolone (which also includes polysorbate 80 and carmellose) due to sensitization to carmellose, one of the excipients in this formulation. Possibility of performing a prick-test with lubricant *eye drops* as screening of allergy to carmellose must be highlighted. Allergy to excipients should be always ruled out in drug hypersensitivity reactions.

1287 | Multiple allergic contact blepharitis due to azithromycin and tropicamide eye drops and povidone iodine solution

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Introduction: Blepharitis is an acute or chronic inflammatory process of the eyelids, caused by infection, allergies or other conditions. Allergic blepharitis may occur in atopic or non-atopic subjects, and may be induced by multiple substances acting as direct or indirect antigens.

Azithromycin and moxifloxacin are antibiotics used topically for the treatment and prevention of bacterial conjunctivitis. Tropicamide and cyclopentolate are cycloplegic agents used in ophthalmology for the induction of mydriasis due to its parasympatholytic action.

We present a case of contact blepharitis due to povidone iodine, Azydrop® and tropicamide.

Objectives: A 63 years old man, with hypertension and dyslipidemia, followed in treatment with different eye drops for infectious prophylaxis in relation to ophthalmologic intervention, who refers eight hours after third tropical administration of Azydrop® (azithromycin and medium chain triglycerides), Vigamox® (moxifloxacin, boric acid and hydrochloric acid) and tropicamide (benzalkonium and edetate disodium), light conjunctive hyperemia, pruritic erythema of the eyelid with parchment of the skin. Previously he presented similar symptoms with a topical povidone iodine solution application.

Prick tests were performed with tropicamide, Azydrop®, povidone iodine, Vigamox®, tetracaine, oxybuprocaine and cyclopentolate. Also, patch test with povidone iodine, Azydrop®, Vigamox®, tropicamide and cycloplegic. Finally, controlled exposure test with Azydrop®, tropicamide, Vigamox® and cycloplegic were performed.

Results: * Prick tests with tropicamide, Azydrop®, povidone iodine, Vigamox®, tetracaine, oxybuprocaine and cyclopentolate were negative.

* Patch test with povidone iodine was positive.

* Patch test with Azydrop®, Vigamox®, tropicamide and cyclopentolate were negative.

* Controlled exposure test with Azydrop® and tropicamide were positive, presenting at 8 hours of administration, erythema and edema of eyelids that yielded after two days.

* Controlled exposure test with Vigamox® and cyclopentolate were negative.

Conclusions: We report a case of a multiple allergic contact blepharitis caused by Azydrop® and tropicamide eye drops and povidone iodine solution. In addition we have demonstrated tolerance to Vigamox® and cyclopentolate.

1288 | Concomitant immediate and delayed type hypersensitivity to amoxicillin in the same patient: two case reports

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Case Report: Adverse drug reactions to amoxicillin (AMX) usually present with urticaria or exanthema resulting either from type I or type IV sensitization. We present two cases showing clinical manifestations of both immediate and delayed type hypersensitivity to AMX with corresponding skin test reactivity.

Patient 1: A 54-year-old female patient developed a generalized pruritic, partly maculopapular exanthema after two doses of AMX/clavulanic acid (AMX/CL) administered for an erysipelas on the abdomen. Antibiotic therapy was switched to clindamycin for 14 days. The

exanthema persisted and was accentuated in the large folds, and facial angioedema occurred despite administration of antihistamines and prednisone. Subsequently, the patient showed disseminated desquamation. A diagnosis of Symmetric Drug Related Intertriginous Flexural Exanthema (SDRIFE) was retained. Skin tests with AMX and AMX/CL were positive after 20 minutes and at 24 hours. PPL and MDM were negative, benzylpenicillin and piperacillin/tazobactam were positive after 24 hours only, clindamycin was positive in the immediate reading only. Reexposure with aztreonam and cefuroxime was tolerated. SDRIFE was attributed to amoxicillin, angioedema may have been caused by clindamycin.

Patient 2: A 23-year-old female patient was treated for helicobacter pylori gastritis with AMX/CL, clarithromycin and pantoprazole for 7 days. On day 8 she developed a maculopapular exanthema persisting for 3 days. Dizziness, facial swelling and dyspnea occurred at the same time for one day only. Skin tests were positive for AMX and AMX/CL after 20 minutes and persisted for more than a week. Skin tests for clarithromycin and pantoprazole were negative.

Both patients had an unusual both immediate and delayed skin test reactivity to AMX. In both patients clinical manifestations represent more likely a T cell mediated mechanism, although also immediate type symptoms were present.

Investigations are ongoing with basophil activation tests (BAT) and lymphocyte transformation tests (LTT) to elucidate the concomitant presence of immediate and delayed type hypersensitivity in the two patients. So far it is unclear whether one single epitope or two different determinants on the AMX molecule are responsible for this unusual concomitant sensitization pattern.

1289 | Performance of the basophil activation test and skin test in a patient with sugammadex-induced anaphylaxis and his monozygotic twin brother

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Case Report: Introduction: The role of genetics in allergy development is well accepted. However, the relative contributions of genetics to development of IgE-mediated anaphylaxis have not been well clarified. To examine this issue, the subjects of this case report included a patient with perioperative anaphylaxis and his monozygotic twin brother. The patient developed severe anaphylaxis during laparoscopic appendectomy when he was 13 years old. Postoperative skin prick tests revealed that sugammadex, a newly developed agent for reversal of neuromuscular blockade, was the causative agent. Several other cases of sugammadex-induced anaphylaxis have also been reported. However, the causative epitopes have not been fully elucidated.

Objective: We performed skin tests for sugammadex on the two brothers to compare their results. Basophil activation tests (BATs) were also performed using flow cytometry, to compare the ratio of activated basophils after adding five different concentrations of sugammadex to blood specimens obtained from both of them. Basophils were selected on a CD3-/CRTH2 + gate and at least 500 basophils were counted. We used both CD63 and CD203c as markers for activated basophils. We then tested γ-cyclodextrin as a candidate epitope for the BAT, because sugammadex is a modified form of γ-cyclodextrin containing eight thiopropionate side chains.

Results: The patient, but not his brother, showed a positive reaction to sugammadex in skin prick tests. Subsequently, intradermal tests were performed on the patient's brother, which showed negative reactions to sugammadex. The BAT revealed that the rate of activated basophils in the patient, but not in his brother, increased in a dose-dependent manner. The number of activated basophils in the patient's brother was comparable to the average value we previously obtained from healthy volunteers. Significant basophil activation was induced by adding 10^4 μg/mL of γ-cyclodextrin only in the patient.

Conclusion: The genetically identical twins evaluated in this report showed different reactions to skin tests and BATs, suggesting that pre-sensitization to the antigen, rather than genetic factors, likely play an important role in the development of sugammadex-induced anaphylaxis. Moreover, γ-cyclodextrin might be the epitope of sugammadex. We believe that these findings might be helpful in unveiling the mechanisms of sugammadex-induced anaphylaxis.

1290 | Allergy to daptomycin

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Introduction: Daptomycin (a natural cyclic-lipopeptide) is a bactericide active against Gram positive microorganisms. It was approved for clinical use in Europe in 2006 for the treatment of skin infections, as well as *S. aureus* bloodstream infections and infectious endocarditis. Its mechanism of action includes an attack to the bacterial membrane with depolarization and cell death. Studies confirm that it is a well tolerated antibiotic. The most common adverse reactions include headache, diarrhea, exanthema and high levels of hepatic transaminases. Severe adverse effects occur in <2% of cases, including hypersensitivity reactions, which have an unknown frequency of onset.

Objectives: We report the case of a 68-year-old female. She had a history of intrinsic asthma, arterial hypertension, severe gastroesophageal reflux and gastric polyps. She was admitted to Surgical Department in our hospital because she presented a duodenal fistula after a Roux-en-Y gastric bypass, suffering a septic shock. She also developed a postoperative biliary fistula and catheter infection.

She started antibiotic treatment with piperacillin+tazobactam and linezolid. During her admission she need multiple antibiotics due to persistent leukocytosis and high levels of c-reactive protein.

She developed, after the second intravenous infusion of daptomycin, an itchy erythematous rash on her chest, abdomen, back, legs and arms. When first seen by us physical examination revealed a symmetrical diffuse erythematous papular rash predominantly in abdomen and flexural areas, spreading through legs and arms. Discontinuation of daptomycin and treatment with antihistamine and corticosteroids improved skin symptoms.

Several months later she was referred to our department for further evaluation. Intradermal test with daptomycin (0.5 mg/mL) was performed to the patient.

Results: We achieved a complete resolution of the symptoms with symptomatic treatment and discontinuation of daptomycin.

Cutaneous test with daptomycin was positive and confirm the relationship with skin rash. She was advised to avoid treatment with daptomycin.

Conclusions: Daptomycin is an antibiotic with a very good safety profile. There are few references about hypersensitivity reactions associated with daptomycin. It has been described a generalized exanthematous pustulosis, acute angioedema, urticarial rash and anaphylaxis.

In our case, positive skin tests and improvement of skin symptoms after drug discontinuation suggest that type I hypersensitivity reaction is involved.

1292 | Looking beyond the chemotherapy: A case of anaphylaxis to mesna

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Case Report: Introduction: Studies have found that cyclophosphamide is the treatment of choice for patients' progressive multiple sclerosis. Sodium 2-mercaptoethane sulfonate (mesna), is a well-known adjuvant to cyclophosphamide that is widely used for the prevention of hemorrhagic cystitis. Cutaneous reactions (such as rash) and angioedema have been described as drug eruptions to mesna.

Case Report: We report the case of a 76-year-old man, with no atopic history, who has experienced two anaphylactic episodes during the twenty-sixth infusion of cyclophosphamide and mesna for a multiple sclerosis. About 10 minutes after the beginning of the infusion, he presented urticarial rash and mild hypotension. The infusion was stopped and he was given a histamine1-receptor antagonist. The patient's symptoms resolved within 15 minutes.

Skin prick tests (SPTs) were performed, three months later, with cyclophosphamide and mesna. Histamine and codeine were used as positive controls.

Results: SPTs were positive for mesna at the concentration of 1 mg/mL (10-2). SPTs stayed negative with cyclophosphamide at the concentration of 10 mg/mL (10-3).

Controls were both positive with histamine (7 mm) and codeine (5 mm).

Conclusion: We report a case of anaphylaxis to mesna with positive SPTs. Physicians should be aware that this drug can be responsible for anaphylaxis. This observation also highlights the necessity to perform a full-allergy assessment with all potential culprit drugs.

1293 | Functionality of specific IgE to penicillins investigated by passive cutaneous sensitization

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Introduction: Immediate reactions to penicillin are considered mediated via specific IgE on mast cells. However, only the minority of patients with penicillin-allergy have, positive specific IgE, and patients with full-blown anaphylactic shock may be IgE negative.

Objectives: The aim of this study was to investigate the functionality of specific IgE to penicillin.

Method: Based on the classical Prausnitz-Küstner technique, passive sensitization of the skin of non-allergic recipients with sera from six penicillin-allergic IgE-positive (median 5.0, range 0.4-9.0 kU/L) donors was performed. Subsequently skin testing, oral and intravenous challenges with penicillin and ampicillin were performed in six recipients. Dose-time responses in the sensitized areas were registered.

Results: With 2/6 sera it was possible to obtain reactions. With one serum (IgE-positive to penicillin V and G), skin prick test with penicillin V and intracutaneous test with benzylpenicillin and ampicillin were consistently positive in all recipients, and all were also positive to oral challenge with penicillin V. With the other reactive serum (IgE-positive to ampicillin and amoxicillin), skin prick test was negative, but intracutaneous test with ampicillin elicited reactions in all recipients. With the two reacting sera, oral pivampicillin only elicited reactions in 2/6 and 1/6 recipients respectively. Both sera elicited reactions in all recipients upon administration of 1000 mg of ampicillin intravenously as a bolus. When ampicillin was titrated intravenously, difference in dose-time-response relationship between the two reacting sera was revealed; the serum with s-IgE to ampicillin elicited wheals faster (median 18.5, range 11-45 minutes) than the serum with s-IgE to penicillin V/G (median 69.5, range 60-75 minutes) ($P = .002$), and the cumulated dose needed for wheal development was lower (median 15 mg, range 10-30 mg, for serum

with IgE to ampicillin and median 145 mg, range 60-160 mg, for serum with IgE to penicillin V, respectively) ($P = .002$).

Conclusions: The results points towards differences in the quality of specific IgE to penicillins that may explain why some patients with measurable specific IgE tolerate penicillin and why others experience full blown anaphylaxis without measurable specific IgE.

1294 | Buccal provocative test in saliva for determination of hypersensitivity to dental materials

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Introduction: A method for diagnosing allergy to dental materials (prosthetic materials and local anaesthetics) was described. For this the increase of peroxidase activity in 54 patients with positive clinical history of allergy to dental materials and negative results of the other tests was determined in the saliva before and after challenging allergen. The presence or absence of sensitization of leucocytes of the oral mucosa was determined according to the color intensity of substrate-chromogen mixture.

Objectives: Investigation of hypersensitivity reactions to dental materials due to the formation of IgE-antibodies fixed on leukocytes in the mouth.

Results: It was revealed that in 30.4% of cases with a positive history of intolerance to dental materials and negative data from other diagnostic methods, peroxidase test was positive.

Conclusions: (i) Saliva is a preferred material for the non-invasive study since receiving material, and also due to the fact that a place In situ biodegradation of dental materials, and of allergic reactions. (ii) Determination of peroxidase activity in the saliva reveals antibodies to immunoglobulin E receptors associated with the cell membrane of neutrophils. (iii) Further research is needed, which would have allowed to identify all the possible mechanisms of intolerance to dental materials.

1295 | The phenotypes of patients with immediate drug specific hypersensitivity to nonsteroidal anti-inflammatory drugs

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) are the second most reported cause of drug hypersensitivity reactions (HSR). Oral provocation tests (OPT) are considered the gold standard for diagnosis of HSR to NSAIDs and the contribution of skin testing is not fully determined.

Objectives: In this study we aim to characterize the clinical manifestations, the results of skin test (ST) and tolerance to acetylsalicylic acid (ASA) in patients with immediate HSR to one specific NSAID drug.

We retrospectively studied all patients with suspected immediate reaction (within 1 hour after drug intake) to one NSAID and tolerance ASA or other NSAIDs-specific COX1-inhibitor presenting to our Drug Allergy Outpatient Department in the last two years. We reviewed the clinical patient files, particularly the detailed manifestations of the reactions related to NSAID ingestion, the results of skin prick tests (SPT), intradermal tests (IDT) to the culprit drugs and OPT to ASA in cases of doubt in tolerance.

Results: Thirty-five patients were included, 66% female, mean age 52 years-old (max. 75, min. 21). Culprit drugs were metamizol (10), diclofenac (9), ibuprofen (4), paracetamol (4), etoricoxib (3), naproxen (2), ASA (2), piroxicam (1), nimesulide (1) and aceclofenac (1).

Clinical manifestations included anaphylaxis in 18 cases (51%) and urticaria/angioedema in 17 cases (49%). ST with the suspected drug were performed in 17 patients: all SPT were negative and IDT were positive in immediate reaction in 7 cases (3 for diclofenac, 3 for metamizol and 1 for paracetamol). No late reactions to IDT occurred. Five of the patients with 7 positive IDT were submitted to ASA OPT and all were negative.

Conclusions: In our case study, 51% of the patients with NSAID-specific HSR presented with anaphylaxis. The most frequently drugs involved were metamizol (10), diclofenac (9) and, paracetamol and ibuprofen (4 each). Forty-one percent of the patients that were submitted to ST had a positive reaction, which is in favor of an IgE mediated mechanism. ST can be useful diagnosing NSAIDs type I HSR, particularly if metamizol, diclofenac and paracetamol are involved.

1297 | Skin tests positivity in consecutive pediatric and adult patients referred to an outpatient department for preoperative allergy risk assessment

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Introduction: The incidence of perioperative allergic reactions to anesthetic agents varies from 1 in 3500 to 1 in 20 000. Skin tests (ST) are considered standard part of the preoperative workup of patients in many countries. Their diagnostic value varies broadly between the separate drugs. The possibility of both false-positive and false-negative results of the testing could have serious implications in terms of prevention of life-threatening intra- and

perioperative allergic/anaphylactic reactions. Preoperative decision-making could be all the more challenging in the pediatric age. We conducted a retrospective analysis on skin testing log-books over a period of one year for children and the last two months of the same year for adults in an attempt to draw conclusions about their utility in preparing patients for subsequent surgical treatment.

Objectives: We compiled a database of the ST we did on patients referred to our outpatient clinic for preoperative allergological assessment over a period of one year for children (0-17 years) and two months of the same year for adults (≥18 years). Data collected included age, gender and the tested anesthetic agents. The spectrum of the medicinal substances tested involved atropine, promethazine, diazepam, ketamine, pipecuronium, suxamethonium, metamizol, fentanyl, lidocain, bupivacaine, atracurium, galantamine, midazolam, thiopental, pethidine, propofol, levobupivacaine. All tests were done by 'scratch' technique, diameters of the wheal and flare ≥3 mm were recorded.

Results: We ended up with ST of 380 children (258 boys) and 116 adults (50 men). In the separate pediatric strata we had 232 children aged 0-6 years, 94 aged 7-12 years, and 54 aged 13-17 years. In 21 (5.5%) of all children (12 boys) we had diameters for wheal and flare ≥3 mm. For 4 of the tested agents no ST ≥3 mm were documented, while for 2 drugs (atropine and diazepam) ST of ≥3 mm were recorded in 5 children. In the pool of 116 adult patients ST ≥3 mm were documented in 9 subjects (7.8%): 7 to pethidine and 6 to galantamine. During the same 2 months, for which we had data for the adults, no ST ≥3 mm for children were recorded.

Conclusions: ST positivity to anesthetic agents is a rare phenomenon, especially in children, and cannot replace clinical judgement. Positive ST are more prominent in adults, mostly to the non-specific histamine liberators pethidine and galantamine.

1298 | Late reaction to clavulanic acid

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Case Report: Introduction: Clavulanic acid (CA) is a potent beta-lactamase inhibitor whose prescription in combination with amoxicillin has increased in daily medical practice. Initial studies considered CA to have poor immunogenicity, more recently hypersensitivity reactions have been reported.

Clinical cases: 1) A 45-year-old man described a pruritic maculopapular generalized exanthema on the 7th day of treatment with amoxicillin + CA for pharyngitis. In order to evaluate beta-lactams allergy, beta-lactam-specific IgE were performed and negative, skin prick tests (SPT) and intradermal (ID) with major (PPL) and minor (MDM) determinants and penicillin, amoxicillin, amoxicillin + CA, ampicillin and cephalosporins were also negative in immediate and late reading as the epicutaneous tests. Provocation test (PT) with amoxicillin + CA with prolongation for 8 days was performed, starting on the 5th day a pruritic, maculopapular and generalized exanthema. SPT and ID were then run to CA alone with positivity observed at 48 hours in the ID with the 20 mg/dL. He was then challenged with amoxicillin for 8 days without complications. The diagnosis of delayed hypersensitivity reaction to CA was established.

2) A 26-year-old man previously studied for suspected penicillin allergy that was excluded. After that he performed 5 cycles of amoxicillin and 1 of amoxicillin + CA, without reactions. In May 2016 is treated again with amoxicillin + CA and started a generalized exanthema on the 2nd day of treatment. A new evaluation was made: specific IgE for beta-lactams negative, SPT and ID tests with PPL, MDM, penicillin, amoxicillin, amoxicillin + CA, ampicillin and cephalosporins negative on immediate and late reading, such as epicutaneous tests. He was submitted to PT with amoxicillin + CA with appearance of pruritic maculopapular exanthema generalized at the 5th day of treatment. After that, SPT and ID with CA isolated were conducted with immediate positive reading in the ID with the 20 mg/dL. He did PT with amoxicillin with prolongation for 8 days, without reactions, thus leading to late hypersensitivity to CA.

Conclusion: The number of hypersensitivity reactions to CA described has increased. Usually immediate reactions are involved, but later reactions are rarely reported. The authors describe 2 cases of late reaction to CA where the possibility of testing the isolated molecule was essential for diagnosis.

1299 | Ace inhibitor-associated angioedema

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Introduction: Angiotensin converting enzyme inhibitor (ACEi)-mediated angioedema (AE) is an infrequent adverse drug effect (prevalence between 0.1% and 0.3%), resulting from a decrease in the bradykinin catabolism, which increases endothelial permeability and produces swelling of soft tissues

Objectives: To analyse a series of cases of ACEi-mediated AE submitted to an allergy department in one-year time in order to identify the demographic and clinical characteristics and to investigate potential risk factors

Results: We performed a retrospective descriptive analysis of cases attended at the Allergy Department and identified by searching the terms "angioedema" and "Angiotensin converting enzyme inhibitors" in the medical database from January 2015 to January 2016. Demographic, clinical and therapeutic data were collected from the electronic medical records.

Thirty-four patients were identified, 19 male (56%) and 15(44%) female, mean age 72.1 years (41-87), 32 Caucasians (94.1%). The most frequent localization of the oedema was facial, involving the lips in 12 cases (21.4%), tongue in 10 (17.8%) and uvula in 7 (12.5%). None of the patients reported associated clinical manifestations or oedema involving other localizations. Enalapril was the most frequent ACEi implicated in the clinical manifestations (19 patients, 55.9%), followed by captopril (4 cases, 11.8%), lisinopril and ramipril (3 cases each, 8.8%). Other antihypertensive drugs were the most common concomitant medications (21 patients, 15.4%), followed by hypolipidemic drugs (17 patients, 12.5%) and proton pump inhibitors in 13 (9.5%) patients. Time from the first intake of ACEi to the episode of angioedema varied from several years in 11 cases (32.3%) to months in 4 cases (11.8%) or few days in 3 cases (8.9%), although it was not reported in 15 cases (44.1%). Recurrence despite ACEi discontinuation was reported in 5 cases (14.8%), but in 6 cases (17.6%) no information about recurrences was provided

Conclusions: ACEi-mediated angioedema characteristically involves the orofacial area and must be suspected in patients undertaking any ACEi. Time from ACEi introduction to the angioedema event is highly variable. Angioedema may relapse after discontinuation

1300 | Anaphylaxis due to lysine clonixinate during hemodialysis—First case report of lysine clonixinate allergy

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Case Report: Background: Anaphylaxis during hemodialysis is reported as a low-frequency event. When it happens, latex, ethylene oxide, heparin and ACE Inhibitors are the main culprits. Nonsteroidal anti-inflammatory drugs (NSAIDs) are less frequent as an anaphylaxis culprit during hemodialysis. For the diagnosis of hypersensitivity reactions to NSAIDs, cutaneous tests are not standardized for most of them. The usefulness of skin testing has been documented for pyrazolones, but for the rest of the NSAIDs group the sensitivity and specificity is very variable, requiring most of the time considering oral provocation challenges.

Case Report: 63 years old, male, caucasian, in hemodialysis, because of diabetic nephropathy. At the beginning of the hemodialysis session, heparin is administered in the blood circuit. Later due to a toothache secondary a molar exodoncia in the process of dental implant treatment, lysine clonixinate is administered. One minute after the start of the infusion, the patient presented generalized pruritus, eyelids angioedema, diaphoresis, dyspnea, audible wheeze, abdominal pain, vomiting, hypotension, bradycardia and conscious compromise. The management included glucocorticoids, H1 antihistamines and crystalloids. The patient responded after the administration of large amounts of crystalloids. Allergologic study 8 weeks after the reaction: latex, unfractioned heparin and lysine clonixinate prick tests: negatives. Intradermal test (IDT) to unfractioned heparin: negative. IDT to lysine clonixinate: positive (1:1.000 dilution). Due to the lack of standardization in dilutions and concentrations for lysine clonixinate skin testing. We performed IDT to lysine clonixinate 50 mg/mL in 1:1000 and 1:100 dilutions to 10 healthy controls subjects, discarding irritative skin reactions. The diagnosis of Anaphylaxis due to Lysine Clonixinate was made, and the use of the drug was prohibited.

Conclusion: NSAIDs hypersensitivity reactions have widely variable clinical presentations. In NSAIDs anaphylaxis, Naproxen, Diclofenac and Ibuprofen are reported as the main culprits. We present the first case report of Allergy due to Lysine Clonixinate according to the literature, a NSAID widely used in Latin America. Also this case report occurred during hemodialysis, where anaphylaxis is reported as a low-frequency event. The lack of use of adrenaline as the first line of treatment is an important concern especially in Chile, where local anaphylaxis guidelines don't exist.

1301 | Flare-up reaction of beta-lactam patch tests after administration of cephalosporins

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Case Report: Introduction: Hypersensitivity reactions with cephalosporins are infrequent, and with uncertain cross-reactivity, according to whether the antigenic determinant is the beta-lactam ring, the dihydrothiazine ring or one of their side chains. Cross-reactivity due to side chains is complex and, in case of cefuroxime and ceftriaxone, some authors report that they have different (Kim et al. Mirakian et al) or similar (Blanca et al) R1 side chain. A recent publication (Romano et al) considers that they share a methoxyimino group in R1 side chain that could be responsible for cross-reactivity.

Case Report: We present a 44 year-old woman undergoing a treatment with levetiracetam after surgery because of cerebral bleeding in 2012. A brain abscess was developed fifteen days later, beginning treatment with vancomycin and ceftazidime for one month with a good tolerance. This treatment was finished and then, ceftriaxone 2 g iv per day was started. Twenty four hours after the second dose, she developed an exanthema on the face and neck, which became generalized, after another two doses. She was diagnosed of drug erythrodermia and ceftriaxone was suspended, receiving treatment with systemic corticotherapy. Erythrodermia was reactivated after step down corticotherapy, so corticosteroids were increased and levetiracetam was replaced for valproic acid. The reaction progressively disappeared, with no residual lesions.

Materials and Methods: We performed an allergy study including prick, intradermal and patch tests with benzylpenicillin, amoxicillin, ampicillin, clavulanic acid, cefuroxime, ceftriaxone, ceftazidime and levetiracetam, as well as prick and intradermal test with PPL and

MDM. Challenge tests with benzylpenicillin, amoxicillin, cefuroxime and ceftriaxone were carried out one month later.

Results: All skin test performed were negative. Twenty four hours after challenge tests with both oral cefuroxime and intramuscular ceftriaxone, the back area where the patches were applied showed a strong itching erythema. Challenge tests with oral benzylpenicillin, and amoxicillin during 5 days were negative.

Conclusion: We present a flare-up reaction of beta-lactam patch tests after the administration of several cephalosporins. Good tolerance to benzylpenicillin and aminopenicillins, together with adverse reactions presented with two cephalosporins with similar R1 side chains (cefuroxime and ceftriaxone) would suggest that the dihydrothiazine ring and/or the methoxyimino group could be responsible for the cephalosporin allergy in our patient.

TUESDAY, 20 JUNE 2017
TPS 49
HEREDITARY ANGIOEDEMA

1302 | The evaluation of the adherence to the prophylactic treatments in hereditary angioedema patients and the potential factors which may affect the adherence: a real life study

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Introduction: There is not any study appraising the level of adherence to prophylactic treatment of hereditary angioedema patients in Turkey.

Objectives: To assess the adherence to the prophylactic treatment in hereditary angioedema (HAE) patients and the potential factors which may affect the adherence.

Method: Sixty patients were asked to full fill a questionnaire including the questions about demographic and clinical features as well as their attitudes related to their medications for HAE.

Results: Sixty-five percent of the patients were female, the mean age was 38.07 ± 12.38 years, 93.3% of the patients were type 1 HAE and 71.7% of the patients were under prophylaxis including danazol and tranexamic acid. In 12 of them danazol were ceased because of the reasons such as pregnancy (n = 8), side effects (n = 3) and inefficacy (n = 1). Fourteen patients were not using the prophylactic treatment regularly due to the fear of the side effect development (n = 11) and the forgetfulness (n = 4). It was observed that the patients who were the only case in their families, had less relatives with HAE and had no exitus due to HAE in their families were more adherent to the prophylactic treatment (P = .008; P = .018; P = .028). 78.3% of the patients stated that the course of the disease improved after the diagnosis and treatment. However the patients using prophylaxis regularly experienced less abdominal pain (P = .03).

Conclusions: The majority of the patients used prophylactic treatment regularly and the major cause of not to use regularly was the fear of the side effect development.

1303 | A clinical care program to evaluate and support individualized treatment in patients with hereditary angioedema (HAE-C1-INH)

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Introduction: Hereditary angioedema due to C1-inhibitor deficiency (HAE-C1-INH) is a rare autosomal dominant inherited disease. The recurrent symptoms are subcutaneous edema and colic-like abdominal pain. Laryngeal edema is rare, but life-threatening if untreated. One of the major goals in the management of HAE-C1-INH patients is the immediate treatment of attacks which can be achieved by self-infusion/self-treatment at home. However, many patients live far away from their treatment center so that educational and medical support might be difficult. In addition, not all attacks are treated adequately, perhaps because they are underestimated. So, on the one hand patients are able to control attacks immediately on the other hand self-medication without support at home may cause considerable mental stress.

Our aim is to set up and evaluate a clinical care program including modern communication platforms (e. g. e-mail, face time, phone call, cell phone 24/7/365, what's app etc.) which might support individualized home treatment in patients with HAE-C1-INH.

Objectives: A patient questionnaire was developed in order to evaluate the current well- being of the patients, how they deal with their current therapeutic approach, the individualization of their treatment regimen and the potential implementation of a communication platform using modern communication platforms. The questionnaire was distributed to the patients during their routine visits after giving informed consent.

Results: A total of 50 patients with HAE-C1-INH type I or type II, age ≥ 18 years were enrolled in this study: 27 females and 23 males aged 18-77 years. The majority of patients (64%) used more than one treatment option (i.v. and s.c.) dependent on their clinical/personal situation. One of the major patient's treatment preferences was the possibility to perform home treatment but with a medical support using modern communication channels such as 24/7/365-phone call service, e-mail, what's app or face time.

Conclusions: Our data indicate the need for the implementation of communication platforms using modern communication channels to support individualized home treatment in C1-INH-HAE patients.

1304 | Blindness, tetraspasticity, and other signs of irreversible brain damage in hereditary angioedema

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Introduction: Hereditary angioedema (HAE) due to a genetic C1 esterase inhibitor (C1-INH) deficiency (HAE-C1-INH) is clinically characterized by recurrent skin swellings, abdominal pain attacks and upper airway obstruction. Patients with undiagnosed HAE-C1-INH are particularly at risk to asphyxiate.

Objectives: Here we report on two patients with HAE-C1-INH who survived severe laryngeal attacks, but, due to a hypoxic brain damage, had irreversible sequelae including central blindness and tetraspasticity.

Results: Patient 1. An actually 29-year-old man had approximately three undiagnosed hand and foot swellings on average per year from age 14 to age 18. Family history for angioedema was negative. At age 18, the patient attended a tattoo studio for tongue piercing. A few minutes after piercing a severe tongue swelling started followed by an upper airway obstruction and loss of consciousness. In an intensive care unit a hypoxic brain damage and a HAE-C1-INH type I were diagnosed. Sequelae of the brain damage were cortical blindness, tetraspasticity with a dystonic component, and an organic delusional disorder with hearing voices as well as various organic intellectual performance deficits, motoric deficits and changes in personality. The patient requires a wheelchair. For the following 11 years up to the present the patient is living in a nursing home. Patient 2. A 20 year-old man with a known HAE-C1-INH had recurrent skin swellings, abdominal attacks and laryngeal attacks since age 8. The family history was negative for angioedema. One night he developed increasing dysphagia and severe dyspnea within 30 minutes. The patient lost consciousness, breathing stopped and the pulse was no longer palpable. In the ambulance, the patient immediately received oxygen, heart massage and defibrillation and was transported to the next intensive care unit. There, a hypoxemic brain damage was diagnosed. The cortex as well as brain stem and cerebellum were damaged. The irreversible sequelae of the brain damage included cerebral cortical blindness, tetraspasticity and athetotic movement disorders.

Conclusions: Patients with HAE-C1-INH may survive a far advanced laryngeal attack having irreversible disabilities as sequelae of brain damage following cardiac arrest and hypoxemia.

1305 | The Turkish version of the angioedema quality of life questionnaire and angioedema activity score: cultural adaptation, assessment of reliability and validity

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Introduction: Recurrent angioedema is a common condition characterized by cutaneous and mucosal swellings which may lead to dyspnea and laryngeal edema. It has a substantial impact on patients' quality of life. Disease-specific tools to assess quality of life impairment and severity of the disease, the Angioedema Quality of Life Questionnaire (AEQoL) and Angioedema Activity Score (AAS) has been generated recently. In this study we aimed to adapt the original German version to the Turkish language and to evaluate its reliability, validity, and sensitivity to change.

Objectives: The Turkish version was developed by performing forward- and back-translation. It was then applied first to 10 pilot patients to test for cognitive debriefing. After establishing its conveniently for Turkish patients, 94 patients with angioedema was asked to fill the AAS, visual analogue scale (VAS), AEQoL and Short Form-12 (SF-12) along with the patient's global assessment for disease severity and quality of life impairment. Sensitivity to change was measured in 63 patients, who completed the instruments again after 4 weeks.

Results: Chronic spontaneous urticaria constituted 62.4% and hereditary angioedema type 1 constituted 28% of the cases while other types were represented in a small proportion. AAS scores had a positive correlation with the VAS scores and number of days with angioedema ($P < .05$). AEQoL scores had a positive correlation with AAS and VAS scores ($P < .05$) but interestingly had no correlation with number of days with angioedema. The instruments showed good correlations with other PRO-tools used and found to be able to discriminate patients with different AAS scores and were sensitive to change. Results of confirmatory factor analysis, convergent validity and multiple linear regression analysis will be presented.

Conclusions: Turkish versions of AEQoL and AAS are sensitive instruments, which will determine efficiently the clinical impact of angioedema and treatment outcomes in Turkish patients.

1306 | Turkish patients' perception about the C1 inhibitor concentrate in the treatment of the acute attacks of hereditary angioedema

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Introduction: C1 inhibitor concentrate is a crucial drug to treat the acute attacks of hereditary angioedema patients.

Objectives: To evaluate patients' opinions about the C1 inhibitor (C1-inh) concentrate which is used in the treatment of acute attacks of hereditary angioedema and to determine the level of satisfaction with this drug.

Method: Fifty-seven hereditary angioedema (HAE) patients who have used C1-inh concentrate before in the treatment of their angioedema attacks were asked to fulfill a questionnaire including various questions about demographic, clinical features and C1-INH concentrate using.

Results: Sixty-five % of the patients were female, 94.7% of them were type 1 HAE, the mean age and age of diagnosis were 38.11 $\pm$ 12.6 and 29.95 $\pm$ 13.85 years respectively. Thirteen patients did not have the family history. Forty patients were under prophylaxis (mostly danazol, n = 39). The mean duration of the C1-INH concentrate using was 4.07 $\pm$ 1.76 years. Patients have used this drug on average 6 times over the past year. All the patients stated that they had difficulties to be injected with this drug in emergency units due to the unawareness of the healthcare professionals about HAE and C1-INH concentrate. A 61.4% of the patients reported overall satisfaction about the effects of drug. On the other hand, 43.8% of the patients stated that the drug should have more practical application while 52.6% told that the drug should be more easily accessible and should be found in the emergency rooms of all the hospitals.

Conclusions: The patients with HAE generally considered that C1 inh concentrate treated their angioedema attack effectively. The level of satisfaction with the drug was high but the patients were worried about that awareness of the health care professionals about HAE and its treatment is low.

1308 | Angioedema attacks related to endometrial hyperplasia in a case of estrogen dependent FXII-hereditary angioedema

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Case Report: Background: Hereditary angioedema associated to factor XII gene mutations (FXII-HAE) is characterized by skin or mucosal AE attacks, affecting mainly women, with family history of AE and normal C1-inhibitor. AE attacks may be exclusively related or influenced by hyperestrogenic situations like pregnancy or exogenous estrogen exposure. There are no reports in the literature relating this condition to endometrial hyperplasia (EH). EH usually occurs after menopause or during perimenopause, when ovulation ceases or becomes irregular and therefore progesterone decreases or is no longer produced, causing an imbalance between endogenous estrogens and progesterone with a relative excess of estrogens.

Case Report: A 43-year old woman was diagnosed with FXII-HAE in 2006 at the age of 35. At that time, she started with recurrent AE attacks during her first pregnancy. AE episodes stopped after delivery. She avoided exogenous estrogens and ACE-inhibitors and she had no more pregnancies, remaining asymptomatic. In 2015, she was diagnosed with EH. At the same time, on March 23rd, she suffered an episode of feet swelling followed by intense acute abdominal pain with nausea and vomits. Abdominal pain lasted for 8 hours and feet swelling for 36 hours with no specific treatment. C1-inhibitor concentrate and icatibant acetate was provided to the patient and she was trained in auto-administration for early home on-demand treatment. On April 1st, oral medroxyprogesterone acetate (MPA) was started (10 mg/day for 12 days from day 14th of every menstrual cycle). The same day she had swelling of one hand finger lasting for 10 hours. On April 24th, after a first cycle of MPA, she had another abdominal attack lasting for 18 hours. The patient did not use specific treatment in spite of given indications. She completed a total of 7 cycles of MPA until September 2015. Endometrial biopsy was normal in October 2015. In November 24th she had swelling of one finger lasting for 5 hours. Re-starting progestogen treatment was then considered but the patient did not suffer any other AE attack. Endometrial biopsy was normal in October 2016 and she had no more AE episodes by the last visit in January 2017.

Conclusions: We propose EH as a hyperestrogenic state causing AE attacks in a patient with estrogen dependent FXII-HAE. Treatment with progestogens avoided AE attacks while EH was also reversed.

1309 | Off-label intramuscular prophylactic treatment with conestat alfa (4200 μ/20 mL) in HAE patient with difficult peripheral venous access

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Case Report: Introduction: Conestat alpha (CA) is registered for intravenous treatment of hereditary angioedema (HAE) attacks. Intravenous application requires access to medical facilities and personnel which is often difficult and time consuming for patients. Nevertheless, some patients have compromised veins, making the treatment of the attacks even more arduous. Prophylactic treatment (PT) with C1-inhibitor concentrate is displayed to be a good opportunity to treat HAE patients afflicted with frequent and/or severe episodes.

Objective: This is a case report of a 71 year old HAE type I patient weighing 84 kg, who reported to our Clinic much more frequently with severe abdominal HAE attacks during the past 6 months (2-3 times per week). The patient suffers compromised veins and difficult peripheral venous access which often resulted in treatment impediments. Everyday activities were suspended and great anxiety was present in the life of the family members. Off-label twice weekly prophylactic intramuscular administration of CA was initiated in order to cope the untoward course of the disease. The dose used per application—4200 U/20 mL (2 vials solved in 10 mL solvent, each) was injected intramuscularly in two different sites, either into the m. gluteus maximus or the m. quadriceps femoris. All ethical implications were discussed and consent was obtained before the common decision for this off-label therapeutic approach. Patient diary was analyzed.

Results: During the 6-week follow-up no breakthrough attacks occurred. No hematoma, infection or other side effects at the places of application were observed. The patient reported significant improvement in the quality of life and daily activities were restored.

Conclusion: Prophylactic intramuscular administration of CA could be an alternative to the intravenous route of application, especially when the patient has difficult peripheral venous access and approach to medical care facilities might cause delay and obstruction. Intramuscular application of 10 mL solution of 2100 U of the drug seems to be safe and well tolerated.

1310 | Angioedema by acquired c1inhibitory deficit case report

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Case Report: Introduction: Angioedema with C1 inhibitor deficiency is a rare disease characterized by recurrent, unpredictable episodes of cutaneous and/or mucosal edema. Our patient is 86 years old woman without family history of angioedema, no personal history of interest and without treatment with IECAS, ARA II and estrogens.

Case Description: First episode was 68 years old (1998), consisted lips and tongue edema and upper respiratory tract produced respiratory failure no response to treatment with corticoids intravenous and Adrenaline intramuscular, required emergency tracheotomy, orotracheal intubation and Intensive care unit. The clinical picture was resolved in 6 days. Complement study requested C4,C1 INH quantitative and functional were normal.

In 2004 presented new episode of laryngeal edema with dyspnea and dysphagia no response to treatment with corticoids and Adrenaline and required orotracheal intubation. Complement study were C1q: 5.37 mg/dL (10-25), C4: <1.36 mg/dL (7.7-50.5), C1 inh quantitative: 16 mg/dL (22-34), C1 inh functional: <0.7 UC1inh/mL (0.7-1.3)

She was diagnosed of Angioedema by Acquired C1inhibitory deficit and treated with Tranexamic acid 500 mg every 8 hours. She was derived to the Internal Medicine Service, infectious, immunology, solid and hematological tumor were excluded.

Controls performed in 2005, 2006 and 2007 were normal. Our patient was asymptomatic and we reduced Tranexamic Acid treatment ending in 2008.

On 2014 had an episode of facial and submaxillary edema was treatment with corticoids and Adrenaline, complement study C4,C1 INH quantitative and functional were normal and C1q: 8.9 mg/dL (10-25).

On March 2015 study was repeated. C1q: 1.63 mg/dL (10-25); C4 < 1.48 mg/dL dl (7.7-50.5); C1 inhibitor quantitative 4.95 mg/dL (22-34); C1 inh functional 0.04 UC1inh/dL (0.7-1.3).

Prophylactic treatment with Tranexamic acid and bradykinin B2 receptor antagonist on demand was prescribed.

Since then our patient has presented 4 episodes of lip edema with good result to bradykinin B2 receptor antagonist with complement C4; C1q; C1inhibitor decreased, Autoantibodies anti-C1-INH positive were appeared.

Conclusion: We present the case of a patient with Angioedema by Acquired C1 inhibitory with normalization of complement values for 9 years and subsequent clinical appearance and decrease of the values that currently remain partially controlled with Tranexamic Acid.

1311 | Design and rationale of the optima study: retreatment or step-up therapy with omalizumab in patients with chronic idiopathic/spontaneous urticaria (CIU/CSU)

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Introduction: Pivotal Phase 3 studies have demonstrated that subcutaneous administration of Omalizumab 150 or 300 mg every 4 weeks for 24 weeks is safe and effective in treating symptoms associated with CIU/CSU. OPTIMA (NCT02161562) is a novel study addressing remaining gaps in the knowledge of optimal CIU/CSU treatment.

Objectives: OPTIMA is a Phase 3b, international, multicenter, randomized, open-label, non-comparator trial. The purpose of the study is to gather data on: (i) retreatment efficiency upon return of symptoms once omalizumab treatment is withdrawn from well controlled patients (UAS7≤6) and symptoms have returned (UAS7≥16); (ii) dose step-up from 150 mg if patients are not well controlled after ≥8 and ≤24 weeks of treatment to 300 mg; (iii) treatment extension beyond 24 weeks in patients who are not well-controlled with 300 mg at 24 weeks. Patients with CIU/CSU and symptomatic despite H_1-antihistamine treatment are randomized 4:3 to 150 or 300 mg omalizumab for 24 weeks of initial treatment and then enter one of the following phases: (i) withdrawal phase (if UAS7 ≤ 6 at either dose); (ii) step-up to 300 mg (if 150 mg initially and UAS7 > 6); (iii) extended treatment for 12 more weeks (if 300 mg initially and UAS7 > 6). Patients in the withdrawal phase are monitored and retreated at the randomized initial dose if relapse occurs (UAS7 ≥ 16). The entire study is 53 weeks, including the final follow-up. There are six distinct treatment groups as a result of this treatment optimization design. Three hundred and fourteen patients were required to observe a sufficient number of relapses after initial dosing with 150 or 300 mg.

Results: Endpoints/Analysis: The primary endpoint is the proportion of patients who were clinically well controlled (UAS7 ≤ 6) after the initial dosing phase, relapsed (UAS7 ≥ 16) when treatment was discontinued, and who achieved a UAS7 score ≤6 at the end of the second dosing Phase. Key secondary endpoints include: change in UAS7 score and proportion of patients UAS7 ≤ 6 in those who step-up from 150 to 300 mg; change in UAS7 score in patients who extend 300 mg treatment; time to relapse in both doses.

Conclusions: The OPTIMA study will allow better characterization of appropriate omalizumab treatment regimen in CIU/CSU patients who relapse or are not well controlled after initial treatment.

1313 | Etiological reasons and prognosis of acute urticaria in children under 5 years of age

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Introduction: Urticaria is a skin lesion that is characterized by erythematous, raised, itchy plaques. It is termed as acute, chronic or recurrent. In most cases of acute urticaria etiological reasons are unknown. Aim of this study was to determine etiology of acute urticaria in children under 5 years of age and to reveal clinical and laboratory characteristics of patients.

Objectives: Children less than 5 years old who were referred to our clinic between July 2015 and July 2016 for acute urticaria were enrolled into the study. Informed consent was taken from the parents of the patients. Their clinical and laboratory data were recorded.

Results: A total of 83 patients [male (n = 49)] with a median age of 2.12 (1.27-3.39) years were included into the study. Angioedema was more common in the patients under 2 years of age (P = .001). Trigger factor could be detected in 62.6% of patients of whom 78.8% had active infections. Other etiologic factors were foods in four patients; vaccines in two patients, drug in one patient, grass pollen in 2 patients, animal fur in 1 patient, dermographism in 1 patient. There was no relationship between steroid intake and urticaria activity score (UAS) or duration of urticaria. Urticaria recurred in 33.2% of the patients and resolved with antihistamine treatment in 86.7%. Median score of UAS was 15 (8-21). 55.4% of the patients had mild urticaria (UAS < 16). There was no relation between eosinophilia and urticaria type (acute-chronic-recurrent), steroid intake or having atopy. All patients who had atopy for foods were under 2 years old. Serological positivity was detected in twenty patients (24%) [herpes simplex type (HSV) 1 (n = 10), EBV (n = 5), *Streptococcus* (n = 4), *Mycoplasma pneumoniae* (n = 1)]. The most common infectious cause was upper respiratory tract infection (URTI). Urticaria recurred in 33.2% of the patients and 7.2% out of 83 occurred as chronically. Urticaria did not recur in patients with positive viral serology (P = .02).

Conclusions: The most common etiological reason of acute urticaria in the preschool period was URTI. HSV type 1 was the most frequently reported among the agents that could be determined by serologic methods. The other causative agents were foods, followed by vaccines, drugs and aeroallergens.

1314 | Autologous serum skin test in chronic urticaria—comparative study and procedure assessment

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Introduction: Autologous serum skin test (ASST) is used to assess autoreactivity in patients with chronic spontaneous urticaria (CSU). Autoreactivity demonstrated by positive AAST does not define autoimmune urticaria but may be an indication of mast cell activating autoantibodies. Mast cells (MC's) distribution throughout skin surface is uneven, with more MC 's at peripheral anatomical sites. However, the pattern of distribution in the same subject is unknown.

Objectives: To characterize the patients undergoing ASST in our Allergy Department in the year 2016. Secondarily, to evaluate ASST reproducibility when performed in both volar forearms, as the pattern of MC's distribution in the same subject is unknown.

Results: Medical records review of all patients with suspected chronic urticaria, who performed ASST being studied at our department during 2016. Data on demographics and clinical history was collected, as well as information on atopy, psychiatric comorbidities, ASST result, urticaria severity and laboratory test results (IgE, ANA [antinuclear antibodies], rheumatoid factor, Helicobacter pylori, thyroid hormones and autoantibodies [TA]).

Twelve patients were included, 11 female, median age 46 (IQ range 16.75). Mean duration of disease was 9 years (SD 12.1). Seven reported recurrent angioedema episodes. Only 1 patient was sensitized to aeroallergens and none had food or drug allergy. Ten patients reported a previous history of psychiatric disorders (anxiety and/or depression). Four patients were on 4 antihistamines per day for CSU. Of those, 3 presented severe CSU activity (UAS 7>28) and were also on treatment with systemic corticosteroids, while waiting authorization to receive omalizumab. Nine had a positive ASST; of those, 2 tested negative for ANA or TA. Of the 3 patients with negative ASST, 1 tested negative for ANA or TA. None presented a positive rheumatoid factor. Only 1 patient had an active auto immune disease (type 1 diabetes)—presented a negative ASST.

In 7 patients ASST was performed in both volar forearms, with the test result being reproducible in all.

Conclusions: ASST is a simple, cheap office-based procedure with clinical relevance, since a positive test has been found to correlate with the CSU severity and course of the disease. As in previous reports, ASST showed reproducibility when performed in both volar forearms.

1315 | Angioedema related to angiotensin-converting-enzyme inhibitors: A case series

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Introduction: Angiotensin converting enzyme inhibitor-related angioedema (ACEI-AAE) occurs in 0.1-0.7% of patients treated with ACE-inhibitors (ACEI),with potentially serious consequences requiring immediate attention. ACEI-AAE is a nonpitting edema that can affect any area of the body, usually involving the face and upper airways. There are no specific diagnostic biomarkers, so the diagnosis is based on exclusion of other causes of angioedema in patients taking ACEI.

Objectives: In this study we present the clinical features of a cohort of patients (pts) with ACEI-AAE followed up at the Angioedema Centers of Universities of Naples and of Zagreb.

Patients who presented to our Departments with history of angioedema without wheals after the initiation of ACEI therapy, were studied. C1-INH deficiency angioedema and all allergological causes were ruled out. Patients' demographic information, duration of ACE-I use, onset of symptoms after starting therapy, attacks frequency and duration, symptoms and anatomic sites involved, were obtained from each patient's chart and interview.

Results: Twenty Caucasian patients (50% F; median (m.) age 59.9 years, range (r.) 46-75 years) were diagnosed with ACEI-AAE. The average time of symptoms onset after starting therapy was 4.8 years (r.0.25-20 years); 6.1 years was the average of therapy duration. The estimated diagnostic delay was 1.6 years. Lips were the most common affected site (15 pts,75%); 55% of pts described tongue involvement. In 3 cases there was larynx edema (15%).Other affected sites were eyelids (10%),ears (5%) and genitalia (10%).Frequency of attacks varied greatly from pts to pts (m.6.95 attacks/year, r. 1-48 episodes/year),such as edema duration (m. 34.5 hours, r. 3-168 hours). 65% of pts required hospitalization, with no endotracheal intubation. We followed up pts up to 10 years after the diagnosis. During the follow up 85% of pts referred no attacks. One patient had 1 attack/3 months during the first year; another one had 1 attack/week during the first month. Before diagnosis, all pts were treated with steroids and antihistamines without response. Four pts complained itching during attacks and two of them presented wheals too.

Conclusions: ACEI-AAE is a rare side effect but it can be a medical emergency. Our data confirm that the majority of ACEI-AAE are severe enough to require hospitalization. Discontinuation of ACEI can stop the edema attacks but sometimes is not enough to break up symptoms. The presence of itching and wheals may not be sufficient tips to exclude ACEI-AEE.

TUESDAY, 20 JUNE 2017
TPS 50
URTICARIA AND ANGIOEDEMA

1316 | Economic and humanistic burden associated with angioedema in patients with chronic spontaneous/idiopathic urticaria

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Introduction: The current analysis used data from the ASSURE-CSU study to assess the economic and humanistic burden associated with angioedema in patients with chronic spontaneous/idiopathic urticaria (CSU/CIU).

Objectives: The ASSURE-CSU study, conducted in 7 countries (Canada, France, Germany, Italy, Spain, Netherlands and the United Kingdom), enrolled patients with CSU aged ≥18 years with disease persisting for ≥12 months and symptomatic despite current treatment. Physicians reported angioedema from medical charts and patients reported angioedema via a survey and a 7-day diary. Angioedema was defined as: YES-ANGIO when both physician and patient reported angioedema, NO-ANGIO when neither reported angioedema, and Misaligned, where only one source recorded angioedema. Patients completed Dermatological Life Quality Index (DLQI) and Chronic Urticaria Quality of Life (CU-Q2oL) questionnaires at enrolment, Urticaria Activity Score for 7 days (UAS7) after enrolment and Work Productivity and Activity Impairment- Specific Health Problem (WPAI-SHP) questionnaire on the 8th day. All outcomes were evaluated for the 3 angioedema groups; significance tests were performed between YES-ANGIO and NO-ANGIO patients.

Results: Among 643 patients with complete angioedema data, there were 259 (40.3%) cases in YES-ANGIO, 173 (26.9%) in NO-ANGIO, and 211 (32.8%) cases in Misaligned groups. The majority of Misaligned cases were based on patients reporting angioedema but not the physicians. YES-ANGIO patients reported significantly higher mean [SD] DLQI and CU-Q2oL scores vs NO-ANGIO patients (10.4 [6.85] vs 6.6 [5.21]) & 37.6 [20.81] vs 23.4 [17.12]) respectively (both $P < .0001$). Mean [SD] UAS7 score was significantly higher in YES-ANGIO compared to NO-ANGIO patients (17.6 [10.55] vs 14.6 [8.97], $P < .01$). YES-ANGIO patients experienced significantly greater mean [SD] % absenteeism (9.1 [23.22] vs 1.4 [9.08]), overall work impairment (29.2 [28.48] vs 19.1 [21.37]) and overall activity impairment (34.5 [29.86] vs 23.8 [23.92]) than the NO-ANGIO group, respectively (all $P < .01$). Outcomes in Misaligned patients followed the same pattern as YES-ANGIO patients.

Conclusions: CSU patients with angioedema experienced substantially higher economic and humanistic burden compared to those without angioedema. Patients in the misaligned angioedema group reported similar burden to patients with angioedema. Overall, angioedema is associated with incremental humanistic and economic burden in CSU and appears to be under-reported in medical charts.

1317 | Effectiveness of omalizumab in a daily practice cohort of adults with chronic spontaneous urticaria

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Introduction: Efficacy and safety of omalizumab was proven in chronic spontaneous urticaria (CSU). However, in randomized controlled studies only data up to 6 months of treatment are available and in addition patients in clinical trials often differ from daily practice patients.

Objectives: We assessed effectiveness of omalizumab in adult CSU patients in daily practice in terms of disease control, relapses, quality of life (QoL) and side effects.

Methods: A monocenter prospective cohort study was performed. Patient-reported outcomes investigated effectiveness, defined as an urticaria control test (UCT) score ≥12. Relapse was defined as UCT <12 after initial effectiveness. QoL was measured with a disease specific measure. Demographics, disease characteristics, side effects

and (concomitant) treatment regimens were retrieved from patients' records.

Results: Fifty-two patients (median age 39.5 years, 75% female) were treated with a median of 11 omalizumab administrations (range 4-38). Thirty-seven (71%) were previously treated with antihistamines higher than fourfold, and 37 (71%) with chronic immunosuppressants. Omalizumab was effective in 49 patients (94%) after a median of 1 administration (range 1-5). Intervals between omalizumab administrations were successfully elongated in 33 patients (63%), 4 (8%) stopped omalizumab after achieving remission (after 9-18 administrations). Relapse was observed in 30 (58%); in 12 (23%) after interval elongations, in 11 (21%) after concomitant treatment adjustments, in 3 (6%) after a flare-up of comorbidities, in 1 after side effects and in 3 (6%) with unknown associations. In 10 patients (19%) omalizumab was up-dosed or the interval was shortened yielding effectiveness in 2. QoL improved significantly after 3.6 and 12 months compared to baseline. Side effects including headache, dizziness, malaise, fatigue, and hair loss, were reported by 38 (73%), in 19 (37%) repeatedly occurring at more than three administrations. Five patients (10%) discontinued omalizumab due to side effects.

Conclusions: Omalizumab was highly effective in daily practice. However, more than half experienced relapse. Intervals could be elongated individually. Side effects occurred in a majority, and but were only in a minority a reason for discontinuation of treatment.

Funding: Treatment for the first 12 patients was sponsored by Novartis Pharma NL within the Patient Urgency Initiative, from April 2014 until reimbursement of the drug in April 2015

1318 | Omalizumab for severe chronic spontaneous urticaria (CSU)- real life experience of 251 patients

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Introduction: To evaluate the real life efficacy of omalizumab in the treatment of CSU patients unresponsive to standard therapy.

Objectives: Two hundred and fifty-one patients with unresponsive (combination of high dose antihistamines, montelukast, corticosteroids and/or cyclosporine) active CSU patients were treated with (≥3 doses) Omalizumab (300 mg every 4 weeks) for a period of 10.4 ± 6.4 (range 3-48) months (approximately 3000 injections). 121 (48%) patients also had angioedema. Disease severity was defied by UAS7 score. Response was defined as complete (UAS7≤6, or improvement of >70% in UAS7 from baseline), partial (improvement of 50-70% in UAS7) or failure (<50% improvement).

Results: The patients (74% females, mean age 45 ± 16 years) had CSU for 4.5 ± 5.4 (range 0.5-50) years. Their mean UAS7 prior to Omalizumab treatment was 30 ± 8 (range 14-42). Following Omalizumab, the mean UAS7 decreased to 7 ± 9 ($P < .001$).The Response rate was complete in 130 (51%), and partial in 102 (41%) patients. 19 (8%) patients failed Omalizumab. The mean time to response was short (1.9 ± 2 months).Thus, 57% of the patients respond after the first Omalizumab treatment and another 25% after three injections. Only 9 (3.5%) patients respond following >6 month of Omalizumab treatment. 10% of the patients complained of local discomfort or mild systemic reactions. Only three patients discontinued Omalizumab due to adverse events.

Conclusions: As was shown in clinical trials, real life experience demonstrates that Omalizumab is a highly (and rapidly) effective, well tolerated and safe treatment for severe CSU.

1319 | Evaluation of the clinical utility of the Spanish version of urticaria activity score and urticaria activity score-7 for chronic urticaria

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Introduction: The Urticaria Activity Score (UAS) and UAS seven days (UAS-7) are two routinely used questionnaires used to assess disease activity in patients with chronic urticaria (CU).

Objectives: The objective of this study was to validate the Spanish version of the UAS questionnaire.

Results: Observational, prospective, multicentre study in adult patients with CU, which were treated previously or have had symptoms at the inclusion date. The UAS is a two-item questionnaire (number of wheals/hives and intensity of itching/pruritus) completed by the general practitioner, scoring 0-3 for each item with a total sum of the two items ranging 0-6 (lowest to highest disease activity). The UAS7 is a patient completed questionnaire of the UAS for 7 consecutive days ranged between 0 and 42 (lowest to highest disease activity). Both UAS and UAS-7 were completed at baseline visit or week respectively and after 6 weeks. The treatments received by the patient according to the normal clinical practice were recorded.
166 patients were included (average age ± SD of 49 ± 14 years, 66% female and a median CU evolution of 2 years). 40% of patients had inducible urticaria associated with CU (30% dermographism). Most frequent co-morbidities were: atopic diseases (17%), CU exacerbation by NSAIDs (15%) and thyroid diseases (16%). Most patients experienced hives and/or itch 24 hours before baseline visit as shown by UAS (hives [76%] and itch [83%]) or UAS7 (hives [74%] and itch [77%]) The mean (SD) UAS and UAS7 scores at baseline

were 2.8 ± 1.7 and 16.4 ± 10.5 respectively. In UAS-7 an increase in patients without hives (26% to 40%) or itch (15% to 32%) was observed between day 1 and 7 of the baseline week. An improved symptomatology was observed between baseline and final visit (mean difference of UAS: −0.7, $P < .0001$; Hives: −0.3, $P = .0003$; Itch: −0.3, $P = .0002$; UAS7: −2.6, $P = .0006$; Hives: −1.1, $P = .0024$; Itch: −1.4, $P = .0009$). Patients defined the UAS7 as easy/very easy to complete (91%) and suitable/very suitable for CU activity measurement (71%). UAS reliability (internal consistency) was good (0.7-0.8).

Conclusions: The results validate the Spanish version of the UAS/UAS7 as a suitable patient-reported outcome to measure and monitor disease activity in patients suffering from CU. It confirms the guidelines recommendation to always measure CU activity with UAS.[querry: 1320 missing]

1321 | Increased risk of chronic spontaneous urticaria in patients with autoimmune thyroid diseases: a nationwide population-based study

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Introduction: Although there have been some reports on the relationship between chronic spontaneous urticaria (CSU) and autoimmune thyroid diseases (AITD), there have been no large population-based study on the comparison of the risk of CSU between AITD and control group.

Objectives: The primary objective of this study was to evaluate the risk of CSU after diagnosis of AITD using national registry data from Korea. The secondary objective was to evaluate other risk factors of CSU.

Results: This study was a population-based study using the Korean National Health Insurance Service National Sample Cohort 2002-2013 made by the Korean National Health Insurance Service. Based on the disease code diagnoses in 2003-2005, we composed an AITD group (N = 3659) and an age- and gender- matched disease control group (N = 18 295). Each subject was tracked for whether CSU occurs or not until 2013. To identify the hazards associated with CSU, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated via univariate and multivariate Cox proportional hazard regression.

After adjusting for demographic differences and comorbidities, subjects with AITD had a significantly higher rate of CSU compared to the control group (HR, 1.46; 95% CI, 1.25-1.70; $P < .001$). Among the AITD group, the adjusted risk for CSU in patients with Hashimoto's thyroiditis (HR, 1.50) was higher than that with Grave's disease (HR, 1.33). Analysis of CSU patients associated with AITD to evaluate other risk factors of CSU showed that female patients had a significantly higher risk of CSU, compared to male ones (HR, 1.35; $P = .001$), and the patients with allergic rhinitis (HR, 1.51; $P < .0001$), atopic dermatitis (HR, 2.44; $P < .0001$), and asthma (HR, 1.50; $P = .0001$) had a significantly higher risk of CSU compared to patients without each disease.

Conclusions: Our results demonstrated that AITD could be significantly associated with an increased risk of CSU.

1322 | Positive CD63 basophil activation test is common in patients with chronic spontaneous urticaria and concomitant autoimmune thyroiditis and therefore may represent a good marker for immunoreactivity

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Introduction: Chronic spontaneous urticaria (CSU) is defined as the recurrent occurrence of transient wheals and/or angioedema for at least 6 weeks. The symptoms occur spontaneously and are not attributable to a specific trigger. It has been shown that autoimmune thyroiditis (AT) is a frequent comorbidity in patients with CSU. The basophil activation test (BAT) using CD63 expression has been described as a sensitive and specific tool for the diagnostic workup of autoimmune CSU. We analyzed occurrence of positive BAT results in patients with CSU and concomitant AT.

Objectives: We investigated patients which were diagnosed with CSU our department during the period from 2007 to 2013. BAT was performed using commercially available BAT purchased from Buhlmann (Flow Cast®). The CD63 expression on the surface of donor basophils after the incubation with patients' sera was determined by flow cytometry according to the protocol provided by the company and adapted for use in CSU patients.

We also investigated patients' sera for the presence of anti-thyroid autoantibodies (anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies) and interviewed patients for the history of AT. The results of BAT were compared with the presence of anti-thyroid autoantibodies and history of AT.

Results: We analyzed 66 patients with CSU. 22 (33%) were male and 44 (67%) were female. The age varied from 17 to 82 with the

median of 42. Mean IgE level was 214 kU/L. 38 (58%) of these patients had positive CD63 BAT. 10 patients hat elevated at least one of the anti-thyroid autoantibodies, 12 patients reported a history of AT (e.g. Hashimoto disease) and overall 15 (23%) patients showed elevated at least one of the anti-thyroid autoantibodies or reported a history of AT. From these patients 12 (80%) showed also a positive CD63 BAT.

Conclusions: An autoimmune subset of CSU is increasingly being recognized internationally, based on laboratory and clinical evidence. Currently, the autologous serum skin test is used as a screening tool to detect the presence of pathogenic autoantibodies in CSU patients. However basophil CD63 expression assay become a useful diagnostic tool. Herein we were able to show that almost one third (12/38) of the CSU patients with positive CD63 BAT presents the evidence for AT. Therefore we recommend screening the CSU patients with positive CD63 BAT for anti-thyroid autoantibodies even if there is no clinical history or symptoms of AT.

1323 | Chronic cold urticaria—experience of an allergy department of north of Portugal

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Introduction: Chronic cold urticaria (CCU), often results in a significant morbidity. First line treatment includes second-generation H1 anti-histamines (AH) up to 4 times the standard dosage as well as lifestyle modification.

Objectives: To review the clinical features, diagnosis and response to therapy in a group of patients with CCU followed in an Allergy Department.

Patients with CCU between 2009 and 2016 were included retrospectively. The data collected were: age, gender, age of symptoms onset, duration of symptoms and disease severity at initial appointment, atopy, triggers of symptoms, other forms of urticaria, underlying disease, cold stimulation tests (ice cube test and Temp Test®), treatment and follow-up.

Results: We assessed 26 patients with a median age of 41 years (5-77), 69% (n = 18) were female, median age of onset of symptoms was 36 years (4-72) and the median duration of symptoms at initial appointment was 1 year (3 months-23 years). Severity disease: type I (65%, n = 17), type II (19%,n = 5) and Type III (15%,n = 4). Atopy was found in 31% (n = 8). Triggers were cold water and cold air (96%, n = 25), aquatic activities (65%, n = 17), cold surfaces (42%, n = 11) and cold foods/liquids (19%, n = 5). One patient had also cholinergic urticaria. At initial evaluation all patients performed the ice cube test (positive in 18, stimulation time: 1 to 20 minutes) and 13 the Temp Test ® (positive in 6, threshold temperature: 9-24°C). The majority of patients (n = 17) were classified as idiopathic acquired urticaria (IAU) and 7 as atypical urticaria. Secondary causes of CCU were identified in 2 patients (primary cryoglobulinemia and HIV infection). No familial types of CCU were found. Atypical urticaria was associated with a younger age of symptoms onset (P = .006). All patients underwent lifestyle modification and AH treatment (on demand n = 6; standard dosage n = 14; twice daily n = 5; 4 times/day n = 1). Patients with type III disease did not need an epinephrine auto-injector during follow-up. The median time of follow-up was 7 months (1 month-7 years). During this period 73% (n = 19) of patients improved, 19% (n = 5) did not improve and symptoms resolved completely in 8% (n = 2).

Conclusions: Type I severity and IAU were the most frequent. Cold water and cold air were the main triggers. Most of the patients were controlled with lifestyle modification and AH therapy. Cold stimulation tests are important to confirm the diagnosis and during the follow-up to monitor disease control.

1324 | Omalizumab in chronic spontaneous urticaria and angioedema; lessons from an Irish cohort

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Introduction: Chronic spontaneous urticaria and angioedema is a common debilitating skin condition that results in significant quality of life impairment. The management of recalcitrant CSUA is challenging, but has been revolutionized by the use of omalizumab.

Objectives: We carried out a retrospective review of patients treated with omalizumab for CSUA and related disorders at our immunology clinic.

Results: 25 patients treated with omalizumab were included in the study. In 4 (16%) cases omalizumab was being used off label (Chronic spontaneous angioedema (2), Delayed pressure angioedema (1), Urticarial vasculitis (1)). The mean duration of disease prior to commencement of omalizumab was 79 months (range 8-360 months). Anxiety/depression was the most common comorbidity, noted in 14 (56%). Rescue steroid use was common (92%). All patients had failed high dose antihistamines ± montelukast. 10 (40%) patients had failed ciclosporin. The mean number of ED admissions and unplanned healthcare attendances due to CSUA over 24 months prior to commencement of omalizumab was 1.5 (0-5) and 5 respectively (2-9). Pre-treatment UAS7 (n = 21) was 30.2 and UCT was 2.2. The mean duration of treatment with omalizumab was 11 months (4-20). One patient with chronic spontaneous angioedema discontinued due to treatment failure. 17 (70%) were on monthly injections with 7 being dosed less frequently. One patient (4%) required 450 mg monthly for control. The mean post treatment UCT was 14.2. No patients on omalizumab required rescue steroids. There were no CSUA related hospital admissions during omalizumab

treatment and unplanned healthcare interactions were also reduced (mean = 0.2).

Conclusions: Omalizumab is an effective treatment for refractory CSUA. Use of omalizumab resulted in symptomatic improvement, prevented rescue steroid use and reduced emergency attendances and unplanned healthcare interactions in the Irish setting. Funding omalizumab is challenging. Innovative strategies are required to ensure that this effective medication is more widely available in the restrictive Irish Healthcare setting.

1325 | Patient tailored omalizumab treatment in chronic urticaria—our experiences

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Introduction: Omalizumab is effective treatment in chronic spontaneous urticaria (CSU). There are reports that treatment schedules should not be uniformed, but patient tailored.

Objectives: We have analysed clinical response to omalizumab 300 mg/4 weeks in 52 CSU patients (41 females, median age 48 years). Treatment was started by 300 mg/4 weeks. Patients daily reported urticaria activity score (UAS.)via a web based application. We analysed UAS7 at the beginning, 2 weeks (W2), 3 months (M3), and 12 (M12) months after first omalizumab application. The following definition of response to treatment were based on UAS7: complete response (UAS7 = 0), well controlled (UAS7 = 1-6), not well controlled (UAS7 > 6) and among last group significant improvement if reduction of UAS7 was 90-30%. In patients with complete response omalizumab dose was stepwise decreased and interval extended to the minimal dose/interval on which patients stayed symptom free.

Results: Complete response was achieved in 24/52 (46%) patients already at W2, in 11/52 (21%) patients at M3 and in 5/52 (10%) patients at M12. In 33/40 (82%) patients with complete response omalizumab treatment could be reduced to median 150 mg/6 weeks. In five patients a remission was achieved after median 7 months of treatment (2-19 months) and were able to discontinue the treatment.

In 4/52 (8%) patients CSU was well controlled at M12. 8/52 (15%) patients were not well controlled although in 4 patients significant improvement was achieved and patients continued with omalizumab 300 mg/4 weeks. In 4 patients with no significant improvement treatment was stopped after median 6 months (3-13 months).

Conclusions: Half of the patients with CSU completely respond to omalizumab very rapid and in these patients lower dose (150 mg/6 weeks) is sufficient. In third of the patients completely response is achieved in several months and also in these patients less intensive treatment is needed. In patients with partial response, even after year of treatment, higher omalizumab dose is needed, while minority of patients did not respond to treatment and omalizumab was stopped

1326 | Treatment and retreatment with omalizumab in chronic spontaneous urticaria: real life experience with twenty-five patients

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Introduction: Previous data has shown the high efficacy of omalizumab in chronic spontaneous urticaria (CSU). However, factors that may be effective on response to the therapy, relapse rates after drug discontinuation, and efficacy of retreatment remain unclear.

Objectives: We aimed to determine the efficacy of omalizumab in CSU refractory to conventional therapy, to identify possible factors on treatment response and relapse, and also to evaluate the efficacy of retreatment on relapsed disease.

Results: Data of CSU patients treated with 300 mg/month in an experienced university hospital allergy clinic for at least 3 months were retrospectively analyzed. In order to evaluate efficacy of treatment and retreatment, baseline and follow-up concomitant medication score (CMS) and urticaria activity score (UAS) were calculated. Possible factors on treatment response and relapse were identified.

Twenty-five patients were included. Median duration of omalizumab therapy was 6 (6-12) months. Of the patients with baseline UAS 6 (5.5-6) and CMS 13 (10-15), 8 (32%) had complete response (UAS = 0) and 3 (12%) were non-responder after 3 months of therapy. None of the complete responders were positive for IgG-anti-TPO. After discontinuation of omalizumab therapy, 11 (61%) patients experienced relapse and 10 of them received retreatment with omalizumab. Half of the patients had complete response, and half had partial response (UAS = 1-4) after retreatment (duration of therapy between 1 and 5 months). No treatment related adverse events were documented.

Conclusions: Omalizumab has high efficacy in both treatment and retreatment of CSU; however, relapse rates after discontinuation are high. Autoimmune markers may be helpful in predicting treatment response and relapse.

	Baseline n = 25	3rd month n = 25	6th month n = 21	9th month n = 10	P
CMS	13 (10-15)	2 (0-6)	2 (0-6)	3 (0-7.3)	<.001
UAS	6 (5.5-6)	1 (0-2)	1 (0-2)	1 (0-1.3)	<.001

CMS: concomitant medication score, UAS: urticaria activity score.

Variables	Non-relapsed n = 7	Relapsed n = 11	P
Age	39 (33-43)	38 (31-47)	.82
Eosinophil count	170 (120-190)	160 (68-233)	.68
Total IgE; IU/mL	101 (37-308)	229 (54-371)	.62
IgG anti-TPO positivity; n (%)	2 (29)	5 (42)	1
ANA positivity; n (%)	0	4 (36)	.12
Duration of initial therapy; months	6 (6-9)	8.5 (6-14)	.32
3rd month CMS	2 (0-4)	3 (0.5-5.5)	.64
3rd month UAS	1 (0-2)	2 (0-3)	.33

TPO: thyroid peroxidase, CMS: concomitant medication score, UAS: urticaria activity score.

1327 | Successful prophylactic treatment of acquired angioedema with plasma derived C1-inhibitor

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Introduction: Acquired angioedema (AAE) is a rare condition clinically characterised by recurrent episodes of cutaneous and/or mucosal painful, even life-threatening edema. It results from C1-Inhibitor (C1-INH) deficiency, which could be caused from production of C1-INH antibodies or directly consummation of C1-INH in association with lymphoproliferative diseases.

Objectives: Therapy of AAE comprises treatment of the deficiency of C1-INH with C1-INH concentrates, tranexamic acid or Icatibant and treatment of the underlying disease.[3]

Results: We report two female patients in their 6th decade of life, who developed first symptoms of swellings involving parts of their body. Laboratory findings showed low levels of C1-Inhibitor function (normal range 70-130%) and C4 (normal range 0.100-0.400 g/L). Family history was unremarkable regarding hereditary angioedema and immunoelectrophoresis showed monoclonal gammopathy of unclear significance (MGUS) in both cases, without detectable underlying haematological malignancy. Both patients had frequent attacks (1-2 per week) which negatively influenced their quality of life. Treatment with tranexamic acid was unsuccessfully therefore due to absence of C1-Inhibitor antibodies treatment with plasma derived nanofiltered C1 INH concentrate (Cinryze®, 1000 U intravenously twice a week) was initiated leading to a significant decrease of attacks.

Conclusions: AAE is a very rare disease and treatment might pose a great challenge. So far prophylactic treatment of AAE with a C1 INH concentrate hasn't been reported and in our experience might be of great benefit for the patients affected.

1328 | Characteristics of patients attending the allergy clinic for chronic spontaneous urticaria

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Introduction: Chronic spontaneous urticaria (CSU) is a common condition. However, its attention in the Allergy clinics is often delayed.

Objectives: The aim of this study was to describe the clinical characteristics of patients evaluated at the Allergy Unit of a tertiary hospital between 2012 and 2014. Demographic data, clinical symptoms, and laboratory findings including autoimmunity, complement, total IgE, IgE against parasites, acute phase reactants, and D-dimer levels were retrieved.

Results: 306 patients were included. Age range 3-89 years old. The mean age was 46.5 (y/o) 75.16% of them were female. Patients were classified in groups according to their age (0-19 years old (y/o), n = 26 (A), 20-39 (y/o), n = 83 (B) 40-59 (y/o), n = 125 (C) and 60-89 (y/o), n = 72 (D)). The time of evolution when they were first attended in the Allergy Unit was high and increased with the age. Mean 37.21 median time in months: 8 (sem). Group A: mean: 21.41 months, median: 5 months (2.67 sem), group B: 29.74, 8.5 months (1.06 sem), group C: 38.40, 9 months (1.08 sem) and group D: mean 45.78, median 7 months (1.63 sem). AE was present in a 42.81% of patients (A): 16% patients with AE, (B):36% patients, (C):56% patients and (D):23% patients. Inducible urticaria was associated in 4.25% (cholinergic 1.63%, dermographism 1.31%, delayed by pressure 0.66% and contact 0.33%). Previous history of atopy was found in 41.5%. Total IgE measured higher than 120 KU/L in 41.2% of the patients, average 294.67 KU/L, mean (A): 308.79 KU/L (2.42sem), group (B): 291.23 KU/L (1.40 sem), (C): 294.88 KU/L (1.05 sem) and (D): 290.57 KU/L (1.78 sem). Laboratory findings included Hypothyroidism in 7.24%, anti-TPO Ab in 4.6%, antithyroglobulin Ab in 3.7%, low C4 levels in 19.60% of the patients, average C4 was 14.66 mg/dL (normal range 17.0-51.0), *Anisakis simplex* IgE in 29%, *Ascaris lumbricoides* 8.9%. VSG was increased in 40/249 patients with an average value of 29.7 mm/hour, LDH 50/261 161.76 UI/L, high D-dimer levels were found in 19/89 patients, mean value 838.74 mcg/L.

Conclusions: Chronic spontaneous urticaria patients who attend the Allergy Unit support a difficult long-lasting disease rarely associated with inducible urticaria. The delay of the first consultation increases with age. The angioedema association seems more frequent in patients between 40 and 59 y/o. Previous history of Atopy is commonly found.

1329 | Diagnostic and therapeutic profiles of patients with chronic urticaria at a reference center

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Introduction: Chronic urticaria/angioedema (CU) has been defined as wheals, angioedema or both lasting for more than 6 weeks. Management of CU is often a challenge to the Allergist/Immunologist. We aimed to evaluate diagnostic and therapeutic profiles among patients with CU.

Objectives: Retrospective analysis of medical records of 383 CU patients followed at a reference center from 2011 to 2016. Autoimmune basis was suspected by presence of positive autologous serum skin test (ASST), anti-thyroid and/or antinuclear antibodies (ANA).

Results: The majority of patients were female (81%), with median age at diagnosis of 41 years (12-91 years). Angioedema was associated with urticaria in 61.2% of the patients. Isolated angioedema was present in 7.3%; isolated chronic inducible urticaria in 11.4% of the patients; isolated chronic spontaneous urticaria in 32.6%; and concomitant spontaneous and inducible chronic urticaria in 27.9%. Personal history of atopic disease occurred in 51% of the patients, with family history of atopic diseases and of urticaria/angioedema in 36% and 14% of the patients, respectively. Overall, features of autoimmunity were observed in 149 (39%) patients. Of the 220 patients to whom ASSTs were performed, 93 (42.2%) gave positive results, with 10.7% associated positive ANA and/or anti-thyroid antibodies. Anti-thyroid antibodies and ANA without positive ASST were positive in 15.4% and 12%, respectively. More than half of the patients (55%) presented elevated serum IgE. Seven patients presented positive serology to hepatitis B, C and/or syphilis, and went into remission after treatment of the specific infection. All patients were treated with second-generation antihistamines (AH), including 138 (37%) who used regular doses of AH, 147 (39%) using doubled dose, 15 (3.9%) using tripled dose, and 76 (20%) who needed fourfold doses of AH. Anti-leukotrienes as add on therapy were used in 12.8% of the patients, and use of oral corticosteroids for more than 15 days were reported by 15.2% of the patients. Seventeen patients were on anti-IgE as an add on therapy. Seven responded within 8 days (fast responders), 9 responded between 8 days and 3 months (slow responders); and 1 went into partial remission.

Conclusions: In accordance with the literature, a high proportion of our CU patients presented features of autoimmunity. Differently from observed in the literature, our study found an important association of CU with atopy.

1330 | Analysis of the efficacy and safety of omalizumab in treatment of idiopathic chronic urticaria in Vietnam

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Introduction: Urticaria, also known as hives, is a very common disorder and is thought to afflict up to 20% of the population at some point in time. The condition is characterized by the appearance of pruritic, and hives. Chronic urticaria (CU) generally is defined by the presence of urticaria on most days of the week, for a period of 6 weeks or longer.

Omalizumab is a unique monoclonal antibody IgE was approved by FDA for the treatment of idiopathic chronic urticaria. This is a new promising therapy for patients with idiopathic chronic urticaria. However, so far, in Vietnam no studies have observed the efficacy and safety of omalizumab in the treatment of idiopathic chronic urticaria.

Objectives: Patients who were diagnosed with idiopathic chronic urticaria in the Center of Allergy and Clinical Immunology in Bach Mai Hospital, failed to 1st, 2nd and 3rd grades under the guideline of WAO.

Subjects were injected subcutaneously at a dose of 150 mg omalizumab at week 0-4-8-12. Efficiency of the treatment was measured by scale UAS-7, Adverse events were closely monitored from the beginning up to 16 weeks after the last injection of omalizumab.

Results: 26 patients were enrolled from 5/2014-9/2016. The proportion of male/female was 1/1, average age was 42.7 $\pm$ 13.4 years (min: 6 year olds, max: 67 years old). The average disease duration is 31.2 $\pm$ 12.0 months. Drugs were prescribed for patients before enrolment include corticosteroids (23.1%),cyclosporin (19.2%), hydroxychloroquine (30.8%), montelukast (73.1%), ranitidine (80.8%) and 100% patients were treated by H1 antihistamines. Average level of total IgE after treatment was 247.7 $\pm$ 389.1U/L, significantly lower than total IgE levels before treatment 435.1 $\pm$ 632.8U/L ($P < .05$). The percentage of patients responded completely after the 1st, 2nd, 3rd and 4th injection were respectively 34.6%, 69.2%, 88.5% and 88.5%. At week 12, the mean change of UAS-7 pre- and post-treatment was -17.5 ± 5.6 ($P < .001$).

During treatment, only one case appeared erythema at the injection site. No cases had anaphylaxis, bronchospasm or drug-induced severe skin reactions.

Conclusions: Omalizumab is well control clinical symptoms and sign of idiopathic chronic urticaria in patients who had remained symptomatic despite the use of other grade of guideline of WAO, is also not observe any severe adverse reactions to omalizumab.

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IMMUNE RESPONSE AND MECHANISMS OF ALLERGY

1332 | Pru p 3-epitope-based immunotherapy in murine model for the treatment of peach allergy

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Introduction: Food-specific immunotherapy (sIT) is a promising treatment for LTP-syndrome. Although sublingual sIT (SLIT) has been shown as safe and effective, it is less so than oral immunotherapy. The use of T-cell peptides from major allergens can increase effectiveness without increasing IgE reactivity. Moreover, their weak responses may be enhanced using Toll-like receptor ligands as adjuvants. We propose a novel SLIT that combines a Pru p 3 peptide and a ODN with CpG motifs (ODN-CpG) to induce a specific Th1/Treg response.

Objectives: We aimed to determine if anaphylactic-response of Pru p 3-sensitized-mice can be reverted into tolerant response, using mono- and tetravalent systems with a Pru p 3 peptide. To achieve this goal, LTP-peach anaphylactic mice were treated sublingually with a combination of a CpG sequence and mono- or tetravalent systems including a Pru p 3 peptide (D_1Prup3, D_4Prup3). Mice were challenged intraperitoneally with Pru p 3 one and three weeks after SLIT. Tolerance was assessed by changes on body temperature, determination of Pru p 3-sIgE, -sIgG1 and -sIgG2a immunoglobulins by ELISA and Pru p 3-sIgE, -sIgG1 and -sIgG2a secreting cells by ELISpot assay, studies of $CD4^+$ and $CD8^+$ cellular proliferative response of spleen cells by flow cytometry and cytokine production.

Results: Mice receiving D_1Prup3+CpG were protected from anaphylaxis after challenge with Pru p 3. They showed no change in body temperature, a decrease of Pru p 3-specific IgE and IgG1 antibodies and an increase in sIgG2a compared to the non-treated group. Similar results were obtained for immunoglobulin-secreting cells. Moreover, a significant decrease of Pru p 3-specific $CD4^+$T-cells and an increase of Treg cells were found, alongside shifts to a Th1 cytokine pattern. These changes were maintained for three weeks after stopping the treatment.

Conclusions: The monomeric compound D_1Prup3+CpG administered sublingually represents a promising new IT approach since it is easily synthesized, safe, induces protection from anaphylaxis and persists in suppressing clinical symptoms after ending the treatment.

1333 | Effects of subcutaneous immunotherapy (SCIT) on the numbers of IL-10-producing CD4+ T cells and IL-10-producing B cells in peripheral blood of pollinosis patients

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Introduction: It has been suggested that mechanisms underlying effectiveness of antigen-specific immunotherapy are related to increases in IgG4 antibody and regulatory T (Treg) cells, whereas their precise roles have been unclear. Different from naturally occurring Treg cells that express a transcription factor, Foxp3, there is another subset of Treg cells, which are induced by antigen challenges and activated by the antigen to produce an anti-inflammatory cytokine, IL-10. In addition, it has been reported that IgG4 antibody is produced from IL-10-producing regulatory B cells.

Objectives: Numbers of IL-10-producing $CD4^+$ T cells and IL-10-producing B cells, and levels of antigen-specific IgE and IgG4 levels in the peripheral blood were comparably assessed among normal subjects, patients of Japanese cedar pollinosis, and the patients who have been treated with subcutaneous immunotherapy (SCIT) for more than 3 years.

Results: 1) By ELISA analyses of sera collected after the pollen season in 2016, increase in antigen-specific IgE antibody level was not statistically reduced by SCIT, whereas antigen-specific IgG4 level was dramatically increased in the SCIT-treated patients. 2) By flow cytometry analyses, the number of antigen, Cry j1-induced IL-10-producing $CD4^+$ T cells in peripheral blood mononuclear cells (PBMC) of the pollenosis patients was significantly lower than that of the normal subjects. However, the number of antigen-induced IL-10-producing $CD4^+$ T cells of the SCIT-treated pollenosis patients was comparable to that of the normal subjects. Additionally, the number of anti-CD3/CD28 mAb-induced IL-10-producing $CD4^+$ T cells in SCIT-treated patients was higher than those of other 2 groups. Most of the IL-10-producing $CD4^+$ T cells were negative for Foxp3. 3) The number of IL-10-producing B ($CD19^+$) cells of the pollenosis patients was not different from that of normal subjects, whereas that of SCIT-treated patients was significantly higher than those of other 2 groups.

Conclusions: The number of antigen-induced IL-10-producing $CD4^+$ $Foxp3^-$ T cells was reduced in the pollinosis patients. SCIT has increased not only the IL-10-producing $CD4^+$ T cells but also IL-10-producing B cells. Regulatory functions of the IL-10-producing lymphocytes may be involved in mechanisms underlying the clinical effects of SCIT.

1334 | Dose-response of skin prick tests with native and glutaraldehyde-polymerised allergen extract of alternaria alternata

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Introduction: Allergens polymerized with glutaraldehyde (allergoids) are commonly used in immunotherapy. Allergoids have less allergenicity (specific IgE binding) than their corresponding native unmodified allergens. Alternaria alternata is one of the fungal species most commonly causing type I allergies. The allergoid of Alternaria alternata, has been developed and in vitro hypoallergenicity (specific IgE binding) has been demonstrated.

Objectives: The aim of this study was to compare the *in vivo* dose-response skin prick test (SPT) of the allergoid with the corresponding native preparation.

Results: Twenty-four patients, known to be allergic to *Alternaria alternata* were included (11 male and 13 female, mean age 19 years, range 7-43 years). The native allergen was tested at three different concentrations of the major allergen Alt a 1: N 10 (Alt a 1 10 μg/mL and protein content of 333 μg/mL); N 2.5 (Alt a 1 of 2.5 μg/mL) and N 1 (Alt a 1 of 1 μg/mL). The allergoid, obtained from the same batch as the native allergen at 10 μg/mL, contained 353 μg/mL. The area of the wheal size induced by each preparation was recorded and measured using PrickFilm® and expressed in mm^2. The median, with the corresponding first and third quartiles, were used as descriptive statistics. Friedman's test was used to compare the results between the 3 concentrations and the Nemenyi procedure was used for pairwise comparisons. The regression line dose-response was calculated with the native allergen concentrations for establishing the loss of *in vivo* allergenicity of the polymer.

The median value of the wheal size was 20.3 (13.4-25.3) for N 10, 10.6 (7.0-27.3) for N 2.5 and 9.8 (7.7-18.9) for N 1. The result obtained with the allergoid was 5.5 (4.3-8.9) mm^2. The reduction of the mean wheal size of the polymer with respect to the different concentrations of the corresponding native was of 73% for N 10 ($P > .0001$), 48% for N 2.5 ($P = .005$) and 44% for N 1 ($P = .049$). The quantity of Alt a 1 of native allergen that produces a wheal of the same size as the wheal induced by the preparation of the allergoid is of 0.16 μg. This means that there is a loss of allergenicity *in vivo* of a factor of 61.

Conclusions: Polymerized allergens of Alternaria alternata show a significant reduction of in vivo allergenicity, as measured in vivo with SPT, compared to their respective native preparations. This fact provides a safe preparation for specific immunotherapy.

1335 | Prospective RT-PCR analysis of chosen genes expression in patients with hymenoptera venom allergy

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Introduction: The treatment of choice for patients with hymenoptera venom allergy (HVA), at high risk of systemic reaction after the sting, is insect venom immunotherapy (VIT). Effectiveness of immunotherapy is well documented. However there are still patients treated with VIT, who do not achieve protection from anaphylaxis. Therefore we still need tools to proper qualify the patients, improve treatment regimen and also to predict the course and effectiveness of immunotherapy.

Objectives: Aims: (1) Assessment of the expression of selected genes using an RT-PCR method in peripheral blood cells of patients with wasp venom allergy compared to healthy controls. (2) Analysis of the changes in gene expression using MFC RT-PCR in peripheral blood cells in patients with wasp venom allergy in the course of venom immunotherapy.

Methods: Among patients under VIT, 45 with wasp venom allergy were qualified to assess the gene expression analysis using MFC RT-PCR. The control group included 38 healthy volunteers without allergy in their medical history.

Results: Significantly lower gene expression were found for 11 genes (*CLDN1* ($P = .000023$), *CNGB3* ($P = .000035$), *FADS1* ($P = .03385$), *HES6* ($P = .007665$), *HLA-DRB5* ($P = .010112$), *HTR3B* ($P = .00004$), *PRLR* ($P = .037961$), *SLC16A4* ($P = .027395$), *SNX33* ($P = .000763$), *SOCS3* ($P = .000848$), *TWIST2* ($P = .004828$) and higher expression for 1 gene (*COMMD8*; $P = .000515$) in wasp venom allergic patients compared to controls. Furthermore significant lowering was found in expression for *COMMD8* after about 3 months of immunotherapy ($P = .012413$).

Conclusions: (1) Our data revealed significant differences between patients and control group, in expression of 12 genes believed to be involved in pathogenesis of inflammation. This data can serve for implementing new diagnostic methods in the future. (2) COMMD8 gene expression was lowered in the course of VIT what, due to its function, makes it likely to become a marker of immunotherapy.

1336 | Reducing allergic symptoms with oral immunotherapy supported by a non-digestible oligosaccharide supplemented diet in a peanut allergy mouse model

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Introduction: Although prevalence of food allergy is increasing, no curative treatment is available yet. Improving oral immunotherapy (OIT) for food allergy is necessary to reduce side effects and achieve tolerance. Non-digestible oligosaccharides, like scFOS/lcFOS (FF), have been shown to reduce allergy development in murine models.

Objectives: This study evaluated the capacity of scFOS/lcFOS to support OIT in a peanut allergy mouse model.

Methods: After sensitization (d0-d35) using peanut extract (PE) and CT, mice were put on a 1% FF (9:1) or control diet and received OIT by intragastric dosing of PE (0, 1.5 or 15 mg, 5 times/wk) for three weeks (d41-d59). Hereafter, mice were exposed to PE via the intradermal (d64), intragastric (d70) and intraperitoneal (d77, i.p.) route, to determine clinical efficacy (acute allergic skin responses, mast cell degranulation, anaphylactic shock symptoms and body temperature). Furthermore, we determined PE specific antibody and cytokine production and number of various immune cells were measured at different time points during the study (d50, d63 and d78).

Results: OIT reduced the mast cell degranulation (1.5 mg) and anaphylactic shock symptoms and drop in body temperature upon PE challenges (1.5 and 15 mg). In addition, FF was able to lower the acute allergic skin response. The combination of OIT with FF limited the drop in body temperature induced by PE challenge. OIT as well as FF appeared to have various immunological effects. OIT raised the serum levels of IgE, IgA, IgG1 and IgG2a, which appeared due to induction of antibody production because increased number of IgG1 and IgA producing cells were also observed. OIT-induced increases in antibody levels were not influenced by FF, but the increase of IgG1 production on d50 was reduced by FF treatment. OIT caused an increase in the number of regulatory T cells (d50) and Th1 cells (d50). OIT + FF lowered IgE-mediated basophil activation caused by αIgE stimulation, and increased the caecum content of short-chain fatty acid, in particular of butyric acid.

Conclusions: These data show that OIT protects against allergic responses upon peanut exposure in allergic mice. Furthermore, cellular parameters suggest Treg induction after OIT. FF itself reduced a range of clinical and immunological parameters compared to control diet but, how the observed changes contribute to the safety or efficacy of the OIT protocol needs further evaluation.

1337 | Bioavailability of house dust mites allergens in sublingual tablet allergy immunotherapy is highly dependent on formulation

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Introduction: Allergy immunotherapy (AIT) is an established treatment option for respiratory allergic disease. In sublingual immunotherapy (SLIT), the immune system is addressed through interactions between solubilized allergen and antigen-presenting cells of the oral mucosa, the efficiency of which is governed by the two main factors of SLIT allergen bioavailability: allergen concentration and mucosal contact time. Recently, three house dust mite (HDM) SLIT-tablets were developed. All showed clinical efficacy, but the tablets differ markedly with regard to allergen content, nominal strength and formulation.

Objectives: The physical properties of the three SLIT-tablets and the importance of tablet formulation for allergen bioavailability were examined.

Methods: HDM major allergen content, tablet disintegration times, and allergen release kinetics during tablet dissolution were determined for two freeze-dried HDM SLIT-tablets, (ACZX, 12 SQ-HDM) and (MTC, 6 SQ-HDM), and a compressed tablet, (ACT, 300IR). Dissolution kinetics of Der f 1, Der p 1 and Der 2 were measured, and the area under the curve (AUC) was used as a proxy for HDM major allergen bioavailability.

Results: ACZX and MTC disintegrated immediately, within a second, upon contact with assay buffer, and almost the entire contents of HDM major allergens were released into solution within 30 second, where a stable plateau was reached. The disintegration time of ACT was much longer, 45 second, and the HDM major allergens were dissolved more slowly, without reaching a plateau even after 10 minutes. incubation. After a minute, the recommended sublingual holding time for MTC, the AUCs for ACT (300IR) were only 8% (Der 2), 19% (Der p 1) and 46% (Der f 1) compared to the AUCs obtained with MTC. This means that the freeze-dried tablet achieved higher levels of HDM major allergen bioavailability at an early time point after dissolution-initiation than the compressed tablet.

Conclusions: SLIT-tablet allergen bioavailability depends highly on tablet formulation. The fast-dissolving freeze-dried tablets comprise the more efficient SLIT-tablet formulation, and provide maximal solubility of allergens well within the recommended sublingual holding time. Consequently, and of importance to both patients and prescribing physicians, the nominal strengths of SLIT-tablets cannot be compared unless the tablets are based on the same formulation, and contain allergen extracts of the same composition.

1338 | Antibody responses to sublingual treatment with recombinant bet v 1 and mal d 1

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Introduction: Birch pollen-associated apple allergy affects more than 70% of birch pollen-allergic individuals and mainly results from immunological cross-reactivity between the major birch pollen allergen Betv1 and the structurally related major apple allergen Mald1. Still, allergen-specific immunotherapy (AIT) with birch pollen has limited effects on the associated apple allergy. To investigate whether this food allergy should be treated with the apple allergen we conducted a single center, double-blinded placebo controlled pilot study including 60 Betv1-sensitized patients with apple allergy randomized to the daily sublingual administration of placebo (n = 20), or 25 μg of recombinant (r) Mald1 (n = 20) or rBetv1 (n = 20). Serum samples were collected before and after the treatment period of 16 weeks.

Objectives: The aim of this study is to compare the quantity, specificity and blocking activity of IgG4 antibodies (Abs) induced by SLIT with rBetv1 and rMald1.

Results: SLIT with rBetv1 significantly increased Betv1- and Mald1-specific IgG4 levels. In contrast, SLIT with rMald1 significantly enhanced Mald1-specific but not Betv1-specific IgG4. The placebo group showed no changes of allergen-specific IgG4 Abs. To assess the primary specificity of SLIT-induced Mald1-specific IgG4 Abs in the active groups sera were incubated with titrated amounts of rBetv1 or rMald1 prior to the analysis of binding to rMald1 in ELISA. In sera from rBet v 1-treated patients incubation with rBet v 1 completely abrogated IgG4-binding to rMal d 1 whereas incubation with rMald1 showed a weaker inhibiting effect. In sera from rMald1-treated patients rMald1 completely inhibited IgG4-binding to rMal d 1 whereas incubation with rBet v 1 showed a weaker inhibiting effect. Currently, we are studying the capacity of Mald1-specific IgG4 Ab in both groups to block allergen-specific IgE-binding by means of basophil activation tests and ELIFAB.

Conclusions: So far, our results indicate that SLIT with rMald1 induced IgG4 primarily specific for Mald1. As expected, SLIT with rBetv1 induced rBetv1-specific IgG4 Abs cross-reactive with rMald1. As this treatment did not improve apple allergy, it will be interesting to see whether cross-reactive Betv1-specific IgG4 Abs show any activity to block IgE-binding to the apple allergen. Another interesting aspect will be to see whether Mald1-specific IgG4 Abs induced by SLIT with rMald1 are able to block IgE-binding to Betv1.

1339 | Immunotherapy with depigmented-polymerized peanut extract. Mouse model of peanut allergy

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Introduction: Immunotherapy for peanut allergy has been an exploding topic of study within the last few years. The availability of animal models has allowed the investigation of different forms of food immunotherapy.

Objectives: This study aims to investigate the efficacy of immunotherapy with a depigmented-polymerized peanut allergen extract (PE) in a mouse model of peanut allergy.

Results: Four weeks-old CH3/HeOUJ female mice were divided in four groups of seven mice. Mice were orally sensitized with native extract (NE) (10 mg) 6 times at weekly intervals. At week 7, animals were intraperitoneally vaccinated with NE and PE receiving a total of 7 doses every 3 days. Finally animals were challenged in week 10 with 100 mg of NE. Serum samples were collected at 0, 30 and 45 days. Rectal temperature was measured every 10 minutes after challenge and the clinical score recorded.

Group 1: Control group. Vaccinated with saline solution

Group 2: Vaccinated with 3, 10 and 30 μg of PE

Group 3: Vaccinated with 30, 100 and 300 μg of PE

Group 4: Vaccinated with 30, 100 and 300 μg of NE

The group 4 experienced a higher production of Th2 related immunoglobulins (IgE and IgG1) when compared to group 2 and 3. After antigen challenges, group 1 showed a mortality of 71.5% while in groups 2, 3 and 4 the mortality was 85.7%, 28.5% and 42.9% respectively. The evolution of the body temperature correlated with the symptom score results.

Conclusions: Immunotherapy with high doses of depigmented-polymerized peanut extract decreases significantly the mortality of animals after peanut challenges. Animals treated with native extract showed also a reduction of mortality but a higher Th2 response was promoted.

1340 | Delineation of T cell responses after COP immunotherapy in birch pollen allergic patients

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Introduction: Contiguous Overlapping Peptides (COPs) based vaccines provide the novel tool for empowering allergen immunotherapy (AIT). Because COPs allergy vaccines show enhanced immunogenicity they require shorter AIT regime and trigger long-term immune memory against natural birch pollen.

Objectives: Effect of COPs desensitization on allergen-specific T-cell response in birch pollen allergic patients was analysed.

Methods: PBMCs from patients that participated in a double blind, placebo controlled, phase II study (NCT02271009) were collected before, during and after COPs AIT and were stimulated with recombinant Bet v 1 for 7 days. Frequencies of Th1, Th2, Th17, Th22 and Treg cells were analysed by flow cytometry. Cytokine levels were measured in supernatants after 5 days of culture.

Results: Allergen-specific T-cell responses showed decreased frequencies of allergen-specific Th2 cells and increased numbers of allergen specific T-regulatory cells with a concomitant increase of IL-10 levels during the course of COPs AIT. Frequency of Th1 cells was not affected by AIT but increased levels of Th1 cytokines were measured in cell supernatants (IL-2, IFNγ, TNFα). Th22 and Th17 subpopulation frequencies were not affected by COPs AIT. Still, increased levels of IL-17 were detected.

Conclusions: Enhanced T-regulatory cell potential associated with increased IL-10 production as well as the decrease in Th2 cell frequency is the well-defined hallmark of successful allergen extract-based AIT. Here we report that the same scenario can be attributed to COPs desensitization. These results suggest that both whole-allergen- and fast COPs based AIT utilize similar tolerance pathways.

1341 | Sublingual immunotherapy with 5-grass allergen suppresses the "spilling" of the airway inflammation to the lung periphery during the pollen season

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Introduction: In a series of studies we have demonstrated that exhaled breath temperature (EBT), a surrogate marker of airway inflammation, consistently increases during the pollen season in subjects with symptoms of allergic rhinitis sensitized to grass. We have also proved that sublingual immunotherapy (SLIT) with 5-grass allergen vaccine reduces this EBT increase. We have further developed the EBT measuring technique to allow the assessment of the differential contribution of the central airway (Caw) and peripheral airways (Paw) in making up the overall EBT. We now present the results comparing EBT for Caw and Paw in SLIT treated and immunotherapy naïve patients.

Objectives: We recruited 40 immunotherapy naïve volunteers with seasonal allergic rhinitis, all sensitized to grass pollens. Of these, 20 subjects (median age 33 years, age range 17-52 years, 10 men) were prescribed local medications to relieve their symptoms, while the other 20 subjects (median age 29.5 years, age range 12-59 years, 14 men) were started on SLIT with 5-grass mix 2 months before and through the grass pollen season. We measured EBT by means of a hand-held device, requiring multiple breaths into a thermal chamber to achieve a highly reproducible accurate estimate. We also measured the fractions corresponding to Caw (the first 10% of the expired air volume) and Paw (the last 70% of it) sampled with a fast reacting inflatable balloon valve system operated by a computer during a single breathing cycle. The ratios between EBT for Paw and Caw [%] were calculated and compared across the 2 visits.

Results: In line with our previous experience, the in-season EBT increased from 34.08 $\pm$ 0.09°C [mean $\pm$ SEM] at V1 to 34.64 $\pm$ 0.09°C at V2 (P = <0.001) for the subjects on SLIT, and from 34.04 $\pm$ 0.07°C at V1 to 34.75 $\pm$ 0.06°C (P = <0.001) for those on local treatment. The increase was smaller for the SLIT group, but not statistically different from the other group (P = .18). However, the Paw/Caw EBT ratios between V1 and V2 did not increase for the SLIT group (P = .635), while it increased significantly for the local treatment group (P = .005).

Conclusions: As the higher Paw/Caw EBT ratios suggest increased involvement of Paw, it appears that in allergic rhinitis subjects not on immunotherapy the seasonal increase of EBT is at the expense of the Paw, and that SLIT is preventing this increase in the periphery of the lung.

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MISCELLANEOUS

1342 | The horse allergen Equus caballus Equ C 4 in horse saliva

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Introduction: Allergy, which includes asthma, rhinitis and eczema, is one of the most common diseases globally. In Sweden, the most common allergies are caused by pollen allergens followed by an increasing incidence of allergy to allergens from furry animals. The prevalence of horse allergy among the Swedish population is uncertain, but preliminary figures indicate that about 6% are allergic to horses. Allergic sensitization to horse allergen, without direct or occupational exposure, has been shown and is more frequent than expected in urban-living individuals.

The horse (*Equus caballus)* allergens that have been identified are Equ c 1, 2, 3 and 4. Equ c 4 is believed to belong to a family of proteins known as latherins that are known to be present in horse sweat and saliva.

Objectives: The objective of this study was to investigate the allergen profile in ten breeds of horses by analysing the level of the allergen Equ c 4 in saliva.

Method: The study population included horses from ten breeds: American Curly (AC), American Quarter horse (AQ), Gotland pony (G), Icelandic horse (I), North Swedish horse (N), Russian Bashkir horse (B), Shetland pony (SP), Standardbred (S), Swedish warmblood (SWB), and Thoroughbred (T). All 248 horses were registered with their respective breed association, and included a variety of ages (<1–31 years, with a mean of 10 years) and all three sexes (stallion, gelding and mare).

Horse saliva was obtained using Salivette®. The horse allergen Equ c 4 levels were quantified using a two-site sandwich ELISA (mAb 103 and mAb 14G4 from Mabtech AB). Arbitrary units (U) were used since no international standard was available. The level of allergen in saliva was expressed as U Equ c 4/mL.

Results: The horse allergen Equ c 4 was present in saliva from all horse breeds included in this study with small variation in levels. However, the North Swedish horse, adjusted for age, sex and changes over time, showed lower levels of Equ c 4 than any other breed. The levels of Equ c 4 were significantly higher in the samples from stallions, compared to mares and geldings, independent of breed in samples taken both in 2013 and 2014.

Conclusions: The horse allergen level of Equ c 4 in saliva was lowest in the North Swedish horse and significantly higher in stallions, independent of breed.

1343 | Particle size distribution of aluminium hydroxide adsorbed allergen preparation by laser diffraction

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Introduction: In the manufacture of injections containing dispersed particles, measures should be taken to ensure a suitable and controlled particle size (PS) with regard to intended use (Ph. Eur. Monograph on Parenteralia, 0520). Aluminium hydroxide adsorbed allergen preparations are typically polydisperse products. A method was developed to measure the particle size distribution (PSD) of an aluminium hydroxide adsorbed allergen preparation.

Objectives: PS analysis was performed by laser diffraction according to Ph. Eur. 2.9.31 on a Mastersizer 2000 equipped with a Hydro 2000S sample dispersion module. Calculation of the PS is based on the Mie theory (general purpose mode). Assuming that the particles are spherical, PSD will be expressed as volume sphere equivalent. Data are reported as cumulative undersize distribution at 10, 50 and 90%, denoted as d10, d50 and d90, respectively. Impact of concentration range (obscuration), dispersion procedure (stirring rate & lag time) and method duration were investigated. PS of several batches of an aluminium hydroxide adsorbed allergen preparation of different ages were measured with the developed method.

Results: An obscuration value between 7.5 and 12.5% was most optimal. Sample concentration was fixed at the quantity necessary to obtain an obscuration around 10%. At lower stirring speed complete dispersion of the samples takes some time. At higher stirring speeds size increases at later time points suggesting early onset of aggregation. A stirring speed of 1000 rpm was found to be most optimal. The %RSD on the 6 consecutive measurements for d10, d50 and d90 and all measurements times is well below the acceptable values (≤15% for d10 and d90, ≤10% for d50). Depending on the measurement time, either a slight decrease in size (short measurement time) or an increase in size (long measurement times) is observed. Consistent PSD with a median value generally between 8 and 10 μm, and 90% of the particles having a size around 20 μm were obtained. Comparable PSs were observed in fresh and elderly batches, which suggests particles size is not changing in time.

Conclusions: Laser diffraction seems to be a promising method to measure PSD of aluminium hydroxide adsorbed allergen preparations, and could be used to further characterise aluminium hydroxide adsorbed allergen preparations.

1344 | Circular dichroism as a valuable tool to characterise allergen products

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Introduction: Circular Dichroism (CD) is a technique increasingly applied to study protein structures in pharmaceutical products. The value of CD has now been assessed as a tool to characterise various allergen (intermediate) products: (i) purified allergens, (ii) allergen extracts and allergoids, (iii) aluminum hydroxide adsorbed allergoids. CD was tested on these products for monitoring (i) chemical modifications, (i) consistency and (iii) stability.

Objectives: *CD:* Far-UV CD spectra (260-190 nm) were recorded on a J-815 Spectropolarimeter. A purified peanut allergen and peanut allergen extract were reduced and alkylated. CD-spectra were analysed before and after modification. Various batches of tree pollen extract and aluminum adsorbed mites allergoid were investigated via their CD-spectra and a CD-ratio. Temperature interval measurements from 20 to 90°C were performed on a purified bee venom allergen and a tree pollen extract and aluminum adsorbed mites allergoid were incubated at elevated temperatures, exposed to freeze-thawing or shaking. CD-spectra and a CD-ratio were used to study the effect of stressing.

Results: *Purified allergens*: CD was applied to study the chemical modification of a peanut allergen. The CD spectra demonstrated a classical unfolding of the protein (loss of α-helix structures). Additionally, the thermal stability of a bee venom allergen was studied by monitoring its CD spectrum from 20-90°C (structural alterations occurred at 60°C). *Allergen extracts and allergoids:* Consistency of tree pollen extracts was established via CD and the effect of stressing a tree pollen extract was demonstrated (protein unfolding). Next, CD was also shown to be applicable to monitor the chemical modification of a peanut allergen extract (loss of α-helix structures). *Aluminum hydroxide adsorbed allergoids:* CD was able to characterise complex protein suspensions like aluminum adsorbed mite allergoids (mixture of α-and β-structures) for consistency and stability. The use of a CD ratio appeared to be a sensitive tool to monitor consistency and protein stability.

Conclusions: CD was demonstrated to be a valuable tool to characterise allergen products during the whole manufacturing process (from purified allergens up to complex aluminum adsorbed allergoids). CD was shown to be applicable for monitoring chemical modifications, consistency and stability of allergen products.

1345 | Development of an aluminium-based ragweed allergoid immunotherapy using quality-by-design

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Introduction: Development of aluminum-based allergoid vaccines is complex and multi-disciplinary. To enable an integrated approach to process and analytical development for a Ragweed immunotherapy with reduced allergenicity, the quality target product profile of a chemically modified extract coupled to aluminum hydroxide ($Al(OH)_3$) was defined. A risk-based approach was used for the development (process development, analytical development, and protein characterization) of the immunotherapeutic product.

Objectives: The desired effect of process steps on product quality attributes was assessed using Quality-by-Design. The effect of source material, pollen concentration, time, temperature, pH, and of protease inhibitors was investigated for different extraction conditions using total protein, total allergenic activity (Relative IgE potency), Immunoblot and SDS-PAGE for testing. Mass Spectrometry (MS) was used to identify bands in the SDS-PAGE protein profile. Development of filtration and ultrafiltration was focused on the selection of the UF/DF module. Finally, the chemical modification was investigated together with coupling of the modified extract to $Al(OH)_3$ using HP-SEC, residual allergenic activity, immunoblot (cross-linking) and quantification of unbound protein (formulation).

Results: Extraction of Ragweed pollen was robust across all tested conditions as assessed by Total Protein, Total allergenic activity (Relative IgE Potency), allergen profile (immunoblot) and protein profile (SDS-PAGE). UF/DF was robust across all modules tested. With MS Amb a 1 (intact form and alpha/beta chain), Amb a 3, Amb a 4, Amb a 5, Amb a 6, Amb a 8 and Amb a 11 were identified. Crosslinking was robust and reproducible as shown by HP-SEC, allergen profile and protein profiles. IgE activity was reduced as shown by residual allergenic activity assay. A robust formulation was established across a range of product strengths and concentrations of aluminium hydroxide using the concentration unbound protein as a read-out.

Conclusions: A manufacturing process for ragweed immunotherapy with reduced allergenicity coupled to $Al(OH)_3$ was developed. The process was robust and reproducible.

1347 | A sensitive, specific, and validated immunoassay for cat allergen, Fel d 4

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Introduction: A majority of mammalian allergens belong to the lipocalin family of proteins which are small proteins present in body fluids and secretions that promote the induction of IgE responses. Previously, a cat lipocalin allergen, Fel d 4 was identified as another major cat allergen, second only to Fel d 1 in its allergenic importance. Approximately 63% of sera from cat allergic patients contained Fel d 4 specific IgE. Our aim was to develop a sensitive ELISA that could be used to measure Fel d 4 for both environmental exposure assessment and allergen standardization.

Objectives: A two-site ELISA was developed using an affinity purified monoclonal antibody raised against recombinant Fel d 4 for capture and polyclonal rabbit anti-Fel d 4 for detection. The assay was calibrated using purified recombinant Fel d 4 reference standard, with total protein content determined by amino acid analysis.

Results: A full method validation was performed to determine parameters of linearity, range, limits of quantification and detection, accuracy and precision. The ELISA standard curve ranged from 10-0.2 ng/mL, with a limit of quantitation of 0.8 ng/mL. Intra- and inter- assay accuracy results for three known samples run in triplicate on six occasions ranged from 87%-102% and 91%-99% recovery, respectively. Similarly, inter- and intra-assay precision results were calculated and the coefficient of variation ranged from 4%-10% and 5%-8%, respectively. The specificity of the assay was tested and detected Fel d 4 in cat saliva (<0.008-1.6 μg/g; n = 17), epithelial and fur (0.5-30.7 μg/mL; n = 27) preparations. Cross-reactivity with known mammalian lipocalin allergens were tested by measuring Fel d 4 in various urine, epithelial, hair and purified natural allergen samples of cat, dog, horse, cow, mouse, rat and guinea pig (

Conclusions: A sensitive, accurate and precise ELISA with defined specificity for cat allergen, Fel d 4 has been developed. This assay will be useful for the quantitative assessment of environmental exposure to Fel d 4 and may also be used as a potency assessment tool for determining Fel d 4 potency in standardized cat hair extracts used by allergen manufacturers.

1348 | Strategy for quality and safety assessment of hydrolyzed whey-based infant formula

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Introduction: Hydrolyzed infant formulas, generally categorized as partial and extensive based on the degree of hydrolysis, are commonly used for infants genetically predisposed at risk for allergy, and infants diagnosed with cow's milk allergy.

Objectives: To ensure the safety and quality of this specific category, the hypoallergenicity and/or sensitizing capacity of the hydrolysates should be assessed with validated and generally accepted assays. Therefore a program was initiated to develop comprehensive and detailed analyses of the residual allergenicity of whey-based hydrolyzed infant formulas using both in vitro and in vivo approaches.

Results: By assessing the sensitizing capacity in an in vivo mouse model for cow's milk allergy using oral sensitization in combination with the in vitro capacity to cross-link chimeric whey-specific IgE antibodies using the humanized rat basophilic leukaemia cell line RBL-2H3 (transfected with the α-chain of human IgE receptor), both the sensation and challenge phase of the allergic response can be studied. Data will be presented of different ring trial studies aiming to validate the mouse model as well as the RBL-2H3 assay to assess the potential allergenicity of hydrolyzed infant formulas.

Conclusions: This combination of assays is proposed as a strategy for the quality and safety screening of hydrolyzed formulas aimed at preventing sensitization in high-risk infants, and/or resolving clinical symptoms in infants suffering from cow's milk allergy.

1350 | Objective indicators substantiating the benefits of micronized methylcellulose use by sensitized subjects during the grass pollens season

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Introduction: Previous research has demonstrated that nasally insufflated micronized methyl-cellulose (hydroxyl-propyl-methyl-cellulose powder, HPMC) provides protection in subjects with allergic rhinitis by acting as nasal barrier against airborne allergens. We documented the ability of HPMC squirted into the nose right after nasally applied drugs to better relieve and control allergic rhinitis symptoms. What we found worth of further exploration was the possible "healing" effect of HPMC, as symptoms tended not to relapse for days after discontinuation of HPMC, which was not the

case with placebo. The aim of our study was to document objective indicators, which could explain this sustained therapeutic effect.

Objectives: Out of 42 subjects recruited for the study, 35 (median age 31 years, range 18-55 years, 24 men) completed the pre- and end- pollen season objective measurements. They were randomized to treat by locally applied drugs: decongestant (oxymetazoline), and/or antihistamine (azelastine) and/or corticosteroid (mometasone), immediately followed by insufflation in the nose of either HPMC (n = 18) or placebo (lactose powder) (n = 17). They were instructed on how to pick the appropriate drug(s) depending on the nature and severity of the leading symptoms. The objective outcomes documented prior to the pollen season and at the end of it were peak nasal expiratory flow (PNIF), saccharine test (ScchT) and exhaled breath temperature (EBT, a surrogate marker of airways inflammation, which we have proven to significantly increase during the pollen season in subjects with allergic rhinitis without overt asthma). The before/end of season differences were compared by independent t-test.

Results: All three before/end of season differences favoured the HPMC using group compared to the placebo users: for PNIF -60.5 ± 7.9 (mean $\pm$ SEM) vs -30.4 ± 7.6 [L/min], $P = .01$; for ScchT -105.1 ± 82.6 vs 182.6 ± 103.2 [seconds], $P = .036$; for EBT 0.02 ± 0.10 vs -0.38 ± 0.10 [°C], $P = .007$. We hypothesized that HPMC augmenting the local therapeutic response in the nose by further suppressing the nasal congestion (PNIF), by supporting normal cilia beat (ScchT) and suppressing the seasonal surge of airway inflammation (EBT).

Conclusions: HPMC may be valuable adjunct to nasally applied drugs enhancing their pharmacological effects on top of its primary function as barrier to airborne allergens.

1351 | Fel d 1 and fel d 4 allergen levels in fur, urine and saliva of domestic house cats

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Introduction: Cat dander is a common cause of perennial allergies. Although several allergens are present in cat dander, Fel d 1 is considered to be primarily responsible for allergic symptoms. Little is known about levels of other antigens such as Fel d 4. The purpose of this study was to compare the levels of Fel d 1 and Fel d 4 in fur, saliva and urine of male and female domestic house cats.

Objectives: Cats coming for general surgical procedures at a local animal hospital were volunteered by owners for this study. Owners signed an informed consent prior to any sample collection. Fur samples were obtained from 26 male and female cats of various breeds and ages. Urine and saliva samples were obtained from 20 and 17 cats, respectively. Commercially available ELISA kits were used to measure Fel d 1 and Fel d 4 levels.

Results: Study consisted of 26 cats, 13 males and 13 females, age 5.6 ± 4.3 years (mean $\pm$ SD). Urine Fel d 1 (0.02, 0.065-0.071 μg/mL, median, 25-75 percentile) and Fel d 4 (<0.4 μg/mL, the limit of detection) levels were low. In fur, Fel d 4 (0.09, 0.03-0.19 μg/g) was much lower than Fel d 1 (12.24, 5.0-25.0 μg/g), ($P < .001$). Conversely, Fel d 4 was higher than Fel d 1 in saliva (7.62, 1.32-18.5 vs 2.45, 0.75-5.73 μg/mL, respectively, $P = .039$). Allergen levels were not dependent on age, gender or breed.

Conclusions: It appears that the distribution of Fel d 4 differs from that of Fel d 1 in domestic cats. Saliva rather than fur appears to be the main source of Fel d 4. It is possible that levels of Fel d 4 in fur arise from saliva deposited when grooming rather than from secretion from the sebaceous glands.

1352 | Dog allergy to meat: is IDT and specific IgE of any usefulness?

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Introduction: Cutaneous adverse food reactions are a current problem in dogs, with beef, dairy products, chicken and wheat as the most implicated food components. As in humans, cutaneous and serological tests do not show enough individual diagnostic reliability for the diagnosis of food allergy. A wider diagnosis approach, including dietary restriction-provocation trials, is often necessary.

Objectives: Evaluate combined IDT and sIgE for food allergy prediction.

Methods: From 85 dogs attending the Veterinary Hospital of the University of Évora (Portugal) and Rof Codina University Hospital (Lugo, Spain) outpatient consultations, 11 (5 males and 6 females) were selected by means of clinical inquiry and IDT for probable food allergy. All of them presented with pruritic dermatitis and at least 6 of the Favrot's criteria for atopic dermatitis. None of them showed noticeable digestive signs. IDT were performed for Dac g, Phl p Der f, Der p, Aca s, Tyr p, Lep d, beef, pork, lamb, chicken, egg and milk. sIgE panels were determined in a commercial lab for pollens, molds and mites. Assessment of specific IgE for beef, pork, lamb, chicken,

egg and milk was performed in Dot Blots with mouse anti-dog IgE McAb.

Results: Mean sIgE (EAU) was Dac g = 547, Phl p = 601, Der f = 1665, Der p = 297, Aca s = 2063, Tyr p = 1644 and Lep d = 105. IDT were found positive in 4 patients (Dac g), 3 (Phl p), 5 (Der f), 6 (Der p), 4 (Aca s), 1 (Tyr p), 3 (Lep d), 10 (beef), 5 (pork), 5 (lamb), 6 (chicken), 4 (egg) and 2 (milk). Specific IgE Dot Blots showed positive for all patients to beef, pork and lamb, and in 8 of them to chicken. Semi-quantitation was found possible in Dot Blots. Strong positive correlation was observed between specific IgE and IDT to Der p ($P = .048$), IDT and Dot Blots to beef ($P = .015$) and to chicken ($P = .0003$), and the intensity of Dot Blots between beef and lamb ($P = .006$). Semi-quantitative difference was found between meat sources for mean IDT/Dot Blots scores: beef (3.2/3.73), pork (3/3.27), lamb (1.8/2.91) and chicken (1.8/1.3). In dogs presenting positive IDT to beef, pork, lamb or chicken, avoidance of those specific meats was recommended, with significant clinical improvement, especially when beef or chicken were implicated.

Conclusions: IDT and sIgE as less invasive and quicker diagnosis tools, may, along with dietary restriction-provocation trials, be useful for the diagnosis of food allergy as in several clinical cases positive results revealed to be predictive.

1353 | Publication trends of Allergy and Clinical and Translational Allergy journals: a MeSH term-based bibliometric analysis

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Introduction: New tools for bibliometric analysis may provide useful insights into Allergy research meta-structure.

Objectives: We aimed to compare the most frequent topics of research of Allergy and Clinical and Translational Allergy (CTA) journals, as well as whether the creation of CTA had repercussions in the topics published by Allergy.

Methods: We performed a MeSH term-based bibliometric analysis of Allergy and CTA publications We assessed original articles, reviews, and brief communications published in Allergy from 1991 to 2015, and in CTA from its inception (in 2011) to 2015. We analysed all CTA publications, as well as 20% of studies (randomly selected on an annual basis) published in Allergy. The title, abstract, and keywords of these publications were retrieved and converted into MeSH terms, using the online application Syn4Data (available at http://www.syn4data.med.up.pt/). We validated the obtained MeSH terms, and compared their frequency for studies published in Allergy before and after 2011, as well as the frequency of terms retrieved for CTA and post-2011 Allergy publications. In particular, we compared the frequency of MeSH terms in relation to the populations studied and to the related subject categories.

Results: We analysed 985 Allergy and 181 CTA publications, yielding a total of 3382 different MeSH terms. The ratio of studies performed in animals *versus* those with the MesH term "Humans" was significantly higher post-2011 Allergy journal papers compared to studies published prior to that date (34/118 vs 43/440; $P < .001$), as well as to CTA publications (9/138; $P < .001$). The percentage of children-related MeSH terms was significantly higher post-2011 Allergy publications in humans compared to CTA publications (65% vs 42%; $P < .001$). Allergy studies published after 2011 had a significantly higher frequency of basic immunology and molecular biology MeSH terms than pre-2011 publications (45% vs 34%; $P < .001$). On the other hand, post-2011 Allergy studies had a significantly lower frequency of MeSH terms on the subject of allergic rhinitis and allergy to aeroallergens (10% vs 18%; $P < .001$).

Conclusions: When compared to previous publications and with CTA articles, Allergy publications published after 2011 have a higher frequency of animal- and basic immunology-related topics. MeSH terms-based bibliometric analysis identified publishing trends in both journals.

1354 | Behavioural and immunological effects of early life prebiotic and omega-3 poly-unsaturated fatty acid dietary supplementation in healthy mice

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Introduction: Prebiotics and omega 3 poly-unsaturated fatty acids (n-3 PUFA) have microbiota modulating properties that can lead to immuno- and neuromodulation.

Objectives: The objective of this study was to evaluate the dietary effect of a combination of short chain galacto- and long chain fructo-oligosaccharides (scGOS:lcFOS) and n-3 PUFA on behaviour and the immune system in mice.

Method: Postnatal dietary supplementation with 3% scGOS:lcFOS (9:1) and/or n-3 PUFA was tested in healthy male BALB/c mice. Explorative behaviour and anxiety were assessed by an open field and a marble burying test, respectively, at 4, 6 and 8 weeks of age (n = 8-10 per group). In addition, caecal short chain fatty acids (SCFA) and splenic and mesenteric lymph node (MLN) levels of $CD4^+$ cells were measured. All dietary groups including a control diet were compared using two-way or one-way ANOVA analysis.

Results: At 6 weeks of age scGOS:lcFOS and n-3 PUFA separately did not significantly change explorative behaviour of mice. Combination of scGOS:lcFOS with n-3 PUFA resulted in reduced explorative behaviour of mice when compared to the scGOS:lcFOS diet alone. At 8 weeks of age all enriched dietary groups showed a trend towards more explorative behaviour compared with the control group. In addition, the scGOS:lcFOS group buried less marbles compared with the control. In the n-3 PUFA and in the combination diet groups no differences in number of buried marbles were observed compared with the control group. Caecal SCFA levels were only significantly increased in the scGOS:lcFOS group compared with the control group. Although no significant difference was detected in caecal iso-SCFA levels in the scGOS:lcFOS and the n-3 PUFA groups compared with the control group, the levels were decreased by the combination diet. Furthermore, the percentage of $CD4^+$ cells in the spleen was not significantly different between the dietary groups, but in the MLN a trend towards an increased percentage of $CD4^+$ cells was only observed in the scGOS:lcFOS group.

Conclusions: Early life dietary supplementation with scGOS:lcFOS had the highest beneficial effect on explorative behaviour and reduction of anxiety. In addition, only scGOS:lcFOS had an effect on the percentage of $CD4^+$ cells in the MLN and enhanced the levels of caecal SCFA in mice. Further studies are needed to investigate the possible interaction between the dietary components.

1355 | Insect bite hypersensitivity (IBH) in horses: in silico selection of "major" culicoides allergens

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Introduction: Salivary *Culicoides* allergens are causative agents of equine IBH in horses. Only recently several of these allergens have been identified by different means. Those proteins now can be produced as recombinant proteins and employed in e.g. allergen specific IgE ELISA for correlation analyses with the diagnosis of IBH, to determine the sensitization pattern and investigate their relative impact for IBH.

Objectives: The first objective of the present study was to create a short list from the numerous *Culicoides* allergens described so far. Our in-silico selection was based on a local alignment of Culicoides peptides to proteins annotated to be "allergens" in various databases (Uniprot, AllergenOnline, Allergome) and corrected those databases for redundancies. For the pairwise local alignment we employed 10-15 amino acid residues with 5-7 spanning residue overlap. Additionally, the same alignments were performed against a random database of the same size (excluding "allergens") to subtract random hits. The cumulative hit count per *Culicoides* protein was determined and served to compile a short list. Several highly ranked *Culicoides* proteins were produced in eukaryotic expression systems.

The second objective was to verify the relevance of these proteins in IBH by in-vitro tests. Blood samples of IBH and healthy horses were employed and IgG, IgE measurements as well as functional in-vitro basophil activation tests (histamine or sulfide-leukotriene release) were performed.

Results: The most prominent result is, that in all data bases the in silico analysis of the peptide sequence of the *Culicoides obsoletus* antigen-5-like allergen, Cul o 3 (UniProt Acc.No. M4X062) gave outstanding total numbers of hits and multiple "allergenic motifs" within the protein sequence. Results of the in vitro assays in equine blood samples confirm that Cul o 3 is putatively a major allergen in IBH. Notably, this result was reproducible in samples of IBH/healthy horses living in 2 climatically very different regions in Europe – i.e. northern Germany and Switzerland as well as in samples derived from horses in different regions of the United States of America.

Conclusions: In conclusion, results of the bioinformatics analysis compared well with the putative relevance of certain allergens in IBH as determined by (functional) in-vitro tests.

1357 | Hypersensitivity pneumonitis after lung volume reduction with endobronchial valves in a patient with nickel contact allergy

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Case Report: Endobronchial valve (EBV) treatment is a relatively new procedure to improve lung function and exercise capacity in patients with severe pulmonary emphysema. Since EBVs consist of silicone and Nitinol (metal alloy of nickel and titanium), concerns exist regarding the release of nickel which may have a clinical impact in patients allergic to nickel.

Case Report: A 53-year-old smoker with severe emphysema was admitted for bronchial lung volume reduction (BLVR) with EBV. His otherwise medical history was uneventful, except acute intermittent porphyria and an allergy to nickel with a positive scratch test. Four EBVs were implanted bronchoscopically in the right upper lobe. The post-interventional course was uneventful. One month later, the patient reported cough, increasing dyspnea and a new itching exanthema on his trunk and face. Treatment with prednisolone resulted in temporary improvement, but recurred after stopping the steroids with new onset of fever up to 39° Celsius and chills. Laboratory

parameters revealed an increased C-reactive protein, normal procalcitonin and normal BCC. Pulmonary function testing showed decreased diffusion capacity, but otherwise improved lung volumes compared to the pre-EBV situation. In bronchoalveolar lavage, there was marked lymphocytosis (57%) with low CD4/CD8 coefficient and slight eosinophilia (6%), but no infectious cause was found. Thus, hypersensitivity pneumonitis was suspected. The patient's history was negative for inhalative allergies, the blood tests were normal (IgE, tryptase, Sx1, Rx2). The known sensitization to nickel was confirmed, but direct epicutaneous testing to EBVs with and without silicone jacket was negative. Two EBVs (one new and one explanted from another patient) were investigated by electron microscopy and nickel release. There was in-vitro evidence of nickel release from EBV during the first 48 h (mass spectrometry) which is maybe due to an incomplete Silicone layer. Silicone-free areas were larger in the explanted compared to the new EBV. The concentration of released nickel was below the toxic range. However, in patients with nickel allergy, the release is concerning and may lead to a systemic hypersensitivity reaction. As a successful treatment oral prednisolone was restarted, and the symptoms improved gradually.

Discussion: This is the first report describing hypersensitivity pneumonitis after BLVR with EBVs in a patient with proven allergy to nickel. The in-vitro nickel release is concerning in patients with nickel allergy and may lead to a systemic hypersensitivity reaction.

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RISK FACTORS AND MANAGEMENT OF FOOD ALLERGY

1358 | Peanut allergy in Chile: First clinical series of 10 Chilean cases

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Introduction: Prevalence of peanut allergy (PA) has increased over the last years, affecting about 1.1% (3 million people) of the United State population. In line with these data, a recent study by our group showed that PA comprises the most frequent food allergy (FA) among Chilean children, with 1.1% prevalence. However, there are no data regarding clinical characteristics and pattern of sensitization concerning peanut allergic Chilean patients.

Objectives: To evaluate demographic characteristics, clinical manifestations and sensitization profile of peanut allergic patients in Chile.

Ten Chilean patients were recruited with confirmed PA. Demographic characteristics and clinical manifestations were evaluated. Skin prick test with commercial extracts to peanut, other foods, inhalants, lipid transfer protein (LTP) and profilin was made. Specific IgE to peanut was assessed by ImmunoCAP.

Results: The median age was 7.5 years (3-21 years), with a predominance of male gender (60%). Ninety percent of the patients presented another allergic disease, especially allergic rhinitis (6/10) and atopic dermatitis (5/10). Five patients had anaphylaxis, and 8 had another FA in addition to PA. All the patients had a positive prick test to peanut, with an average of 5.8 mm of diameter (ds: 2.75). Fifty percent of the patients presented sensitization to panallergens, 4/10 to LTP and 2/10 to profilins.

Conclusions: In our sample, half of the patients presented anaphylaxis as first manifestation of PA. Most patients had another type of allergy disease (90%) and allergy to another food (70%). Although this is the first study of patients with PA in Chile, it is necessary to carry out studies with a greater number of patients in order to have more representative data of the Chilean population.

1359 | Visual recognition of peanuts and tree nuts in 440 allergic children and their parents

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Introduction: Peanuts and tree nuts frequently cause allergic reactions and accurate identification is essential for avoidance.

Objectives: The purpose of this study was to evaluate the ability of allergic children and their parents to recognize their allergen(s) visually, and to evaluate the impact of therapeutic education.

A retrospective (2012-2016) descriptive analysis was conducted with patients aged >3 years (and their parents) who were allergic to peanuts or tree nuts. The patients were on an avoidance schedule for more than 3 months and participated in therapeutic education sessions at the Saint-Vincent de Paul Hospital Allergology Unit (recruitment from northern France including Paris) in Lille, France. The routine educational sessions presented a standard set of peanuts and tree nuts with and without shells.

Results: Recognition tests (738 allergens) were conducted with 440 patients (mean age 9 years). At baseline, 19% of patients (average) recognized the allergen they were to avoid. There was no significant difference by gender, age, or presentation with or without shell. Variability was observed between allergens but did not reach significance. Recognition tests (73 allergens) were also conducted with 49 parents.

For patients, baseline rate of allergen recognition (with and without shell; mean) are: Peanut 38%, Pistachio 30%, Hazelnut 22%, Walnut 22%, Cashew 17%, Almond 14%, Pecan 0%. For parents: Peanut 93%, Pistachio 100%, Hazelnut 100%, Cashew 85% (not determined for Walnut, Almond and Pecan).

After one therapeutic education session, 57% of patients recognized their allergen(s). The therapeutic education effect was significant, irrespective of age, gender or allergen.

Conclusions: Patients exhibited very low recognition rates for their allergens compared with their parents. The problem is thus not a question of knowledge but of transmission of information from parents to their children, the consequence of very strict avoidance behavior instituted around allergic children. Awareness of this problem could help therapeutic education contribute significantly to better probability of allergen recognition.

Therapeutic education enables better visual recognition of allergens, crucial for successful avoidance, non-recognition remaining an important risk factor.

1359A | Early risk factors for sensitization to food allergens in children up to 3 years

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Introduction: It was indicated that perinatal factors may affect the increased risk of developing food allergy.

Objectives: The aim of the study is to analyze the early risk factors for sensitization to food allergens in children up to 3 years of age with suspected food allergy.

Material and methods: The study included 318 children under 3 years of age hospitalized in 2015 at the Department of Pediatrics, Allergology, and Gastroenterology. IgE-sensitization was established on the basis of the presence of specific IgE-antibodies at a concentration of >0.15 kU/L (Polycheck Allergy, Germany). The positive results of atopy patch tests (APT) using the native food allergens applied on a filter paper covered with IQ Chambers (Chemotechnique Diagnostics, Sweden) formed the basis for non-IgE-mediated sensitization. Patients with negative test results were qualified as the control group.

Results: The sensitization to foods was confirmed in 203 children (63.84%), including IgE-mediated sensitization in 52 (16.35%) and non-IgE-mediated in 151 children (47.48%). In 115 (36.16%) children test results were negative. Majority of children with non-IgE-mediated sensitization were infants (58%), while patients with IgE-mediated sensitization more frequently were older than 12 month (62%; $P = .047$). Compared with the control group, patients with non-IgE-mediated sensitization significantly more often inhabited rural than urban environment (23% vs 39%, P .015). The frequency of caesarean deliveries were similar in both studied groups (35%; 40%) and controls (41%) ($P > .05$). There was no correlation between sequence of pregnancy, average duration of pregnancy, infant birth weight and its assessment with the Apgar score with the sensitization to food allergens ($P > .05$). In the group of children with non-IgE-mediated sensitization, the average time of breastfeeding was significantly longer than in the control group (3.00 vs 1.50 month; $P = .023$). Modified formulas were introduced in the patients with IgE-mediated sensitization later then in the control group (2 vs 1 month; $P = .033$). Compared with the control group, the children with a positive APT, were more often exclusively breastfed (28% vs 10%; $P = .03$).

Conclusions: The way of feeding in the first year of life and place of residence were associated with the development of sensitization to food allergens. There was no evidence that perinatal factors were crucial for the development of food sensitization in children up to 3 years of age.

1360 | Effect of egg and folic acid supplement consumption by pregnant women on food allergies in their children

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Introduction: According to a meta-analysis, consumption of eggs by pregnant mothers was found to have no effect on food allergies in their children. However, we believe that careful study is required because eggs are allergens in the majority of food allergy cases in infants. On the other hand, it was reported that excessive intake of folic acid supplements during pregnancy can increase the risk of development of asthma in children, suggesting that folic acid could influence the immune system of children.

Objectives: We conducted a study on the effect of egg and folic acid supplement intake by pregnant mothers on food allergy onset in their children. In order to study the influence of egg consumption during pregnancy, 7924 expectant mothers with no egg allergy during or prior to the study were recruited as subjects of this study. The questionnaire was distributed during an 18-month checkup targeting all infants.

Results: In the group in which folic acid was taken (FA+ group), 11.6% of children developed food allergies, whereas in the group in which no folic acid was taken (FA− group), 9.9% of children developed food allergies. After adjusting the data according to the order of birth and whether the child was delivered by cesarean section, in the FA− group (3539 mothers), the adjusted odds ratio for mothers who consumed no eggs compared with mothers who consumed two or more eggs a week was 1.45 [95% confidence interval (CI): 1.06-1.97]. When the allergies of the parents were considered, among 900 boys whose mothers had either food allergies or atopic dermatitis or whose fathers had atopic dermatitis, 18.6% and 17.2% developed food allergies in the FA+ and FA− groups, respectively. Among the 186 mothers who consumed no eggs, 11.5% and 32.9% of their children developed food allergies in the FA+ and FA− groups, respectively. The adjusted odds ratio was 0.25 (95% CI: 0.12-0.55), suggesting that the onset of food allergies in children was suppressed by maternal folic acid intake. However, in a comparison of 198 girls under the same conditions, 15.4% developed food allergies in the FA+ group and 19.8% developed food allergies in the FA− group, indicating a minor level of suppression based on material folic acid intake.

Conclusions: Analysis based on the presence of allergies in parents or the sex of the child suggested that the consumption of eggs and folic acid supplements by women during pregnancy can influence the onset of food allergies in young infants.

1361 | Evaluation of L. Rhamnosus GG heat-stability during formula preparation according to FAO/WHO recommendation

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Introduction: It has been demonstrated that dietary intervention with extensively hydrolyzed casein formula (EHCF) supplemented with the probiotic *Lactobacillus rhamnosus* GG (LGG) accelerates tolerance acquisition in infants with cow milk allergy (CMA). Concerns have been raised on LGG stability because FAO/WHO recommend powdered infant formula (PIF) reconstitution with water that is no less than 70°C.

Objectives: We aimed to evaluate if LGG, contained in EHCF could survive during the formula preparation procedure indicated by FAO/WHO.

We boiled drinking water for 10 min. Water was left at room temperature until a temperature of 70°C was achieved, then EHCF containing LGG powder (Nutramigen LGG, Evansville IN, US) was dissolved in the bottle. Bottle was immediately cooled to feeding temperature by holding the bottom under cold running tap. EHCF supplemented with LGG dissolved in water at room temperature served as control. Samples were diluted 1:1000 in distilled water and 100 μL of each samples was spread on the MRS agar plates. The plates were incubated under anaerobic conditions for 72 hours at 37°C.

Results: Manufacturer's specification indicates a LGG concentration from 2.5×10^7 to 5×10^8 CFU/gr with a guaranteed level of 1.46×10^7 CFU/100 mL (approximately 1×10^6 CFU/gr). After EHCF containing LGG preparation according to FAO/WHO recommendation the total LGG counts was 2.7×10^7 that exceeded the guaranteed level of CFU/100 mL.

Conclusions: Reconstitution of EHCF + LGG according to FAO/WHO recommendation for PIF preparation allows an adequate degree of the probiotic survival. Our result suggest that this dietary approach could be efficiently adopted also in Countries where FAO/WHO recommendation are mandatory.

1362 | Baked egg challenges: A 6-year clinical experience from a large, paediatric allergy specialist centre in the UK

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Introduction: The majority of children with egg allergy can tolerate the baked form of egg; studies have shown that regular consumption of baked egg may accelerate the resolution of raw egg allergy.

Objectives: A review of positive baked egg challenges with the aim to assess severity of allergic symptoms and treatment of reactions during the challenge.

Results: 66 children (mean age 6.4 years) had a positive baked egg challenge between Feb 2010- Jan 2016. Male to female ratio was 1:1. Mean time for symptoms to appear was 42 minutes (5-170 mins).

The mean SPT results were: egg extract 7.4 (0-15 mm), raw egg 9.1 (0-23 mm) and the mean specific IgE to egg white was 3.99 (0.02-14.7 kUA/L).

Allergic symptoms recorded are shown on table 1.

With regards to treatment, 60/66 (90%) of patients received antihistamines, 3/66 (4%) were given bronchodilators. Steroids were used in 3/66 (4%). Intramuscular adrenaline was used on four occasions (6%); none of the children required a repeat dose.

Conclusions: Most children, who react while undergoing a baked egg challenge, suffer from mild/moderate symptoms. However, anaphylaxis can also occur (6% in our cohort) and requires prompt treatment with intramuscular adrenaline.

Symptoms	Number of patients (%)
Skin	
Hives/urticaria	17/66 (26%)
Pruritus	11/66 (17%)
Erythema/flushing	11/66 (17%)
Angioedema	7/66 (10%)
Respiratory (upper and lower)	
Sneezing	5/66 (8%)
Cough	5/66 (8%)
Rhinitis	4/66 (6%)
Wheeze	2/66 (3%)
Shortness of breath	1/66 (1.5%)
Gastrointestinal	
Abdominal Pain	26/66 (39%)
Vomiting	15/66 (23%)
Nausea	12/66 (18%)
Oral itching/sore throat	11/66 (17%)
Diarrhoea	1/66 (1.5%)
Behavioural change	9/66 (14%)
Anaphylaxis	4/66 (6%)

1363 | Epicutaneous immunotherapy (EPIT) for peanut allergy modifies igG4 responses to major peanut allergens

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Introduction: Epicutaneous immunotherapy (EPIT) for peanut has been shown to increase significantly the threshold levels of peanut allergic patients, especially in children.

Objectives: We sought to analyze immunologic effects induced by peanut EPIT in children by assessing serological changes. Sera were collected from children (6-11 years) before and after 1 year of treatment with Viaskin® Peanut (250 μg dose, n = 25) or placebo (n = 26) in the VIPES trial. IgE and IgG4 peanut component levels were determined with two methods. ImmunoCAP (Thermo Fisher Scientific) was used to assess immunoglobulin levels for selected allergens. The multiplex assay ISAC (Thermo Fisher Scientific) was used to evaluate immunoglobulin levels to a broader range of allergens. The ISAC results are expressed in units used by the manufacturer (ISU), for IgE indirectly standardized against WHO preparation 75/502.

Results: ImmunoCAP and ISAC correlated well for those individual peanut allergens that are available on both platforms, demonstrating the suitability of the ISAC method to assess the global sensitization profile of children in the VIPES trial. Peanut-sensitization at baseline was dominated by Ara h2 and Ara h6 (median (lower quartile; upper quartile): 29.5 (12.0; 56.7) and 25.5 (8.5; 36.5) ISU, respectively) and all 51 subjects were positive for these two allergens. IgE for Ara h1 was found in 44/51 subjects (9.7 (1.5; 23.4) ISU) and for Ara h3 in 36/51 subjects (3.0 (0.0; 24.8) ISU). 25/51 subjects had IgE to Ara h8, and IgE levels were low (0.0 (0.0; 0.7) ISU) compared to those of Ara h2 and Ara h6. ISAC analysis showed that IgE to Ara h6 correlates closely with IgE to Ara h2. IgG4 induction after 1 year of treatment was most pronounced for Ara h2 and Ara h6, followed by Ara h1 and Ara h3 (*P*-value from Wilcoxon-signed-rank test <.001 for Ara h2, Ara h6 and Ara h1, and <.005 for Ara h3). Corresponding median fold increases were 21, 18, 3, and 1.2 fold respectively. No significant increases were observed for Ara h8 and Ara h9. No induction of IgG4 was observed in the placebo group.

Conclusions: In terms of sensitization, Ara h2 and Ara h6 are believed to be the most important allergens in this population. Peanut EPIT induces IgG4 in particular to these allergens, and to Ara h1 and Ara h3 as well. This demonstrates that peanut EPIT induces a humoral response to the most relevant peanut allergens.

1364 | Long term outcomes of oral immunotherapy for cow's milk allergy

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Introduction: Oral immunotherapy (OIT) for cow's milk (CM) allergy is a highly controversial treatment modality. Long term outcomes are very important for evaluating success of the treatment.

Objectives: In this study we aimed to investigate long term outcomes of our OIT patients.

Results: Twenty-two girls, 45 CM allergy patients treated with OIT was included to the study. After a mean 3.3 ± 1.3 (1-6) years follow-up period only one patient couldn't drink milk and had reactions such as urticaria/angioedema especially with infections but he could drink yogurt drink without a problem. Two patients didn't drink milk and two patients didn't eat cheese or yogurt because they didn't like. Ninety-seven percent of the patients could consume milk and milk products.

Laboratory tests showed no difference of total IgE levels before and after follow-up period. Mean CM-spIgE which was 21.9 ± 27.2 kU/L at the beginning was found 1.9 ± 0.7 kU/L with a 50% negativity to date. Alpha-lactalbumin-spIgE, beta-lactoglobulin-spIgE, casein-spIgE levels decreased significantly especially more distinctly at casein. We also saw a significant regression at SPT endurations for CM (9 ± 6.8 mm/0 mm) and goats milk (8.7 ± 6.7 mm/0.5 ± 1.7 mm). We didn't find any significant difference of laboratory tests between the groups who drink milk liking or not liking or the one with reactions.

Aeroallergen sensitivity rate before and after treatment was 31.8% and 40%, respectively. Four of these patients had no symptoms but the others were followed-up for allergic rhinitis or asthma. Skin prick tests (SPT) revealed grass-pollen (41.1%), dermatophagoides (41.1%), cat (23.5%) and mold (17.6%) sensitivity.

Conclusions: OIT is a successful therapy for CM allergy when applied by experienced centers.

1365 | Soti for wheat allergy in a one-year-old girl: a case report of a modified protocol

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Case Report: Introduction: IgE-mediated allergy to wheat has been reported to affect up to 1% of the pediatric population. Although strict avoidance of the culprit allergen remains the cornerstone of its management, specific oral tolerance induction (SOTI) may also

represent an alternative to dietetic restrictions. SOTI has been successfully implemented in children, mainly in the setting of cow's milk allergy, but its safety and efficacy in achieving tolerance to wheat remains poorly investigated.

Objectives: We present the case of a one-year-old girl with wheat allergy, who successfully underwent SOTI to wheat in the Allergy Department of Sotiria Athens General Hospital.

Results: Our one-year-old patient was referred to our department for further evaluation of suspected food allergy (to cow's milk, egg and wheat). The patient had a previous episode of urticaria after first-time consumption of wheat, at the age of 10 months, and had not been exposed to wheat ever since. Her remaining personal atopic history was positive for atopic dermatitis; her family history of atopic diseases was also positive. Specific IgE to Triticum aestivum (f4) and gluten (f79) was 9.63 KUA/L and 9.56 KUA/L, respectively. Total IgE was 77.6 KUA/L. The SPT to wheat was 6 mm. SOTI was decided, with parental consent. Taking into account the patient's age and in order to be able to have as accurate wheat quantity measurements as possible, we decided to use mashed pasta and measure its quantity in milliliters. The initial dose was 5 drops of a solution made from a drop of mashed pasta and 10 mL of water. Each subsequent dose was increased by 20%-50% from the previous one. The final dose was 50 mL of undiluted pasta, achieved on the 12th day. On days 2, 4 and 8 of the above protocol, exacerbation of atopic dermatitis and urticaria was observed, promptly treated with oral antihistamines. The patient's parents were instructed to gradually increase the quantity of pasta at home by 2 mL every day, until 200 mL were reached. No other complications were noted until completion of SOTI. At the latest six months follow-up evaluation, following completion of SOTI and unrestricted consumption of wheat, the patient remained well and symptom-free.

Conclusion: SOTI to wheat was successful and safe for our patient. Our modified protocol using mashed pasta was practical and easy to follow. Additional studies are warranted to confirm the efficacy and safety of wheat SOTI in routine pediatric practice.

1366 | Safety and tolerability of subcutaneous immunotherapy (SCIT) with a modified peanut extract in peanut-allergic adults, adolescents and children

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Introduction: HAL-MPE1 is a chemically modified, aluminum hydroxide absorbed peanut extract being developed for SCIT for treatment of peanut allergy. The first-in-human safety and tolerability study with HAL-MPE1 in adult patients with peanut allergy was recently successfully completed in Denmark (EudraCT 2013-004238-13). The results of this randomized, placebo-controlled study in 17 adult patients, with dose escalation to 375 μg peanut protein during 14 weeks, showed that treatment with HAL-MPE1 was generally safe and well tolerated and that the immunological response was supportive of the pharmacological action of HAL-MPE1. The second study is currently ongoing with primary objective to investigate the safety and tolerability of HAL-MPE1 in adults, adolescents and children and secondary objective to evaluate the immunological response compared to placebo.

Objectives: This is a prospective, randomized, double blind placebo controlled, multi-centre study in 42 patients with documented peanut allergy. In order to increase the experience in the adult population, the study will start with a group of 12 adult patients (18-50 aged years). After completion and evaluation of the safety results in the adult population, the study is planned to continue with 15 adolescents (12-18 years) and 15 children (5-12 years). HAL-MPE1 or placebo will be administered subcutaneously once weekly, using a dose titration schedule starting with 0.05 μg modified peanut protein and gradually increasing the dose to reach the maximum dose of 375 μg after 13 weeks of treatment. This maximum dose will be repeated twice, with an interval of 1 and 2 weeks. The safety and tolerability of HAL-MPE1 treatment will be assessed by recording immediate, early and late local and systemic allergic reactions, and other adverse events. As a secondary outcome, the immunological response will be evaluated by determination of serum specific immunoglobulins (IgE, IgG, IgE-FAB), a basophil activation test and a histamine release test.

Results: This safety study with HAL-MPE1 was initiated at 3 academic sites in the US in Q4 2016

Conclusions: The described study with a modified peanut SCIT product is the next step in developing this novel immunotherapy for peanut allergy.

1367 | Oral immunotherapy and follow-up in highly sensitized egg allergic children

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Introduction: Egg is one of the most common causes of food allergy in children. Egg avoidance causes significant dietary limitations, and patients are at risk of severe allergic reactions in case of accidental ingestion. Oral Inmunotherapy (OIT) is an immunomodulatory treatment in use over the last decade.

Objectives: The purpose of this study was to describe the demographic characteristics, length and reactions during OIT, tolerance, and clinical follow-up in highly sensitized patients.

A retrospective, descriptive study was designed. Patients with persistent egg allergy and high sensitization (sIgE to ovalbumin—OVA- and/or ovomucoid—OVM- > 80 kU/L) that underwent OIT from January 2006 to May 2016 were included. Informed consent was obtained for all patients.

Results: Twelve patients were included. All patients had other atopic condition, like rhinitis-asthma (11), other food allergy (8), atopic dermatitis (7). 5 patients had undergone a previous failed egg OIT.

Median age at the beginning of OIT was 11.5 years (range: 7-14 years), median sIgE: OVA 93.2 kU/L (range: 52.5-594), OVM 86 kU/L (range: 42.7-234). All patients had positive skin prick test for egg, OVA and OVM.

Median OIT duration was 12 weeks (range: 8-24). 9 patients presented reactions during induction phase, with a median of 5 reactions (range: 2-10). Mild (oral itchy, mild abdominal ache): 33%, moderate (hives, moderate abdominal ache): 44%, severe 22% (anaphylaxis). 2 reactions were associated with cofactors (exercise, menstruation).

10 patients (83%) required premedication with antihistamines. Because of repeated reactions throughout induction phase and/or previous failed egg OIT, omalizumab was used like adjuvant in 5 patients (42%).

9 patients (75%) completed the treatment. Three patients were withdrawn due to repeated digestive symptoms. All patients continued 3-cooked eggs/week.

During maintenance phase, 6 patients had reactions. Mild: 67%, moderate: 33%, severe: 17%. Five patients (56%) achieved complete tolerance (including raw egg white) and 4 patients (44%) partial tolerance (cooked egg lone).

Conclusions: -OIT seems a valid treatment option for persistent egg allergy even in highly sensitized patients. Most of them achieved tolerance (partial or complete); in these case omalizumab appear to be a hopeful adjuvant treatment.

-During induction phase, most of the reactions were moderate-severe, while in maintenance phase were mild.

-Digestive symptoms were the cause for withdrawals in our group.

1368 | Adverse reactions during oral food immunotherapy in patients allergic to cow's milk or egg proteins: our experience

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Introduction: Oral food immunotherapy (OIT) is an experimental technique, not exempt of adverse reactions of varying severity, allowing complete dose or traces of food tolerance in a significant percentage of allergic patients. We evaluated the adverse reactions during OIT that occurred in one year in our department.

Objectives: Descriptive, retrospective study in 25 patients between 4 and 24 years old treated with OIT to cow's milk (M) and egg (E). We use a modified protocol based on the *Spanish-approved OIT protocol of the Society of Clinical Immunology and Pediatric Allergy* (SEICAP).

Results: A total of 25 patients received OIT, 8 for cow's milk (M) and 17 for egg (E). The mean age was 12.12 years in M (range: 4-24) and 7.94 years in E (range: 4-21). Eight patients were treated with M-OIT, 6 presented adverse reactions (75%) and 17 patients were treated with E-OIT, 8 presented adverse reactions (47.60%). A total of 31 adverse reactions (15 M-OIT, 16 E-OIT) occurred. In the induction phase, 14 patients had 1 adverse reaction (6 M-OIT, 8 E-OIT) and 8 patients more than one adverse reaction (3 M-OIT, 5 E-OIT). One patient had an adverse reaction in maintenance phase in M-OIT. The most frequent severity reaction degree, according to Sampson scale, was II (33.33% M-OIT, 62.50% E-OIT). Patients with adverse reactions to M-OIT had a mean total IgE of 2854.52 kU/L, casein-sIgE 37.87 Ku/L (0.10- >100), milk skin prick test (SPT) 5.5 mm (3-7) and casein SPT 3.47 mm (0-10). Patients with adverse reactions to E-OIT had a mean total IgE of 934.50 kU/L, ovomucoid-sIgE 27.46 kU/L (0.10-99), egg SPT 6.12 mm (0-10) and ovomucoid SPT 5 mm (0-10). Cofactors were identified in 10 adverse reactions, 7 for M-OIT and 3 for E-OIT.

Conclusions: Adverse reactions during OIT are common. Our percentage and severity of adverse reactions are similar to those of other published series. It is important to know the risk of them during OIT.

1369 | Current management and use of oral immunotherapy for peanut allergy across Western Europe

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Introduction: Peanut allergy is a major health burden in Europe, affecting 4.4 million people. Treatment is largely limited to avoidance and management of acute reactions; peanut oral immunotherapy (OIT) remains experimental, its responses varied, and longevity uncertain.

Objectives: To understand current practice protocols for experimental peanut (OIT) in France, Germany, Italy, Spain, Switzerland, and UK.

To this end, we conducted qualitative, in-depth, telephonic, interviews with 93 physician and nurse food allergy specialists across the six countries between September 2016 and January 2017. Eligibility criteria included managing >100 unique peanut allergy patients per year and offering immunotherapy.

Results: Widely differing practice patterns were observed in the diagnosis and management of peanut allergy (e.g. use of food challenges, prescription of adrenaline autoinjectors, etc.); however, the starkest differences were seen in the administration of experimental OIT.

Use of OIT for peanut allergens is not EMA approved; however, a few physicians (e.g., in France and Germany) have developed and use experimental peanut OIT protocols. These OIT protocols vary substantially in terms of:

Patient selection: Differing opinions about treating very severe patients for fear of anaphylaxis

Peanut material: Includes whole peanuts (Spain), peanut candy (France), pharmacy compounded peanut flour capsules (Germany)

Starting dose: Can be patient-tailored (e.g., in France, patients initiated at 0.1× the reactive food challenge dose) or fixed (e.g. in Germany, dose ranges from 0.1 to 10 mg in different practices)

End-dose: Ranges from 500 mg to ~1 gm

Up-dosing interval: Every few days, up to one month

Clinician oversight during updosing: Ranges from no oversight (patients updose themselves at home) to intensive monitoring (patient observed for 3-4 hours following peanut administration, monitored by physician or nurse)

Amongst those physicians not offering peanut OIT, major barriers include the lack of an EMA approved therapy, standardized protocols, or national guidelines.

Conclusions: Substantial variability in the approach to experimental peanut OIT exists within and across countries. Differing practice standards lead to uncertainty in patient selection and treated patients achieve widely varying tolerability levels. Use of unconventional practices to serve peanut allergy patients suggests an unmet need for a standardized, EMA approved OIT protocol to treat peanut allergy.

1370 | Omalizumab combined with oral immunotherapy for the treatment of severe cow's milk allergy: Our 2-year-long experience

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Introduction: Oral immunotherapy (OIT) combined with omalizumab (O) can be an effective and safe approach treatment to rapid desensitization in children with severe cow's milk allergy (CMA). We report our experience.

Objectives: To evaluate the safety and efficacy of OIT combined with O.

Methods: Volunteers with severe CMA that had previously interrupted a conventional OIT for dose-related severe anaphylactic reactions were enrolled. Informed written consent was obtained by parents before the treatment. As off label treatment, O was administered according to the package insert for asthma. Each pts undertook s.c. injections of O for 8 wks prior to and 8 wks following the initiation of OIT. On the initial escalation day, dosing began at 1.5 mL of cow's milk (CM, 5 mg of proteins) and were slowly increased until the pt reached a final dose of 200 mL or if any adverse event (AEs). The highest tolerated dose (i.e. with no clinical reactivity) determined the pt's starting daily home dose. The pts returned to the clinic every 2 wks for a dose escalation visit. OIT protocol did not advance according to a fixed calendar, but, rather were individualized according to pts allergic reactions and safety outcomes. After the up-dosing regimen the maintenance phase was performed (200 mL of CM daily and dairy products ad libitum).

Results: We have enrolled 6 children (n male = 4), aged 9.8 ± 2.31 years (mean ± SD) suffering from severe CMA. 4 children had concomitant allergic asthma (A) and one of the latter atopic dermatitis, too.

EFFICACY: 2 pts reached the maintained dose of CM 200 mL after 17 wks; 1 reached the dose of 150 mL of CM and dairy products after 7 months. All of them are going on daily maintenance intake since a 12 months.

Three points interrupted OIT during the build- up phase: 1 for severe AE (2 mL CM); 1 for concomitant severe A; 1 for personal problem.

SAFETY: 2 pts developed severe anaphylactic reactions after dose intake: 1 at the increasing dose of 2 mL [rhinitis (R), cough, A, angioedema-urticaria (U), hypotension]; 1 at the maintenance dose of 150 mL (U&A). All of them have history of A.

The same 2 pts developed mild AEs during the induction phase: 1 reacted at 8 mL (R) and 25 mL of CM (U); another at 150 mL of CM (R & U).

Conclusions: This combined approach could allow for a more successful and safer desensitization in children with high-risk CMA that had failed a conventional OIT protocol. However, in pts with concomitant A, it could be less effective.

1371 | An adult-onset kiwi allergy case not accompanied by multiple drug allergy with a history of latex allergy

Örçen C; Bulut I; Tepetam FM; Keren M

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Case Report: A patient (N.H.) with diagnoses of HT and bronchial asthma, as well as with a history of admissions on separate occasions to the emergency service due to anaphylaxis following the use of penicillin or proton pump inhibitor, stated that she has experienced swelling in face and eyelids after eating kiwi within the last two years for a total of three times.

Method: Skin prick test was performed with respiratory and food allergen panels in the patient. No sensitization was detected. Prick test was applied to the patient in order to evaluate the possibility of cross-reactivity with latex, and it was found as negative. Also, prick test with kiwi was performed by prick-to-prick method in the patient.

Results: After 20 minutes, an induration of 6 × 6 mm accompanied by hyperemia was detected against kiwi. Kiwi allergy of the patient was thus confirmed by prick-to-prick test. Adrenaline auto-injector was prescribed for the patient, and kiwi was removed from her diet. She was put into follow-up in our polyclinic.

Conclusion: With this kiwi allergy case which is not accompanied by latex allergy, we wanted to highlight that food allergy may also be seen in adults, and food allergy in anamnesis should be taken into consideration and confirmed.

1373 | An late-onset multiple food allergy case

Örçen C; Bulut I; Tepetam FM; Keren M

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Case Report: A male patient (B.B.) at the age of 40 with complaints of food allergy applied to our immunology and allergy polyclinic. Patient stated that he has been suffering from swallowing difficulty starting with feeling of itching and swelling in throat immediately after eating kiwi and certain half-cooked fish species for about 15 years. He also told that he does not experience any complaints with the cooked forms of the same foods.

Method: Skin prick tests (ALK-Abello-Denmark) were carried out with standard ready-to-use respiratory and food allergen extracts and latex in the said patient. No positivity was detected. In accordance with the kinds of foods described by the patient, several prick-to-prick tests were made with kiwi, raw and cooked anchovy, bream, chicken and turkey. In prick-to-prick tests, positivity accompanied by hyperemia and induration 7 × 7 mm with kiwi, of 8 × 8 mm with raw anchovy, of 11 × 11 mm with raw chicken, of 7 × 7 mm with cooked chicken and of 5 × 5 mm with raw turkey was detected. On the other hand, prick-to-prick tests carried out with cooked anchovy and cooked turkey were accepted as negative.

Results: As a result of confirmation of the presence of food allergy stated by the patient in his history, adrenaline automatic injector was prescribed for the patient. The foods responsible for allergy were removed from his diet.

Conclusion: With this multiple food allergy case, we wanted to show that in adults food allergy may also be seen in advanced age period, and to highlight that if a patient describes a history of food allergy it should be taken into consideration and confirmed.

1374 | A late adult-onset egg allergy case

Örçen C; Bulut I; Tepetam FM; Keren M

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Case Report

Introduction: Egg allergy is rarely seen in adult age group. We herein present a case about a patient who has presented to our allergy and immunology polyclinic with a complaint of egg allergy.

Case: A female patient (H.G.) at the age of 48. As reported by the patient, she has presented to the emergency service 2 years ago due to swollen tongue, swallowing difficulty and shortness of breath developed following nasal discharge and tickly throat which had occurred immediately after eating egg. Within these 2 years, she has presented to the emergency service for a total of three times with similar complaints after eating egg.

Method: A prick test (ALK-Abello-Denmark) was performed with a ready-to-use allergen solution in the patient, and potent positive reactions were detected against egg white and yolk. Adrenaline auto-injector was prescribed for the patient. She was advised not to eat egg and egg-containing foods by any means.

Conclusion: We wanted to show that a late-onset egg allergy may also be seen in adults though it is rare, and to highlight that patients describing a history with such complaints should be cared with due importance.

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1375 | A multiple fruit allergy clinical case—co-sensitization or cross-reactivity?

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Case Report: Background: Multiple fruit allergy may be due to co-sensitization or more often to cross-reactivity. Several proteins are described as being responsible for cross-reactivity, in particular nsLTP, Profilin and PR-10. Thaumatin-like proteins (TLPs) are also responsible for cross-reactivity, although they are less frequently reported in the literature.

Report: A 24-year-old caucasian female, cook, with previous history of rhinitis and three gynecologic surgeries without complications was referred to our outpatient clinic for suspected food allergy. She presented with rapid-onset rhinorrhea, oropharyngeal itching and acute urticaria after banana milkshake intake. After this episode, she presented several reproducible reactions with vomiting, diarrhea and dysphonia after grape, wine, olives, olive oil, cantaloupe, melon, kiwi, persimmon, fig, papaya, nut, açai, peach and tomato intake. She also referred rhinoconjuntivitis while frying banana and hand pruritus while preparing fruit salad. She had no complaints with latex contact. She tolerates orange, apple, pear, cucumber and lettuce. Skin prick tests to aeroallergens were positive to D. pteronyssinus, plane tree, pellitory, birch and dog. Skin prick tests with commercial extracts were positive to banana, kiwi, avocado, grape, fig, mango, pineapple, tomato, latex and negative to LTP and profilin. Prick-prick tests were positive to grape, olive, olive oil, peach peel and walnut and negative to peach pulp and melon. ImmunoCAP ISAC® was positive only to TLP nAct d 2 (kiwi). Adrenaline auto-injector, fexofenadine and prednisolone were prescribed as emergency treatment.

Discussion: TLPs have been identified in several fruits, vegetables and pollens. They are considered a putative panallergen but cases of allergy to multiple fruits are rarely described. In this patient with severe reactions to several fruits and vegetables the positive IgE to TLP and the negative result to other panallergens strongly indicate TLP as the causative allergen.

1376 | Jackfruit allergy—An increasing exotic problem linked to the oral allergy syndrome

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Case Report: Introduction: Jackfruit (*Artocarpus heterophyllus*), otherwise known as breadfruit, is a member of the mulberry family. Jackfruit allergy is extremely rare and previous reports have been restricted to subjects with Silver Birch pollen-related oral allergy syndrome (OAS).

Objectives: We report five cases of people from the Indian subcontinent who have settled in the UK for over 10 years, and developed jackfruit allergy on a background of the oral allergy syndrome.

Cases: All of the five patients had all suffered seasonal allergic rhinitis, particularly in the spring, which affected their eyes and nose. After 5-6 years they had initially developed oral mucosa-limited immediate reactivity to raw but not cooked apples and peaches and had subsequently avoided fruit of the Rosacaea family with no symptoms. All but one had developed oral itching, dysphagia, and facial swelling following the ingestion of raw jackfruit (the remaining patient did not have an acute episode of systemic reactivity to jackfruit, but reported oral itching following ingestion).
Skin testing with the raw jackfruit was confirmatory in all cases but blood tests were mixed in their positivity.

Conclusion: Jackfruit allergy is likely to increase in Western countries owing to the increasing export of this fruit by Asian, African and Caribbean countries and global migration trends. Jackfruit contains proteins that cross react with the silver birch BetV1 protein that underlies the OAS. Physicians should be aware that most cases are related to the oral allergy syndrome and blood tests may be negative while skin tests with the raw fruit are positive. While jackfruit allergy is extremely unlikely to occur in people who remain resident in Asia it is possible that it may occur in people who return to Asia having resided in Europe and developed Silver birch pollen allergic rhinitis and the oral allergy syndrome. Similarly, European patients with birch pollen-related oral allergy syndrome travelling to Asia are at risk of significant allergic symptoms on eating jackfruit.

1377 | Kiwi allergy—a case series

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Introduction: Kiwi, *actinidia deliciosa*, allergy was first described in 1981 and it is now an important and increasing cause of food allergy. Symptoms can vary in severity from oral allergy syndrome (OAS) to anaphylaxis. Kiwi allergy is frequently associated with birch and grass pollinosis or latex hypersensitivity; however monosensitization has been reported, suggesting a possible primary sensitization to this fruit.

Objectives: To access clinical characteristics of patients with kiwi allergy suspicion and patterns of cross sensitization in kiwi allergic patients.

Results: A review of medical records of all patients with suspected kiwi allergy followed in our department from 2010 to 2016. Demographic and clinical history data, specific IgE, skin test results (skin prick tests with kiwi commercial extract (SPT) or skin prick-to-prick tests with kiwi) and oral food challenges results were collected.

A total of 32 patients, 18 (56%) female, with a mean (±SD) age of 22.3 (14.9) years were included. Regarding allergic comorbidities, 44% had asthma, 69% rhinitis, 3% atopic dermatitis, 72% suspected allergy to other foods (10 to fresh fruits, 5 to egg, 4 to nuts, 4 to shellfish, 1 to milk and 4 to other foods). Of the 24 patients sensitized to aeroallergens, 64% were sensitized to pollens (4 patients to birch, 12 to grasses, 10 to weeds). Furthermore, 2 presented positive SPT to latex, 1 to LTP and 1 to profilin.

With respect to clinical manifestations, isolated cutaneous symptoms were the most common manifestation with kiwi (41%), followed by oral allergy syndrome (25%), anaphylaxis (19%), gastro-intestinal symptoms (6%) and respiratory symptoms (3%).

Sensitization to kiwi was confirmed in 78% patients (56% with both positive skin tests and sIgE, 32% with positive skin tests alone and 28% with sIgE alone). Eight patients were sensitized to kiwi but not to profilin, LTP, birch, grass or weed pollen, nor latex.

Four open food challenges with kiwi were performed and all were negative.

Conclusions: In this population, sensitization to kiwi was found in the vast majority of patients with suggestive history and almost a third were monosensitized to kiwi. Cutaneous symptoms were the most common manifestation but anaphylaxis occurred in almost one fifth of the patients.

1378 | Kounis syndrome; an underdiagnosed entity

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Introduction: Kounis syndrome is defined as the coincidental occurrence of an acute coronary event and an anaphylactic allergic reaction. The main physiopathological mechanism appears to be a coronary vasospasm. Drugs are the most common trigger, but food also could be implicated.

Objectives: We report a patient without history of food allergy who developed an anaphylactic reaction with elevation of cardiac enzymes and alterations in the electrocardiogram after the ingestion of cashew.

Results: We present a 22 years old male outpatient clinic with history of conjunctival erythema on contact with walnuts, asthma in relationship with physical exercise and smoker, without other cardiovascular risk factors. Five minutes after the ingestion of Indian rice which containing cashew, he present a skin pruritus and erythema in trunk, dizziness, vomiting and dyspnea. At the arrival of the paramedics, he presented hypotension and bronchospasm. It was treated with 0.5 mg of adrenaline, 200 mg of hydrocortisone and fluid replacement intravenously. He was immediately transferred to the emergency room where, additionally, he presented generalized erythema and lips edema, therefore it was treated with 40 mg of methylprednisolone and 5 mg of dexchlorpheniramine. Symptoms went down 30 minutes later. In this context, electrocardiogram showed a decrease on T waves in leads II, III and aVF. The blood analysis revealed high levels of troponin T values (maximum value of 28 ng/L), eosinophil count was in normal range. 14 hours later observation, the patient was discharged.

When the patient was evaluated in our Allergy Service, skin prick test with cashew and the rest of nuts were not performed because the patient did not consent.

The laboratory data showed a serum total IgE of 172 KU/L (normal <120), IgE specific for cashew of 8.75 KUA/L, peanut 0.45 KUA/L, hazelnut 13.1 KUA/L, pistachio 12.1 KUA/L, pinion 0.25 KUA/L, nut 33 KUA/L, sunflower seed 0.67 KUA/L (normal <0.35). The serum tryptase basal level was 7.74 μg/L (normal <11.5).

Control electrocardiogram demonstrated the completed resolution of the T waves decrease as well as a normal echocardiogram.

Conclusions: We report the first published case of Kounis syndrome type I by cashew nuts.

Food inducing Kounis syndrome by nuts is rare and a few cases have been reported.

The cardiac manifestations and electrocardiographic findings are very varied, this makes diagnosis even more difficult. For this reason Kounis Syndrome is an under-diagnosed illness.

1379 | Interspecies cross reactivity beyond parvalbumin in allergy food: a case report between tuna and grouper

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Case Report: Background: The major allergen causing allergy to fish is parvalbumin but many others allergens, which remain unknown, are also responsible for many allergic reactions.

Method: We present a case report of a 24 years old man who presented immediate abdominal pain and urticaria after fresh or tin tuna fish ingestion. Since the same symptoms occurred after grouper ingestion, he consequently stopped fish ingestion. Patient was subjected to a prick-prick analysis, prick tests and open oral challenge. Serum specific IgE was determined by Hycor-ELISA. In order to determine the reactivity to the different fish at molecular level, proteins were subjected to SDS-PAGE, transferred to PVDF membranes, blocked and subsequently incubated with patient's serum. Immunoreactive bands were resolved by incubation with anti IgE-HRP antibodies and detection by chemiluminescence

Results: Among all the prick-prick analysis performed (including fresh tuna, cod, anchovy, harvest fish, gilt head bream, hake and monkfish, but not grouper), only tuna resulted positive. Regarding the prick tests using commercial extracts, they were exclusively positive to tuna. Conversely, for self-prepared extracts (including tuna, grouper, fresh hake, perch and orange roughly), both tuna and grouper were positive. Open oral challenge was carried out with hake and orange roughly, and they both were well tolerated. Specific IgE determinations revealed values of 1.08 IKU/L and 0.58 IKI/L to tuna and orange roughly, respectively. All the other specific IgE analysis performed were negative to cod, perch, hake, grouper and Cod parvalbumin (rGad c1). In terms of Immunoblotting, a strong smeary reactive signal was found in tuna fish for very high molecular weight (range 80-180 KDa) proteins, probably including the different collagen allergens and other proteins as transferrin. Among all the species analysed, the grouper was the only one where a non identified high molecular weight (~175 KDa) protein was shared with tuna fish. In contrast to the restricted pattern for high molecular weight proteins, two bands of ~50 KDa (probably corresponding to enolases) and ~35 KDa (probably corresponding to fish tropomyosin) were detected in all fish extracts. A major band of ~25 KDa was detected (as previously described) in orange roughly and also in perch and grouper. In the last specie an additional band of ~18 KDa (the same molecular weight of an allergenic protein described in other fish as Pangasius) was found. No reactivity at all was observed for any of the species analysed to parvalbumin.

Conclusion: Although the patient recognises different bands from the different studied fishes at molecular level, he is able to tolerate some of them, suggesting a subclinical sensitisation. However, the recognised ~175 KDa protein, common for both tuna and grouper extracts, seems to be cause of his allergy. So far, no protein of about that molecular weight has been described in the scientific literature for allergy to fish as tuna and grouper.

1380 | A case report of a patient allergic to mushrooms

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Introduction: The most commonly consumed edible mushrooms belong to the Agaricus, Boletus and Lentinus genera. Their implication in food allergy is rare.

Objectives: Methods: 35 year-old male patient with a history of seafood allergy, professional cook, that in two occasions developed generalized pruritus, urticaria, facial swelling and abdominal pain after consuming a raw mushroom (Agaricus bisporus).

Intraepidermal skin prick test, in vitro study and oral food challenge were performed.

Results: Skin prick tests were negative for Alternaria, Aspergillus, Cladosporium and Penicillium spores.

Prick-Prick: Negative for raw and cooked mushroom.

Rubbing with cooked mushroom (lower lip): Negative.

Rubbing with raw mushroom (lower lip): Positive, inducing immediate pruritus and labial angioedema. Oral Dexchlorpheniramine and Methylprednisolone were used to treat the symptoms.

Blood test CAP: Total IgE 328.6 kU/L. Specific mushroom IgE <0.35 kU/L.

SDS-PAGE immunoblotting (IgE-binding protein study): mild/low binding around 30kD (MW:Molecular Weight in kD) with Agaricus bisporus extract and no binding with the extract of Agaricus brunnescens.

Conclusions: It has been proven by the edible raw- mushroom oral challenge the patients' diagnosis of food allergy.

It is important to take into account mushrooms' implication as etiologic agents of urticaria and angioedema cases.

1381 | High allergy to guar gum and to xanthan gum

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Case Report: Guar gum (GG) and Xanthan gum (XG) are polysaccharide water-soluble used as food additives (A) under the code E412 and E415. We find them in sauces, and products of bakery. The XG is present also in some medicines. We present here the case of a patient having made several allergic reactions and the method diagnosis.

Clinical Case: Julie S 20 year-old consults in the beginning of 2016 for 8 allergic reactions arisen from October 2015 to December 2015 to type of generalized urticarial, oral pruritus in immediate post-prandial, followed by 4 severe reactions in January 2016, with thoracic oppression (TO) and palpitation, requiring every time an auto-injection of Adrenaline.

Food investigation: scenes arising after eating industrial salad dressing except the last front after taking Gluten free pancake, (contain all GG).

In November, 2016: Metopimazine tablet taken (containing XG) immediate urticaria, oral pruritus, TO, taking antihistamine (AH1).

Allergic review: Skin prick tests (SPT) with natives A and the diluted solutions; 1 g of GG put in 99 mL of water, mixed during 30 seconds, extracted of 11 mL forming the mother solution (MS), taken 1 mL of the MS put in 9 mL of water realization of the solution to 10-1 and so on to form the S to 10-2, 10-3 and 10-4; labial tests of provocations (LTP), same technical used for the XG; measure of the specific IgE and Tryptase Seric (TS).

Results: SPT return <0 for the GG, the XG and the various dilutions; positive control 8/28 mm; IgE GDG <0.10 Ku/L; TS 13.5 μg/L. 09/2016: External LTP GG SM, light lips pruritus (4/10); LTP intern solution to 10-1 (0, 2 mL drop under the tongue 2mn and spit out); immediate oral pruritus (5/10) urticarial of the trunk after 15 mn; TO (fall in Peak flow (PF) of 25%); TA constant; prescription of AH1 and Salbutamol; rise of the PF in 20 mn; amendment of the clinical scene in 1 hour.

12/2016: LTP XG >0 for 0, 2 mL of the solution to 10-2, with the same symptoms that for the GG.

Total: LTP return positive for 0, 2 mg of GG and 0, 02 mg of XG.

Conclusion: The GG and the XG are often used in the industry food-processing but also in some medicines. In front of unexplained severe allergic reactions repeating it seems judicious to think about it. The SPT and the measure of the specific IgE can be taken as faulted. Food and drug investigations are necessary, accompanied by LTP with increasing dilutions which seems to be an interesting technique to insure the diagnosis. Cross reactions between gums may exist.

1382 | Mustard allergy: diagnostic and identification of specific allergens by immunoblotting

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Case Report: Introduction: We describe a clinical case study of severe allergy to a variety of mustard, *Sinapis alba*, in an adult patient without any previous food nor respiratory allergy history.

Objectives: The diagnosis of allergy to mustard is based on anamnesis, skin prick test and specific IgE (sIgE) measurement to total mustard extract. Actually, the in vitro diagnostic tools cannot help the physician to define the precise mustard allergens involved in the allergic reaction and are unable to support evaluation of potential cross-reactions. Indeed, no molecular allergen component is commercially available for mustard. We aimed to adapt a 2D immunoblot method to mustard. Afterwards, mass spectrometry (LC-MS/MS) was used to identify precisely the allergens bound to sIgE.

Methods: We analyzed the serum of a 37 y.o. man presenting a grade 2 reaction (facial quincke edema with respiratory distress) after eating food containing the mustard species *Sinapis alba*. He had positive sIgE results for mustard extract (0.62 KUA/L) and a positive realistic SPT to foods containing mustard. We extracted total proteins of *Sinapis alba* seed. The different proteins were separated based on their isoelectric point and their molecular weight. The patient serum was analyzed by 2D Western blot in order to evaluate its sIgE reactivity against the different protein spots. Finally, the protein spots recognized by the patient sIgE were precisely identified by LC-MS/MS.

Results: The patient sIgE sensitization profile showed three specific protein spots. The first protein spot was observed at 18 kDa and pH 5-6. A second protein spot was localized around 14 kDa and pH 5. Finally, the third protein spot was situated around 15 kDa and pH 7. The LC-MS/MS analysis of these 3 spots pointed out 2 allergens already described in mustard allergy: sin a 1 (2S-albumin) and sin a 2 (11S-globulin).

Conclusion: In this study, a 2D immunoblot provided a specific sensitization profile for a patient presenting a grade 2 allergy to mustard with low sIgE to total mustard extract and without any other history of allergy. The protein spots recognized by the sIgE concerned two main allergens identified by LC-MS/MS as sin a 1 and sin a 2. Those allergens are classified in the storage protein family which is associated to severe reactions to food and could be highly cross-reactive. We pointed out specific mustard allergens that could be associated to severe reactions such as facial quincke edema with respiratory distress.

1384 | Disease progression of lipid transfer protein syndrome: clinical case

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Case Report: Background: Non-specific lipid transfer proteins (LTP) are pan-allergens present in many plant foods and pollens. Significant cross-reactivity occurs between food LTPs but not between food LTPs and pollen LTPs. In Portugal and Southern Europe, severe allergic reactions to foods containing LTP occur frequently in patients primarily sensitized to peach LTP.

Clinical Case: A 24 year-old male patient presented with a 8 year history of recurrent episodes of abdominal pain 30-60 minutes after the ingestion of peanuts; several episodes of acute urticaria during exercise after meals without any identified food trigger; and severe events of abdominal pain, malaise and loss of consciousness during exercise after drinking beer together with other alcohol beverages. At the age of 23 years-old, he had a severe episode of anaphylaxis (rhinoconjunctivitis, abdominal pain and distension, and generalized urticaria) developing twenty minutes after the ingestion of hazelnuts and almonds, without exercising or other known cofactors. The patient had symptoms of rhinoconjunctivitis since 18 years-old.

Skin tests with commercial extract to inhalants allergens and to food allergens accordingly to case history were performed. Serum specific IgE determinations to some plant foods and to molecular components (LTP and profilins) were performed. Specific IgE detection (skin prick tests and/or specific serum IgE) was positive to several pollens (plane, grass mix, olive, mugwort and cypress), dog, mites, peanut, almond, hazelnut, chestnut, walnut, peach, apple, malt, wheat, oat, rice, chestnut, lupin and sunflower seed. Prick test to profilin and LTP (Pru p 3) were positive. Specific IgE were positive to rPru p 3 (82.5 kU/L) and rTri a 14 (15.8 kU/L).

Conclusion: The clinical severity and cross-reactivity among two different LTPs are in accordance with an LTP syndrome in progression. We emphasize that these patients must be aware of the complexity of this syndrome as a great variety of foods can be responsible for severe reactions, particularly if cofactors are involved.

1385 | Development of food allergy to fish in elderly patient

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Case Report: Seventy-seven years old woman complained of suddenly developing angioedema of the eyelids, face, redness and itching of the skin of the whole body, hands, shins for the first time after eating fish in April 2016. She hadn't any symptoms of allergies before.

Comorbidities: Chronic gastroduodenitis, colitis, cholecystectomy in 1985, diabetes type 2, arthritis of the shoulders, knees. Three weeks before, neurologist prescribed some homeopathic medicines for intramuscular injection because of joint pain. One of the drugs included bioactive concentrate from small sea fish, the other—mixture of plant products (Arnica montana; Calendula officinalis; Hamamelis virginiana, etc.) On the 15th day of injection of the drug with fish components, the patient ate minced surimi. In 15 minutes an acute angioedema of eyelids, face, throat, generalized itching of the palms occurred for the first time, intravenous corticosteroids were effective. She occasionally used to eat boiled cod with no reactions till May 2016, when after eating minced surimi in 15 minutes an acute itching of the palms, body, throat swelling occurred again. In June 2016 after eating boiled cod, in 15 minutes the itching of palms, angioedema of the eyelids. All the symptoms regressed after intravenous injection of prednisone. In August 2016 she tried a small amount of boiled trout. In 20 minutes there was itch and tremor of the hands, weakness. A few minutes after intravenous injection of prednisone all symptoms disappeared.

Examination: General blood analysis—normal. Slight increase of glucose of 6.2 mmol/L, alkaline phosphatase to 147 IU/L (30-120), lipase 161.5 μ/L (21-67) was found. Colonoscopy: Diverticulosis of the sigmoid colon without evidence of diverticulitis. Endoscopy: chronic atrophic gastritis. Ultrasound of the abdomen: signs of diffuse changes of liver and pancreas. Skin prick tests with atopic inhalant allergens-negative. Skin prick tests with the standard food allergens: cod 8 mm, hake 8 mm. Phadiatop—negative. Total IgE-normal. sIgE to mixed fish: cod, herring, mackerel, flounder—positive. Skin prick—prick tests: 8 mm surimi, tilapia 8 mm, trout 6 mm, fresh shrimp 8 mm, boiled shrimp-negative.

Conclusion: Thus, the patient has the diagnosis of food allergy to fish. We can assume that sensitization to fish developed due to parenteral administration of homeopathic drugs containing antigens of fish with strong sensitizing activity.

1386 | A late adult-onset multiple food allergy case

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Case Report: Although food allergy is not frequently seen in adults, it may cause serious reactions. In this regard, we herein present a case of late adult-onset multiple food allergy.

A male patient (İ.S.) at the age of 40 applied to our immunology and allergy polyclinic with complaints of food allergy. Patient stated in his history that he has been suffering from burning in subcutaneous areas and hair roots, swelling, itching in mouth and throat, swelling in tongue, and shortness of breath, all of which occurring immediately after eating foods containing chicken, calf meat and tomato, for the last 6 months. He also stated that he has presented to the emergency service six times with these complaints, and his complaints have been eliminated by intervention made in the emergency service. Patient showed no abnormality in routine tests, and his C4 and Tryptase levels were also normal.

Skin prick test (ALK-Abello-Denmark) was performed with standard ready-to-use respiratory and food allergen extracts in the patient. In food panel, positivity was not detected. Prick-to-prick tests were carried out with raw and boiled chicken and calf meat in the patient. According to evaluation made after 20 minutes, in prick-to-prick test carried out with raw and cooked calf meat, positivity accompanied by hyperemia and induration of 5 × 5 mm was detected with raw calf meat, and in prick-to-prick test carried out with raw and cooked chicken meat, positivity accompanied by hyperemia and induration of 7 × 7 mm was detected. In prick-to-prick tests carried out with hot green pepper, sweet green pepper and raw tomato, positivity accompanied by hyperemia and induration of 7 × 7 mm, 6 × 6 mm and 6 × 6 mm, respectively, was detected. Food allergy in patient's history was thus confirmed with skin prick test positivity. Patient was prescribed with adrenaline automatic injector. The foods responsible for allergic reactions were removed from his diet, and patient was put into follow-up in our polyclinic.

With this multiple food allergy case, we wanted to highlight that food allergy may also be seen in adults in advanced age period, and food allergy in clinical history should be taken into consideration and confirmed.

1388 | A late adult-onset food allergy case

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Case Report: A female patient (E.E.) at the age of 35 with complaints of food allergy applied to our immunology and allergy polyclinic. Patient reported that she has been suffering from itching, itchy throat, swallowing difficulty and respiratory distress after eating red meat for about 4 years. Patient also stated that these complaints do not occur every time she eats red meat, but rather sometimes.

Method: Skin prick tests (ALK-Abello-Denmark) were carried out with standard ready-to-use respiratory and food allergen extracts in the patient. In food panel, positivity was not detected. Prick-to-prick test was carried out with raw and cooked red meat, and with raw meat, positivity accompanied by typical hyperemia and induration of 7 × 7 mm was detected. Prick-to-prick test performed with cooked anchovy was accepted as negative.

Results: The food allergy in patient's history was thus confirmed by skin prick test. Adrenaline automatic injector was prescribed for the patient. She was advised not to eat raw red meat.

Conclusion: With this red meat allergy case, we wanted to show that food allergy may also be seen in adults, and food allergy may develop to only one form, or to both forms, of the same food, i.e. raw and cooked forms, and to highlight that the presence of food allergy should be confirmed by proper tests.

1389 | An interesting food allergy case displaying angioedema associated with hazelnut consumption

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Case Report: Food allergy may cause serious reactions in adults. In this regard, we herein present an interesting case of food allergy. A female patient (A.O.) at the age of 40 applied to our polyclinic with a complaint of hazelnut allergy. Patient reported that starting from 2 years before her admission to our polyclinic she has been suffering from an allergic reaction characterized by swollen lips, itching in mouth, feeling of enlarged tongue, and swallowing difficulty after eating hazelnut, the last episode of which occurred 6 months ago. According to her anamnesis, her complaints were not accompanied by urticaria. Patient stated that she has presented to the emergency service whenever she experienced these complaints, and she has received necessary treatments therein. Skin prick test was

performed with respiratory and food allergen panels in the patient. When skin prick test obtained from the patient was evaluated after 20 minutes, sensitivity to house dust mite was detected in respiratory allergen panel. On the other hand, positivity with typical hyperemia and induration of 9x9 mm and 5x5 mm was detected against hazelnut and peanut, respectively, in food panel. Hazelnut allergy stated by the patient, who has no clinical complaints of peanut allergy, in her history was thus confirmed by skin prick test. Adrenaline auto-injector was prescribed for the patient, and foods containing hazelnut and/or peanut were removed from her diet. She was put into follow-up in our polyclinic. With this case of hazelnut allergy, we wanted to show that in adults food allergies like hazelnut allergy may be seen though it is rare, and to highlight that complaints of food allergy in clinical history should be taken into consideration and confirmed by clinicians.

1392 | An interesting case of adult-onset kiwi allergy not accompanied by latex allergy

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Case Report: Although food allergy is not a common problem among adults compared to as in children, it may cause serious reactions in adults as well. In this regard, we herein present an interesting case of food allergy.

A female patient (P.K.) at the age of 42 presented to our polyclinic with an alleged complaint of kiwi allergy. She described a history of allergic reactions including swollen tongue and throat, and shortness of breath, which have allegedly occurred two times within the last one year 10 minutes after eating kiwi. Patient reported that she has presented to the emergency service twice because of these complaints.

Skin prick tests were made with respiratory and food allergen panels in the patient. No sensitization was detected. To evaluate the possibility of cross-reactivity with latex, a prick test was performed in the patient, and it was found as negative. Also, a prick test was carried out with fresh kiwi according to prick-to-prick method. The studied latex-specific IgE of patient was negative.

In evaluation of results after 20 minutes, an induration of 6x6 mm accompanied by hyperemia was detected against kiwi. The alleged kiwi allergy of patient was thus confirmed by prick-to-prick test. Adrenaline auto-injector was prescribed for the patient, and kiwi was removed from her diet. Patient was put into follow-up in our polyclinic

With this kiwi allergy case, we wanted to show that in adults food allergy may also be seen in advanced age period, and to highlight that a history of food allergy should be cared with due importance and confirmed.

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1393 | Characterization of a PhL p 6 mutant with increased structural stability

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Introduction: Protein fold stability has been proposed to represent an intrinsic feature contributing to allergenicity. It was recently demonstrated that increased structural stability of an allergen can lead to prolonged survival of endolysosomal degradation, resulting in altered presentation of immunodominant T cell epitopes, thereby promoting T helper 2 type immune responses.

Objectives: In ongoing work, we investigate fold stability mutants of the Timothy grass pollen allergen Phl p 6 with respect to changes in their antigen processing and presentation.

Methods: By employing MAESTRO algorithm, Phl p 6 point mutant S46Y was predicted to have a free energy of −1.27 kcal/mol, indicating an increase in structural stability. The mutant was expressed in *E. coli*, purified by chromatography, and analyzed for thermal stability by circular dichroism (CD). To evaluate its capacity to stimulate T cell proliferation, co-cultures of bone-marrow derived dendritic cells (BMDCs) pulsed with various concentrations of the wild-type and the mutated Phl p 6 together with a T cell hybridoma specific for the immunodominant epitope of Phl p 6 were performed. Finally, the structure of the mutant protein was obtained by X-ray crystallography.

Results: Circular dichroism analysis confirmed the MAESTRO prediction, as Phl p 6 S46Y mutant displayed a higher melting temperature of 72.5°C compared to the wild-type allergen (58.5°C). The high resolution crystal structure revealed an overall high structural similarity of the mutant and the wild-type protein (PDB: 1nlx). The Tyr46 was found to complement the aromatic stacking and thereby to stabilize the hydrophobic core interaction of the four-helix bundle architecture of Phl p 6, explaining the increased thermal stability found by CD. IL-2 production of Phl p 6-specific T cells was weaker following culture with BMDCs pulsed with the mutant, pointing to reduced presentation of the immunodominant epitope.

Conclusions: The replacement of serine 46 to tyrosine maintains the overall structure of Phl p 6 while stabilizing its fold as compared to the natural allergen. Rigidification of the molecule led to reduced presentation of the immunodominant T cell epitope in vitro, suggesting reduced or delayed processing. Whether this also translates to decreased in vivo immunogenicity and/or allergenicity remains to be investigated.

1394 | Evaluation of allergenic relationship between humulus japonicus and humulus lupulus pollens

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Introduction: *Humulus japonicus* (Hop J) pollen is a major cause of autumn allergens in the Far East countries and its allergenic potency has been increasing with climate change. Allergen immunotherapy has been considered for Hop J-sensitized allergic patients, however, Hop J allergen extracts are not currently commercially available. We speculate that *Humulus lupulus* (Hop L) belonged to the same genus may share cross-reacting allergens with Hop J and evaluated allergenic relationships between these two pollens.

Objectives: Thirteen patients with allergic rhinitis and/or asthma sensitive to Hop J pollens were enrolled from Ajou University Hospital, Suwon, Korea. Hop J pollens were collected locally and lyophilized extracts were prepared, while lyophilized Hop L extracts were provided by Lofarma (Milano, Italy). IgE-ELISA/ELISA inhibition tests, SDS-PAGE and IgE-immunoblot/immunoblot inhibition analysis using sera from the enrolled subjects were performed.

Results: All patients had high serum specific IgE to both Hop J and Hop L extracts by ELISA, but no significant correlation was found between two pollens. ELISA inhibition test showed significant dose-dependent inhibitions on IgE-binding to Hop L with serial addition of Hop J extracts in dose-dependent manners, while minimal inhibitions on IgE binding to Hop J were noted with additions of Hop L. IgE-immunoblot analysis demonstrated the major allergenic component of Hop J at 12 kDa which was inhibited by Hop J, not by Hop L extracts in IgE immunoblot inhibition analysis.

Conclusions: These findings suggest that there is no significant cross-allergenicity between Hop J and Hop L pollens.

1395 | Carbohydrate composition of house dust mite allergen extracts and its relevance for IgE binding

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Introduction: Glycosylation plays an important role in the recognition and uptake of allergens by antigen presenting cells (APCs) and

the modulation of immune responses. In addition, cross-reactive carbohydrate determinants (CCDs) are known to constitute epitopes for human IgE. Thus, elucidation of carbohydrate structures and investigation of their biological function is essential to understand characteristics of natural allergens.

Objectives: In the present study, carbohydrate structures of proteins in house dust mite (HDM) extracts and their interaction with IgE were assessed to elucidate physicochemical and immunological properties of HDM allergens.

Results: *D. pteronyssinus* and *D. farinae* extracts and natural major HDM allergens were investigated for the presence and identity of glycans by Periodate-Schiff staining, c-type lectins, carbohydrate-specific antibodies and mass spectrometry. Glycan structures were detected by Periodate-Schiff staining to be present on high molecular weight proteins in HDM extracts from both species. Binding of the lectins GNA, PNA and DSA to proteins from both HDM species indicates the presence of N-linked mannose and O-linked glycans comprising a core Gal-$GalNAc_1$. Investigation by a fucose-specific antibody excluded the presence of this CCD in the investigated samples. Applying mass spectrometry, the presence of various N-linked high mannose structures linked to a core $HexNAc_2$ glycan was confirmed.

To elucidate the relevance of glycans for IgE binding, periodate- and mock-treated HDM extracts were incubated with pools of sera from HDM allergic subjects and individual human sera with CCD reactivity. IgE from pools of sera reacted with HDM allergens including the major group 1 and group 2 allergens. IgE reactivity of HDM extracts was unaltered after periodate treatment, thereby excluding that mite carbohydrate structures constitute epitopes for human IgE of HDM allergic subjects. In line with this finding, HDM carbohydrate structures were not recognized by a purely CCD reactive human serum.

Conclusions: Our results reveal a complex glycosylation pattern of proteins in *D. pteronyssinus* and *D. farinae* extracts. However, the detected glycans on HDM allergens apparently do not to constitute epitopes for IgE of HDM allergic subjects and do not comprise CCDs. The immunological relevance of the individual identified carbohydrate modifications needs to be further elucidated in continuing studies.

1396 | House dust mite component allergens as diagnostic markers

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Introduction: House dust mite (HDM) is composed of various component allergens. As HDM can be sensitized through skin and respiratory tract, it can cause various diseases through lifetime; atopic dermatitis, asthma and allergic rhinitis. Therefore, sensitization patterns of the component HDM allergens can be different between diseases and its severity.

Objectives: The aim of this study was to investigate the sensitization profiles of Korean HDM allergic patients. Sensitization patterns of major (group 1, 2) and minor (group 10, 11, 13, 14, 30, 32) component allergens are compared at respiratory (allergic rhinitis or asthma) and atopic dermatitis patients.

Results: In this study, sensitization profiles of 161 HDM-allergic patients were analyzed using ELISA and western blot method. Respiratory allergy group (asthma or allergic rhinitis) were mainly sensitized group 1 or group 2 allergens. However, patients who suffered from atopic dermatitis were poly-sensitized by major and minor HDM allergens, especially Der f 11 ($P = .034$), Der f 13 ($P < .001$), Der f 14 ($P < .001$), Der f 32 ($P < .001$). Among the allergen, Der f 14 is the prominent difference between the airway and cutaneous diseases by western blot and ELISA assay. In addition, there were 15 patients (9.3%) who neither sensitized to group 1 or 2 allergens.

Conclusions: Sensitization profiles of house dust mite are different between airway and cutaneous disease. Der f 14 sensitization is a main difference between respiratory allergy and atopic dermatitis patients.

1397 | The COMPARE allergen database: a comprehensive Protein Allergen resource

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Introduction: The COMPARE database, publicly available as of January 2017, is a comprehensive list of protein allergen sequences (www.comparedatabase.org), provided as a resource to multiple stakeholders to meet the needs for allergy risk assessment in order to support public safety. The database is a collaborative effort of academic, government, and industry scientists sponsored by the Health and Environmental Sciences Institute (HESI).

Objectives: Objectives for the database include development of a sustainable, reproducible, and reliable process to identify new allergens for use in allergy risk assessment by the biotechnology industry, and by regulatory agencies responsible for food and feed safety.

Additional stakeholders include medical personnel and consumers who may be interested in identifying sources of allergens. As advances in genomic sequencing technologies have dramatically increased the volume of sequence data, identifying potential new allergens has become increasingly complex. The COMPARE process accommodates this growth by using a high-throughput bioinformatic algorithm to identify candidate allergens for review by a group of recognized allergy experts. This poster provides a description of the COMPARE process, to be applied annually for regular updates, which: 1) captures new listings of potential allergen sequences, 2) identifies likely allergen sequences, 3) collects published support for each sequence, and 4) uses transparent, standardized criteria. A key goal for the COMPARE process is to include or reject protein sequences based on the presence or absence of well-documented proof of IgE recognition. To provide an unbiased review, academic experts operate as an independent panel to make final decisions for selecting sequences to include. The HESI collaboration provides for a thorough examination of the transparent decision points supporting the COMPARE process.

Results: In its first year of operation, the COMPARE scientific advisory team has validated its initial allergen identification process, selected candidate sequences via bioinformatic screening of all proteins entered into NCBI between May 2015 and May 2016, and completed the independent review. The complete 2017 database consists of 14 new unique sequences as well as all the allergens listed in the 2016 Allergen Online (AOL) database, for a total of 1970 allergens.

Conclusions: The COMPARE database is a new, freely available resource for comparison of protein sequences to known allergens to ensure a safe food supply.

1398 | Extracts freeze dried and stable purified allergens from HDM for diagnostic, research and immunotherapy purposes

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Introduction: House dust mite allergy is one of the most widely spread allergic diseases. Most patients allergic to house dust mites react to group 1 and 2 allergens. The need for consistent house dust mite (HDM) extracts, especially extracts freeze dried (FD), as well as purified major allergens, can be used for diagnostic, research and immunotherapy purposes. Currently, commercially available ELISA kits do not distinguish between group 2 allergens and as such large deviations in group 2 are observed. Therefore, individual antibodies for Der p 2 and Der f 2 are necessary.

Objectives: To obtain defined extracts FD, as well as stable purified major allergens from HDM Whole cultures and separated antibodies for group 2 from HDM Whole cultures.

Methods: Whole cultures (WC), extracts freeze dried (FD) and purified allergens from HDM (*Dermatophagoides pteronyssinus* (DP) and *Dermatophagoides farinae* (DF)) are all produced by Citeq. An extract FD is prepared from mite whole cultures, extraction in a suitable buffer, a concentration step by ultra filtration and the obtained liquid is freeze dried. Purification of major allergens of group 1 and group 2 from DP and DF were purified as described in literature, with small modifications. Rabbit-polyclonal antibodies were obtained from rabbits immunized with purified allergens and monoclonal-antibodies were obtained from a hybrid between BALB/c spleen cells and a myeloma cell line.

Results: DP and DF HDM extracts FD show that group 1 levels are 10 times higher and group 2 levels are 5 times higher than determined for WC extracts. Endotoxin levels are slightly higher in extracts FD. Purified Der p 1, Der f 1, Der p 2 and Der f 2 are 98% pure as determined by SDS-PAGE. Stability analysis for Der p 1 and Der p 2 show that both proteins are stable for prolonged time at 4°, ambient room temperature and 37°C, with minor loss of intensity at 37°C. Antibodies against Der p 2 do not show cross-reactivity with purified Der f 2 as is shown by ELISA and immunostaining.

Conclusions: *Extracts FD*; Extracts FD produced by Citeq are consistent and can be used for a mouse model for allergic asthma. *Purified allergens*; Stable major allergens from DP and DF HDM can be purified up to 98%. *Antibodies*; There is no cross-reactivity between anti-Der p 2 and Der f 2 purified allergen. Future research will be necessary to develop a ready-to-use-ELISA for Der p 2. Extracts FD and stable purified allergens produced by Citeq can be used for diagnostic, research and immunotherapy purposes.

1399 | Inhalation antigens sensitisation in Czech hypersensitivity pneumonitis patients

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Introduction: Hypersensitivity pneumonitis (HP) develops after repeated exposure to inhalation antigen in susceptible individuals. Different serological methods testing association between antigen exposure and humoral response have been used in the past. Specific immunoglobulins G (IgG) testing is one of those more frequently used and commercially available.

Objectives: The aim of this pilot study was to estimate sensitisation of Czech HP patients to different inhalation antigens.

Patients: 254 HP patients diagnosed in years 2007-2015 were included. Diagnostic criteria concerned appropriate history and high resolution computed tomography finding eventually supported by bronchoalveolar lavage fluid lymphocytosis and histology (if

available). Antigen exposure was detectable in history of 169 persons, in 85 no source of exposure could have been found.

Methods: All included patients underwent evaluation of specific IgG in serum, using ImmunoCAP method (Phadia, Sweden). Used specific IgG panel included mites, moulds, avian antigens, mammal proteins and professional antigens.

Statistical differences between HP patients with known and unknown exposure were estimated using Mann-Whitney test. For antigens with statistically significant difference in serum concentrations in specific IgGs in patients with detectable and undetectable exposure, sensitisation values were regarded as mean (unexposed group) + SD (mg/L) and percentages of sensitised patients in the whole group were counted .

Results: In 63 patients we detected sensitisation to more than one antigen group (mould, mite, professional, avian)—39 patients exhibited sensitisation to moulds and mites, 28 mites and avian antigens, 25 moulds and avian antigens, 20 professional antigens (isocyanates) and moulds, 17 professional antigens and mites and 12 patients avian and professional antigens.

Conclusions: Presented study shows that the Czech HP patients in our study group are most commonly sensitised to hexamethylene diisocyanate (27.6% of HP patients) and diphenylmethane diisocyanate (26.3% of HP patients). Mite sensitisation is on the other hand the less common (*D. pteronyssinus* 14.6% of HP patients, *D. farinae* 15.5% of HP patients). Sensitisation to more than one antigen seems to be frequent.

Antigen	Cut off for sensitisation (mg/L)	% of sensitised patients
D. pteronyssimus	53.4	14.6
D. farina	51.3	15.5
D. microceras	39.3	20.2
Acarus siro	48.2	20.7
Lepidoglyphus destructor	26.1	17.0
Tyrophagus putrescentiae	44.2	23.5
Glycophagus domesticus	NA	NA
Euroglyphus maynei	NA	NA
Moulds 1: Penicillium notatum, Cladosporium herbatum, Aspergillus fumigatus, Alternaria alternata	86.3	25.1
Moulds 2: Penicillium notatum, Cladosporium herbatum, Aspergillus fumigatus, Alternaria alternata, Setomelanomma rostrata	64.2	20.3
Cladosporium herbatum	NA	NA
Aspergillus fumigates	56.9	15.7
Candida albicans	NA	NA
Alternaria alternate	20.2	24.9
Micropolyspora faeni	18	18.4
Thermoactinomyces vulgaris	15.5	24.7
Epithelium 1: cat, dog, horse, cow, Epithelium 2: dog, guinea pig, rat, mouse	NA	NA
Epithelium + fur: Guinea pig, rabbit, rat, mouse, hamster	NA	NA
Cat − fur	NA	NA
Dog − fur	NA	NA
Dog- epithel	NA	NA
Feather 1: goose, hen, duck, turkey	56.8	22
Feather 2: parrot, budgerigar, canary, alexander, finch	64.2	21.2
Feather 3: goose, hen, duck, parrot	37.4	23.7
Budgerigar—feather, droppings, serum	NA	NA
Pigeon—feather, droppings, serum	75.4	22
Parrot—feather, droppings, serum	NA	NA
Isocyanate TDI (toluene diisocyanate)	NA	NA
Isocyanate MDI (diphenylmethane diisocyanate)	16.3	26.3
Isocyanate HDI (hexamethylene diisocyanate)	15.3	27.6

1400 | A sensitive two-site immunoassay for quantification of Japanese cedar pollen allergen, Cry j 1

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Introduction: Allergy to Japanese cedar pollen (*Cryptomeria japonica*) is the most common form of pollinosis in Japan, affecting nearly 10% of the population. Of those who are sensitized, more than 90% have specific IgE antibodies to Cry j 1, a 41kD glycoprotein. Our aim was to develop a sensitive immunoassay for the detection of Cry j 1.

Objectives: Natural Cry j 1 was extracted and purified from Japanese cedar pollen and used to immunize mice for monoclonal antibody production. Antibodies were screened by ELISA for reactivity to Japanese cedar pollen allergens, Cry j 1 and Cry j 2, birch pollen allergen, Bet v 1, and ragweed allergen, Amb a 1. Additional screening by Octet analysis was performed to identify potential antibody pairs with non-overlapping epitopes. Selected antibodies were used to develop a two-site monoclonal antibody ELISA with natural Cry j 1 as the assay standard.

Results: Eleven positive clones producing Cry j 1-reactive antibody were identified. Three antibodies were selected for production based on ELISA screening for Cry j 1 specificity and Octet analysis for epitope binning. Purified antibodies reacted strongly with Cry j 1 and showed minor cross-reactivity to Cry j 2 (<5%) in ELISA. Additional screening with tree pollen extracts from birch, olive, hazelnut, privet, and ash were negative. The assay standard curve ranged from 250-0.49 ng/mL with a limit of quantification of 3.9 ng/mL.

Conclusions: A sensitive, highly specific ELISA for the quantification of Cry j 1 has been developed. The assay has applications for measuring Cry j 1 in diagnostic and therapeutic allergenic products and for aerobiologic studies of exposure to Japanese cedar pollen allergen and clinical outcomes.

1401 | The influence of the East Asian mushrooms ganoderma lucidum and lentinula edodes and the belarusian mushroom boletus edulis on immune cell function

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Introduction: Over 140 000 species of fungi have been identified, many with immunomodulatory and anti-tumor capabilities. Reishi (Ganoderma lucidum) and shiitake (Lentinula edodes), which contain polysaccharides that suppress cancer growth and influence immunity, are often used in East Asian traditional medicine. Boletus edulis is the most commonly distributed mushroom in Belarus. It is found in Poland, Ukraine and Belarus, being a common constituent of soups and gravies and also frequently pickled or dried for long term storage. The effects of reishi, shiitake and boletus mushrooms on the Reactive Oxygen Species (ROS) production by peripheral blood neutrophils and monocytes.

Objectives: We assayed effect of reishi, shiitake and Boletus mushroom ethanol and water extracts (0.05%-0.2% w/v final concentration in the culture media) on the ROS production by peripheral blood neutrophils and monocytes using the Dihydrorhodamine DHR123 probe and CD69 expression by T-cells. PSB culture medium was used as negative control and PMA (phorbol, 12-myristate, 13-acetate) as positive control.

Results: The 3 mushroom water extracts increased ROS production by peripheral blood neutrophils and monocytes (negative control—2.74 ± 0.75%, PMA—98.9 ± 1.15%, reishi (0.2%) 20.2 ± 1.4%, shiitake—19.4 ± 2.2%, boletus—38.3 ± 3.5%.) The 3 ethanol extracted mushroom extracts had no effect on ROS production in any concentration studied. The investigated water extracts weakly induced CD69 expression by T-cells.

Conclusions: Mushrooms also have immunomodulatory properties. All three of the mushroom extracts caused an increase in ROS production by peripheral blood neutrophils and monocytes. Each of the extracts of the mushrooms gave ROS production which was at least 20% greater than the negative controls. The Boletus edulis mushroom, a popular food ingredient from Poland, Ukraine and Belarus, has been shown to enhance immune responses including production of reactive oxygen species by immune inflammatory cells similar to the medicinal mushrooms of East Asia. These mushrooms should be further studied for their potential use as immune modulators in new pharmacologic preparations or perhaps for use in alternative medicine for viral and oncologic diseases.

1403 | Major peach allergen pru p 3 has structural features similar to saposins

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Introduction: CD1 receptor proteins can present lipids and glycolipids to iNKT, a subtype of T cells. In the trafficking and loading of lipids onto their binding grooves, CD1 molecules are assisted by saposins, small lipid transfer proteins that facilitate non-enzymatically the hydrolysis of disparate glycosphingolipids in lysosomes. Pru p 3, the major allergen from peach fruit, is a lipid transfer protein carrying a ligand with a phytosphingosine domain.

Objectives: To study the structural relationship between Pru p 3 and saposins regarding their functional role in transporting and loading of lipids onto CD1d receptors.

Results: The crystal structure of Pru p 3 (PDB id 2B5S) was used together with those of saposins A (2DOB), B (1N69), C (2GTG), and D (2RB3). Firstly, the identification of secondary structure was performed with DSSP and geometrical characteristics of tertiary structures were analysed with tools implemented in Chimera. Then, three different methods to determine structural alignments were used to compare the 3D structures of Pru p 3 and saposins: FATCAT rigid, CE, and TM-align. Pru p 3 exhibited the same architecture as the four existing saposins A, B, C, and D: a highly conserved conformation with four a-helices in spite of having pairwise sequence identities lower than 39%. Other structural features such as a local disruption of main chain hydrogen bonds in the longest a helix, a conserved proline starting the shortest a helix, the existence of inter-helices disulfide bridges, and the presence of 3-residue 3_{10} helices are also shared by Pru p 3 and saposins. Within the confidence levels of the corresponding superposition scores, the different structural alignment methods agree in predicting a significant structural relationship for Pru p 3 and saposin A

Conclusions: Peach major allergen Pru p 3 shares structural features with saposins that would facilitate the presentation of the ligand of Pru p 3 to CD1d receptors, and trigger an immune response.

1404 | Assessing potency of various peanut allergens in germ-free murine model using Ara h1, Ara h2, and Ara h3

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Introduction: Peanut allergy is a significant health problem because of its prevalence and severity of the reactions elicited in some individuals. We used a germ-free C3H/HeN mouse model to evaluate sensitization and elicitation of allergenic peanut proteins Ara h1, h2, and h3. The aim of this study was to determine if we could assess the potency of various peanut allergens in this animal model. Purified Ara h1, h2, and h3 were tested as model allergens with varied potency as reported by in vitro serum IgE, basophil histamine release, and skin prick tests from peanut-allergic individuals.

Objectives: Determine if our mouse model can differentiate peanut allergens Ara h1, Ara h2, and Ara h3 based on allergenicity. Allergenicity is assessed on the basis of established benchmark responses that include clinical and serological markers associated with allergy including hypothermia post challenge, clinical symptoms, allergen-specific IgE, and murine mast cell protease (mMCP-1; a marker of mast cell degranulation). Germ-free C3H/HeN mice were sensitized with 60 μg Ara h1, h2, or h3 by three weekly intraperitoneal injections (IP) with alum adjuvant followed 7 days later by IP challenge with 500 μg of the allergens.

Results: Mice sensitized with Ara h1 and h3 exhibited significantly less-severe clinical scores (mean 2 and 1 respectively) compared to mice sensitized with Ara h2 (mean = 4). Hypothermic responses post-challenge of Ara h1, h2 and h3 were [average −2.5 (SD = 1.6), −8.8 (SD = 0.9), and −0.29°C (SD = 0.5), respectively ($P < .05$)].

Conclusions: Preliminary results based on clinical scores and hypothermia confirmed that the germ-free C3H/HeN mouse model can differentiate between the potency of Ara h1, h2 and h3. Interestingly these results correlate with previously reported in vitro and in vivo analyses of human subjects, providing insight into the individual potency of various peanut allergens.

1405 | Different sensitizations in the lombardia region (Italy)

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Introduction: Allergic diseases have increased over the last few years and new technology are available in order to reach in vitro diagnosis. The aim of the present study was to evaluate the present epidemiology of allergen sensitization in a cohort of patients, evaluated by the immunoallergology laboratory of the Foundation IRCCS Policlinico San Matteo of Pavia (Italy). The study included patients from the entire Lombardia region, divided into three different sectors (North, Center, South).

Objectives: The present analysis was conducted on 318 consecutive patients. ImmunoCap ISAC® was used to evaluate specific IgEs, in order to differentiate false positives due to multiple cross-reactivity. Patients were divided into three groups, depending on their geographical residence: those who lived in the Northern part of the Lombardia region (158/257, 61.5%), those from the Center (64/257, 24.9%) and those from the Southern area (34/257, 13.2%). Chi-squared test was performed to verify if there was a statistical difference in allergen sensitization in the three different geographical areas.

Results: The results showed that 16.7% of patients are sensitized to at least one of the tested allergens, 5.7% to food allergens, 20.3% to pneumo-allergens, 2.2% to other components, and 14.3% to cross-reactive allergens. Chi-squared analysis was significant for tested molecules on their whole ($P < .0001$). We reached the same results for food allergens ($P < .0001$) and pneumo-allergens ($P = .0004$). No statistical difference was found for other components ($P = .2126$) and cross-reactive allergens ($P = .3534$).

Conclusions: In the Lombardia region the pattern of allergen sensitization differs in the three geographical areas we analyzed, both when considering overall sensitization and when considering only pneumo- or tropho-allergen components.

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1406 | Increased risk of developing depressive and anxiety disorders in patients with systemic lupus erythematosus: a matched case-control study

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Introduction: Systemic lupus erythematosus (SLE) is a chronic, systemic autoimmune disease that may involve the central nervous system, which is known as neuropsychiatric SLE. Both depressive and anxiety disorders have been reported as comorbidities of SLE, but the relationship remains controversial.

Objectives: The aim of this study was to evaluate the risk of developing depressive and/or anxiety disorders in patients with SLE. We performed a matched case-control study using data from the Longitudinal Health Insurance Database 2000, 2005, and 2010 (LHID2000, LHID2005 and LHID2010, respectively), which are part of National Health Insurance Research Database (NHIRD). Study subjects were diagnosed as SLE during our study period (from the start of 2002 to the end of 2010), without psychiatric diagnoses before enrollment. Proportional hazard analyses with and without important covariates were applied to determine the relationship between SLE and depressive and/or anxiety disorders.

Results: We identified 904 SLE patients and age-, gender-matched 4520 controls in this study. We found a significantly increased risk of depressive and/or anxiety disorders (adjusted hazards ratio (HR): 1.79; 95% confidence interval (CI): 1.08-2.97).

Conclusions: To our knowledge, this is one of the few studies reporting a significantly increased risk of depressive and/or anxiety disorders in patients with SLE after adjusting for important risk factors in a national healthcare database. The findings suggest SLE is a significant risk factor for the development of depressive and/or anxiety disorders. Further investigation on underlying mechanisms will be warranted.

1407 | The role of dysregulation of the immune system in the formation of immunodeficiencies and autoimmune disorders

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Introduction: The immune system is functioning at the harmonious interaction of the activation and regulation of immune suppression. Violation of the consistency of these processes underlies the different clinical variants of immunopathology. Purpose of the study—to study the mechanisms of dysregulation in the formation of the different phenotypes of immune deficiency.

Objectives: The survey was attended by 50 patients, who were in the dynamics of the progression of HIV infection and 89 patients with multiple sclerosis (MS). In assessing the parameters of the immune system using flow cytometry, RBTL to PHA, ELISA, RID. 40 healthy blood donors consisted of the control group.

Results: The number of naive T-cells, which provide the primary antigen recognition, was reduced in the terminal stage of HIV infection ($0.03 \pm 0.002 \times 10^9$/L, in control $0.4 \pm 0.01 \times 10^9$/L). We can observed increasing of the amount of peripheral CD3 + CD4 + Foxp3 + -cells to $0.046 \pm 0.005 \times 10^9$/L (in control $0.023 \pm 0.006 \times 10^9$/L), the high level in the serum of IL-4 (69.60 ± 21.75 pg/mL, in control 1.90 ± 0.20 pg/mL) and IFN-γ (53.49 ± 23.03 pg/mL, in control 6.2 ± 3.3 pg/mL). Patients with MS in clinical manifestation period had low level of peripheral CD3+ CD4 + Foxp3 + -cells ($0.014 \pm 0.002 \times 10^9$/L), high amount of naive T-helper cells ($1.17 \pm 0.06 \times 10^9$/L), activated RBTL on PHA (SI 72.12 ± 1.97, in control 63.60 ± 0.87). The level of IFN-γ (38.37 ± 16.91 pg/mL) and TNF-α (9.48 ± 0.96 pg/mL, in control 1.14 ± 0.16 pg/mL) was increased.

Conclusions: Various clinical manifestation of secondary immune deficiency associated with different mechanisms intraimmune dysregulation. Inhibition of processes of proliferation and recognition in the immune system leads to the formation of immunodeficiency with infectious variant of immune deficiency. The activation of recognition, proliferative properties of lymphocytes and immunoregulatory weakening suppression, dysregulation processes lead to the formation of autoimmune phenotype.

1408 | Sputum anti-neutrophil cytoplasmic antibodies in eosinophilic granulomatosis and polyangiitis patients with respiratory involvement

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Introduction: Eosinophilic granulomatosis with polyangiitis (eGPA) is a systemic small-vessel vasculitis characterized by hypereosinophilia, with a pathophysiology linked to the autoinflammatory effect of anti-neutrophil cytoplasmic antibodies (ANCA). However, of clinically diagnosed eGPA patients only 40% are ANCA seropositive.

Objectives: We hypothesized that ANCA-negative patients with severe respiratory involvement (severe asthma and/or sinusitis) would present with ANCAs 'localized' to the lungs.

Results: We collected matched sera and induced sputum from 20 eGPA patients (diagnosed as 4 or more of the 6 criteria outlined by American College of Rheumatology), 11 prednisone-dependent severe eosinophilic asthmatics, and 13 healthy volunteers. To reduce signal-to-noise ratio immunoglobulins were immunoprecipitated and ANCA reactivity was tested by immunofluorescence (IIF) (Immco Diagnostics Buffalo, NY, USA). The IIF-staining intensity was scored by three blinded observers. To negate false peripheral (p) ANCA patterns portrayed by anti-nuclear antibodies, both ethanol, and formalin-fixed neutrophil-substrate slides, in addition to Hep-2 IIF were employed. 14 out of 20 eGPA patients (70%) showed a significant increase in sputum-ANCA intensity scores compared to eosinophilic asthmatics and healthy controls (Kruskal-Wallis, $P > .0001$). 9/11 ANCA-seronegative patients, and 5/9 seropositive patients with demonstrable sputum-ANCA reactivity presented with significant clinical manifestations of severe asthma (determined by methacholine challenge test and/or bronchodilator reversibility) and/or presence of sputum eosinophilia >3%, compared to the 6/20 sputum-ANCA-negative patients who had more vasculitis-related symptoms (Table 1, Chi Square, $P = .01$). In contrast to the characteristic pANCA pattern associated with eGPA, sputum immunoglobulins from 12/14 sputum-ANCA-positive patients produced a cytoplasmic staining pattern (cANCA). This further corroborated the discordance with sputum anti-MPO reactivity analyzed by ELISA. However, the two patient samples with sputum-pANCA-type staining patterns showed increased anti-MPO absorbance values (>90th percentile of healthy controls).

Conclusions: For the first time, we report ANCA-reactivity in the sputum of eGPA patients in whom the disease severity is driven by respiratory rather than vasculitis complications. The sputum-cANCA staining pattern suggests possible autoantigen targets like proteinase 3 in the lungs, investigations for which are currently ongoing.

Clinical Manifestations (n = 20)	Sputum-Positive Sero-negative	Sputum-Positive Sero-positive	Sputum-negative Sero-negative	Sputum-negative Sero-positive
Vasculitic symptoms	1	0	1	4
Respiratory symptoms	5	0	0	0
Combined	3	5	1	0

Chi-Square, *df* 16.23, 6; *P* value = .012.

1410 | Vasculitis in rheumatoid arthritis/RA/

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Introduction: We investigated some clinical and immunological parameters in 17 patients with vasculitis and RA.

Objectives: We followed the 17 patients with RA and vasculitis at the University Hospital—city of Stara Zagora, including 14 women and 3 men, Caucasian type, aged 21-65 years, with disease duration of 2-7 years. The study is open. Were examined following indicators: biopsy, Doppler sonography, X-ray change, RF, CRP, ANA, levels complement and other.

Results: All patients completed the study. Skin tissue biopsy, obtained from all patients, showed typical fibrinoid necrosis with neutrophil infiltration in 14/82%/patients and lymphocytic infiltration at 3/18%. All of our patients were made Doppler sonography. Complete arterial obstruction was observed in six patients with peripheral gangrene, while 11/65%/was observed incomplete obstruction and that those with numbness and tingling in the fingers. Performed X-graph of phalanges of the upper limbs, all of our patients and observed these Rö change—chronic symmetrical erosive synovitis with pannus formation of peripheral joints found in 15/88%/patients, and in two patients radiologists described and specific for RA "Cysts Baker" with expressed osteoporosis.. In our sick positive ANA observed in 16/94%/patients—in low titer at 5/29%/and 1:80 titer in 12/71%/patients with vasculitis. The main clinical symptoms, except vasculitic changes, are morning stiffness and joint damage in 16/94%/patients and weight loss at 14/82%/.

Conclusions: (i) We observed a typical fibrinoid necrosis with neutrophils in the walls of small and medium-sized blood vessels. (ii) Skin disease with palpable purpura was found in all patients. (iii) All patients were positive RF, high values of CRP and low levels of complement. Positive ANA observed in almost all patients, but in a different titer.

1416 | Investigation of IL-17 producing CD26-/low memory Treg cells in patients with psoriasis

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Introduction: Defects in frequency and function of regulatory T cells (Treg) have been shown in Psoriasis. Under ex vivo stimulation, IL-17+ Treg cells were significantly increased in psoriasis patients compared to normal subjects. CD26, a surface molecule with dipeptidyl peptidase activity, is expressed mainly on effector T cells which is negative or low on Treg cells. We aimed to evaluate IL-17+ $CD26^{-/low}$ memory Treg cells in patients with psoriasis.

Objectives: In this study, we isolated memory T cells from 10 patients and 10 sex and age matched controls. The cells were activated with anti CD3/CD28 for 48 h and stimulated with PMA/ionomycin for 4.5 h. IL-17 + Foxp3 + CD25 + $CD26^{-/low}$ and $CD26^{hi}$ subpopulations in memory T cells were evaluated. The samples were acquired on flow cytometry and data were analyzed by FlowJo 7.6.

Results: Our results revealed that the percentage of IL-17 producing Foxp3 + CD25 + $CD26^{-/low}$ memory T cells decreased in patients compared to controls. (mean ± SEM; 32.4 ± 5.2, 39.1 ± 4.6, respectively), although it was not statistically significant. Investigation of intracellular IL-17 producing Foxp3 + CD25 + $CD26^{hi}$ memory T cells indicated that there was a significant decreased of percentage of Il-17 producing cells in patients compared to controls. (mean ± SEM; 53.2 ± 3.6, 64.7 ± 4.2, respectively, $P = .056$).

Conclusions: Taken together, our results were in contrast with previous evidences regarding to IL-17 production in ex vivo stimulated Treg cells in patients with psoriasis. Present finding propose that the major of IL-17 producing cells migrate to skin to involve in inflammatory responses.

1417 | Recalcitrant cutaneous sarcoidosis—paradoxical worsening with anti-TNFa therapy despite a dramatic improvement in pulmonary function

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Introduction: TNF-α (tissue necrosis factor) antagonists have been shown to be an effective treatment for multiple inflammatory and autoimmune cutaneous, rheumatic and gastrointestinal diseases. However, the increasing use of these agents has led to the recognition of several paradoxical cutaneous adverse effects. New onset or exacerbation of cutaneous psoriasis, cutaneous vasculitis and sarcoidosis has been described.

While new onset of sarcoid-like granulomatous disease has been well documented with this class of drug in non-dermatological patients, to our knowledge our patient is the first reported case of pre-existing cutaneous sarcoidosis which has worsened during infliximab treatment.

Objectives: We present the case of a 49 year old female with a history of multi-system sarcoidosis. Pulmonary sarcoidosis preceded cutaneous involvement by eight years. She has a background history of cardiomyopathy, hypertension and an unprovoked deep venous thrombosis (DVT).

The patient's cutaneous sarcoidosis had failed to respond to multiple therapies and she was intolerant of many others. These included pulsed methylprednisolone (psychiatric side effects), methotrexate (headaches, insomnia), hydroxychloroquine (possible cardiomyopathy) and mycophenolate mofetil (poor response). Thalidomide was contraindicated due to a previous thrombotic event.

Results: Infliximab was commenced in October 2014 but was subsequently discontinued in February 2015 due to dramatic paradoxical worsening of cutaneous sarcoidosis. A further course of pulsed IV methylprednisolone (half the standard dose) temporarily improved cutaneous ulceration. She subsequently commenced pentoxifylline, azathioprine and doxycycline. However, due to disease progression she is currently undergoing rituximab therapy with multi-disciplinary input.

Conclusions: While infliximab is often effective in the treatment of recalcitrant sarcoidosis, to our knowledge this is the first case of infliximab induced deterioration of pre-existing cutaneous sarcoidosis. Genetic variation of the TNF-α gene is emerging as an important factor in determining sarcoidosis predisposition and course.