DOI: 10.1111/all.15096

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

994 | TARGET - impact of authorized microcrystalline tyrosine (MCT)-adsorbed pollen SCIT allergoids on allergic rhinitis (AR) under real life conditions

Vogelberg C.[1]; Becker S.[2]; Klimek L.[3]
[1]*Department of Pediatric Pneumology and Allergology, University Hospital Carl Gustav Carus, Dresden, Germany*; [2]*Department of Otolaryngology, Head and Neck Surgery, University of Tuebingen, Tuebingen, Germany*; [3]*Center for Rhinology and Allergology, Wiesbaden, Germany*

Background: Subcutaneous immunotherapy with allergoid preparations (SCIT allergoids) represent the market leading application route in allergen immunotherapy (AIT) in Germany. The safety profile of SCIT allergoids is favorable and the efficacy has been proven in DBPC trials and meta analysis for various preparations. However, the treatment outcomes always reflect the effects under artificial conditions. The aim of the '**T**yrosine-**A**llergoid – **R**eal World Evidence in **G**ermany – **E**ffectiveness in AI**T**" (TARGET) study program is to investigate the "effectiveness" of authorized MicroCrystalline Tyrosine (MCT)-adsorbed grass and tree pollen (pollen) SCIT allergoids in clinical practice routine.

Method: TARGET is designed as a retrospective cohort study and is based on the IMS® LRx database (IQVIA, Germany). It accesses prescription data of German patients within the statutory health insurance system (GKV). The information collected is patient related with a unique anonymized identification number, allowing a patient follow up over time. One objective of the TARGET study program is to assess the impact of authorized pollen SCIT allergoids (MCT-adsorbed allergoid, allergoid 2, allergoid 3) on allergic rhinitis (AR) patients vs. control group (patients not receiving AIT). The progression of AR is measured by the prescription of symptomatic medication.

Results: Within the index-period (09/2009–08/2013) 181.496 patients aged between 5 and 65 years received prescriptions within the AIT group (all three preparations). Patients with at least four prescriptions of the focus products within three years from index date were included into the study. After the end of the treatment (and expiry of the last prescription) statistically significant more patients treated with MCT-adsorbed allergoids (with AR at baseline) vs. control group were AR treatment free in the follow up period. This was also shown for the entire AIT group.

Conclusion: Real world evidence studies add important information about the effectiveness of AIT under natural conditions. TARGET is based on real world prescription data and demonstrates the effectiveness of authorized MCT-adsorbed allergoids on AR in clinical practice routine.

985 | Clinical efficacy and safety of combined house dust-mite subcutaneous immunotherapy (HDM -SCIT) and omalizumab in five cases of allergic rhinitis & asthma

Rai M.; Kathuria P.
National Allergy Centre, New Delhi, India

Allergen immunotherapy (AIT) is a well-recognized treatment for alter the natural course of respiratory allergy which builds immune tolerance and prevents progression of allergic diseases. In our five cases of House Dust Mite (HDM)- driven Allergic Rhinitis and Asthma, combined House dust mite subcutaneous Immunotherapy (HDM-SCIT) for 2 years with Omalizumab for more than 12 months has achieved disease remission in four cases and disease-control in one case along with long term effect for three years after discontinuation of AIT. We hypothesize that combining HDM-SCIT and Omalizumab is a promising strategy as it is effective, safe, synergistic having immune-modifying activity in cases of HDM-driven Allergic Rhinitis and Asthma.

Our five patients underwent Skin Prick Test (SPT) to various groups of aeroallergens after giving an informed consent. House Dust Mite Sub-Cutaneous Allergen Immunotherapy (HDM-SCIT) was given with effective concentration of 1000 AU per ml. Omalizumab (Anti-IgE) was prescribed 15 days before the start of build-up dose of HDM extract by Cluster-Immunotherapy with incremental concentration 0.05/0.05 ml, 0.1/0.1 ml, 0.2/0.2 ml, 0.3/0.2 ml till maintenance dose (MD) of 0.5 ml of 1000 AU per ml) was achieved. Further MD of HDM-SCIT was continued every 4 weeks for 2 years along with Inj Omalizumab 150 mg given every 4 weeks varying from 14-21 months. None of our patients had systemic life-threatening reaction during build-up phase. Pre-medication with anti-histamine and OCS was given two hours before cluster doses of HDM-SCIT.

We hypothesize that combination of Omalizumab & HDM-SCIT has excellent safety profile and might be a promising strategy having immune-modifying activity. This combined therapy not only improved symptom and medication scoring but also enabled our patients to achieve maintenance dose of AIT faster in just four visits. We also hypothesize that if history is consistent with HDM sensitization then, single AIT with HDM-SCIT (for two years) combined with Omalizumab (for one year) is enough to achieve remission even if the patient is sensitized to other cross-reactive allergens. We have three years follow-up of these five cases with remission of four cases and disease-control of one case with long-term effect for three years after discontinuation of AIT.

Table 3: Schedule and duration of Combined House Dust Mite Subcutaneous Cluster Immunotherapy (HDM-SCIT) (Dp-50%, Df-50% 500 AU per MD) along with Inj Omalizumab therapy.

No. of Visits	1st Visit	2nd Visit	3rd Visit	4th Visit	5th Visit	6th Visit
Cluster Dose AIT (500 AU per 0.5ml per MD) Combined with ***Inj Omalizumab (150mg)****	0.05/0.05ml @ 60 mts interval (100 AU)	0.1/0.1 ml @ 60 mts interval (200 AU)	0.2/0.2 ml @ 60 mts interval (400 AU)	0.3/0.2 ml @ 60 mts interval (500 AU)	0.5 ml (500 AU)	0.5 ml (500 AU) M.D (500 AU)
Cluster Dose frequency	First day	10-12 days	10-12 days	15-20 days	20-30 days	Every 4 weeks
Inj Omalizumab (150mg) X 15 days before AIT followed by once in a month in variable duration ***[case 1 for 14 months, case 2 for 20 months, case 3 for 14 months, case 4 for 21 months, case5 for 17 months X omalizumab given]***						

AU-Allergy Unit, MD-maintenance dose (500 AU), conc.-concentration, AIT-Allergen Immunotherapy, HDM-Hose Dust Mite

983 | House dust mite sublingual immunotherapy in patients with receiving subcutaneous immunotherapy maintenance phase: A randomized controlled trial

Kiatiwat P.; Sangasapaviliya A.; Pradubpongsa P.; Sangkanjanavanich S.; Chiewchalermsri C.; Boonpiyathad T.; Mitthamsiri W.

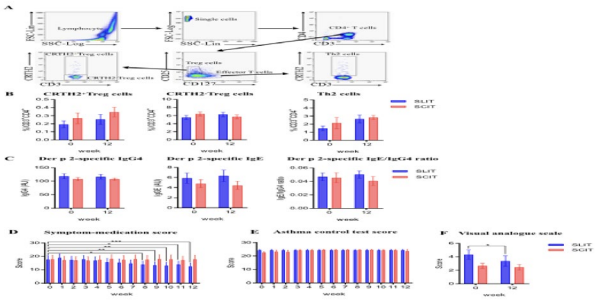
Phramongkutklao hospital, Bangkok, Thailand

Background: Allergen-specific immunotherapy (AIT) is the only treatment that cures allergic diseases. Subcutaneous immunotherapy (SCIT) is a conventional treatment which introduced more than 100 years ago. Novel oral formulation sublingual immunotherapy (SLIT) has shown equal efficacy to SCIT, while it is safe without life-threatening allergic reaction. Amid a pandemic of COVID-19, patients are advised to avoid hospital visits. SLIT might be the right choice because patients can take the tablets at home and no need to go to the hospital for weekly injections like SCIT. However, no recent report on the efficacy of changing the route of immunotherapy from SCIT to SLIT. The study aims to assess the efficacy of switching SCIT to SLIT in patients with house dust mite (HDM) allergy.

Method: A randomized controlled study was undertaken in 40 patients with allergic rhinitis with/without asthma and receiving maintenance phase of HDM SCIT (TCTR20200606002). HDM SLIT tablet was given daily for 12 weeks and compared to patients with continue SCIT. The principle outcome measure was symptom-medication score (SMS) and asthma control test (ACT) score. immunologic changes in fresh whole blood to monitor T cell subsets, including regulatory T cells (tregs), dysfunctional tregs, and T helper 2 cells were investigated by the flow cytometry method and Der p2-specific IgE, Der p2-specific IgG4 and Der p2-specific IgE/IgG4 were investigated by ELISA method at baseline and 12 weeks after switching treatment.

Results: Of 40 patients, 19 patients in the SLIT group and 20 patients in the control group achieved the study. There were no significant differences in SMS and ACT scores between the SLIT group and SCIT group during 12 weeks of treatment. Significantly reduced SMS after 8 weeks compared to baseline (17.6 ± 2.9 to 14 ± 2.4, $p = 0.028$) was demonstrated in the patients with SLIT. T cell subsets' frequency, specific IgE, IgG4 and IgE/IgG4 ratio did not change significantly in both groups at the end of the study. No severe adverse drug reactions were reported.

Conclusion: SCIT can switch to SLIT in the immunotherapy maintenance phase. SLIT was safe and efficacious by reducing the symptoms and medication consumption



1198 | Ameliorating allergic symptoms by supplementing micronutritional deficiencies in immune cells with a holoBLG-based FSMP (food for specific medical purposes)- lozenge in a double-blind placebo-controlled trial

Bartosik T.[1]; Jensen S. A.[2,3]; Afify S. M.[2,3,4]; Bianchini R.[2]; Hufnagl K.[2]; Hofstetter G.[2]; Berger M.[1,5]; Bastl M.[1,5]; Berger U.[1,5]; Rivelles E.[6]; Schmetterer K.[6]; Eckl-Dorna J.[1]; Vyskocil E.[1]; Kramer M. F.[7,8]; Guethoff S.[7,8]; Jensen-Jarolim E.[2,3,9]; Roth-Walter F.[2,3]

[1]Department of Otorhinolaryngology, Medical University of Vienna, Vienna, Austria; [2]Comparative Medicine, The Interuniversity Messerli Research Institute of the University of Veterinary Medicine Vienna, Medical University Vienna and University Vienna, Vienna, Austria; [3]Institute of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria; [4]Laboratory Medicine and Immunology Department, Faculty of Medicine, Menoufia University, Menoufa, Egypt; [5]Aerobiology and Pollen Information Research Unit, Department of Oto-Rhino-Laryngology, Medical University of Vienna, Vienna, Austria; [6]Department of Laboratory Medicine, Center of Translational Research, Medical University of Vienna, Vienna, Austria; [7]Bencard Allergie GmbH, Munich, Germany; [8]Allergy Therapeutics Ltd, Worthing, United Kingdom; [9]Biomedical International R+D GmbH, Vienna, Austria

Background: Functional iron deficiency not only facilitates allergy development, but also amplifies the clinical symptom burden in allergy sufferers. Our preclinical studies document that iron can be selectively delivered to immune cells with beta-lactoglobulin carrying ligands such as retinoic acid and polyphenol-iron complexes (holo-BLG) resulting in immune resilience and allergy prevention. Here, we assessed in allergic subjects the clinical efficacy of a FSMP (food for specific medical purposes) lozenge containing beta-lactoglobulin with iron, retinoic acid, zinc and polyphenols (holoBLG lozenge).

Method: In a double-blind placebo-controlled study, grass- and/or birch pollen allergic women ($n = 45$) were given holoBLG lozenge (verum) or placebo lozenges twice daily over 6 months. Prior and

after dietary supplementation, participants were nasally challenged with birch- or grass pollen extracts, and their blood was analyzed for immune and iron parameters. Participants made daily electronic entries in a pollen diary to record the study participants' symptoms, medications and well-being during the pollen seasons. Peripheral blood mononuclear cells were isolated, stimulated and assessed by flow cytometry.

Results: Allergic symptoms after nasal provocations improved by 42% in the verum versus 13% in the placebo group. During the birch as well as grass pollen seasons 2019 and 2020 daily symptom burden was significantly reduced in birch- and or grass pollen allergic subjects supplemented with the holoBLG lozenge compared to the placebo lozenge. Allergic participants ingesting the holoBLG lozenge improved their iron status with increased hematocrit values and decreased red cell distribution width compared to subjects from the placebo group. Moreover, after 6 months ingestion the circulating CD14+ cells of allergic participants receiving the holoBLG lozenge contained significant higher iron-levels compared to the placebo-group.

Conclusion: In this double-blind placebo-controlled trial, targeted micro-nutrition with a holoBLG based FSMP lozenge was effective in elevating immune iron levels and reducing the symptom burden in allergic women. This allergen-independent mechanism redefines our understanding of allergies and highlights the great benefits of targeted micro-nutrition to combat allergies.

981 | The health and economic impact of allergen therapy in patients with allergic rhinoconjunctivitis: Real-word evidence from the czech republic

Dolezal T.[1]; Janickova N.[2]; Velackova B.[1]; Strosova D.[1]; Filkova B.[1]; Dolzealova H.[1]

[1]*Value Outcomes, Prague, Czech Republic;* [2]*Allergy Therapeutics, Worthing, United Kingdom*

Background: To compare the changes in clinical outcomes and healthcare costs during the usage of subcutaneous allergen immunotherapy (AIT) with tyrosine adsorbed allergoids in patients with allergic rhinoconjunctivitis (AR) before and after initiation of AIT in the Czech Republic.

Method: Allergen therapy data were based on prospective, non-interventional, single arm, multi-centre cohort clinical study with 3-year follow-up. Data were obtained from routinely collected medical records and only patients with three completed pollen seasons with AIT were included (n = 317). Each patient was assessed before the start of AIT and then during three consecutive years treated with subcutaneous AIT. Information about the daily occurrence, severity and symptomatic treatment used in the pollen season was obtained from patient questionnaires. In addition, demographic data and healthcare resource use and costs connected to allergic rhinoconjunctivitis were collected.

Differences between patient outcomes before and after third season with AIT therapy were tested at the 5% significance level. The costs were based on actual list prices, reimbursement tariffs and expert opinion as of 12/2020.

Results: The data showed improvement in frequency and severity of clinical symptoms reported by clinicians and patients: from 78% to 29% with persistent AR and from 87% to 10% with moderate or severe AR (both p-values < 0.001). The mean ARMS score (Average Rescue Medicine Score) which represents the amount of the usage of symptomatic medicine decreased from 1.8 points to 0.9 points (p-value < 0.001). The regular use of antiallergic medications (antihistamines, glucocorticoids and cromons) decreased significantly during the study follow-up.

Total healthcare costs apart from administration of tyrosine adsorbed allergoids decreased during AIT treatment by 54%. Healthcare costs of medication including antihistamines, glucocorticoids, antileukotrienes and cromons decreased by 49% and the cost of unscheduled physicians visit by 73%.

Conclusion: AIT treatment is a clinical effective and cost-saving treatment of AR based on medical records from the real clinical practice in the Czech Republic. However, it should be taken into the account that the environmental changes between the seasons might affect the results.

1232 | IgG response of rabbits immunized with different subcutaneous immunotherapies against ragweed allergy

Zbircea L. E.[1,2]; Grijincu M.[1,2]; Buzan M. R.[1,2]; Cotarca M. D.[1,2]; Tamas P. T.[1,2]; Tanasie G.[1,2]; Paunescu V.[1,2]; Valenta R.[3,4,5,6]; Panaitescu C.[1,2]; Chen K. W.[2]

[1]*Center of Immuno-Physiology and Biotechnologies, Department of Functional Sciences, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*OncoGen Center, Pius Brinzeu County Clinical Emergency Hospital, Timisoara, Romania;* [3]*Department of Pathophysiology and Allergy Research, Division of Immunopathology, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria;* [4]*Laboratory for Immunopathology, Department of Clinical Immunology and Allergology, Sechenov First Moscow State Medical University, Moscow, Russia;* [5]*Karl Landsteiner University of Health Sciences, Krems, Austria;* [6]*NRC Institute of Immunology FMBA of Russia, Moscow, Russia*

Background: Ragweed (*Ambrosia artemisiifolia*) pollen is one of the most important sources of respiratory allergies in Europe. Allergen-specific immunotherapy (AIT) is considered the only long-lasting treatment, able to prevent the progression of IgE-mediated allergic rhinitis to asthma. However, the content of individual allergens in different extract-based AITs may vary.

The goal of this study was to assess the IgG induction towards various ragweed allergens upon vaccination with commercially available subcutaneous allergen immunotherapies (SCIT) in rabbits.

Method: Three ragweed extract-based SCIT available in Europe - from now on referred to as SCIT 1, 2 and 3 - were selected for this study as antigens for rabbit immunization. Each SCIT was administered to two rabbits with the recommended doses and time schedule recommended by the manufacturer. Test bleedings were taken every four weeks, while final bleeding was performed 4 weeks after the last immunization. IgG antibodies against ragweed allergens were detected by ELISA using recombinant ragweed allergens Amb a 1, Amb a 3, Amb a 4, Amb a 5, Amb a 6, Amb a 8, Amb a 9, Amb a 10, Amb a 11 and Amb a 12. Preimmune serum was used as negative control.

Results: Very high levels of anti-Amb a 1 IgG antibodies were detected in sera from rabbits immunized with SCIT 3; high levels of anti-Amb 5 antibodies were detected in sera from rabbits immunised with all three immunotherapies, whereas medium levels of IgG antibodies against Amb a 8 were detected in sera from rabbits immunised with SCIT 2 and 3. Low IgG levels against Amb a 4, Amb a 6 and Amb a 11 were detected in sera from one rabbit immunised with SCIT 3. IgG antibodies levels against allergens Amb a 3, Amb a 9, Amb a 10 and Amb a 12 were very low in all immunotherapies.

Conclusion: Our study showed that different extract-based immunotherapies induced different IgG profiles which may refer to different allergen content or allergen concentration in the extract. Also, the duration of the therapy and/or the number of applied doses seems to affect the IgG induction. These findings may be helpful for allergist when prescribing allergen-based immunotherapy.

1124 | Tolerance of an olea 100% cluster build-up schedule

Garcia-Nunez I.[1]; Algaba-Marmol M.[2]; Mistrello G.[3]
[1]*Hospital Quironsalud Cordoba, Cordoba, Spain;* [2]*SAS, Ecija, Spain;*
[3]*Research Department, Lofarma SpA, Milan, Italy*

Background: Olea europeae sensitization is the most common seasonal rhinitis and/or asthma reason in South Spain, with high pollen levels every year. Immunotherapy is the best treatment to improve the quality of life of patients with these symptoms. Cluster schedule is postulated as a safe built-up phase in all patients. Our objective was to describe a population referring allergic symptoms with Olea europeae as the main reason and the tolerance of a cluster build-up phase with Lais in Olea 100%.

Method: Patients referring allergic symptoms (rhinitis and/or asthma) due to Olea Europeae sensitization were included. After a skin prick test (with the main house dust mites, pollens, moulds, epithelia, profiline and Pru p3) and a in vitro test (total IgE, specific IgE (sIgE), Ole e1 and Ole e7 levels) a cluster build-up phase with Lais in Olea 100% was performed following the schedule (see table 1). Immediate and non-immediate tolerance was evaluated.

Results: Nine patients (6 males and 3 females; mean age 42, 34 years (15-66 years) were included. All of them referred allergic rhinitis and 7 (77.7%) mild to moderate asthma. Three patients (33.33%) presented a positive skin prick test to Lolium or 2 (22.22%) to dog dander. Medium total IgE was 165.35. Olea medium sIgE was 35.5 (75.4-15.3) with medium Ole e1 levels 14.8 (70.1-6.7) and medium Ole e7 levels 9.56 (15.2-0). Built-up schedule was well tolerated by all patients, with no local or systemic reactions (immediate and non immediate observation) after the injections.

Conclusion: Our patients present a high sensitization to Olea pollen, with high levels to major (Ole e1) and minor allergens (Ole e7).
Lais in Olea 100% in a cluster schedule is well tolerated by patients from an Olea europeae high exposure zone.
More patients are needed to confirm these results and to reduce the built-up phase schedule.

TABLE 1 cluster built up schedule

Day	Dose	Observation period
0	0.1 + 0.2	30 minutes between doses
7	0.2 + 0.3	30 minutes between doses
14	0.5	30 minutes

1283 | Allergenicity and immunogenicity profile of depigmented-polymerized phleum pratense extract for use in allergen-specific immunotherapy treatments

Layhadi J. A.[1]; Lenormand M. M.[1]; Sharif H.[1]; Parkin R. V.[1]; Vilà-Nadal G.[1]; Moya R.[2]; Durham S. R.[1]; Carnés J.[2]; Shamji M. H.[1]
[1]*Imperial College London, London, United Kingdom;* [2]*LETI Pharma S.L.U, Madrid, Spain*

Background: Allergoids are chemically modified allergen extracts with reduced capacity to crosslink IgE receptors on the surface of mast cells and basophils, providing a better safety approach for use in allergen immunotherapy (AIT). We hypothesized that allergoids derived by depigmentation and polymerization have reduced allergenicity, allergen-specific Th2 (Th2A) and T follicular helper (Tfh) cell responses. We further hypothesized that allergoids can promote B regulatory (Breg) cell responses with the capacity to produce IL-10.

Method: Whole blood and peripheral blood mononuclear cells were collected from 16 grass pollen allergics (GPA) and 8 non-atopic controls (NAC). The allergenicity of native *Phleum pratense* (Phlp) extract, depigmented (DPG Phlp) extract and depigmented-polymerized (DPG-POL Phlp) allergoid were measured by their ability to elicit basophil activation and histamine release using flow cytometry. Allergen-specific Th2A, Tfh cells and IL-10$^+$ Breg cells were quantified by flow cytometry. Moreover, unbiased analyses were performed using FlowSOM to generate clusters based on cell surface expression and their abundance profile to identify cell subsets targeted by DPG-POL Phlp.

Results: Unmodified Phlp extract elicited a dose-dependent increase in basophil responsiveness as illustrated by CD63$^+$CRTh2$^+$ (EC_{50} = 10.37 ± 4.48 ng/mL) and DAO$^-$CD63$^+$CRTh2$^+$ (EC_{50} = 25.16 ± 10.86 ng/mL) basophils in GPA, but not NAC. A

similar dose response was observed in response to DPG Phlp stimulation. DPG-POL Phlp demonstrated hypo-allergenic profile when compared to unmodified Phlp extract (31.54-fold, $CD63^+CRTh2^+$ and $DAO^-CD63^+CRTh2^+$; all $p < .001$). DPG-POL Phlp had reduced capacity to elicit proliferation of Th2A, $IL\text{-}4^+$ Tfh and $IL\text{-}21^+$ Tfh cells compared to Phlp extract in GPA (all, $p < .05$). Moreover, DPG-POL Phlp was the most prominent at inducing $CD19^+CD5^{hi}IL\text{-}10^+$ and $CD19^+CD5^{hi}CD38^{int}CD24^{int}IL\text{-}10^+$ Breg cell subsets compared to Phlp extract in GPA (all, $p < .05$). The effect of DPG-POL Phlp on Th2A, Tfh and IL-10-producing Bregs were validated using an unbiased clustering analysis using FlowSOM. FlowSOM identified 2 distinct metaclusters corresponding to Tfh cells, that were targeted by DPG-POL Phlp, while 3 distinct metaclusters were identified corresponding to Breg cell subsets.

Conclusion: We confirmed the hypo-allergenic nature of DPG-POL Phlp and for the first time, we demonstrate their capacity to elicit reduced Th2A, Tfh response and enhanced $IL\text{-}10^+$ Breg responses. This highlights their beneficial use for AIT.

1229 | Remission of a case of hymenoptera sting-associated chronic urticaria during venom immunotherapy

Dubini M.[1]; Pravettoni V.[2]; Sangalli A.[1]; Cappelletti C.[1]; Rivolta F.[2]
[1]*Università degli Studi di Milano, Milan, Italy;* [2]*IRCCS Foundation Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy*

Background: The role of immunotherapy in Chronic Urticaria is unclear, except for isolated circumstances. Hymenoptera sting mostly causes acute urticaria and no report of CU after Hymenoptera sting can be found in the literature.

Methods: We report a case of 34-year-old man with CU that appeared after a grade I Mueller reaction to Hymenoptera sting and remitted during venom immunotherapy (VIT), after months of unsuccessful therapy for CU.

Results: Routine blood tests, D-dimer, complement components and acute phase reactants were normal. Other causes of CU, such as acute or chronic infections and thyroid gland disorders, were excluded. Autologous serum skin test was negative. Serum baseline tryptase was 7 mcg/mL. Skin tests and specific IgE were positive for vespid venoms, and venom-specific component revealed allergy to *Vespula* spp.

After three months of CU the patient agreed to start VIT because of the impairment of quality of life and the close beginning of wasp season. Venom-specific immunotherapy was started with *Vespula spp* extract, according to a 6-week cluster schedule with weekly incremental doses, until a maintenance dose of 100,000 SQ-U/ml.

Discussion: The hypothesis behind urticaria progression can be explained from several perspectives. First, vespid sting and urticaria onset could be coincidental and CU remitted spontaneously.

Alternatively, CU progression, from onset to remission, might be associated with some specific effects of venom allergens. Supporting this hypothesis, we observed a clear-cut association between exposure to venom allergens and urticaria symptoms. In fact, type I allergy may be causative in a small number of CU patients and specific immunotherapy (AIT) with these allergens may be beneficial in those patients. Moreover, besides its specific effects, immunotherapy exerts non-specific effects. AIT changes type 2 lymphocytes, eosinophil, basophil and mast cell homeostasis and reduces the skin sensitivity not only to specific allergens, but also to histamine and non-specific mast cell stimuli.

As a matter of fact, reduced immune cells reactivity could contribute significantly to the improvement of urticaria symptoms, even if they have not been related to venom allergens. Therefore, in our patient VIT might have played a positive role, increasing the sensitivity threshold to non-specific stimuli.

1043 | Correlation between total ige results in newly released multiplex allergy panel and fluoroenzimoimmune single-parameter assay. characteristics of the studied population

Landaveri Sánchez L.; Lopez Salgueiro R.; Stein Coronado C.; Catalán Cácares N.
Hospital Universitari i Politècnic La Fe, Valencia, Spain

Background: The use of new multi-parameter assays (which includes total IgE value determination) in complex allergy study has extended in the past years.

We aimed to determine the correlation of the results for total IgE and specific IgE (sIgE) in house dust mite (HDM) and Lipid transfer protein (LTP) allergic patients, using the available single-parameter assay and new multiplex assay. Second objective was to clarify the principal pathologies in the tested population.

Method: We analyzed 114 samples from patients attended at the Allergy Department (January 2020–March 2021). Total IgE, sIgE for Der p1, Der p2 and Pru p3 were performed with ImmunoCAP© (Phadia AB, Uppsala, Suecia) and $ALEX^2$ (MacroArray Diagnostics, Vienna, Austria). Quantitative correlation between methods was analyzed with Pearson coefficient (r). Statistical significance level of 5% ($p < 0.05$) was considered. Correlation is considered weak if $r < 0.5$, moderate if $0.5 < r < 0.8$ and strong if $r > 0.8$.

The principal patient's diagnosis were also registered.

Results: Multiplex panels were demanded in poly-allergic patients: 20% had multiple food allergy, 15.5% rhinitis with inadequate response to immunotherapy, 13% rhinitis and asthma, 13% rhinitis and food allergy, 9.5% asthma and food allergy. The remaining 19% had other diagnoses (such urticaria, eosinophilic esophagitis, mastocytosis)

Values of total IgE using both methods were obtained for 90 samples. Correlation index between methods was 0.71 (p-value <0.0001) for total IgE. Results in 15 samples of allergic patients to HDM showed a high correlation degree between Derp1: 0.99 and Der p2: 0.97 (p-value < 0.0001). Five allergic patients to LTP, Pru p3 showed a correlation of 0.99 (p-value < 0.014)

Conclusion: Multi-parameter was demanded in poly-sensitized patients (mainly to food allergens) and in case of immunotherapy fail. A

strong correlation degree was found for main HDM components and Pru p 3 using both methods. Therefore, when soliciting a multiplex assay, there is no need to perform parallel testing of single sIgE to these components. In case of total IgE, the correlation detected is moderate so a parallel determination by a single total IgE could be useful.

Further and larger studies with sIgE for these and other components are needed.

1113 | Allergy burden in luxembourg: A population-based, cross-sectional health survey paralleled by component-resolved-IgE-diagnosis

Czolk R.[1,2]; Roth L. E.[1,3]; Scheuermann T.[1]; Graf T.[1]; Klueber J.[1,4]; Hilger C.[1]; Rösch N.[3]; Le Coroller G.[5]; Vaillant M.[5]; Ruiz-Castell M.[6]; Fagherazzi G.[6]; Huiart L.[6]; Ollert M.[1,4]; Kuehn A.[1]

[1]Department of Infection and Immunity, Luxembourg Institute of Health, Esch-Sur-Alzette, Luxembourg; [2]Faculty of Science, Technology and Medicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg; [3]University of Applied Sciences Kaiserslautern, Faculty of Computer Science and Microsystems Technology, Campus Zweibrücken, Zweibrücken, Germany; [4]Department of Dermatology and Allergy Center, Odense Research Center for Anaphylaxis, Odense University Hospital, University of Southern Denmark, Odense, Denmark; [5]Competence Center for Methodology and Statistics, Integrated Bed to Bench Operations, Luxembourg Institute of Health, Strassen, Luxembourg; [6]Department of Population Health, Epidemiology and Public Health Research Unit, Luxembourg Institute of Health, Strassen, Luxembourg

Background: Allergy is the most common chronic health condition in Europe. The European Health Examination Survey (EHES) study is a population-based, cross-sectional survey on baseline characteristics of the general health status representative for adults. The aim of this study was to establish a first national dataset on allergies in Luxembourg by extracting relevant disease-specific data from the EHES survey in Luxembourg (EHES-LUX) and identifying molecular sensitization patterns in bio-banked serum samples from potential allergy cases.

Method: Data were extracted from the EHES-LUX questionnaire (*N* = 1,529 participants; age 25–64) using the software R Studio and participant groups were compared using descriptive statistics (Chi-Square, T-test, Spearman's correlation). All participants with reported allergy (*N* = 458) were tested by multiplex IgE-testing using a macroarray with 299 allergens from food and environmental sources. All other participants (876) were tested with a Phadiatop assay for respiratory sensitization. Positive Phadiatop cases were also analyzed on the macroarray.

Results:: A self-reported overall allergy percentage of 40.2% was determined in the EHES-LUX cohort (25.2% nasal, 20.9% skin, 17.8% eye, 9.0% food allergy, 8.1% asthma). IgE sensitization was found in 43,0 % of the cohort. This sensitization group reported higher discomfort on specific aspects of their physical and mental needs, such as more work-absence due to health issues and tiredness. The most common sensitization was against grass pollen. 45.4% of the cohort was sensitized against Timothy grass (Phl p 1), followed by Rye grass (Lol p 1 40.1%) and Bermuda grass (Cyn d 1 29.5%). Very high significant correlation was found between Birch allergen Bet v 1 (29.2% sensitized) and its cross-reactive allergens Strawberry Fra a 1/3, Hazelnut Cor a 1, Apple Mal d 1, characteristic for the "pollen-fruit-syndrome ". A high number of participants (26.3%) presented with high co-sensitizations to multiple respiratory sources, pollens and other environmental allergens (mites/animal dander/mold), suggesting a high respiratory allergy burden.

Conclusion: In Luxembourgish adults, a high overall allergy burden was found, with respiratory allergens being a major contributor. Reported food allergy symptoms can be explained by the "pollen-fruit-syndrome".

1136 | IgE binding to component allergens in a cohort of crustacean allergic subjects in Australia

Johnston E. B.[1,2,3]; Kamath S. D.[1,2,3,4]; Karnaneedi S.[1,2,3,4]; Nugraha R.[1,5]; Lopata A. L.[1,2,3,4]

[1]Molecular Allergy Research Laboratory, College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, Australia; [2]Australian Institute of Tropical Health and Medicine, James Cook University, Townsville, Australia; [3]Centre for Molecular Therapeutics, James Cook University, Townsville, Australia; [4]Centre for Food and Allergy Research, Murdoch Children's Research Institute, Melbourne, Australia; [5]Department of Aquatic Product Technology, Bogor Agricultural University, Bogor, Indonesia

Background: Shellfish allergy affects up to 3% of children and adults worldwide, and persists for life for most people. The diagnosis of shellfish allergy is often challenging due to structural similarity of allergens in other allergen sources and geographic differences in shellfish exposure. Despite significant clinical importance, the IgE recognition frequency of different allergen components remains unclear. The aim of this study was to compare and characterise crustacean allergen recognition profiles of people with confirmed shellfish allergy in Australia.

Method: A total of 54 subjects were recruited for this study with confirmed clinical history of shellfish allergy and a positive diagnostic result by either skin prick test or ImmunoCAP. Specific-IgE (sIgE) was quantified using the ALEX Allergy Explorer macroarray system (Macro Acro Diagnsotics, Vienna) containing 117 allergen extracts and 178 purified allergen components, including five crustacean allergen components: tropomyosin (TM), arginine kinase (AK), myosin light chain (MLC), sarcoplasmic calcium binding protein (SCP), and troponin C (TpC).

Results: IgE binding to any crustacean allergen/extract was observed in 74% of investigated adults. sIgE was detected against all five component allergens present on the array, including 40% of

subjects positive to TM, 26% to TpC, 22% to AK, 13% to SCP and 4% to MLC.

When comparing IgE reactivity to homolog shrimp components in other allergen sources, considerable binding was demonstrated to TM from dust mite (48%), cockroach (44%) and Anisakis (43%), and AK from mite (24%) and cockroach (20%).

Conclusion: This is the first study in Australia to use an allergen multiplex system to determine the IgE binding profile to crustacean allergen components and homologous allergenic proteins from other allergen sources. The number of people with sIgE to the main crustacean allergen TM was lower than expected, while binding to the homologous allergens TM and AK in dust mite, cockroach and Anisakis indicated the same or higher frequency of binding compared to crustacean, in this cohort. This highlights the difficulty in determining true cross-reactivity and the role that TM and AK may play as important cross-sensitising pan-allergens.

1159 | Impact of blood specimen age on cell reactivity and possible strategies to implement basophil activation testing in multi-centric studies

Bourgoin P.; Busnel J.
Beckman Coulter, Marseille, France

Background: Based on the use of whole blood, the Basophil Activation Testing (BAT) is a flow cytometry based functional approach that enables the *ex vivo* characterization of basophil reactivity against specific allergenic molecules and/or raw extracts. The main focus now revolves around standardizing and democratizing this tool. After having recently developed a simplified and streamlined approach to BAT, with dry and room temperature stable reagents and an optimized workflow, herein, we wanted to characterize and further compare two possible strategies for implementing BAT in multi-centric studies. The main question was whether it was preferable to store blood before or after sample stimulation and processing.

Method: Fresh heparin and EDTA whole blood samples were collected and processed in parallel following two workflows: "collect, store, process & analyze" or "collect, process, store & analyze". Storage times between 0 and 7 days at temperatures of 18–25°C or 2–8°C were considered. Basophil reactivity to increasing doses of anti-IgEs ranging from 0.01 to 100 ng/test was assessed using dry and ready-to-use BAT reagents consisting of 5 markers, including CD45 and CD294 as gating markers, CD3 to exclude CD294+ T cells, and CD203c and CD63 as activation markers.

Results: The "collect, store, process & analyze" workflow showed that blood can be kept at least 2 days at 18–25°C or 2–8°C before further processing without impact on basophil reactivity. A careful analysis of the basophil activation phenotype revealed that significant upregulation of CD203c and slight CD63 decrease occurred after 2 days of storage.

The "collect, process, store & analyze" workflow demonstrated that blood can be processed and then kept at least 5 days at 18-25°C or 2-8°C before being analyzed with no significant impact on CD203c or CD63 expressions, thereby enabling the accurate characterization of basophil reactivity to increasing doses of anti-IgEs.

Conclusion: These results demonstrate that various strategies can be implemented to integrate BAT in multi-centric studies. The "collect, store, process & analyze" workflow remains a simplified logistical approach but depending on the time available between clinical centers and reference laboratories. The "collect, process, store & analyze" workflow, made possible by the format of the new BAT, can thus constitute a workflow improvement to provide significant flexibility without impact on the level of basophil reactivity detected.

1215 | "allergoeye" fully automatic quantitative conjunctival provocation test based on artificial intelligence

Yarin Y.; Kalaidzidis Y.; Kalaidzidou A.
ENT & Allergy Praxis, Dresden, Germany

Background: The significance of the conjunctival provocation test in allergology continually raises due to its simplicity, precision and sensitivity, which are comparable to those of a nasal provocation test. However, until now there is no simple way to analyse an allergic reaction through a conjunctival provocation in quantitative manners.

Method: The platform "Allergoeye", based on neural networks and artificial intelligence, was developed to completely automatically, quickly and easily quantify the allergic reaction of the sclera. AllergoEye consists of an Android-based camera with a controlled light stand and a PC-based AI server module. The camera and the server are linked by a local, non-routable, wireless protocol that ensures the protection of personal data. The result of the analysis is transferred back to the Android-based camera, which offers the doctor real-time control for fully automatic quantitative evaluation. There are interfaces that allow data to be exported from the AI module to the statistics and medical software.

Results: Preclinical investigation in 10 patients showed a strong correlation between therapy effectiveness (symptom reduction during KPT) and reduction of redness and quantification in the results of the "AllergoEye".

Conclusion: "Allergoeye" platform is used to diagnose allergic rhinoconjunctivitis, to control the effectiveness of desensibilisation therapy and as a quantitative method for clinical studies.

1219 | Case series of food cofactor anaphylaxis syndrome (FCAS): A new proposal for anaphylaxis associated with pathogenesis-related to protein 10 or non-specific lipid transfer protein sensitivities

Moon E.; Herwadkar A.; Crump V.; Elkhalifa S.
Salford Royal Hospital, Mancheser, United Kingdom

Background: Food-Dependant Exercise-Induced Anaphylaxis (FDEIA) due to non-specific Lipid Transfer Proteins (ns-LTP) sensitization has been well established. Recently sensitization to pathogenesis-related proteins 10 (PR10) has been reported to cause systemic symptoms following ingestions of fruits, nuts, and vegetables in the presence of cofactors such as exercise, alcohol, fasting, and taking gastric acid suppression medications. We propose to rename these syndromes as Food Cofactor Anaphylaxis Syndrome (FCAS).
Method: We retrospectively reviewed 30 cases presented to a Large Regional Immunology and Allergy Tertiary Centre in the North West of England in the period: March 2018 to March 2021. All cases presented with Anaphylaxis in the presence of variable cofactors and were found to be sensitized to either PR10 or ns-LTP.
Results: Our case series demonstrated the association between the occurrence of systemic symptoms and the sensitization to either PR 10 or ns LTP in the presence of the following cofactors were identified: consumption of a large amount of allergen exposure, physical activity, environmental factors, concomitant medications/drugs, emotional stress, and fatigue. The type of physical activity and the minimum threshold of physical activity required for eliciting an anaphylaxis reaction found to be variable in this cohort of patients.
Conclusion: We propose that co-factors induced anaphylaxis syndromes with sensitization to PR10 or ns LTPs be renamed as Food Cofactor Anaphylaxis Syndrome (FCAS) and that the management pathway should be considered for risk stratifying this cohort of patients in advance. Further studies on the pathogenesis of cofactors and triggers of systemic symptoms in the context of PR10 sensitization are required to gain a better understanding of this syndrome.

1241 | Comparison of reactivities of serum IgE from atopic dermatitis patients and dogs to dust mite allergens

Song H.[1]; Jeong K.Y.[1]; Cheon D.S.[2]; Park J.W.[1]
[1]*Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul, South Korea;* [2]*POSTBIO Co., Ltd, Guri, South Korea*

Background: Dust mite (DM) causes atopic dermatitis (AD) in human and dog. However, reactivities of canine IgE to DM component allergens have not been compared yet.
Method: We identified canine IgE-reactive components of *Dermatophagoides farinae* and *Tyrophagus putrescentiae* by 2D gel and tandem mass spectrometry. IgE-reactivities of 8 recombinant DM allergens (Der f 1, Der f 2, Der f 11, Der f 18, Tyr 4, Tyr 8, Tyr 11, Tyr 28) were determined by ELISA using sera from 30 AD patients and 27 AD dogs.
Results: Canine IgE-reactive proteins (Der f 1, Der f 11, Tyr p 4, Tyr p 8, Tyr p 11, Tyr p 28) were identified by proteome analysis. AD patients showed highest sensitization to Der f 1 (93.3%) followed by Der f 2 (86.7%), Tyr p 11 (83.3%), Der f 11 (53.3%), Der f 18 (50%), Tyr p 4 (46.7%) and Tyr p 28 (46.7%). Interestingly, AD dogs showed IgE-reactivities to Der f 2 (94.1%), Der f 18 (84.6%), Der f 1 (73.1%), Tyr p 4 (46.2%), Tyr p 11 (46.2%), and Der f 11 (42.3%) in descending order.
Conclusion: Der f 2 and Der f 18 were the most important allergens in AD dogs while Der f 1 and Der f 2 were the important allergens in AD patients. Information on different sensitization pattern between AD human and dog may be useful for better diagnostics of AD canine.

1127 | Comparison between linear and conformational epitopes of most frequent ltp's sensitizers

Lopez-Salgueiro R.[1]; Sanchez Gomez H.[2]; Garcia Caballero N.[2]; Poveda Alberola J.[2]
[1]*Hospital Universitario y Politácnico La Fe, Valencia, Spain;*
[2]*Universidad de Valencia. Biology Faculty, Valencia, Spain*

Background: LTPs are the main elicitors of food allergy in Southern Europe and there is a high cross-reactivity among them. However, the molecular cause of cross reactions observed in patients is not well known.
Objective: To evaluate the structural homology among the residues that set up the linear and conformational epitopes in most frequent LTP sensitizers (Pru p 3, Jug r 3, Ara h 9, Cor a 8) and compare this with levels of specific IgE (sIgE) to these components in LTP profiles previously described (Peach profile (PP) and Peanut profile (PeP))
Method: Linear and conformational epitopes were identified by sequences from previous experiments based on the analysis of IgE-binding capacity of decapeptides bound to membrane, a phago display random peptide library and analysis of the surface electrostatic potential and solvent exposure in the case of Pru p 3 and based on *in silico* approach for linear and conformational epitopes of Ara h 9 .To analyze the homology we counted the number of different amino acids. Levels of sIgE to LTP components were previously measured by Immuno®CAP ISAC (levels >0.35 ISU were considered positive) and profiles were determined by higher level of sIgE to every LTP
Results: Homology degree according to Pru p 3 was ranked as follows: linear epitopes Ara h 9> Cor a 8>Jug r 3 and conformational epitopes Ara h 9>Jug r 3=Cor a 8. Levels of sIgE in PP were ranked as Pru p 3>Ara h 9>Jug r 3>Cor a 8 matching the homology results with regarding conformational epitopes. Comparing Ara h 9 with other LTPs linear epitopes Pru p 3 obtained the greatest similarity followed by Cor a 8 and Jug r 3. At conformational level the result was Ara h 9>Pru p 3=Jug r 3>Cor a 8 and this rank matches with the sIgE results in PeP.

Conclusion: Hierarchical order of homology according to conformational epitopes of LTP components matches perfectly with the order of sIgE levels measured in patients classified in PP and PeP. These results confirm the relevance of conformational epitopes in LTP allergy and the practice utility of the homology degree between different LTP components to prescribe dietary restrictions.

1228 | Utility of specific-to-total IgE ratios: The golden ratio for cannabis allergy?

Decuyper I. I.[1,2]; Rihs H.[3]; Mertens C.[1]; Van Gasse A.[1,2]; Elst J.[1]; Faber M.[1,2]; Hagendorens M.[1,2]; Sabato V.[1,2]; Ebo D.[1,2]
[1]University of Antwerp, Antwerp, Belgium; [2]University Hospital of Antwerp, Antwerp, Belgium; [3]Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Bochum, Germany

Background: In the past decade, cannabis allergy (CA) has been recognized as an increasing health issue and its prevalence is likely underestimated because of cannabis's illegal status in many countries and the absence of reliable diagnostics.

Method: Here, we sought to investigate whether serological diagnosis of CA could benefit from an adjustment for tIgE by exploring sIgE hemp-to-tIgE, sIgE rCannabis sativa (Can s) 3-to-tIgE and rCan s 5-to-tIgE ratios. All three ratios were performed and compared between cannabis allergic patients and pollen and/or nsLTP sensitized controls. Only patients with a positive sIgE for each allergen were taken into account as negative results cannot benefit from additional ratios.

Results: Specific IgE hemp-to-tIgE ratio differed significantly between CA patients and controls (cut-off 0.02, specificity 93% (95% confidence interval (CI), 85-98%)). A significant difference was also found for sIgE rCan s 5-to-tIgE (cut-off 0.01, 95% CI 61% (36-83%)), although small group numbers resulted in very wide confidence intervals. No additional benefit was found for sIgE rCan s 3-to-tIgE. When all three ratios were compared between CA patients with and without anaphylaxis, no significant difference was found either.

Conclusion: These results indicate that there is a place for sIgE-to-tIgE ratios in the diagnostic approach of CA. However, these should not be used to estimate the risk for cannabis related anaphylaxis. In the case of a definite history of cannabis related symptoms, we now recommend starting serological confirmatory testing with a sIgE hemp assay as a negative result significantly reduces the chance of IgE-mediated CA. A positive result, however, should be complemented by calculation of a sIgE hemp-to-tIgE value, as this will notably increase test specificity. Where available, it is still worthwhile using cannabis component resolved diagnostics as for example, it was previously shown that over two-thirds of CA patients who experienced anaphylaxis are Can s 3 sensitized. The utility of rCan s 5-to-tIgE is promising but should be further explored in larger groups as is the case for sIgE rCan s 2-to-tIgE and sIgE rCan s 4-to-tIgE which could not be explored in this analysis due to insufficient data.

	sIgE hemp-to-tIgE		sIgE rCan s 5-to-tIgE			
	<0.02	≥0.02	<0.005	≥0.005	<0.01	≥0.01
Controls	70	5	59	16	11	7
CSA	58	34	21	71	6	11
Sensitivity (95%CI*)	37% (27–48%)		77% (67–85%)		65% (38–88%)	
Specificity (95%CI*)	93% (85–98%)		79% (68–87%)		61% (36–83%)	
Pearson Chi-square	$p < 0.01$		$p < 0.01$		$p = 0.117$	

1253 | Basophil activation test in the diagnostic management of hypersensitivity reactions to non-steroidal anti-inflammatory drugs in patients with and without lipid transfer protein sensitization

Urbani S.; Aruanno A.; Rizzi A.; Rumi G.; Ferraironi M.; La Sorda M.; Sanguinetti M.; Nucera E.
Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) can act as cofactors exacerbating allergic reactions induced by lipid trasfer protein (LTP). To explain this cofactor role, one theory suggests NSAIDs can have a direct effect on mast cells and basophils degranulation/activation.

Method: Starting from October 2019 until January 2020 the adult patients, with a clinical history of NSAIDs hypersensitivity, independently to food ingestion, have undergone to a complete allergological work-up, comprising:

- skin prick test for food allergens;
- measurement of total serum IgE and specific IgE for rPrup 3;
- basophils activation test performed in three phases: first, only stimulating with rPru p 3, secondly with culprit NSAIDs and finally with a combination of the culprit drug and the food allergen (NSAID + LTP).

Results: Currently, 76 patients are included in the study (19 male and 57 female). The patients reactions after drug administration are variable (Table 1). Among the patients with a clinical history of

NSAIDs hypersensitivity, we have found a prevalence of 62% of LTP sensitization.

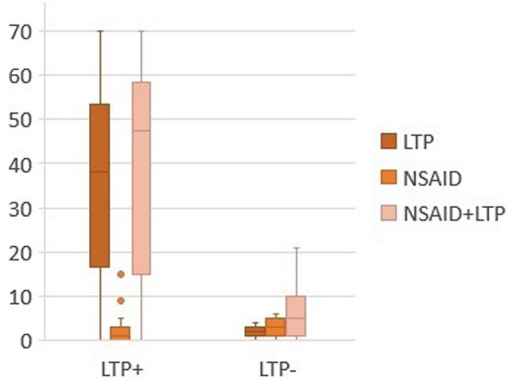
In both group we observed a greater basophils activation after combined exposition to NSAID+LTP. However this activation is higher in LTP+ patients where NSAID clinically acts as a cofactor (Figure 1).

Conclusion: We have shown the importance of search for LTP sensitization in patients with a clinical history of NSAIDs hypersensitivity and the possible role played in vitro by NSAIDs in basophils activation.

Characteristics	Values
Female, *n* (%)	57
Age (years)	39.6 ± 12.8
BMI (kg/m2)	27.6 ± 5.3
Concomitant allegy, *n* (%)	79
OAS, *n* (%)	7.9
Cutaneous symptoms, *n* (%)	83.5
Respiratory symptoms, *n* (%)	2.5
Anaphylaxis, *n* (%)	6.6

Data are presented as mean ± SD or %, as indicated. BMI= body mass index; OAS= Oral Allergy Syndrome

Figure 1



1277 | Frequency of sensitization to cockroach allergens in russian population

Bala A.; Chursinova Y.

M.F. Vladimirskiy Moscow Regional Research and Clinical Institute, Moscow, Russia

Background: Cockroach ubiquitous scavenger organisms have inhabited the planet long ago and domiciliary species are currently a serious problem for humans. There is inter-species cross reactivity (e.g. American, German, Asian and Oriental) and extra-species cross reactivity ("pan allergy") with a number of other arthropods such as crustaceans (shrimp, crab, and lobster), insects (silverfish, butterflies), arachnids (dust mites) and mollusks (oysters, mussels, scallops, clams). Usually Bla g 2 and Bla g 5 have the higher frequency of IgE positivity among cockroach allergens but there are important differences among individual patients and populations. Since both exposure and allergy to cockroach are very common, patients with asthma or rhinitis should be routinely evaluated for this type of allergy.

Aim: To study sensitization to cockroach allergens.

Method: The presence and level of IgE-aB to by ISAC ImmunoCAP technology (Thermofisher Scientific, Sweeden).

Patients: There were 616 pts aged from 1 to 79 with different severity of food allergy observed. All sera from these pts tested to rBla g 1, rBla g 2, rBla g 5 and nBla g 7.

Results: There were 24 pts positive to cockroach allergens. Most frequently the IgE-aB in 62.50% (15/24) pts were positive to nBla g 7 wherein concentrations of IgE-aB were 0.4–82.9 ISU-E. Specific IgE-aB to major components of cockroach allergens rBla g 5 and rBla g 2 identified in 33.33% (8/24) pts and 12.50% (3/24), concentrations differed slightly 0.5–14.0 and 0.5–0.9 ISU-E respectively. Most of pts were sensitized only to 1 allergen component 91.66% (22/24) pts and most of them are sensitized to nBla g 7 (15/22). Only two patients sensitized to two allergic components. They were two women 25 and 33 years old with sensitization to rBla g 2 and rBla g 5. None of the patients was sensitized to three allergic components, and none of the patients was sensitive to rBla g 1.

Conclusion: Sensitization to cockroach allergens available for research in ISAC but not often found in the Russian population in 3,89% of cases (24/616). Moreover, most of patients with IgE-aB to this type of allergens have monosensitization to nBla g 7 in 62,50% of cases and only 2 patients have sensitization to 2 allergic components.

1304 | Going viral: Assessing etiological trends in pediatric urticaria in the absence of immediate historical trigger(s)

Gyaltsen T.; Wu V.; Ohayon J.

Hamilton Allergy, Hamilton, Canada

Background: Pediatric urticaria (PU) involves the development of clearly demarcated or coalescing pruritic wheals (hives), and affects up to 25% of children. Its etiology is suggested by history and often leads to Allergist consultation for further work up. PU presentation is categorized into acute (<6 weeks duration) or chronic (>=6 weeks duration), with etiologies including allergic, infectious, physical (pressure and temperature) and autoimmune triggers. Skin prick testing (SPT) is routinely expected by parents to help diagnose definitive, allergic triggers of their child's urticaria.

Method: A retrospective chart review was conducted at a community allergy referred for evaluation of PU, with absence of immediate allergic trigger(s). History of urticaria presentation; relevant physical examination; and results of investigations including skin prick testing (SPT) to common food/inhalant allergies and physical provocation triggers (ice cube provocation, immediate deep scratch testing, and delayed 15 lb weight) were collected to determine etiology.

Results: A sample of 137 pediatric patients between the ages of 1 and 17 years (mean age = 9.6) were analyzed over a 2 year period. Eighty-eight of 137 (64.2%) presented with acute pediatric urticaria (APU) while the remaining 49 (35.8%) presented with chronic pediatric urticaria (CPU). Sixty-four of the 88 (72.7%) acute presentations identified infection as a trigger by history. Of the total 129 patients who underwent SPT, only 17 (13.2%) had relevant allergens identified as a trigger by history and SPT, with foods representing 5 of 17 (29.4%) and inhalant aeroallergens representing 12 of 17 (70.6%) cases.

Conclusion: In the majority of cases of PU with no immediately-historically suggestive allergic trigger(s), presentations were acute, self-limited, and did not relapse. Infection was identified as the most common presentation. In addition, SPT in PU diagnosis of these cases was of minimal help, suggesting that history provided sufficient information in the majority of APU. SPT however did promote anxiety and discomfort in these children, with little yield of information. These data suggest that the majority of PU presentations in patients with no immediate known trigger are self-limiting, will not relapse, and if acute, most likely bear infection as a trigger.

1306 | Urticaria 'chronic'led: an analysis of pediatric chronic urticaria presentation in the absence of immediate historical trigger(s)

Gyaltsen T.; Wu V.; Ohayon J.
Hamilton Allergy, Hamilton, Canada

Background: Pediatric chronic urticaria (PCU) is characterized by the formation of pruritic wheals (hives) over a period of 6 weeks or greater, and is usually accompanied by local redness and swelling. PCU presentation can stem from various etiologies such as allergy, pressure and temperature (cholinergic), and autoimmunity. It develops when mast cells and basophils receive a trigger to release histamine into the surrounding skin. PCU's etiology is regularly limited by history and physical examinations, often requiring Allergist consultation for further investigation and treatment.

Method: A retrospective chart review was conducted at a community allergy clinic for evaluation of pediatric urticaria, with absence of immediate known trigger. History of urticaria; relevant physical examination; and information from skin prick testing (SPT) to common food/inhalant allergies, ice cube provocation, immediate deep scratch testing, and delayed weight (15 lbs) provocation were collected to help determine causes and retrospectively identify trends in the suspected etiology of PCU.

Results: A sample of 49 pediatric patients (ages 1 to 17 years, mean age = 11.3) were analyzed for their history, result of allergy SPT, and suspected etiology over a 2 year period. Twenty-four of 49 (49.0%) presented with pressure-induced PCU, 12 (24.5%) presented with PCU triggered by changes in core temperature, 6 (12.3%) presented with both pressure and temperature-induced PCU, while only 2 (4.1%) required further work up to establish an autoimmune association. Of the 49 patients who underwent SPT, only 8 (16.3%) had relevant allergens identified as a trigger by history and SPT, with foods representing 3 of 8 (37.5%) and inhalant aeroallergens representing 5 of 8 (62.5%) cases.

Conclusion: In the majority of PCU, presentations were chronic-inducible, as predicted by history and relevant testing. Only a small percentage of PCU presentations displayed an autoimmune association, based on bloodwork. In addition, SPT in PCU diagnosis was of minimal help, suggesting that history and provocation testing were of greater yield in the majority. PCU will often be due to inducible (e.g. pressure and/or temperature) triggers, rarely rheumatic or autoimmune. As an educational point to younger clinicians, provocation testing in CPU is of greater value than SPT (to common foods and inhalant aeroallergens) in its management and treatment.

1294 | Wheat-dependent exercise-induced anaphylaxis – A case report of a rare, but potentially severe and life-threatening syndrome

Shehaj A.[1]; Lazri E.[2]
[1]*American Hospital, Fier, Albania;* [2]*Regional Hospital of Gjirokastra, Tirane, Albania*

Abstract

A 50-year-old male with an uncomplicated medical history, developed two episodes of anaphylactic reaction with generalized itching and urticaria, labial angioedema, wheezing and abdominal pain after consuming pizza and going for a run immediately after. It was performed Specific Ig E and Molecular Allergy Test and after a detailed clinical history, the patient was diagnosed with Wheat-dependent Exercise-Induced Anaphylaxis.

Introduction

WDEIA is a rare, but potentially severe food allergy occurring during or shortly following exercise. It is clinically characterized with urticaria, angioedema, dyspnea, hypotension, collapse and shock. The precise mechanism of WDEIA remain unclear. Diagnosis is made based on the patient's history in combination with SPT, wheat-sIgE test and Molecular Allergy test. Acute treatment includes adrenaline or antihistamines. The most reliable prophylaxis is a gluten-free diet. In less severe cases, a strict limitation of wheat ingestion before exercise may be sufficient.

Case report

A 50-year-old male, was referred to our allergy clinic after 2 anaphylactic reactions in the last 2 months, 20-30 minutes after consuming pizza and gone for a run immediately after. He had manifested generalized itching and urticaria, labial angioedema, wheezing and abdominal pain and received immediate treatment after both episodes. He came to our clinic for further investigation to find the cause of these reactions.The patient does not refer allergic symptoms after consuming cooked wheat products in absence of physical activity. Specific Ig E and Molecular Allergy Test were performed and

resulted in high sIgE for wheat extract 18 kUA/L; for barley extract 12 kUA/L and for Tri- a-19 [ω-5-gliadin], 9.8 kUA/L.

Discussion

Sensitization to wheat by ingestion can lead to WDEIA, a condition in which ω-5 gliadin (Tri a 19), a storage protein and major wheat allergen, is responsible for severe immediate reactions (within 3 h). This particular presentation is difficult to predict and to diagnose as the ingested wheat quantities as well as the exercise level necessary to induce the symptoms are very variable. In conclusion, we report a rare case of WDEIA, which underlines the need to carefully investigate wheat sensitization and most importantly the cofactors with a detailed clinical history. The patient, based on the severity of the reactions, was recommended a gluten free diet and always carrying an epinephrine autoinjector.

1036 | Strategies to improve the requests for specific IgE tests in primary care

Pardo E. F.[1]; Garrigós M. L.[1]; Barbero Á. B.[1]; Sánchez J. F.[1]; Salinas C. L.[2]; Campos M. T.[3]; Lacasta M. S.[1]

[1]*Hospital Universitario San Juan de Alicante, San Juan De Alicante, Spain;* [2]*University of Missouri, Columbia, United States;* [3]*Thermo Fisher Diagnostics, Cornellà De Llobregat, Spain*

Background: The prevalence of allergies has increased notably over recent decades, thus allergy testing needs have become more relevant for healthcare systems. Allergy patients are mainly screened by general practitioners in primary care settings. Unfortunately, these professionals are not sufficiently trained on allergy testing, thus appropriate protocols are crucial for proper first-line management of allergy patients. The experience of clinical laboratories through the analysis of retrospective data, in concert with allergy specialists, plays a key role in developing allergy testing strategies that allow better patient management while being cost-effective.

Method: An observational study consisting of the retrospective analysis of 4,359 interventions on primary care testing requests from 2014 to 2019. Interventions followed a protocol established in 2014, between allergy specialists and the clinical laboratory, and included the following: to override redundant sIgE testing for allergen mixes, sIgE testing for allergen extracts included in mixes, sIgE testing for low-prevalent allergen extracts in our region, sIgE testing for milk and egg molecular components without prior positivity to allergen extracts, and the addition of prevalent allergen testing in patients with respiratory symptoms and/or urticaria.

Results: The strategy, based on demand management by the lab, resulted in a net balance of 683 saved tests. Test drop-offs were primarily driven by the cancelation of 2,186 egg and milk components, while 561 tests were added for mixes together with 942 allergen extracts. 27.6% of the patients with a respiratory allergy and 11.8% of patients with urticaria tested positive for the added whole allergens, whilst none of the cancelled tests were reordered by the general practitioner.

Conclusion: This study shows how the allergy laboratory plays a key role in the active demand management for sIgE testing, leading to a better selection and diagnosis of allergy patients while optimizing investment in resources.

1129 | Comparison of ltp's sensitization profiles according to two component resolved diagnosis in vitro test

Lopez-Salgueiro R.[1]; Sanchez Gomez H.[2]; Poveda Alberola J.[2]

[1]*Hospital Universitario y Politécnico La Fe, Valencia, Spain;*

[2]*Universidad de Valencia. Biology Faculty, Valencia, Spain*

Background: Several clinical profiles had been described for LTP's according to clinical, laboratory and structural alignment criteria. New "in vitro" diagnostic tool is emerging to detect the specific IgE (sIgE) to LTP components but its clinical useful has to be determined.

Objective: To evaluate the ability of new "in vitro" test to identify different LTP profiles and compare the results with the standard multiplex sIgE detection test.

Method: We analyzed 22 patients diagnosed with LTP mediated food anaphylaxis at the Allergy Department. The analysis was performed by two multiplexed sIgE tests (ImmunoCAP© and ALEX$^{2®}$). Results >0,35 kUA/L to LTP's components were considered positive in both tests. Every patient is classified in every profile according to LTP component with higher level of sIgE. The rest of components were ranked according sIgE level. Results obtained with both type of tests were compared.

Results: According to the level of sensitization to a specific LTP component we identified 2 LTP profiles: peach profile (PP) in 72.7% of patients and peanut profile (PeP) in 27.3%. The ranking of sIgE in PP by ImmunoCAP® ISAC was Pru p 3>Jug r 3>Ara h 9>Cor a 8 and in ALEX$^{2®}$ was Pru p 3>Ara h 9> Jug r 3>Cor a 8. Regarding PeP the order of sIgE was in ImmunoCAP® ISAC Ara h 9>Pru p 3>Jug r 3>Cor a 8 and the same hierarchic order was determined by ALEX$^{2®}$.

Conclusion: The two LTP sensitization profiles showed a high degree of concordance when analyzing by the two "in vitro" methods. There is only one different result between tests in PP (ImmunoCAP® ISAC Jug r 3>Ara h 9/ALEX$^{2®}$ Ara h 9> Jug r 3). Cor a 8 is the last component in every profile indicating the lower level of cross-reactivity with other components. Both analytical methods are reliable to identify clinical LTP profiles. This fact is so important to individualized the diet restriction in LTP allergy patients.

1168 | Correlation between dermatophagoides multiplex assays and single-parameter assays

Stein C. I.; Landaveri L.; Catalan N.; Ethel I.; Lopez R.

Hospital Universitari y Politecnic La Fe, Valencia, Spain

Background: In the last years, new detection methods of specific IgE (sIgE) serum levels had been deployed for allergy diagnosis. Singleplex analysis has been the standard method for molecular

allergy diagnosis, but it is a costly method when various determinations are required. Multiplex assays allow analysis of a wide range of related allergens with a capacity up to 34 aeroallergens with only 500 µL of serum.

We aimed to compare multiplex and single-parameter assays for house dust mites (HDM) sIgE, determining their utility for diagnosis.

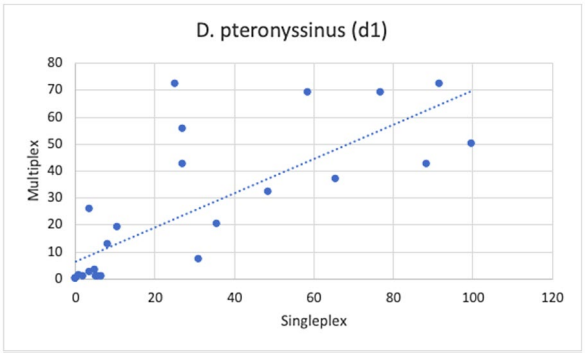
Method: Patients who attended our Department for respiratory allergy from July 2019 to February 2021 were included. Total IgE (tIgE), specific IgE levels and ratio sIgE/tIgE to Dermatophagoides pteronyssinus (d1) and Dermatophagoides farinae (d2) were measured using an immunoblot based multiplex panel and fluoroenzimoimmune single-parameter assay (considered as lab standard test). Values >0,35 kUa/L were considered positive. Quantitative correlation between methods was analyzed with non-parametric Spearman coefficient.

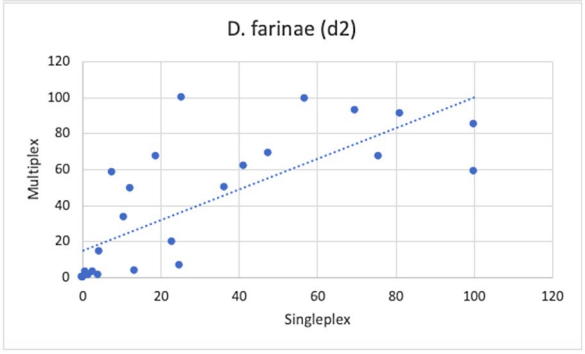
Results: Twenty-six patients were studied (18 females and 8 males, 16-62 years old with a median age of 40). Sixteen as first visits and 10 as follow-up visits. Thirteen presented only with allergic rhinoconjuctivitis, two with asthma and 9 with dual pathology (rhinoconjuctivitis and asthma).

Based on absolute sIgE values, correlation degree was 0,833 for d1 and 0,874 for d2 (p < 0,001 both cases)

According to sIgE/tIgE, correlation degree was 0,756 (p = 0,08) for d1 and 0,833 (p = 0,008) for d2.

Conclusion: There is a very good correlation level about sIgE for d1 and d2 and ratio sIgE/tIgE d2 between both analytical methods, so any method can be eligible for HDM diagnosis. There was no statistical significance found for ratio sIgE/tIgE d1, this could be due to the small amount of the sample. There is a need for more studies to other allergens and an increase in the number of d1 positive patients to reinforce the clinical utility of this new analytical method.





1226 | IgE reactivity profiles in ragweed pollen allergy

Buzan M. R.[1,2]; Zbircea L. E.[1,2]; Grijincu M.[1,2]; Gattinger P.[3]; Stolz F.[4]; Valenta R.[3,5,6,7]; Paunescu V.[1,2]; Panaitescu C.[1,2]; Chen K. W.[2]

[1]Center of Immuno-Physiology and Biotechnologies, Department of Functional Sciences, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania; [2]OncoGen Center, Pius Brinzeu County Clinical Emergency Hospital, Timisoara, Romania; [3]Department of Pathophysiology and Allergy Research, Division of Immunopathology, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria; [4]Biomay AG, Vienna Competence Center, Vienna, Austria; [5]Laboratory for Immunopathology, Department of Clinical Immunology and Allergology, Sechenov First Moscow State Medical University, Moscow, Russia; [6]Karl Landsteiner University of Health Sciences, Krems, Austria; [7]NRC Institute of Immunology FMBA of Russia, Moscow, Russia

Background: Common ragweed (*Ambrosia artemisiifolia*) became both an environmental and a health issue, worldwide. Ragweed pollen contains different protein components responsible for allergic reactions in late summer and fall. Hence, for an accurate diagnosis, detailed investigations about patients' IgE sensitization profile are needed. This study aimed to determine the IgE-reactivity profile of ragweed pollen allergic patients in association with allergy symptoms.

Method: IgE reactivity profile of ragweed pollen allergic patients from Western Romania was determined using blotted ragweed pollen extract. An allergist evaluated the clinical symptoms and grouped them into rhinitis, conjunctivitis, asthma-like symptoms and skin reactions. The reactivity to ragweed pollen allergens other than Amb a 1 was evaluated using immunoblot inhibition assays with two Amb a 1 isoforms (Amb a 1.01 and Amb a 1.03) and two CCD markers.

Results: Immunoblot assays showed 19 different IgE reactivity patterns, but after analyzing their frequency no dominant pattern was observed. Clinical evaluation showed that more than 95% of the patients reported rhino-conjunctivitis, around 60% were complaining of asthma-like symptoms and about 25% had skin reactions. Also, patients with complex sensitization profiles tend to have more clinical symptoms. Inhibition experiments revealed incomplete signal inhibition on ragweed extract immunoblots when the patients' sera were pre-incubated with the two Amb a 1 isoforms. Different degrees of inhibition were seen after pre-incubation with CCD markers.

Conclusion: The sensitization profile of ragweed pollen allergic patients is very heterogeneous and the major allergen Amb a 1 alone was not able to completely inhibit the IgE binding. Therefore, for an accurate diagnosis, the role of other ragweed pollen allergens has to be evaluated and CCD markers should be included to avoid false-positive results.

1130 | Feline atopic syndrome: The current need for a multimodal diagnostic approach

Machado A.[1]; Ferreira D.[2]; Martins L.[3]

[1]*Universidade de Évora/Escola de Ciências e Tecnologia/Departamento de Medicina Veterinária, Évora, Portugal;* [2]*OneVet Group, Vn Gaia, Portugal;* [3]*Universidade de Évora/Escola de Ciências e Tecnologia/Departamento de Medicina Veterinária/MED - Instituto Mediterrâneo para a Agricultura, Ambiente e Desenvolvimento, Évora, Portugal*

Background: Clinical signs of Feline Atopic Syndrome rely mainly on the presence of pruritus, like in dogs. Despite, in cats, specific patterns of skin reaction could point to a primary allergic cause of the atopic syndrome, these patterns are not specific of atopy. Factors such as ectoparasites, food or environmental allergens may also trigger a great diversity of close clinical signs.

Etiologic and pathogenic diagnosis of FAS requires time and dedication, and both the veterinarian and the owner should cooperate. Since none of the clinical signs or global presentation pattern result pathognomonic for FAS, and no "perfect" diagnostic test is still available, a combination of (i) suggestive anamnesis; (ii) clinical signs and (iii) exclusion of other compatible differentials stand so far as the most reliable diagnosis plan. Hence, in face of a compatible clinical history of SAF it is necessary to proceed through a detailed collection of patient's relevant information and to carry out several complementary diagnostic exams as skin cytology and/or histology, trichograms, bacterial and fungal cultures, among others.

Throughout the current plan leading to a positive diagnosis of FAS, several differentials are successively discarded. However, mostly due to pruritic consequences, several skin complications may join the clinical frame, making difficult either the diagnosis or even the treatment options.

Evolution of the clinical condition following the implementation of allergen-avoidance measures also plays a crucial role in the diagnosis confirmation as Feline Dermatitis Extent and Severity Index (FeDESI) or Scoring Feline Allergic Dermatitis (SCORFAD) may evolve positively regarding the avoidance of implicated allergens species.

Method: Three clinical cases of FAS are described, exemplifying the current multi-modal diagnosis approach. Diagnosis of FAS was obtained by differential exclusion, combining anamnesis, clinical signs, dermatology complementary tests, prophylactic flee prevention and exclusion diets.

Results: All of the patients presented with FAS and #2 and #3 also with secondary pyoderma; #3 also with ceruminous external otitis, a not so common manifestation in cats with FAS, needing specific treatment.

Conclusion: FAS positive diagnosis allowed effective control of clinical signs with significant gain in wellbeing.

1049 | Allergy leading to a reproductive disorder: A story of two sisters

Irastorza M. J.[1]; Cavallo M. C.[2]

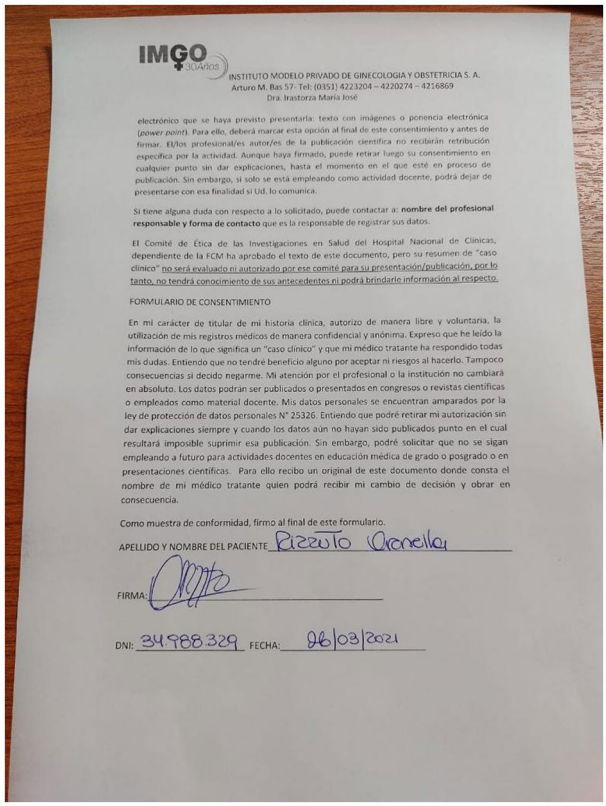
[1]*Model Institute of Gynecology and Obstetrics, Cordoba, Argentina;* [2]*Hospital San Martin, Paraná, Argentina*

Background: A semen allergy or human seminal plasma hypersensitivity (HSP) is an allergic reaction to the proteins found in most men's sperm. This rare condition is more common in women that can be the cause of impaired reproduction. Hypersensitivity to seminal fluid is uncommon and encompasses a wide variety of clinical manifestations ranging from local pruritus and localized dermal reactions, to life-threatening situations such as anaphylaxis, which are generated by skin contact with semen.

Objective: Present two cases report of allergy in a reproduction institute.

Clinical cases: A 28-year-old female patient with a history of Allergic Rhinitis. Consulted for sensation of vaginal burning and genital edema after sexual intercourse, for which she received treatments with corticosteroids and polyvalent ovules, without results. Vaginal infections are ruled out and she is sent to psychological therapy, where pathology is ruled out. After 2 years she changes partners and begins with the same symptoms but with greater intensity and they do not occur with the use of a prophylactic. Total Ig E is performed: 30 IU/ml (up to 168 IU/ml). Prick Test with Seminal Fluid: 7 mm papule and 40 mm erythema. One year after the diagnosis, her 33-year-old sister, with a history of allergic rhinitis, consulted for sensation of vaginal burning, pain and genital edema after sexual intercourse which does not appear before the use of prophylaxis. Total Ig E is made: 57.8 IU/ml (up to 168 IU/ml). Prick Test with Seminal Fluid: papule 6 mm and 15 mm erythema.

Conclusion: The correct allergological diagnosis allows to rule out infections and dermatitis generated by spermicides, soaps or lotions. Sperm Fluid Allergy has no impact on fertility, however its symptoms may interfere with reproductive capacity. Artificial insemination with sperm devoid of seminal plasma is very useful for establishing pregnancy. These cases make us consider the immunological mechanisms and genetic association



IMGO 30 Años

INSTITUTO MODELO PRIVADO DE GINECOLOGIA Y OBSTETRICIA S. A.
Arturo M. Bas 57- Tel: (0351) 4223204 – 4220274 – 4216869
Dra. Irastorza María José

electrónico que se haya previsto presentarla: texto con imágenes o ponencia electrónica (*power point*). Para ello, deberá marcar esta opción al final de este consentimiento y antes de firmar. El/los profesional/es autor/es de la publicación científica no recibirán retribución específica por la actividad. Aunque haya firmado, puede retirar luego su consentimiento en cualquier punto sin dar explicaciones, hasta el momento en el que esté en proceso de publicación. Sin embargo, si solo se está empleando como actividad docente, podrá dejar de presentarse con esa finalidad si Ud. lo comunica.

Si tiene alguna duda con respecto a lo solicitado, puede contactar a: **nombre del profesional responsable y forma de contacto** que es la responsable de registrar sus datos.

El Comité de Ética de las Investigaciones en Salud del Hospital Nacional de Clínicas, dependiente de la FCM ha aprobado el texto de este documento, pero su resumen de "caso clínico" no será evaluado ni autorizado por ese comité para su presentación/publicación, por lo tanto, no tendrá conocimiento de sus antecedentes ni podrá brindarle información al respecto.

FORMULARIO DE CONSENTIMIENTO

En mi carácter de titular de mi historia clínica, autorizo de manera libre y voluntaria, la utilización de mis registros médicos de manera confidencial y anónima. Expreso que he leído la información de lo que significa un "caso clínico" y que mi médico tratante ha respondido todas mis dudas. Entiendo que no tendré beneficio alguno por aceptar ni riesgos al hacerlo. Tampoco consecuencias si decido negarme. Mi atención por el profesional o la institución no cambiará en absoluto. Los datos podrán ser publicados o presentados en congresos o revistas científicas o empleados como material docente. Mis datos personales se encuentran amparados por la ley de protección de datos personales N° 25326. Entiendo que podré retirar mi autorización sin dar explicaciones siempre y cuando los datos aún no hayan sido publicados punto en el cual resultará imposible suprimir esa publicación. Sin embargo, podré solicitar que no se sigan empleando a futuro para actividades docentes en educación médica de grado o posgrado o en presentaciones científicas. Para ello recibo un original de este documento donde consta el nombre de mi médico tratante quien podrá recibir mi cambio de decisión y obrar en consecuencia.

Como muestra de conformidad, firmo al final de este formulario.

APELLIDO Y NOMBRE DEL PACIENTE Rizzuto Graciela

FIRMA:

DNI: 34988329 FECHA: 06/03/2021

1261 | Is periconceptional maternal sex hormones risk factors for atopic eczema in the offspring: a systematic review and meta-analysis

Baldeh A. K.[1]; Nyassi S.[2]; Nwaru B.[3]
[1]*University of Gothenburg, Gothenburg, Sweden;* [2]*Dalarna University, Dalarna, Sweden;* [3]*Krefting Research Center, Gothenburg, Sweden*

Background: Evidence on the role of periconceptional exposure to sex steroids in the development of allergy in the offspring remains equivocal.
Aim: To synthesize the evidence from studies that have investigated the relation of the use of exogenous sex hormones before pregnancy and serum levels of endogenous sex hormones during pregnancy to the risk of developing atopic eczema in the offspring.
Method: We searched twelve electronic databases from inception to date for observational epidemiological studies. In addition, databases of ongoing studies and grey literature were searched, reference lists of included studies scanned, and contacted experts on the topic. The risk of bias in included studies was assessed using the Effective Public Health Practice Project tool. Meta-analyses were undertaken using the robust variance estimation approach in order to account for dependencies in effect estimates within studies.
Results: Our database searches yielded 5,226 papers, of which nine were included (giving a total of 88,200 subjects). The studies were graded moderate risk of bias. Neither use of exogenous steroids 6–12 months before pregnancy (risk ratio [RR] 1.10, 95% CI 0.97–1.23) no serum levels of estradiol/progestogen/testosterone (RR 1.07, 95% CI 0.64–1.50) was statistically significantly associated with the risk of developing atopic eczema in the offspring.
Conclusion: Although in utero exposure to environmental and intrauterine factors is strongly believed to influence the risk of allergy in the offspring, the current evidence does not support any putative role for periconceptional maternal sex hormones. Nevertheless, the low to moderate quality of available studies on the topic indicates that more robust longitudinal studies are required to provide definitive clarity on the topic, as well as studies investigating the potential mechanism through which periconceptional sex hormones may influence the subsequent risk of allergy in the offspring.

1222 | Adrenaline prescribing in primary care over 5 years: a review of UK longitudinal prescription data

Dua S.[1]; Lacquiere S.[2]; Doyle M.[3]
[1]*Cambridge University Hospitals, Cambridge, United Kingdom;* [2]*ALK, Horsholm, Denmark;* [3]*Indigo Medical, St Helier, JY*

Background: Adrenaline is the first line treatment for anaphylaxis and an adrenaline autoinjector (AAI) should be prescribed for those at risk of anaphylaxis. Regulatory advice recommends that two adrenaline autoinjectors per patient should be prescribed. Training on the use of AAIs is critical and should be device specific. The aim of this study was to review data on AAI prescriptions in primary care.
Method: Longitudinal patient data from anonymous electronic prescription records from general practitioners in the UK were examined retrospectively from August 2020 to October 2015.
Results: Only one AAI device was prescribed in 8% patients. The average interval between renewing prescriptions was 240.7 days (approximately 8 months). The proportion of patients who were carrying expired devices was 29%. There has been a threefold increase in the number of patients being prescribed generic adrenaline over 5 years from 5098 to 15,119; 10,635 prescriptions were written between March 2020 and Sept 2020. Until February 2018, 95% of patients carried one brand of AAI, however between March 2018 and February 2019, 22.5% patients were carrying more than one brand at one time. There were 23,122 prescriptions written in primary care for a specific AAI brand even after it had been withdrawn from the market.
Conclusion: Prescription of AAIs in primary care is suboptimal. An increase in generic prescribing, likely driven by AAI stock issues and recalls, and a high number of prescriptions for a withdrawn AAI brand suggests that device specific training may not be taking place against prescribing guidance. Furthermore, a considerable number of patients are carrying expired devices and carrying multiple brands with different administration techniques. These factors place anaphylaxis patients at risk. Patients renew prescriptions every 8 months which provides an opportunity for device training. Education programmes are needed to ensure that prescribing guidance is adhered to in primary care.

1006 | Incidence, triggers and clinical manifestations of anaphylaxis in hospitalized patients—A retrospective study in Tirana

Asllani J.; Gjeli A.; Kryeziu E.; Vladi J.; Lekli E.; Luku D.; Mesonjesi E.; Hoxha M.; Qirko E.; Priftanji A.
University of Medicine of Tirana, Tirana, Albania

Background: A lot of uncertainty exists regarding anaphylaxis epidemiology, wide range of clinical manifestations, mechanisms and etiology. Foods, drugs and hymenoptera venom (HV) represent most common triggers of anaphylaxis. Cutaneous symptoms are present in 80–90% of patients. We aim to investigate anaphylaxis causes, incidence and symptoms.

Method: We included all consecutive patients with anaphylaxis hospitalized in our department from January 2017 to January 2019. A retrospective form based on patient's medical chart was used to collect data on age, gender, triggers, symptoms, atopy, time of symptoms onset, presence of cofactors. Common triggers and clinical presentation according sex and age were analyzed. A p value <0.05 was considered significant.

Results: From a total of 181 subjects with anaphylaxis only 150 patients fulfilled the inclusion criteria. The median age was 43 years old and 54.7% were female. The incidence of anaphylaxis was 7.8% in 2017 and 10.9% in 2018. The most frequent trigger was HV (42%) followed by drugs (36%), foods (14.7%) and idiopathic in 6%. We found exercise induced anaphylaxis in one case. There was no significant correlation between triggers and gender (p = 0.932). Patients with food induced anaphylaxis were younger (m = 28.8 ± 13 years) than those with drugs as a trigger (m = 46 ± 15.8 years, p < 0.001) and those with HV anaphylaxis (m = 47 ± 12.5 years, p < 0.001). Cutaneous manifestations were observed in 93%, respiratory in 87%, cardiovascular in 63% and gastrointestinal in 53% of patients. In 43% of the cases symptoms started within 30 minutes after exposure. 82.6% of symptom onset between 5-10 minutes were triggered by HV and 71.4% of symptom onset >60 minutes were triggered by drugs (p < 0.001). Cofactors were reported in 22.7% with acute infections being the most frequent. Allergic rhinitis (10%) and asthma (9.3%) were the most frequent allergic comorbidites in our study (Table 1).

Conclusion: This is the first published study about anaphylaxis in hospitalized patients in Albania. HV was the most frequent trigger. Triggers in our study were age dependent. Cutaneous and respiratory symptoms were observed in the majority of patients. Symptoms onset were trigger dependent. Further research is needed for understanding anaphylaxis trends.

TABLE 1 General characteristic of the patients included in the study

Variables	Total *N* (150)	Frequency (%)
Sex (Female)	82	54.7%
Smoking	41	27.3%
Place of anaphylaxis		
Home	65	43.3%
School	44	29.3%
Health institution	1	0.7%
Restaurant	6	4%
Unspecified	10	6.7%
	14	9.3%
	10	6.7%
Atopy	43	28.7%
Bronchial asthma	*14*	9.3%
Allergic rhinitis	*15*	10%
Urticaria	*12*	8%
Atopic dermatitis	*1*	0.7%
Biphasic	10	6.7%
Hymenoptera venom	63	42%
Bee venom	40	26.7%
Wasp venom	19	12.7%
Unidentified	4	2.7%
Drugs ?	54	36%
Antibiotics	20	13.3%
Non steroidal antiinflammatory drugs	26	17.3%
Angiotensin converting enzyme inhibitors	3	2%
Proton pomp inhibitors	2	1.3%
Antiepileptics	1	0.7%
Foods	22	14.7%
Fish/Sea foods	10	6.7%
Tree nuts	4	2.7%
Vegetables/fruits	3	2%
Others	4	2.7%
Time of symptoms onset		
5-10 minutes	55	36.7%
Within 30 minutes	64	42.7%
30-60 minutes	24	16%
>60 minutes	7	4.6%
Time of arrival in emergency department		
Within 30 minutes	35	23.3%
30-60 minutes	67	44.7%
>60minutes	48	32%
Cofactors		
Alcohol	6	4%
Acute infections	14	9.3%
NSAID	4	2.7%
Exercise	3	2%
Stress	5	3.3%
Menstruations	2	1.3%

1167 | Managing anaphylaxis in a COVID-19 field hospital adapted for oral food challenging using risk management & process mapping

Alsaleemi A. Y.[1,2]; Farren L.[1]; Trujillo J.[3]; Fitzsimons J.[4]; O'carroll C.[5]; Byrne A.[6]; Hourihane J. O.[7]; Mccarthy K. F.[8]; Coghlan D.[9]
[1]*1-Children's Health Ireland at Crumlin, Dublin, Ireland;* [2]*Department of Paediatrics, College of Medicine, Qassim University, Saudi Arabia, Qassim, Saudi Arabia;* [3]*Cork University Hospital, Cork, Ireland;* [4]*Children's Health Ireland at Crumlin,, Dublin, Ireland;* [5]*University College Dublin, Dublin, Ireland;* [6]*Children's Health Ireland at Crumlin, Ireland, Dublin, Ireland;* [7]*Royal College of Surgeons, Dublin, Ireland;* [8]*Children's Health Ireland at Crumlin, Dublin, Ireland;* [9]*Children's Health Ireland at Tallaght,, Dublin, Ireland*

Background: Five paediatric allergy clinics across Ireland joined together at covid-19 field hospital to deliver OFCs for a large number of paediatrics patients over 6 weeks. The aim was to maximise this opportunity to remove children from the waiting list, while providing safe care for patients and a safe environment for healthcare staff. The goal of this project is to report our experience of preparing an alternative care site for the large-scale administration of OFCs.
Method: Funding for this initiative at a hotel in Dublin was received from the NTPF. Standardised food challenge protocols were utilized. OFCs were performed within a pods system, 4 to 6 beds in each pod. A resuscitation room was designed and equipped in situ with an easy access to the pod area and the main exit. Two anaphylaxis simulation sessions were undertaken prior to commencement. We instituted a traffic light system approach according to patient status to guide the role of each team member. We followed a "Go/No Go" principle when moving children across different care sites.
Results: 474 children received an OFC. We did not proceed with OFC in additional 14 children as they were unfit for the challenge. 25 children (5%) had an anaphylaxis reaction. Of those, 7(28%) were treated with two doses of IM adrenaline, 6(24%) had received intravenous fluid, 9(36%) were moved to the resuscitation area and 8 (32%) were transferred to a local paediatric hospital and stayed one night only. No child required advanced airway management. The most frequent unanticipated event was due to lack of consumable stocks. There was one near-miss event that was not anticipated by the process mapping.
Conclusion: Disruption of elective and planned care by pandemics and seasonal viruses is inevitable. Vacant field hospitals provided a potential opportunity for us to perform off-site OFCs safely through a cross-hospitals collaboration. We would advocate for the utilization of field hospitals for non-urgent medical care. We hope that our experience provides a road map for those planning services in the future.

1044 | Vipera latastei anaphylaxis

Torres Pérez B.[1]; Delgado González A.[1]; Reaño Martos M.[1]; Iglesias Cadarso A.[1]; Pineda De La Losa F.[2]
[1]*Allergy Department. Hospital Universitario Puerta de Hierro - Majadahonda, Madrid, Spain;* [2]*Laboratorio de Aplicaciones. DIATER Laboratorios., Madrid, Spain*

Background: Lataste's viper is a species of snake present in the south-west Europe (Spain and Portugal). The toxicity of its venom is lower than the one of other vipers. The most common symptoms of poisoning are local swelling and necrosis. Ig-E reactions can also be present, but they have seldom been described.
Method: A previously healthy 46-year-old male, an animal photographer, presented generalized itching, dizziness, sickness, hypotension, and loss of consciousness immediately after the fifth bite of a viper (*Vipera latastei*) in his right hand. He needed urgent adrenalin treatment and admission to the intensive care unit.
He had presented less severe symptoms with previous viper bites, but it is not clear if they were due to poisoning or an allergic reaction.
Results: The protein profile of the venom by SDS-PAGE showed a range of molecular weight protein between 10 and 70 kDa, particularly three bands between 10 and 15 kDa were exhibited.
The Western Blot showed that the patient's IgE recognized some proteins in the extract of the *Vipera latastei* venom, with a molecular weight between 10 and 15 kDa. These proteins have reportedly been found in the venom of other viper species, therefore, a cross-reactivity between them seems likely.
There was no elevation of his basal tryptase levels.
The patient was diagnosed with anaphylactic shock due to V*ipera latastei* venom hypersensitivity.
Conclusion: Viper (genus vipera) bites lead to a variety of clinical manifestations. Anaphylactic reactions following snake bites can be presented, especially in patients with repeated bites. Immunoblotting can be useful to identify patients that can be sensitized to viper's venom.

1160 | An analysis of anaphylaxis due to unknown trigger at a single emergency department during 10 years

Sim D.W.; Yu J.E.; Koh Y.
Chonnam National University Medical School & Hospital, Gwangju, South Korea

Background: Anaphylaxis due to unknown trigger (AUT) is a diagnosis of exclusion when no cause can be identified. Several studies revealed that AUT accounts for approximately up to 60% of cases of anaphylaxis in adults. Research describing the clinical manifestation and follow up of AUT in Korea is limited. To assess and compare

the demographic and clinical characteristics and the management of adult AUT cases.

Method: Participants were identified between 2010 and 2019 in emergency departments at single tertiary referral hospital. The data of patients who met the diagnostic criteria of anaphylaxis were collected. The data included clinical manifestations, laboratory findings, managements, and anaphylactic triggers. We analyzed patients who was an AUT for this study.

Results: A total of 22 AUT cases (6.4%) were recruited among 346 cases of anaphylaxis in adults. The mean patient age was 43.9 years and 72.7% were female. The most common symptom observed in AUT patients was skin involvement. Half of the AUT patients had a history of previous allergic diseases, the most of which were food allergies, observed in four. All patients received epinephrine promptly. 10 patients were considered severe anaphylaxis. Tryptase was not raised in 68.2% of cases; furthermore, in 53.3% of these patients, no changes were observed in tryptase levels comparing between anaphylaxis and basal condition. Only 10 patients were referred to an allergist, and only 5 of these visited an allergist to further evaluate an AUT.

Conclusion: In our center, AUT is not an uncommon condition of adult anaphylaxis. It is necessary to increase the number of cases referred to an allergist in the emergency department for proper management of patients with AUT.

966 | WDEIA manifestation only in combination with selected drugs

Kinaciyan T.; Gorris A.

Dept of Dermatology, Medical University of Vienna, Vienna, Austria

Background: A 66-year-lady presented to our Allergy Outpatient Clinic with a 10-year history of occasional generalized urticaria, itch, dyspnea and asthmatic symptoms. On 2 occasions she developed emesis and had lost her consciousness. In one case, she remembered to have taken a combination of Naproxen 500mg and Esomeprazole 20mg. She was commonly taking ASA since she often suffered from headache. She had been already seen by an allergist, who found a Tria19 sensitization and suspected a WDEIA. However, she could not comprehend this, since she ate bread every day.

Method: Drug provocation tests (DPT) were performed with Paracetamol, Diclofenac, Naproxen and ASA on the ward and Esomeprazole as well as provocation tests adjusted to real-life conditions with drugs and possible co-factor at different visits.

Results: DPT with all named drugs alone yielded negative results. We then tried a combination of bread feeding and taking ASA and Esomeprazole mono combined with exercise again without any reaction. Thereafter, we tried triple combination on different occasions Bread feeding Paracetamol/Diclofenac/Naproxen/esomeprazole intake and ergometry over 15 minutes. The patient reacted only with generalized urticaria only twice: (i) Bread feeding, ASA intake and ergometry, (ii) Bread feeding, Esomeprazole intake and ergometry.

Conclusion: In WDEIA, gluten-specific IgE-levels are often too low to cause allergic reactions per se. Therefore, exercise as a co-factor is required by definition of WDEIA which increases gliadin absorption leading to higher allergen levels due to increased blood circulation. In our case, even exercise as co-factor alone was not sufficient to elicit WDEIA, requiring more co-factors, such as additional intake of ASA or Esomeprazole. We recommended the avoidance of this two triple-combinations. If necessary, she was allowed to take Diclofenac or Naproxen with bread feeding and be physically active.

1002 | Severe anaphylaxis to laxative in a child

Siebert S.; Bogs T.; Yavuz S.T.

Department of Pediatric Allergy, Children's Hospital, University of Bonn, Bonn, Germany

Introduction: Laxative drugs are commonly used in pediatric patients with constipation. Serious allergic adverse drug reactions are rarely reported.

Case Report: A 4-year old boy with cerebral palsy was treated in hospital after a selective dorsal rhizotomy. Due to constipation a common laxative enema (containing sodium citrate, dodecylsulfoacetat, sodium salt and sorbitol dilution) was administered. After fifteen minutes the patient presented with paleness, hypotension, bradycardia and he was not responsive for a short time. Subsequent he showed an erythema of the skin and an urticarial rush. Symptoms resolved after intravenous administration of antihistamine and corticosteroids. The boy had no history of atopic disease, only rare episodes of urticarial lesions were reported. Fourteen months after the anaphylactic reaction the boy was presented to our pediatric allergy department. A skin prick test with the laxative showed a negative result. Subsequently, we performed a provocation test with rectal application of the enema. The patient showed no reaction after initial administration of one-third of a normal dose, however he suffered from paleness, fatigue, vomiting and decrease of blood pressure and oxygen saturation 20 minutes after the application of remaining two-third dose. Baseline tryptase level was 5,18 µg/l, whereas it increased to 10,5 µg/l during the anaphylactic reaction. Symptoms resolved after the administration of intramuscular adrenalin as well as intravenous antihistamine and corticosteroid. Within the following hours he presented with an erythema of the whole body, which resolved by administration of oral antihistamine and intravenous corticosteroids.

Conclusion: Only few published cases describe serious anaphylactic reactions to laxative drugs, especially concerning polyethylene glycol (PEG) containing preparations. The role of diagnostic procedures is also limited. A provocation test should be performed to confirm the diagnosis.

1240 | Takotsubo cardiomyopathy as complication of exceeded use of adrenalin in anaphylaxis treatment: A case report

Mijanovic R.[1,2]; Srdic Lehocki M.[3]; Plavsic A.[1,2]
[1]*Clinic of Allergy and Immunology, Clinical Center of Serbia, Belgrade, Serbia;* [2]*Faculty of Medicine, University of Belgrade, Belgrade, Serbia;* [3]*Clinic for Cardiology, Clinical Center of Serbia, Belgrade, Serbia*

Background: Massive release of catecholamines is the cause of Takotsubo cardiomyopathy (TC). Here we present a case of patient who received the large amounts of adrenalin i.v. during anaphylaxis treatment and developed TC.

Case report: Female patient 63 years old went on multislice computed tomography (MSCT) of thorax, abdomen and pelvis for regular control of breast cancer, which was diagnosed 9 years ago. Soon after finishing of the diagnostics she felt itch, redness and hives on the skin of the face, neck and thorax, malaise and heart pain. The radiologist examined the patient, and found no detectable arterials pulse, so he administered 2 ml of adrenalin iv, 120 mg methylprednisolone, 1 ampoule chloropyramine iv, and one saline solution. Patient was transferred to Emergency center. At the examination at the hospital patient had no skin marks, arterial tension was 150/90 mm Hg, normal findings on lungs and heart, so the doctor administered captopril 25 mg per os. When consultant allergist came to see the patient, she had chest pain and have no arterial pulse, so he administered adrenalin 0,3 mL i.m., infusions and patient was admitted to Intensive care unit. She had no changes in ST segment in EKG, but had increase in hs troponine T to 381, so she was treated as acute coronary syndrome. Echocardiography (EC) showed typical changes in the movement of the heart for TC (during systole the midsection and apex of the left ventricle balloon out, while the area above contracts normally). Those changes were not registered on control EC a week later and ejection fraction has risen from 31 to 49%. One month later she was examined in Allergy clinic, where she was skin tested negative with ioversol 350. Five months later she performed coronarography with normal finding, which confirmed the diagnose of TC.

Conclusion: In this case we cannot exclude that anaphylaxis per se as the cause of TC, but large amounts of adrenalin could also induce the same disease. It is advisable not to exceed amounts of adrenalin that are suggested in different anaphylaxis guidelines treatment.

1126 | Anaphylaxis to cat in a 7-year-old girl

Bogs T.[1]; Siebert S.[1]; Sabir H.[2]; Müller A.[2]; Yavuz S.T.[1]
[1]*Department of Pediatric Allergy, Children's Hospital, University of Bonn, Bonn, Germany;* [2]*Department of Neonatology and Pediatric Intensive Care, Children's Hospital, University of Bonn, Bonn, Germany*

Introduction: Cat allergy is a common clinical problem, whereas anaphylaxis after cat contact seems to be extremely rare. Herein, we report a patient who had an anaphylaxis after exposure to cat.

Case Report: A 7-year-old girl was admitted to our emergency department suffering from a systemic allergic reaction 2 hours after playing with a cat at a friend's house. She was totally healthy before the contact with the cat. She presented with generalized itching, paleness and dyspnea with wheezing. Blood pressure was stable, heart frequency at 130/min, oxygen level at 91%. Physical examination revealed a bronchial obstruction. Laboratory investigation including inflammation markers, liver and kidney test, serum electrolytes, complete blood count and a blood gas analysis were performed. Complete blood count showed a mild leucocytosis with eosinophilia. Serum IgE levels were also elevated whereas serum tryptase level was normal (Serum tryptase measurement was performed five hours after first symptoms).

In the emergency department, she received intramuscular epinephrine, intravenous clestamine and prednisone, salbutamol inhalation and oxygen. Since symptoms persisted, the patient was transferred to our intensive care unit, where the initiated therapy was continued. Itching of the skin resolved within a few hours. Increased oxygen demand persisted over two days, respiratory symptoms resolved within two days. There were two contacts to a cat reported by the mother before this episode. Symptoms after the first contact were conjunctival redness and itching and dyspnea after the second contact. Allergen-specific IgE antibodies to common inhalant allergens, including cat, were performed and showed a high elevation for cat (class 6) and a mild elevation for dog (class 2) and house dust mite (class 1).

Conclusion: Anaphylaxis to cat is extremely rare and so far only one case after exposure to a cat is reported in the literature. Along with the leading symptoms of cat allergy in childhood, such as rhinoconjunctivitis and coughing, anaphylaxis may be seen after contact with cats especially in highly sensitized children.

1268 | Anaphylaxis during skin prick test with aeroallergen extract: Case report

Oliveira I. A.; Prado A. I. F.; Alberto N. E. S.; Menechino N. T. C.; Kalil J.; Giavina-Bianchi P.; Agondi R. C.
University of São Paulo, São Paulo, Brazil

The objective was to describe a clinical case of anaphylaxis triggered after performing a skin prick test (SPT) with aeroallergen extract in an adult patient with a hypothesis of respiratory allergy.

A 55-year-old man referred to the Clinical Immunology and Allergy service for investigation of atopy due to respiratory symptoms suggestive of allergic rhinitis and asthma. The patient also had a history of anaphylaxis after eating shrimp and other crustaceans, as well as wheals after being stung by bees. He had never done a clinical research. Laboratory tests were requested, including a SPT for aeroallergens and serum specific IgE for shrimp. Attended to be doing the SPT for aeroallergens after 2 weeks, without acute respiratory symptoms at the time of the test. After the application of standardized

extracts of aeroallergens (*Blomia tropicalis*, *Dermatofagoides pteronyssinus*, epithelium of cat and dog, *Penicillium notatum*, *Aspergillus fumigatus*) in the volar region of the right arm, as soon as the puncture started, the patient reported a sensation of itching throughout the body. Immediately after the end of the test, the patient developed generalized itching, skin rash, conjunctival hyperemia, coughing and vomiting. He remained normotensive, but showed a slight drop in peripheral oxygen saturation (94%). The patient received intramuscular adrenaline, hydrocortisone and diphenhydramine, with complete resolution of symptoms approximately 2 h later. The serum value of tryptase collected immediately after the start of the reaction was 11.2 ng/ml, which does not rule out the possibility of mastocytosis, but makes it less likely, since most patients with mastocytosis have serum levels greater than 20 ng/ml. The main hypothesis was cross-reactivity between tropomyosin presente in crustaceans and also house dust mites, causing anaphylaxis triggered by SPT with aeroallergens. This hypothesis is reinforced by the fact that tropomyosin is considered a panalergen, and that it could be involved in cross-reactivity between tropomyosins in invertebrates.

Although the SPT is considered to be effective and safe, it should be performed under medical supervision in a specialized environment to treat any serious reactions such as anaphylaxis.

1288 | Anaphylaxis to beluga caviar: A case report and brief review of the literature

Gabrielli G.[1]; Boni E.[2]; Deleonardi G.[2]; Mancini R.[2]

[1]*University of Bologna - Resident in Allergology and Clinical Immunology, Bologna, Italy;* [2]*LUM, Maggiore Hospital - AUSL Bologna, Bologna, Italy*

Introduction: Fish roe is a rare cause of food allergic reactions in Western world where just a few cases are described. According to literature, the culprit molecule of fish roe allergy is vitellogenin. This is a protein produced by the liver of oviparous and ovoviviparous female animals and carried through bloodstream to the oocytes where it's degraded to the three major yolk proteins: lipovitellin, beta-component and phosvitin. Lipovitellin and beta-component have high IgE-binding ability; the latter is the major allergen and has been isolated in salmon roe (Onc k5).

Patients with fish roe allergy tend to cross-react to other fish roes, but fish roe sensitization is not concomitant to fish allergy.

Methods: We report the case of a 65 y.o. woman who experienced an anaphylactic shock after eating salmon and Beluga caviar.

The allergological work up included skin prick test with commercial extracts of fishes, shellfishes, mussel, octopus, hen's egg and dust mites, as well as prick by prick test with culprit food and other fish roes; detection of specific IgEs to food allergens and basal serum tryptase were performed.

Results: The patient showed positivity below 0.35 kUA/l for shrimp, *Blattella germanica*, egg white. In vivo and in vitro tests were positive for Dermatophagoides farinae without clinical correlation. All remaining tests were negative for fishes, sea fruits, anisakis, egg, CCD, fish parvalbumins and tropomyosin. Basal tryptase level was in normal range. Total IgE level was 205 kU/l. Prick by prick test with salmon, Beluga caviar, Lumpfish roe and Mugil roe (*bottarga*) showed a strong positivity just for Beluga caviar.

Afterwards, the patient tolerated Salmon, Salmon roe and Mugil roe.

Conclusion: We present a rare case of a severe allergic reaction after ingestion of Beluga caviar. Even though in some Countries like Japan salmon roe is listed as a common food allergen due to its major consumption, in Western Countries it's a rare cause of allergy. Selective sensibility for Beluga caviar represents a rarest of a rare case. We speculate that this patient may be sensitized to a protein different from vitellogenin or to a specifin vitellogenin epitope in sturgeon egg. In vitro diagnosis of allergy to fish roe is not currently feasible because, though the major allergen has been isolated, allergen extracts are not commercially available. Therefore, the diagnosis of allergy from fish roe must rely on prick by prick test.

1169 | Asthma and circulating mononuclear cells: an overall increase in mitochondrial metabolism?

Marcozzi N.[1,2]; Ederlé C.[3,1]; Charles A.[1]; Poirot A.[3]; De Blay F.[3]; Geny B.[1,4]

[1]*UR3072 "Mitochondria, Oxidative Stress and Muscle Protection", Unistra, Faculty of Medicine, Translational Medicine Federation of Strasbourg (FMTS), University of Strasbourg, Strasbourg, France;* [2]*Department of Chest Diseases, University Hospital of Nancy, Nancy, France;* [3]*Division of Asthma and Allergy, Department of Chest Diseases, University Hospital of Strasbourg, Translational Medicine Federation of Strasbourg (FMTS), University of Strasbourg, Strasbourg, France;* [4]*Department of Physiology and Functional Explorations, University Hospital of Strasbourg, Strasbourg, France*

Background: Mitochondria (Mt) plays a well-known pro-inflammatory role in asthma. Increased ROS production induced by Mt dysfunction and increased basal Mt metabolism have been described in lung parenchyma of asthmatic patients. High tissular ROS concentration, favored by environmental ROS exposures like ozone, likely induce Mt damages, maintaining Mt dysfunction and local inflammation. Nevertheless, few studies investigated at Mt roles in peripheral immune cells. Peripherical blood mononuclear cells (PBMC) is an easy extractible cellular layer containing amongst 70-90% lymphocytes. Here we show intermediate results from an ongoing study taking place in our University Hospital.

Method: To assess the impact of controlled asthma (CA) on the Mt metabolism of isolated PBMC, we recruited patients with CA, non-smokers, and aged 18 to 75 years. Mt metabolism study was performed using High Resolution Oximetry (Oxygraph-2k; Oroboros Instruments, Innsbruck, Austria), in a buffer containing substrates, after PBMC's extraction and cell count normalization. Substrates were successively added in oximeter closed chambers in the following order: ADP (activate ATP synthase, and so oxidative

phosphorylation, allowing to assess activity of all respiratory complexes, except complex II), Succinate (activate complex II, allowing reach Maximal ADP-stimulated Respiration), Rotenone (inhibits complex I) and TMPD + Ascorbate (maximal activation of complex IV).

Results: 24 patients and 13 controls were recruited. According to GINA 2016, there was 6 patients with GINA 1-3, 6 with GINA 4, and 12 with GINA 5 asthma. Asthmatics and controls were comparable considering age and sex. There was a significant increase of maximal ADP-stimulated respiration of PBMC of CA patients, compared to healthy subjects (+26%, p = 0,02). A significant increase was also found in patients compared with controls after adding ADP (+45%, p = 0,0003).

Conclusion: Our preliminary results show an impact of CA on peripheral immune cells. Indeed, our results show an increase of overall Mt metabolism of PBMC that seems to be mainly mediated by increased activity of respiratory complex I. This increased Mt metabolism might reflect a basal activation of immune cells in CA patients.

1267 | Type 2 inflammation biomarkers in adult asthmatic patients from a tropical environment and IgE sensitized to the helminth ascaris

De Vivero M. M.[1]; Escamilla Gil J. M.[1]; Espinoza H.[2,3]; Regino R.[1]; Florez De Arco L.[4]; Caraballo L.[1]; Acevedo N.[1]

[1]*Institute for Immunological Research, University of Cartagena, Cartagena, Colombia;* [2]*Faculty of Engineering, University of Cartagena, Cartagena, Colombia;* [3]*Division de Informática, CIDIT, Grupo INMEDIT S.A.S, Cartagena, Colombia;* [4]*Clinica Respiratoria y de Alergias, Cartagena, Colombia*

Background: Helminth infections are endemic in tropical developing countries and induce a type 2 immune response that resembles in several aspects that occurring in type 2 asthma. It is possible that these infections affect the measurements of type 2 biomarkers such as Fractional Exhaled Nitric Oxide (FeNO) and periostin. We here compared the differences in type 2 inflammation biomarkers between adult asthmatic patients naturally exposed to *Ascaris*.

Method: We analyzed biomarker data from 57 adult asthmatic patients from Cartagena, Colombia (Mean age 56.8 ± 10 years). Total and specific IgE levels (d1, d201 and p1) were measured by ImmunoCAP. Positive exposure to Ascaris was determined by IgE levels ≥0.35 kU/l. FeNO was measured by the NOBreath (Bedfont Scientific). Eosinophils were quantified by hemocytometry. Periostin was measured by quantitative ELISA (R&D Systems). Protein plasma levels were measured by Proximity Extension Assay using the Olink Inflammation Panel. Biomarker levels were compared between Ascaris-positive (n = 22) and Ascaris-negative (n = 35) patients using non-parametric methods. A p value < 0.05 was considered significant.

Results: There were no differences in FeNO and periostin levels between Ascaris-positive and Ascaris-negative patients. As expected, levels of total IgE and specific IgE to Ascaris, *Blomia tropicalis* and *Dermatophagoides pteronyssinus* were significantly higher in Ascaris-positive vs. Ascaris-negative patients (p < 0.001). Eosinophil counts (cells/μl) were slightly higher in Ascaris-positive compared to Ascaris-negative patients (p = 0.03). In addition, we detected reduced levels of stem cell factor (SCF), matrix metalloproteinase 1 (MMP-1), CXCL1 and CD244 in Ascaris-positive patients. When analyzed as a continuous variable, IgE levels to Ascaris showed a significant inverse correlation with SCF and CD244.

Conclusion: FeNO and periostin levels did not differ between Ascaris-positive and Ascaris-negative asthmatics in a tropical environment, suggesting that these type 2 biomarkers are not influenced by Ascaris sensitization in adult patients. However, Ascaris sensitization was associated with increased eosinophil counts and reduced plasma levels of SCF and CD244, suggesting that exposure to this nematode may affect some biomarkers in asthmatic patients. Since positive IgE reflects parasite exposure but not necessarily active infection, further studies are needed to determine if active infection modifies FeNO levels, in both paediatric and adult populations.

1104 | Characteristics of patients with severe allergic asthma according to atopic multimorbidity

Oliveira I. F.A.; Fonseca L. G.; Franco G. R.; Kalil J.; Giavina-Bianchi P.; Agondi R. C.

University of São Paulo, São Paulo, Brazil

Background: More than 50% of asthmatic patients had atopic disease. It involves a mediated IgE mechanism, resulting in an eosinophilic inflammation of the airways. Some patients have allergic multimorbidity, with the coexistence of asthma, rhinoconjuntivitis and atopic dermatitis (AD), whose mechanisms involved are still a matter of debate. Patients with this phenotype tend to evolve with a more severe and persistent condition, and should receive suitable management in order to prevent exacerbations and morbimortality. The objective of this study was to describe the characteristics of patients with severe allergic asthma according to associated comorbidity (rhinitis, conjunctivitis and or AD), followed up at the asthma outpatient clinic of a tertiary service.

Method: This was a retrospective observational study with data collected from the electronic medical records of patients with severe (step 4 and 5) allergic asthma. Patients were classified according to the presence of other comorbidities: A1Asthma + rhinitis; A2 = asthma + rhinitis + conjunctivitis or AD; and A3 = asthma + rhinitis + conjunctivitis + AD. In addition, demographic characteristics, total serum IgE, peripheral eosinophils (Eo) and specific IgE were assessed in all groups.

Results: One hundred and sixty-six patients were included, of these, 128 (77.1%) were female, with a mean age of 49.8 years, with allergic asthma steps 4 (52.4%) and 5 (47.6%). The mean inhaled corticosteroids (budesonide) was dose 1102.4 mcg/day). The prevalence of rhinitis, conjunctivitis and AD was estimated at 99.4%, 61.4% and

13.3%, respectively. A3 group (asthma, rhinitis, conjuctivitis and AD) were younger compared to other groups (A1 and A2), 3.3 *vs* 14.7 *vs* 13.9 years respectively, $p < 0.01$. Regarding sensitization to aeroallergens, 49.4% are polysensitized, although, there were no statistical differences between groups. Total serum IgE was higher for patients group A3 (A3>A2>A1), 2770.6, 873.4 and 500.6 IU/ml, respectively, $p < 0.01$. Peripheral Eo were also higher for A3 (A3>A2>A1), 430, 282.5 and 196.8 cells/µl, respectively, $p < 0.01$.

Conclusion: The presence of allergic multimorbidities in patients with severe asthma is prevalent, and those with more associated multimorbidities reported earlier age of onset, as well as more expressive values of both serum IgE and peripheral eosinophilia.

1276 | Serum zonulin may be a biomarker of severe asthma

Choi J.[1,2]; Shin E.[3]; Hong S.[2,4]; Kang S.H.[5]; Lee T.[6]; Kim T.[7]

[1]Department of Pulmonology and Allergy, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, South Korea; [2]Allergy and Clinical Immunology Research Center, Hallym University College of Medicine, Chuncheon, South Korea; [3]Department of Pathology, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, South Korea; [4]Department of Otorhinolaryngology, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, South Korea; [5]Hallym University College of Medicine, Graduate School, Chuncheon, South Korea; [6]Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea; [7]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Zonulin is a regulator of epithelial and endothelial barrier function, which was first reported as a key regulator of intestinal permeability by way of tight junction disassembly. Zonulin has been reported to play a role in various chronic inflammatory diseases such as celiac disease, inflammatory bowel disease, type-1-diabetes, and atopic dermatitis. Defective epithelial barrier function is a feature of airway inflammation in asthmatic patients. The aim of this study is to investigate the role of zonulin in severe asthma.

Method: We enrolled 60 adult asthmatics and 33 normal controls. The clinical data, sera, and lung tissues were provided by COhort for Reality and Evolution of adult Asthma in Korea (COREA) and the Biobank of Soonchunhyang University Bucheon Hospital, a member of the Korea Biobank Network. Asthma was diagnosed by a positive bronchodilator response or a positive result of methacholine bronchoprovocation test. Severe asthma were defined as asthma that requires treatment with high-dose inhaled corticosteroids plus additional controllers (long-acting inhaled beta 2 agonists, montelukast, and/or theophylline) for the previous year to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy. Serum zonulin and zonulin expression at lung tissues was measured using ELISA kit and immunohistochemical staining. Statistical analyses were done using R program.

Results: Serum zonulin levels were significantly increased in severe asthma (51.98 ± 19.66 ng/ml) than those in other asthma (26.35 ± 13.70 ng/ml, $p < 0.001$) and normal controls (17.26 ± 10.29 ng/ml, $p < 0.001$), respectively. Zonulin expression in bronchial epithelium was greater in severe asthma than those in other asthma and normal controls.

Conclusion: Zonulin may play a role in the pathogenesis of severe asthma, and serum zonulin may be a biomarker of severe asthma. Further study will be needed.

1054 | Effect of body mass index on pulmonary function in asthmatic children

Lamberti R.[1]; Gasparini C.[2]; Sartorio M.U.A.[1]; D'Auria E.[2]; Zuccotti G.[1]

[1]Department of Pediatrics, Vittore Buzzi Children's Hospital, University of Milan, Milan, Italy; [2]Allergy Unit - Department of Pediatrics, Vittore Buzzi Children's Hospital, University of Milan, Milan, Italy

Background: Paediatric obesity prevalence is increasing and it represents an emerging health problem. Obesity is a risk factor for many conditions including asthma and increased airway resistance. The effects of obesity and overweight on lung functions are not well defined in children.

Method: Fifty-five asthmatic children, twenty-one overweight (mean age 9.83 ± 2.28 years) and thirty-four obese (mean age 10.92 ± 2.79 years) underwent spirometry. Forced vital capacity (FVC), forced expiratory flow (FEF) at 25-75% (FEF 25–75%) and forced expiratory volume in one second (FEV1) were used as measures of ventilatory function. Collected data were analyzed by Pearson correlation.

Results: In our sample, an inverse relationship between BMI z-score and lung volumes was observed. In particular, the correlation coefficient between BMI z-score and FVC/FEF/FEV1 were $r = -0.1232$, $r = -0.0921$, $r = -0.1129$ respectively, showing an inverse relation between these parameters.

Conclusion: Our data suggest that overweight/obesity in asthmatic children lead to an airflow limitation due to obstruction. Further studies should be performed to deeply address this issue and to evaluate the correlation between body composition and lung function.

972 | Comparison of vitamin D receptor gene polymorphisms is patients with asthma and healthy subjects

Tamasauskiene L.; Golubickaite I.; Bastyte D.; Ugenskiene R.; Sitkauskiene B.

Lithuanian University of Health Sciences, Kaunas, Lithuania

Background: There is evidence that adequate vitamin D level is associated with decreased risk and better outcomes of asthma. The biological activities of vitamin D are mediated by vitamin D receptor (VDR). *VDR* genetic variants have been studied as a potential factor

for autoimmune disease and/or allergic disease since they may influence VDR activity.

The aim of this study was to investigate and compare single nucleotide polymorphisms (SNPs) of the *VDR* gene (rs7975232, rs1544410, rs731236, rs3847987, rs2228570, rs4588, rs7041, rs4725, rs11168293, rs3733359) in patients with asthma and healthy individuals, and to evaluate differences in asthma phenotypes.

Method: Individuals with asthma (diagnosed according to GINA) and healthy subjects were involved in the study. DNA from peripheral blood samples was extracted using QIAamp DNA blood mini kit (Qiagen, Hilden, Germany) following the manufacturer's protocol. Ten SNPs on the 12q13.11 chromosomal region were analyzed in this study using TaqMan SNP Genotyping Assay probes.

Results: Sixty-three patients with asthma (45 allergic and 18 non-allergic) and 32 healthy individuals were involved into the study. rs731236 A allele was found more frequently in patients with asthma than in healthy individuals (94.9% vs. 77.4%, p = 0.01). We noticed a tendency, that rs4588 GG and TT genotypes were more common in patients with asthma than in control group (52.5% vs. 43.3% and 15.3% vs. 3.3%; respectively, p = 0.08), whereas rs4588 GT genotype was more common in healthy individuals (53.3% vs. 32.2%, p = 0.08). Moreover, rs4588 G allele tended to be more often found in healthy individuals than in asthmatics (96.7% vs. 84.7%, p = 0.09). Rs7975232 AA genotype showed a tendency to be found more frequently in allergic asthmatics than in non-allergic (31.1% vs. 5.6%, p = 0.08) whereas rs7975232 AC and CC genotypes were more common in non-allergic asthmatics than in allergic (50.0% vs. 42.2% and 44.4% vs. 26.7%, respectively, p = 0.08). Rs7975232 C allele was significantly more prevalent in non-allergic asthmatics than in allergic asthmatics (94.4% vs. 68.9%, p = 0.03). Rs11168293 T allele also tended to be more frequent in non-allergic asthmatics than in allergic (77.8 vs. 51.1%, p = 0.05).

Conclusion: Some of VDR polymorphisms may play a role in asthma, because Rs731236 A allele was found more frequently in patients with asthma than in healthy subjects whereas rs7975232 C allele was more prevalent in non-allergic asthmatics than in allergic.

1220 | Impact of the junction adhesion molecule-A on asthma

Jang A.[1]; Ahn M.[1]; Choi S.[2]; Lee Y.[3]; Lee P.[4]

[1]*Soonchunhyang University Bucheon Hospital, Bucheon, South Korea;* [2]*Soonchunhyang University, Bucheon, Korea, Bucheon, South Korea;* [3]*Soonchunhayng University Bucheon Hospital, Bucheon, South Korea;* [4]*Soonchunhyang University Bucheon Hosppital, Bucheon, South Korea*

Background: Junctional adhesion molecule (JAM)-A is an immunoglobulin-like molecule that colocalizes with tight junctions (TJs) in endothelium and epithelium and is also found on blood leukocytes and platelets. The biological significance of JAM-A in asthma and its clinical potential as a therapeutic target were not fully described. We aimed to elucidate the role of JAM-A on airway hyperresponsiveness and inflammation in asthma using a murine asthma model, and to check blood level of asthmatic patients.

Method: Using mice sensitized and challenged with OVA, as well as mice sensitized and challenged with saline, we investigated whether Jam-a be involved in the pathogenesis of bronchial asthma. The level of JAM-A was checked in the plasma of asthmatic patients and control subjects. The relation of JAM-A with clinical variables in patients with asthma was checked.

Results: JAM-A level had higher concentrations in plasma from patients with asthma (n = 19) than that of healthy controls (n = 12). JAM-A level was correlated with FVC% (r = −0.403, p = 0.006), FEV_1% (r = −0.622, p = 0.001), FEV_1/FVC (r = -0.698, p = 0.000), smoke amount (r = 0.621, p = 0.002), total IgE (r = 0.431, p = 0.014), and blood lymphocyte proportion (r = −0.424, p = 0.002) in patients with asthma. Jam-a protein expression in lung tissue was significantly increased in OVA/OVA mice compared with control mice.

Conclusion: These data suggest that JAM-A be elevated in plasma of patients with asthma, which raise the possibility that JAM-A be involved in asthma.

976 | Development of a tool to measure the clinical response to biologic therapy in uncontrolled severe asthma: The FEOS score

González-Bravo L.[1]; Colás C.[2]; Dávila I.[3]; Domínguez Ortega J.[4]; Laiseca García J.[1]; Pérez De Llano L.[5]

[1]*Department of allergy. Hospital Universitario Fundación Alcorcón, Madrid, Spain;* [2]*Department of allergy. Hospital Clínico-Instituto de Investigación Sanitaria de Aragón, Zaragoza, Spain;* [3]*Department of Allergy. University Hospital of Salamanca, Salamanca, Spain;* [4]*Department of Allergy. La Paz Hospital Institute for Health Research (IdiPAZ), Department of Allergy, Madrid, Spain;* [5]*Pneumology Service. Hospital Universitario Lucus Augusti., Lugo, Spain*

Background: The aim of this study is to develop a valid score to assist clinicians who care for severe uncontrolled asthma (SUA) patients to better assess or quantify the response to monoclonal antibodies (mAbs).

Method: The proposed score was developed in 4 phases:

1. Elaboration of the predicted model of the construct intended to be measured (response to mAbs): a methodologist did a systematic literature review to identify potential domains to be included in the under-development tool.
2. Definition and selection of domains and measurement instruments by Delphi survey: the review results were presented to specialists with proven expertise in SA management (5 pneumologists and 3 allergists). Once the list of domains and items was generated, an online Delphi survey gathered the opinion of 58 pneumologists and 30 allergists.
3. Weight assignment of the selected items by multicriteria decision analysis (MCDA) via the 1000Minds software (a decision-making software based on the presentation of multiple changing

scenarios was presented to a panel of 41 professionals from accredited asthma units).

4. Face validity assessment: this score was verified in a pilot study that compared how 1000Minds software and an investigator ranked 14 real patients in terms of response. The agreement between the two raters was calculated using intraclass correlation coefficient (ICC).

Results: Four core items were finally chosen, with different levels of response for each of them: "severe exacerbations", "oral corticosteroid use", "symptoms" (evaluated by Asthma Control Test: ACT) and "bronchial obstruction" (assessed by FEV1 % predicted value). "Severe exacerbations" and "oral corticosteroid maintenance dose" were weighted most heavily (38% each), followed by "symptoms" (13%) and "FEV1" (11%). Higher scores in the weighted system indicate better response and the range of responses runs from 0 (worsening) to 100 (best possible response). Face validity was high (intraclass correlation coefficient: 0.86).

Conclusion: The FEOS score (FEV1, Exacerbations, Oral corticosteroids, Symptoms) allows clinicians to quantify response in SUA patients who are being treated with mAbs.

Criteria	Points
Maintenance systemic corticosteroid dose	
Increase	0
No change	14
Reduction < 50%	24
Reduction between 50% and 100%	29
Complete withdrawal	38
Severe exacerbations	
Increase	0
No change	11
Reducion <50%	22
Reduction between 50% and 100%	27
100% reduction	38
Symptoms (evaluated by asthma control test: ACT)	
ACT total score decrease	0
<3 points increase	5
≥3 points increase, but total <20	9
ACT ≥20	13
Bronchial obstruction (assessed by fev1 % predicted value)	
>100ml decrease	0
No change or <100ml and < 10% increase	5
≥100ml increase and 10% but <80%	9
FEV1 ≥80%	11
Total score	

1011 | Effectiveness and safety of a microcrystalline tyrosine-adsorbed cupressus arizonica allergoid in patients with allergic rhinitis with and without asthma: Results from a restrospective study

Carretero P.[1]; Mayorgas R.[2]; Blanco R. M.[3]; Pineda R.[4]; Gandolfo M. M.[5]; Mohedano E.[5]; Trujillo M. J.[5]; González E.[5]

[1]*Hospital Universitario de Burgos, Burgos, Spain;* [2]*Alergogranada, Granada, Spain;* [3]*Hospital Nuestra Señora de Sonsoles de Ávila, Ávila, Spain;* [4]*Hospital Universitario del Sureste, Madrid, Spain;* [5]*Hospital Universitario de Fuenlabrada, Madrid, Spain*

Background: Sensitization to *Cupressus* species is the third most frequent one among patients with allergic rhinitis caused by pollens in Spain. To date, there are no efficacy or safety data of a MicroCrystalline Tyrosine (MCT)-adsorbed *Cupressus* specific immunotherapy (AIT). The aim of this study was to acquire knowledge of a *Cupressus* allergoid adsorbed to MCT regarding effectiveness and safety in patients with allergic rhinitis in the real-world setting.

Method: A post-authorization, observational and retrospective study was conducted in children and adults with allergic rhinitis with/without asthma sensitized to *Cupressus arizonica* (monosensitized or sensitized to other pollens) who were treated with an MCT-adsorbed *Cupressus arizonica* allergoid (or a mixture of *Cupressus* with other pollens). Primary objective was effectiveness, assessed comparing data obtained from the first pollen season after starting the AIT (year 2020) versus data obtained from the pollen season previous to starting the AIT (year 2019). It was measured by number of unscheduled medical visits (UMV) and emergency room visits (ERV), ARIA and GEMA classifications of rhinitis and asthma, respectively, use of rhinitis and asthma medication and patient's and physician's perception of the disease according to a visual analogue scale (VAS). Secondary objective was safety, measured by number and severity of adverse reactions.

Results: Out of 52 patients recruited, 34 were evaluated. 55.9% were female, 85.3% were adults and only two (5.8%) were monosensitized to *Cupressus arizonica*. 11.8% were treated with a *Cupressus arizonica* 100% extract. Statistically significant results were detected: UMV (1.47 vs 0.26), ERV (0.26 vs 0), use of nasal corticosteroids (88.2% vs 52.9%), use of inhaled corticosteroids (73.3% vs 33.3%), patient's VAS (7.5 vs 4.6) and physician's VAS (7.2 vs 4). 100% of the patients had persistent rhinitis before AIT and in 67.6% it was moderate, and, after AIT, 23.5% had intermittent rhinitis and in 61.8% it was mild. Regarding asthma, before AIT, 66.7% of the patients had mild persistent symptoms and, after AIT, 73.3% had intermittent symptoms. No adverse reactions were reported.

Conclusion: An MCT-adsorbed *Cupressus arizonica* allergoid was effective and safe in children and adults with allergic rhinitis with and without asthma sensitized to cypress in the real-world setting.

1024 | Fatigue: A forgotten symptom of asthma

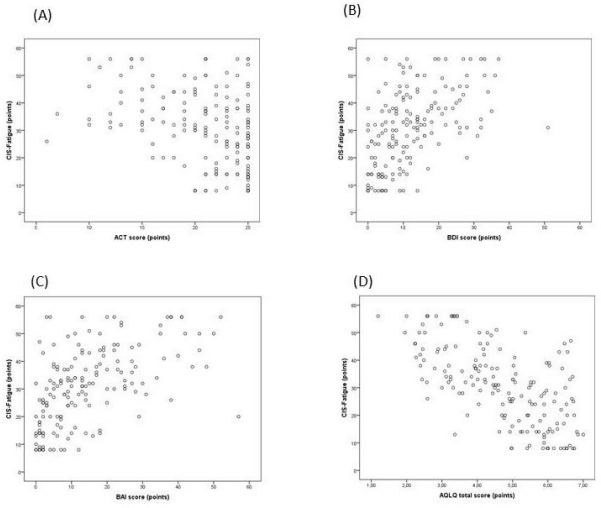
Gunaydin F. E.; Ediger D.; Erbay M.
Uludag University Medical Faculty, Section of Immunology and Allergy Diseases, Department of Chest Diseases, Medical Faculty, Bursa, Turkey

Background: Fatigue is a common symptom frequently reported in many disorders but little is known about the prevalence of fatigue in asthma. The objective of this study was to determine the prevalence of fatigue in asthmatic patients, the effect of fatigue on asthma quality of life and the relationship between fatigue and anxiety/depression

Method: This prospective cross-sectional study was conducted in Uludağ University Faculty of Medicine, Department of Immunology and Allergic Diseases outpatient clinic from June 2019 to December 2019. Fatigue was assessed using the Checklist Individual Strength-Fatigue (CIS-Fatigue), psychological distress was assessed using the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) and quality of life was assessed using the Asthma Quality of Life Questionnaire (AQLQ).

Results: In the present study, A total of 168 patients are included with an average age of 43.8 ± 4.3 years. Nearly sixty four (64.8%) patients had controlled asthma and (35.2%) patients had uncontrolled asthma. Fatigue (CIS-Fatigue ≥27 points) was detected in 62.6% of patients and associated with asthma-related quality of life, asthma control, dyspnea, depression and anxiety ($p < 0.05$). However, the degree of lung function impairment and asthma severity were not associated with fatigue.

Conclusion: Fatigue as a symptom is common in asthmatic patients and correlates with asthma-related quality of life, asthma control, dyspnea, depression and anxiety. Future studies are needed to better understand the physical, psychological, behavioural and systemic factors that precipitate or perpetuate fatigue in asthma.



1072 | Short-acting β_2-agonist prescription patterns in patients with asthma in Turkey: Results from SABINA III

Yorgancioglu A.[1]; Aksu K.[2]; Atis Nayci S.[3]; Ediger D.[4]; Mungan D.[5]; Gül U.[6]; Beekman M.[7]
[1]*Manisa Celal Bayar University, Faculty of Medicine, Department of Pulmonology, Manisa, Turkey*; [2]*University of Health Sciences Atatürk Chest Diseases and Chest Surgery Education and Research Hospital, Division of Immunology and Allergy, Department of Chest Diseases, Ankara, Turkey*; [3]*Mersin University Faculty of Medicine, Department of Pulmonology, Mersin, Turkey*; [4]*Bursa Uludag University Faculty of Medicine, Department of Pulmonology, Division of Allergy and Immunology, Bursa, Turkey*; [5]*Ankara University Faculty of Medicine, Department of Pulmonology, Division of Allergy and Immunology Ankara, Ankara, Turkey*; [6]*AstraZeneca, Istanbul, Turkey*; [7]*AstraZeneca, The Hague, The Netherlands*

Background: Overreliance on short-acting β_2-agonists (SABA) is associated with poor asthma outcomes. The extent of SABA use in Turkey is unclear due to a lack of comprehensive healthcare databases. The SABA use IN Asthma (SABINA) studies assess the current global burden of SABA use. Here, we describe demographics, disease characteristics, and treatment patterns of the Turkish cohort from the SABINA III study.

Method: Patients (aged ≥12 years) with asthma were included in this cross-sectional study and classified by investigator-defined asthma severity (guided by the 2017 Global Initiative for Asthma [GINA] recommendations). Data on asthma symptom control (2017 GINA), severe exacerbation history, and prescribed treatments in the year before the study visit were collected using real-time electronic case report forms. The primary objective was to describe SABA prescription patterns in the past 12 months. ≥3 SABA canisters in the past 12 months was considered over-prescription.

Results: Overall, 579 patients were analyzed (mean age [standard deviation]: 47.4 [16.1] years; 74.3% female), all of whom were treated by respiratory specialists. Most patients had moderate-to-severe asthma (82.7%; GINA steps 3–5), were overweight or obese (70.5%), had never smoked (68.6%), had high school or university/post-university education (51.8%), had fully reimbursed healthcare (97.1%) and ≥1 comorbidity (67%). Overall, 43.7% of patients had well-controlled asthma and 56.3% had partly controlled or uncontrolled asthma, with 46.5% experiencing ≥1 severe exacerbation in the past 12 months. A total of 23.9% of patients were prescribed ≥3 SABA canisters in the past 12 months. As few patients had mild asthma, only 5.7% were prescribed SABA monotherapy. Most patients (61.5%) were prescribed SABA as add-on to maintenance therapy, of whom 42.8% receiving ≥3 SABA canister prescriptions in the past year. Inhaled corticosteroids (ICS), ICS + a long-acting β-agonist fixed-dose combination, and bursts of oral corticosteroids were prescribed to 14.5%, 88.3%, and 28.5% of patients, respectively. SABA canisters were purchased over-the-counter by 10.2% of patients; of these, 27.1% purchased ≥3 canisters in the past 12 months.

Conclusion: Although this Turkish cohort likely represents a "better case scenario," with all patients treated by specialists and most receiving fully reimbursed healthcare, nearly a quarter of all patients received prescriptions for ≥3 SABA canisters in the past 12 months, highlighting a public health concern.

1074 | Omalizumab and mepolizumab in atopic and eosinophilic overlap patients with severe persistent asthma; which biological agent should we choose?

Akyildiz A. B.; Tepetam F. M.

University of Health Sciences, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

Background: Severe asthma is a heterogeneous disease characterized by attacks and hospitalizations, in which asthma control cannot be achieved despite GINA (The Global Initiative for Asthma) step 4 and 5 treatment. Since the need for personalized treatment for each patient has established, anti-IgE mAb, Omalizumab has taken its place in severe allergic persistent asthma, and anti IL-5 mAb, Mepolizumab has taken its place in the treatment of severe eosinophilic persistent asthma. However, it has been shown that approximately 30% of patients may be suitable candidates for both biological agents. We aimed to retrospectively compare the clinical and laboratory effects of biological agents applied in this overlap group of patients with severe allergic and eosinophilic asthma.

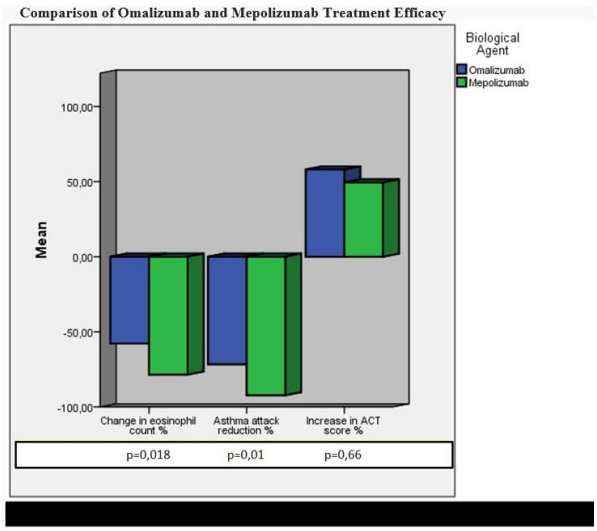
Method: In our Immunology and Allergy clinic, patients who continued Omalizumab or Mepolizumab treatment for at least 16 weeks due to severe asthma were retrospectively evaluated; durations of asthma, smoking habit, body mass index (BMI), allergen sensitivity, comorbidities, and total IgE levels were recorded. Patients with both perennial allergen sensitivity and absolute eosinophil count ≥300/μl when treatment was initiated were included in the study. COPD, bronchiectasis and eosinophilic lung diseases such as EGPA (Eosinophilic Granulomatosis and Polyangitis) were excluded from the study. Asthma control test (ACT), eosinophil count and number of attacks were compared, before and after treatment.

Results: A total of 43 patients, 38 (88.4%) women, with a mean age of 51.2 ± 13.9 were evaluated retrospectively. A total of 28 patients, eosinophilic and atopic, 14 in the Omalizumab arm and 14 in the Mepolizumab arm, were included in the study. There was no significant difference between the groups in terms of gender, disease duration, total IgE, baseline FEV1, number of attacks before treatment and BMI. However, while the mean age of the patients was higher in the Omalizumab arm, the eosinophil level was higher in the Mepolizumab arm (Table 1). When compared in terms of treatment efficacy, Mepolizumab treatment was statistically more successful in reducing eosinophil level and asthma attacks, while in regard of increasing ACT score Omalizumab was found to be more effective, although it was not statistically significant (Figure 1).

Conclusion: Since Mepolizumab treatment targets eosinophils, it is more successful in reducing eosinophil levels and asthma attacks. However, more studies and head-to-head comparisons are needed.

TABLE 1 Baseline characteristics of omalizumab and mepolizumab treatment arms

	Omalizumab (*n* = 14)	Mepolizumab (*n* = 14)	*p*-value
Age; year, mean (±SD)	55.6 (7.8)	41.7 (11.8)	0.001
Sex; *n*, female (%)	13 (92.8)	11 (78.5)	0.59
BMI; kg/cm^2, mean (±SD)	29.9 (8.3)	30.4 (5.8)	0.87
Duration of asthma; year, median (%25-75 percentile)	21 (12–28)	14 (6–25)	0.19
Total IgE; IU/ml, median (%25-75 percentile)	280 (160–586)	473 (149–835)	0.38
History of smoking; *n* (%)	7 (50)	3 (21.4)	0.11
Baseline FEV1; ml, mean (%)	1620 (68.4)	1968 (67.4)	0.35/0.91
Baseline ACT; mean (±SD)	9.4 (2.7)	11.6 (2.5)	0.037
Baseline eosinophil count; cell/μl, median (%25-75 percentile)	395 (320–700)	890 (600–1430)	0.007



1125 | Clinical behavior of patients with asthma during the COVID-19 pandemic

Batalha A. P.; Basili J. O.V.; Pereira G. F.; Kalil J.; Giavina-Bianchi P.; Agondi R. C.

University of São Paulo, São Paulo, Brazil

Background: Asthma is a chronic respiratory disease, and respiratory viruses are well-known triggers for asthma exacerbations. The novel *coronavirus* named *SARS-CoV-2*, which causes *COVID-19*, can

present with pulmonary symptoms. Several studies suggest that IL-13, an allergic asthma mediator, should prevent asthma exacerbations by SARS-CoV-2. The objective of this study was to evaluate the clinical behavior of patients with asthma during the COVID-19 pandemic.

Asthma is a chronic respiratory disease, and respiratory viruses are well-known triggers for asthma exacerbations.The novel *coronavirus* named *SARS-CoV-2*, which causes *COVID-19*, can present with pulmonary symptoms.Several studies suggest that IL-13, an allergic asthma mediator, should prevent asthma exacerbations by SARS-CoV-2.The objective of this study was to evaluate the clinical behavior of patients with asthma during the COVID-19 pandemic.

Method: This was a retrospective study of electronic medical records of adult asthmatic patients, being followed up in a tertiary service and who received telephone calls for rescheduling the face-to-face consultations, during the COVID-19 pandemic period.Demographic data, asthma symptoms, frequency of atopy, presence of comorbidities and symptoms related to coronavirus infection were analyzed. Patients were classified according to their history of asthma attacks.

Results: Two hundred and seven patients were included, and of them, 165 patients (79.7%) were female, with a mean age of 53.3 years and asthma duration of 35 years. Atopy was confirmed in 156 patients (81.7%). The main comorbidities were obesity (32.9%), high blood pressure (47.3%), diabetes mellitus (17.4%) and emotional stress (68.1%). Of the total, 87 patients (42%) had acute symptoms, of which 20 (9.7%) sought emergency care and 15 of 20 patients (75%) were investigated for Covid-19, all of which were negative. Of the total, only 7 patients (3.4%) exacerbated and required systemic corticosteroids. During this study, the more frequent complaints among asthmatic patients with acute respiratory symptoms were dyspnea, cough, asthenia and headache when compared to those without a crisis ($p < 0.05$).

Conclusion: This study found that asthmatic patients had a low prevalence of asthma exacerbation during the coronavirus pandemic period. Patients with acute symptoms may have been underdiagnosed for COVID-19, due to the low demand for emergency care. Previous atopy may act as a protective factor for COVID-19 in asthmatic patients.

1187 | Evaluation of the clinical and laboratory findings of asthmatic children with SARS coV-2 infection

Metbulut A.P.; Mustafaoglu Ö.; sen G.; Kanik Yüksek S.; Külhas Çelik I.; Akça H.; Dibek Misirlioglu E.
Ankara City Hospital, Child Hospital, Ankara, Turkey

Background: There are a limited number of studies about the clinical findings of coronavirus infection in pediatric patients with asthma. We aimed to evaluate the clinical and laboratory characteristics of pediatric patients with asthma and healthy children without chronic disease who were infected with SARS-CoV-2.

Method: This is a retrospective, case-control study comparing the children diagnosed with asthma and healthy children who were diagnosed with COVID-19 in our hospital between March,11 and November,10 2020.

Results: During the study period, 6205 children were diagnosed with COVID-19 in our hospital. Only 54 (0.87%) patients had a diagnosis of asthma. The mean of the age was 10.7 years and 53.7% (*n*:29) of the patients with asthma were male. Cough, shortness of breath, emesis and diarrhea were found to be significantly higher in asthma group than in the control group (respectively $p = 0.002$,0.000, 0.002, 0.019, 0.015). Patients who were given SABA were significantly higher in asthma diagnosed patients ($p = 0.000$). There was no significant difference between the two groups in terms of oxygen treatment and hospitalization requirement. There was no significant difference in laboratory findings between groups.

Conclusion: This study revealed that pediatric patients diagnosed with asthma were in mild clinic state and the clinic of COVID-19 was not different between the groups. According to these findings, asthma may not be a risk factor for the development of COVID-19 and may not affect the course of the disease in children.

TABLE 1 Demographic and clinical characteristics of patients diagnosed with asthma (*n* = 54)

	Patients with asthma
Age	
Age (years), median (IQR)	10.5 (7-15)
Age at diagnosis of asthma (years), median (IQR)	4 (1-9)
Gender (female/male)	0.86
Male, *n* (%)	29 (53.7%)
Concomitant allergic diseases	17 (31.5%)
Allergic rhinitis, *n* (%)	13 (24.1%)
Food allergy, *n* (%)	3 (5.6%)
Atopic dermatitis, *n* (%)	1 (1.9%)
Chronic urticaria, *n* (%)	1 (1.9%)
Family member having allergic disease, *n* (%)	14 (25.9%)
Asthma	10 (18.5%)

	Patients with asthma
Allergic rhinitis	4 (7.4%)
Atopy status	
Aeroallergen sensitization, *n* (%)	18 (33.3%)
Pollen	12(22.2%)
House dust mite	7 (13%)
Mold	2 (3.7%)
Cat and dog dander	3 (5.6%)
Cockroach	1(1.9%)
Used asthma maintenance therapy before COVID-19	
Patients used asthma medications, *n* (%)	23 (42.6%)
Only using Inhaled corticosteroids (ICS), *n* (%)	11 (20.4%)
Only using Anti-leukotrienes, *n* (%)	5 (9.3%)
Both using ICS and anti-leukotrienes, *n* (%)	6 (11.1%)
Both using ICS and LABA, *n* (%)	1 (1.9%)
Admission to clinic control during pandemic	
Patients admitted to control for asthma, *n* (%)	14 (25.9%)
Asthma Control	
GINA assessment of asthma in the last 3 months (*n*:46)	
Well controlled, *n* (%)	36 (66.7%)
Partly controlled, *n* (%)	5 (9.3%)
Uncontrolled, *n* (%)	5 (9.3%)
Patients having asthma attack in the last one year, *n* (%)	2 (3.7%)

TABLE 2 During COVID-19, clinical, laboratory and treatment features of the patients with and without asthma

	Patients diagnosed with asthma *n*:54 *n* (%)	Patients not diagnosed with asthma *n*:162 *n* (%)	*P*-value
Age			
Age (years), median IQR	10.5 (7-15)	11.5 (7-15)	0.863·
Gender			
Male, *n* (%)	29 (53.7)	85 (52.5)	0.875
Contact History			
Family cluster, *n* (%)	24 (44.4)	90 (55.6)	0.157
Unidentified source of infection, *n* (%)	30 (55.6)	72 (44.4)	
Symptoms at admission			
Having symptoms, *n* (%)	51 (94.4)	139 (85.8)	0.091
Duration of symptoms before admission to hospital (days) mean, ±SD	**2.97 ±2.18**	**2.11 ±1.43**	**0.016·**
Symptoms¨			
Fever	13 (27.5)	84 (51.9)	0.814
Throat pain	10 (18.5)	43 (26.5)	0.235
Cough	**32 (59.3)**	**57 (35.2)**	**0.002**
Short of breath	**12 (22.2)**	**7 (4.3)**	**0.000**
Chest tightness	1 (1.9)	6 (3.7)	0.683*
Rhinorrhoea	6 (11.1)	11 (6.8)	0.307
Non-respiratory system symptoms	32 (59.3)	79 (48.8)	0.181
Emesis	**10 (18.5)**	**8 (4.9)**	**0.002**
Vomiting	8 (14.8)	10 (6.2)	0.47

	Patients diagnosed with asthma *n*:54 *n* (%)	Patients not diagnosed with asthma *n*:162 *n* (%)	*P*-value
Abdominal pain	2 (3.7)	11 (6.8)	0.525*
Diarrhea	**13 (24.1)**	**18 (11.1)**	**0.019**
Joint pain	6 (11.1)	16 (9.9)	0.795
Myalgia	2 (3.7)	7 (4.3)	1*
Headache	5 (9.3)	30 (18.5)	0.110
Fatique	9 (16.7)	26 (16)	0.915
Loss of smell or taste	2 (3.7)	8 (4.9)	1*
Loss of appetite	**3 (5.6)**	**0 (0)**	**0.015***
Pyhsical examination			
Having patologic pyhsical finding, *n* (%)	11 (20.4)	48 (29.6)	0.186
Having hypoxia	3 (5.6)	2 (1.2)	0.101*
Having tachypnea	1 (1.9)	4 (2.5)	1*
Having rales, *n* (%)	0	2 (1.2)	1*
Having ronchus	2 (3.7)	1 (0.6)	0.155*
Treatment			
Patients being given drugs during COVID-19, *n* (%)	12 (22.2)	25 (15.4)	0.251
Favipiravir, *n* (%)	1 (1.9)	2 (1.2)	
Hydroxychloroquine, *n* (%)	2 (3.7)	1 (0.6)	
Oseltamivir	2 (3.7)	0	
Antibiotic, *n* (%)	7 (13)	22 (13.6)	0.908
Short-acting beta-agonists	**11 (20.4)**	**2 (1.2)**	**0.000***
Systemic steroid	3 (5.6)	2 (1.2)	0.097*
Hospitalization			
Hospitalized, *n* (%)	14 (25.9)	21 (13)	0.025
Duration of hospitalization (days), mean	3.6	5.5	0.034°
Hospitalised in intensive care unit, *n* (%)	0	1 (0.6)	
Requiring oxygen, *n* (%)	4 (7.4)	5 (3.1)	0.232*
Requiring oxygen via high flow nasal oxygen, *n* (%)	0	2 (1.2)	
Imaging tests			
Having Chest graphy, *n* (%)	**42 (77.8)**	**96 (59.3)**	**0.014**
Having pathologic radiographic findings, *n* (%)	19 (35.2)	49 (30.2)	0.494
Infiltration	4 (7.4)	13 (8)	
Ground glass opacity	0	2 (2.1)	
Stripe shadowing	10 (18.5)	17 (10.5)	
Hilar enlargement	5 (9.3)	17 (10.5)	
Having Thorax CT	3 (5.6)	3 (1.9)	0.167*
Infiltration	2 (3.7)	3 (1.9)	0.10*
Ground glass opacity	2 (3.7)	2 (1.2)	1*

Chi-square test, *Fisher test, ·Mann-Whitney test, °Student-T test/Independent T test, Column percentage

TABLE 3 Laboratory findings of patients with and without comorbid asthma

Laboratory findings	Patients diagnosed with asthma *n*:54 *n* (%)	Patients not diagnosed with asthma *n*:162 *n* (%)	*P*-value
Laboratory test performed, *n* (%)	**40 (74.1%)**	**86 (53.1%)**	**0.007**
Total white blood cell count, median, IQR	5205 (4275–7680)	5960 (4572–7772)	0.708·
Serum haemoglobin level, mean, ±SD	14 (±1.48)	13.7 (±1.55)	0.341 °

Laboratory findings	Patients diagnosed with asthma *n*:54 *n* (%)	Patients not diagnosed with asthma *n*:162 *n* (%)	*P*-value
Serum neutrophil level (absolute number),median, IQR	2920 (2332–4312)	2900 (1935–4622)	0.379·
Serum lymphocyte level (absolute number), median, IQR	1760 (1197–2382)	1845 (1477–2565)	0.263·
Serum eosinophil level (absolute number), median, IQR	70 (40–140)	50 (30–100)	0.079·
Serum eosinophil level (percent), median, IQR	1.30 (0.70–2.60)	1.10 (0.4–1.72)	0.137·
Serum platelet level, mean, ±SD	273.000 (±83.000)	263.000 (±66.000)	0.480 °
C-reactive protein level, median, IQR	0.003 (0.0006–0.007)	0.003 (0.0019–0.007)	0.377·
Procalcitonin level, median, IQR	0.02 (0.003–0.495)	0.035 (0.030–0.05)	0.269·
Ferritin level, median, IQR	36 (13–43)	33 (18–45)	0.902·
APTT level, mean, ±SD	26.5 (±2.17)	26.3 (±2.52)	0.677°
INR level, median, IQR	1.03 (0.99–1.11)	1.03 (1–1.10)	0.994·
D-dimer level, median, IQR	0.3 (0.20–0.63)	0.41 (0.22–0.65)	0.425·
AST level, mean, ±SD	24.2 (±10.6)	24.2 (±11.5)	0.990°
ALT level, median, IQR	17 (14–24)	18 (15–22)	0.636·
Serum urine level, median, IQR	24 (21.2–27.9)	24 (21–28)	0.717·
Serum creatinine level, mean, ±SD	0.57 (±0.20)	0.55 (±0.18)	0.549 °

Chi-square test, *Fisher test, ·Mann-W

1271 | IRF7-associated immunophenotypes have dichotomous responses to virus/allergen coexposure and bacterial lysate-induced reprogramming

De Jong E.[1,2]; Lauzon-Joset J.[1,3]; Leffler J.[1,2]; Serralha M.[1]; Larcombe A.[1,4]; Christophersen C.[5,6]; Holt P.[1]; Strickland D.[1]; Bosco A.[1,2]

[1]Telethon Kids Institute, Perth, Australia; [2]University of Western Australia, Perth, Australia; [3]Centre de Recherche, Institut Universitaire de Cardiologie et de Pneumologie de Québec, Québec, Canada; [4]School of Public Health, Curtin University, Perth, Australia; [5]WA Human Microbiome Collaboration Centre, School of Molecular and Life Sciences, Curtin University, Perth, Australia; [6]Centre for Integrative Metabolomics and Computational Biology, School of Medical & Health Sciences, Edith Cowan University, Perth, Australia

Background: High risk for virus-induced asthma exacerbations in children is associated with an IRF7lo immunophenotype, but the underlying mechanisms and the nature of interactions with other asthma risk phenotypes are unclear.

Objective: To elucidate the mechanism(s)-of-action of the high-risk asthma immunophenotype, and investigate potential risk mitigation via pretreatment with a bacterial lysate.

Method: We utilized an animal model comprising rat strains manifesting high (BN) versus low susceptibility (PVG) to experimental asthma. OVA-sensitized animals from both strains, with vs without bacterial lysate pretreatment, were co-exposed to intranasal mengovirus (hRV mimic) and aerosolised OVA, previously shown to elicit high-intensity airways inflammation. Multiple tissues were sampled during/after ensuing viral clearance for comparative systems level analyses to map underlying inflammation-associated gene coexpression networks.

Results: Virus/allergen coexposure in low-risk PVG rats resulted in rapid and transient neutrophilic and eosinophilic airways inflammation in BAL, and pDC recruitment into lung and airway draining lymph nodes alongside IRF7 gene network formation in lung and bone marrow. In contrast, responses in high-risk BN rats were characterized by severe airways eosinophilia and exaggerated proinflammatory responses in combination with growth factor signaling in the lung that failed to resolve, and complete absence of IRF7 gene networks. Moreover, increased T2 signaling and decreased type-I-interferon signaling were evident in BN bone marrow at baseline. Bacterial lysate pretreatment had more profound effects in high-risk BN rats, inducing immune-related gene expression changes in lung at baseline and reducing exaggerated airway inflammatory responses to virus/allergen coexposure. In low-risk PVG rats, bacterial lysate pretreatment boosted IRF7 gene networks in the lung but did not alter baseline gene expression or cellular influx.

Conclusion: Distinct IRF7-associated asthma risk immunophenotypes have dichotomous responses to virus/allergen coexposure and respond differentially to bacterial lysate pretreatment. Extrapolating to humans, our findings suggest that the beneficial effects bacterial lysate treatment may preferentially target those in high-risk subgroups.

1318 | Bronchial asthma control during pregnancy: Influence of the weight of the newborn and fetal well-being parameter

Baynova K.; Romero Falcón A.; García Diaz L.; Castilla Guerra J.; Medina Gallardo J.F.; Álvarez Gutierrez F.J.
Virgen del Rocío University Hospital, Seville, Spain

Background: Poor asthma control during the pregnancy, caused mainly by abandoning previous bronchodilator medication or by viral symptoms, is related to preterm delivery, low birth weight and therefore higher perinatal mortality. We analyzed the influence of the monographic consultation of asthma follow-up during pregnancy and the puerperium, the control and evolution of the disease; in relation to the weight of the newborn and the signs of fetal well-being (determined by the Apgar test) at the time of delivery.

Method: 138 patients who had given birth in the Virgen del Rocío health area, undergoing previous follow-up in the Asthma-Pregnancy clinic, during the period 2010-2015 were analyzed. The clinical parameters (according to GEMA 4.1 and ACT) and functional parameters (spirometry and fractional exhaled nitric oxide) during each trimester, determined the classification of severity of asthma at the time of the start of the follow-up protocol.

At the puerperal visit, the variables related to the newborn's weight and the Apgar test at the time of birth were collected.

Statistical analysis of means was performed using student's t-test for independent samples and qualitative samples by chi square.

Results: 77% gave birth by natural delivery and 23% by cesarean section.

The mean weight of newborns at birth was 3322 g (± 450), presenting by groups of severity of bronchial asthma an average birth weight in the case of intermittent asthma of 3373 g (± 502), mild persistent asthma- 3185 g (± 449), in persistent moderate asthma- 3411 g (± 547), and in severe asthmatics- 3320 g (± 442). 47% of the women required treatment with inhaled corticosteroids during pregnancy with an equivalent dose of beclomethasone of 1123.68 mcg (SD 860) .No statistically significant differences were found between the severity of asthma that the patients presented at the time of inclusion in the consultation with the weight of the newborn. No differences were found in the Apgar test in any of the groups analyzed.

Conclusion: The data obtained from our study confirm the importance of close monitoring of bronchial asthma in pregnant women, mainly in those with greater severity, which will influence a better weight of the newborn and therefore in the control of possible perinatal complications.

1052 | Real-life effectiveness of dupilumab on symptom control, lung function and oral corticosteroid intake in patients with severe allergic eosinophilic asthma and nasal polyposis

Pelaia C.[1]; Busceti M.T.[1]; Crimi C.[2]; Lombardo N.[1]; Vatrella A.[3]; Pelaia G.[1]
[1]*University "Magna Græcia" of Catanzaro, Catanzaro, Italy;* [2]*University of Catania, Catania, Italy;* [3]*University of Salerno, Salerno, Italy*

Background: Dupilumab is a fully human monoclonal antibody, which specifically recognizes and occupies the α-subunit of the IL-4 receptor, thereby inhibiting the biological actions of both IL-4 and IL-13. Dupilumab is nowadays available in many countries for add-on biological therapy of severe asthma. Although several pre-marketing randomized controlled trials have made it possible to use this monoclonal antibody in clinical practice, real-life investigations are still lacking. The **primary outcome** of this observational study was to evaluate the effectiveness of dupilumab in a real-life environment.

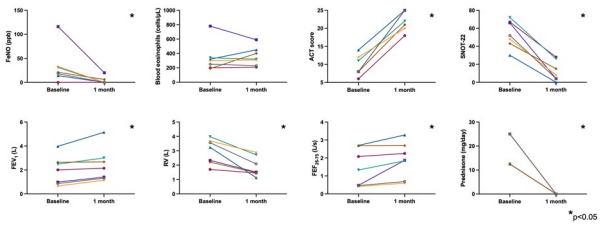
Method: We enrolled **7 patients** with severe allergic eosinophilic asthma and nasal polyposis, currently treated with dupilumab at the **Respiratory Unit of "Magna Græcia" University Hospital-Catanzaro, Italy**. Fractional exhaled nitric oxide (FeNO), blood eosinophil count, asthma control test (ACT) score, sino-nasal outcome test (SNOT-22), forced expiratory volume in the first second (FEV_1), residual volume (RV), forced mid-expiratory flow between 25% and 75% of FVC (FEF_{25-75}), and daily oral corticosteroid (OCS) intake were recorded at baseline and 4 weeks after the first dose of dupilumab.

Results: After 4 weeks of treatment with dupilumab, **FeNO** levels significantly declined in comparison to baseline, from 33.2 ± 38.1 ppb to 3.71 ± 7.52 ppb ($p < 0.05$). Peripheral **blood eosinophil** counts did not significantly change from baseline values (340.5 ± 202.4 cells/μL) at the 4th week (358.6 ± 133.0 cells/μL; $p = 0.89$). With respect to baseline (9.57 ± 2.82), the **ACT** score significantly increased after 4 weeks (22.3 ± 2.81; $p < 0.05$). In the same period, **SNOT-22** decreased from 54.0 ± 15.1 to 12.1 ± 11.1 ($p < 0.05$). These effects were associated with relevant **FEV_1** increases from baseline (1.94 ± 1.20 L) at the 4th week (2.40 ± 1.40 L; $p < 0.05$), and with significant **RV** decreases from baseline (2.96 ± 0.87 L) at the 4th week (1.89 ± 0.68 L; $p < 0.05$). **FEF_{25-75}**increased from baseline (1.45 ± 1.04 L/s) at the 4th week (1.89 ± 0.98 L/s; $p < 0.05$). Moreover, the marked improvement in global health status experienced by our patients allowed them to progressively lower and then completely interrupt, within 4 weeks, their daily **OCS** intake, which fell from 19.6 ± 6.68 to 0 mg ($p < 0.05$) of prednisone.

Conclusion: These preliminary data referring to our observational study highlight, in a real-life world, the **favorable therapeutic effects** exerted by **dupilumab** in patients with **corticosteroid refractory**, **severe allergic**, **eosinophilic asthma** and **nasal polyposis**.

Baseline patient characteristics	
Age (years)	54.29 ± 14.94
Duration of asthma (years)	24.86 ± 13.03

Baseline patient characteristics	
Sex (M/F)	2/5
Weight (kg)	75.00 ± 11.08
Height (cm)	164.3 ± 11.86
BMI (kg/m^2)	27.86 ± 4.71
FEV_1 (% predicted)	62.57 ± 23.61
FEV_1/FVC (%)	66.57 ± 7.43
Serum IgE (UI/mL)	357.7 ± 305.8
Atopy (yes/no)	7/0
Nasal polyposis (yes/no)	7/0



1102 | Overview of severe asthma disease control during the second wave of COVID-19 pandemic in Albania

Lekli E.[1]; Hoxha M.[1,2]; Vyshka G.[1,2]; Qirko Loloci E.[1,2]

[1]*University of Medicine Tirana, Tirana, Albania;* [2]*University Hospital Center, Tirana, Albania*

Background: Under the restriction of direct access to specialized health care, COVID-19 pandemic, has created an "iceberg" regarding disease control data in severe Bronchial Asthma (BA). We aimed to evaluate indicators of asthma control, in severe persistent BA, consequences of pandemic and in-person visits limitations among this patient population.

Method: A cross-sectional study, obtained data from 86 patients with yearly pre-pandemic hospitalizations, at the only tertiary hospital center for severe persistent BA in Albania. Descriptive data analysis was performed through anamnestic and clinical records. Standardized and validated questionnaires for inhalers adherence and asthma control, have been performed though phone interview during January 2021. Patients under treatment with biologic drugs (anti-IgE) and allergen specific immunotherapy have been excluded.

Results: 64% were classified as high TH2 phenotype, predominating late-onset eosinophilic asthma (30.2%), and in low TH2 phenotype, with predominance of obesity associated asthma (18.6 %). 66,3 % were females with mean age of 49.3 ± 13.9. Overall Asthma Control Test (ACT= 19.5 ± 3.8), 43% controlled (20-25 points), with no statistically significant differences, between sex and phenotypes. Among early onset allergic asthma phenotype (25,6%), lower ACT score (18.5 ± 1.5) resulted in outdoor + indoor allergen polysensitization, compared to monosensitization ($p < 0.05$). Seasonal influenza vaccination rate was 16.2%, ACT score between vaccinated and unvaccinated groups, with significant difference ($p = 0.03$). Prevalence of confirmed COVID-19 was 15.1%, only 1,2% severe. ATC score, between confirmed or suspected post COVID-19 severe ABs and COVID-19 negative, was not statistically significant. Coexistence of sporadic and intentional nonadherence affected ACT score ($p = 0.01$), between controlled (ACT, 20-25) and uncontrolled group (ACT<20 points).

Conclusion: Asthma control in severe persistent BA population was <50%, affected by sensitization profile, seasonal flu vaccination and type of non-adherence to inhalers. Differences of disease control in ACT score, were not statistically related with phenotype, sex or post COVID-19 infection condition. Particularly, Severe Persistent Bronchial Asthma needs a periodic specialist care to reach disease control and to lower the burden of indirect pandemic effects on disease progression.

1134 | Work-exacerbated asthma and work-induced asthma: A comparative study

Belhadj Chabbah N.[1,2]; Belhadj N.[1,2]; El Maalel O.[1,2]; Sridi C.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Brahem A.[1,2]; Kalboussi H.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Department of occupational Medicine, Teaching Hospital Farhat Hached, Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine Ibn El Jazzar, Sousse, Tunisia*

Background: Asthma is a serious public health problem. It is the most common respiratory disease related to the work environment. Over the last decade, attention has been focused on the role of occupational exposure on the evolution of asthma. To compare the socio-professional, clinical, and medico-legal characteristics of occupational asthma (OA) and work-exacerbated asthma (WEA) and to identify the factors associated with severe exacerbations of asthmatic disease.

Method: This is a retrospective descriptive study of all cases of work-related asthma diagnosed at the Occupational Medicine and Pneumology Departments of the University Hospital "Farhat Hached" of Sousse-Tunisia during the period from July 2015 to June 2018. The data collection was based on a synoptic sheet containing the socio-professional and medical characteristics of patients as well as data from additional examinations performed.

Results: A total of 202 cases of work-related asthma were enrolled. The mean age of the patients was 41.6 ± 8.5 years with a predominance of females (sex ratio = 0.66). Only 26.7% of cases had asthma before the onset of occupational exposure representing the proportion of WEA. No statistically significant differences were found in terms of gender and mean age between the OA and WEA groups. However, there was a significant difference between the two groups in terms of sectoral distribution of activity and etiological agents. Approximately 67% of work-induced asthma cases were reported as an occupational disease versus 29.4% of WEA cases with a statistically significant difference. The occupational outcome of asthmatics did not vary significantly with the presence of severe exacerbations.

In the multivariate analysis, there were statistically significant associations between WEA on the one hand and occupational rhythmicity (ORa=8.35; 95% CI=[1.8-37.91]), personal allergy (ORa=3.80; 95% CI=[1.32-10.89]), eviction test (ORa=6.64; 95% CI=[2.22-19.86]) and prick tests (ORa=3.64; 95% CI=[1.21-10.89]) on the other hand.

Conclusion: WEA represents a significant proportion of all work-related asthma cases. Therefore, it seems necessary to distinguish between OA and WEA. The socio-economic impact of this entity appears to be as pejorative as OA itself. Only an effective preventive intervention could reduce the occupational morbidity and disability of this disease.

1181 | Occupational asthma and obesity: What links?

Chelly F.[1]; Aloui A.[1]; Maoua M.[1]; Kalboussi H.[1]; Sridi C.[1]; Benzarti W.[2]; Bouhoula M.[1]; Chouchene A.[1]; Kacem I.[1]; Brahem A.[1]; El Maalel O.[1]; Chatti S.[1]; Abdelghani A.[2]; Benzarti M.[2]; Mrizak N.[1]

[1]Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia; [2]Department of Pneumology - Teaching Hospital Farhat Hached, Sousse, Tunisia

Background: Risk factors for the severity of occupational asthma (OA) are often attributed to working conditions and occupational exposure. However, some recent epidemiological data suggest a link with obesity given the parallel growth in the frequency of severe occupational asthma and obesity.

Objective: Analyze the relationship between obesity and the severity of occupational asthma assessed by non-specific bronchial provocation

Method: We conducted an epidemiological study including all patients who were referred to the Occupational Medicine Department of Farhat Hached University Hospital, Sousse, for occupational asthma, and who have completed a non-specific bronchial provocation test to metacholine between 2004 and 2012

Results: Our population consisted of 131 cases of occupational asthma with a mean age of 38.31 ± 8.55 years and a female predominance (sex ratio = 0.48). The average BMI was 27.34 ± 5.30 kg. The majority of the population (34.4%), had a normal BMI and 32.8% were overweight, while obesity was only observed in 29.8% of cases. The non-specific metacholine bronchial provocation test revealed that the average dose of PD20 was 750.4 ± 656.3 µg. Thus, severe occupational asthma was observed in 46 cases (35.1%). After univariate analysis, obesity in asthmatics had a significant association with age (p <10-3), marital status (p = 0.005), average professional seniority (p <10-3), the evolution of complaints (p = 0.035) and pathological initial spirometry (p = 0.044). As for the severity of occupational asthma, the univariate analytical study did not show a significant link with obesity (p = 0.68).

Conclusion: Despite the fact that our study did not reveal an association between the severity of OA and obesity that may be due to certain limits, the data found offer new research opportunities as the pandemic of obesity remains highly suspect in the worsening of occupational allergic conditions such as asthma

1199 | The continuous laryngoscopy exercise test in severe asthma in adults - A systematic review

Thomander T.[1,2]; Malmberg L.P.[3]; Toppila-Salmi S.[2]; Aaltonen L.[4]; Kauppi P.[5]

[1]Doctoral Programme in Clinical Research, University of Helsinki, Helsinki, Finland; [2]Department of Allergy, Inflammation Center, Helsinki University Hospital, Helsinki, Finland; [3]Department of Clinical Physiology, Inflammation Center, Helsinki University Hospital, Helsinki, Finland; [4]Department of Otorhinolaryngology, Head and Neck Surgery, Helsinki University Hospital, Helsinki, Finland; [5]Heart and Lung Center, Helsinki University Hospital, Helsinki, Finland

Background: A systematic review was performed to clarify the role of the continuous laryngoscopy exercise test (the CLE test) in the diagnostics of exercise dyspnea in adult asthma patients, and whether vocal cord dysfunction (VCD) is found in those with a severe disease.

Method: We employed Scopus and PubMed databases. The articles published up to 13 August 2019 were noticed. We excluded manuscripts which did not contain information about adult asthma patients. In this systematic review we included 11 studies from 59 search results in Scopus and none from the 17 search results in PubMed.

Results: The articles covered 734 study individuals and of those, 74 (10.1 %) had diagnosed asthma. Altogether 17/74 (23.0 %) subjects with diagnosis of asthma had exercise-induced laryngeal obstruction (EILO) as comorbidity. The CLE test had been performed on 65/74 (87.8 %) patients with asthma. The method has been implemented only for differential diagnosis of exercise-induced dyspnea to confirm EILO. At least 14 (1.9 %) out of the 734 subjects underwent adverse events.

Conclusion: This systematic review showed that only small proportion of asthma patients had undergone the CLE test in order to analyze exercise-induced dyspnea. The lung function was presented only in three of the included 11 articles. None of the selected manuscripts reported asthma severity. Whether CLE provide a valuable diagnostic tool for severe or difficult-to-treat asthma patients cannot be assessed according this review.

TABLE 1 Summary of the included studies embodying objectives, study design, subjects and methods

Reference number	Objectives	Study design	Subjects	Methods
3	Evaluating the prevalence of EILO in athletes with exercise-induced respiratory symptoms	A retrospective cohort study	*n* = 88. The median (IQR) age 17 (9.0) years. *N* (female in EILO group) = 24 (77 %), *N* (females in non-EILO group) = 26 (46 %)	Comparison of clinical characteristics and bronchial hyperreactivity between athletes with and without EILO
4	Development and validation a diagnostic method for exercise-induced vocal cord dysfunction by combining continuous fiberoptic laryngoscopy with bicycle ergometry test	A validation study	*n* (patients) = 30, median (min-max) age 27.8 (10.6-69.2) years, *n* (females) = 24 (80 %), *n* (asthma) =13 (43 %), *n* (non-smoker) = 29 (97 %); *n* (controls) = 15, median (min-max) age 33.4 (20.9-54.1) years, *n* (females) = 10 (67 %), healthy individuals, *n* (smoker) = 1	CLE test in a bicycle ergometer and during the test rating of perceived exertion by Borg scale, measurements of blood pressure, heart rate and respiratory rate. Baseline measurements: FEV1, oxygen saturation, ECG, blood pressure, heart rate and respiratory rate. A questionnaire of medical history
5	Assessing the prevalence and symptoms of EILOs and their relation to airway hyperresponsiveness (AHR)	An interventional study	*n* (interviewed) = 150, mean (min-max) age 18.65 (14-24) years, median 19 years, OR (females/males) = insignificant. *n* (CLE tested) = 98, age mean 18.48 (14-24) years, OR (females/males) = 1.61 (95% CI 1.03-2.50)	Self-reported and interview-based questionnaire about EILO and EIA (exercise-induced asthma) symptoms, bronchial provocation test, physical stress test, CLE test with video recording
6	Evaluation of the CLE test	A case report	*n* = 1, 31 years of age, female	CLE test in a swimming flume and on land
7	Validation and reliability of CLE test result	A prospective single-blinded case-control study	*n* (EILO subjects) = 17, *n* (healthy controls) = 6. Median (min-max) age 19 (5-45) years. *N* (female) = 19 (83 %). Normal resting spirometry. Nonsmokers	Repeated CLE tests on treadmill, three raters evaluate the video material in a blinded and randomized way
8	Describing therapeutic laryngoscopy during exercise (TLE)	An open label intervention study	*n* (patients with refractory EILO) = 41, mean (min-max) age 17 (14-21) years, gender: 28 (78 %) females	Cycle ergometer sprints, physician-advised breathing techniques and psychological emotion control
9	Elucidate and quantitate the time course of laryngeal obstruction during CLE test	A retrospective evaluation	*n* = 71, mean (min-max) age 15.0 (13.0-17.0) years, 66 % were females. Peak VO2 39.3 ± 9.8 mL/(kg*min), 9 patients with peak VO2 > 50 mL/(kg*min).	CLE with ramp protocols. Reviewers blinded to time sequencing rated inspiratory glottic and supraglottic obstruction.
10	Investigation of consistency between CLE score and EILOMEA method for CLE test recordings evaluation	A method comparison study	*N* = 53, various levels of severity of EILOs	Two blinded raters evaluated the supraglottic and glottic obstruction
11	Examination of similarity of laryngeal obstruction induced by eucapnic voluntary hyperventilation (EVH) testing and exercise testing	A method comparison study	*n* = 39, mean (min-max) age 21.7(15-34) years, no significant difference in gender, 43.6 % reported at least one moderate or severe exercise-related respiratory symptoms experienced within the last four weeks	EVH test (eucapnic hyperventilation test) and MPS (maximal physical stress) test performed during recorded continuous laryngoscopy
12	Exploring laryngeal response pattern to exercise by CLE test in patients with exercise-induced inspiratory stridor	An observational study	*n* (asymptomatic volunteers) = 20, mean (SD) age = 22.7 (7.8) years, *n* (females) 13 (65 %), FEV1 = 103.6% (12.7), FVC = 106.6% (10.3), PEF = 113.5% (14.7), peak VO2 = 53.0 (8.1) mL/(kg*min); *n* (patients) = 166;, mean (SD) age 16.3 (7.3) years, *n* (females) = 99 (65.5 %), FEV1 = 101.9%(15.9), FVC = 105.7% (14.8), PEF = 96.6% (21.0), peak VO2 = 45.1 (9.4) mL/(kg*min)	CLE test to symptom-limiting exhaustion, film recordings of the larynx and upper part of the body, breathing sounds recordings. 20 volunteers demonstrated a normal laryngeal response pattern to exercise

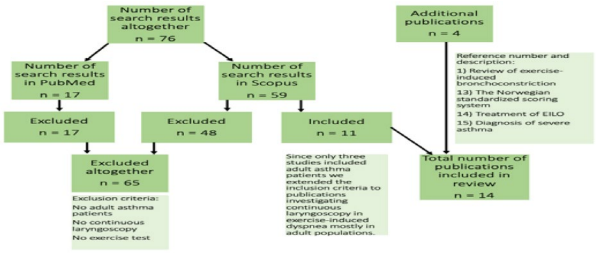
CLE continuous laryngoscope in exercise test, EILO exercise-induced laryngeal obstruction, EVH eucapnic voluntary hyperventilation

TABLE 2 Summary of the included studies embodying summary measures, main results and bias

Reference no	Summary measures	Main results	Bias
2	Supraglottic and glottic obstruction level, FEV1, FVC, FEV1/FVC, bronchial and extrathoracic airway hyperresponsiveness to mannitol, methacholine and bronchodilator reversibility. Asthma diagnosis was based on the consistent symptoms and a positive bronchoprovocation test (BPT) and in those with no BPT (i. e., if baseline FEV1 70 % or less) on symptoms, bronchodilator reversibility, peak flow variation (> 20 %), and asthma history. Extrathoracic airway hyperresponsiveness was defined as a decrease in FIF50 at least 25%. The CLE video recordings were graded applying the Norwegian standardized scoring system by two specialists and EILO diagnosis rested on grade score at least 2 (moderate) for either glottic or supraglottic obstruction	Based on the CLE test 8 (22 % of all female) had EILO, of whom 7 (88 %) had supra-glottic and one glottic EILO. EILO subjects had a slightly higher FEV1/FVC ratio (0.89 vs 0.83: $p = 0.01$). There was no difference in age, level of physical activity, pulmonary function test values including bronchial provocation test results between EILO and non-EILO subjects, neither in diagnosed asthma (63 % vs 62 %). EILO subjects had a lower BMI (20.2 vs 23.6; $p = 0.04$), less frequent rescue medication ($p = 0.04$) usage, symptoms and limitations on daily activities than non-EILO subjects	Subjects not participating in the CLE study ($n = 41$) were more likely test positive in the methacholine challenge test (69 % vs 35 %) or have bronchodilator reversibility (27 % vs 3 %) compared with the subjects who did participate. Subjects were young and physically active
3	EILO diagnosis was based on the presence of symptoms and a Norwegian grade score of 2 or greater (i. e. at least moderate) and asthma diagnosis on the presence of symptoms and a positive bronchoprovocation test (BPT) or bronchodilator reversibility test	EILO was diagnosed in 35.2 % of athletes. Supraglottic EILO appeared in 25 % of all athletes, glottic EILO in 3.4 % and combination in 6.8 %	Day-to-day variability of EILO. Fluctuation of airway hyperresponsiveness. β2-agonist before warm-up. Subjectivity of evaluation by Norwegian standardized scoring system
4	Heart rate (% of maximum), changes in respiratory rate, blood pressure, FEV1, and SaO2, total duration of the test, ECG. The supraglottic and glottic laryngeal adduction was graded on a four-stage scale (described by Maat et al)	The test was successfully performed for 27 (90 %) of the patients and all controls. Nine patients showed signs of diagnostic or highly suspect exercise-induced vocal cord dysfunction, none of the controls	Subjectivity when visually estimating the obstruction
5	FEV1, FVC, PD20, degree of EIL and EI-VCD by visually based severity grading system (0-3) and EILOMEA method	EILOs were verified in 26.1 % of participants with AHR. No symptoms specific for either AHR or EILO were found	Inhaling 1 mg terbutaline (Tubuhaler) prior to the physical stress test. Timing of the symptoms was unobserved. OR (symptomatic female /symptomatic male participating CLE test) = 3.11
6	Feasibility of the method	Stable high-quality diagnostic images	A healthy individual
7	Visual grade scale scores described by Maat RC et al (13)	One third of the subjects retained their initial diagnosis (i. e. diagnostic severity of EILO)	The learning effect

Reference no	Summary measures	Main results	Bias
8	Self-reported estimation on safety and tolerability, educational and clinical benefit	Of the subjects 75 % found that their breathing during exercise had improved	Only young and athletic subjects. Time between the procedure and questionnaire varied
9	Scoring was based on visual scoring scale published by Røksund et al (12)	Observed maximal laryngeal obstruction occurred at peak work capacity and the resolution of it started in less than 30 seconds. Severe forms of obstruction were rare and solved also rapidly	Young subjects, distribution of peak oxygen consumption skewed upward
10	CLE scores for supraglottic (SO) and glottic obstruction (GO) (0 -3). In the EILOMEA method the severity of supraglottic obstruction by EILOMEA SO measure and the severity of glottic obstruction by EILOMEA GO measure 1 and 2	The methods are compatible showing significant differences in the means for clinically important differences	Subjectivity in still frame selection from recording
11	Evaluation of laryngeal obstruction degree by CLE score and Eilomea	No significant differences appeared. EVH test can induce EILO	Elite athletes. Subjectivity in Eilomea evaluation method
12	Peak VO2, FVC (%), FVC (%), PEF (%), max heart rate (%). Glottic and supraglottic movements were scored throughout the exercise session by the protocol of Maat et al (13)	113 (75 %) patients had a normal laryngoscopy at rest and a moderate or severe adduction of laryngeal structures in parallel with increasing inspiratory distress during exercise. Typically adduction started within supraglottic structures	Asthma treatment during the year preceding the CLE test was reported by 10% of the volunteers and by 85% of the patients. Information whether the medication was discontinued before the examination was absent

CLE continuous laryngoscope in exercise test, EILO exercise-induced laryngeal obstruction, EVH eucapnic voluntary hyperventilation, VCD vocal cord dysfunction



1028 | Association between childhood living environment and occupational asthma

Sridi C.[1,2]; Maoua M.[1,2]; Kacem I.[1,2]; Chouchane A.[1,2]; Aloui A.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Occupational Medicine Department, Teaching Hospital "Farhat Hached", Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine "Ibn El Jazzar", Sousse, Tunisia*

Background: Occupational asthma (OA) is one of the most common respiratory diseases in the workplace. It is a heterogeneous and multifactorial disease.

Objective: To determine the association between childhood living environment and occupational asthma to vegetable textile dusts.

Method: A case-control study was conducted. The cases and controls were enrolled from the occupational medicine department of the Teaching Hospital "Farhat Hached" of Sousse (Tunisia) among patients attending from 2009 to 2016. Case group was composed of patients diagnosed with OA to vegetable textile dusts. Controls were age and gender matched, working in the textile sector and not suffering from any allergic diseases. Data collection was based on a synoptic sheet containing the socio-demographic characteristics of the participants and data related to their living environment during childhood.

Results: A total of 57 OA cases and 112 controls were enrolled. Our population was predominantly female with a sex ratio of 0.023. The mean age of the cases was 42.3 ± 6.6 years versus 43.4 ± 6.5 years for the controls. The majority of our patients had a primary study level: 54.4% of cases and 75% of controls with no statistically significant difference (p = 0.07). OA was statistically associated with living in urban areas in childhood (OR = 7.2; 95% CI: 3.3-15.8), passive smoking as a child (OR = 2.7; 95% CI: 1.4-5.3) and first rank in siblings (OR = 2.5; 95% CI: 1.1-5.6). Contact with animals in childhood and father's occupation as a farmer were protective factors for OA (OR = 0.61; 95% CI: 0.03-0.13 and OR = 0.29; 95% CI: 0.13-0.68 respectively).

Conclusion: The development of OA begins at an early age. The environment is an important model for understanding the mechanisms involved in the development of allergic asthma. Urbanization may explain the increase in allergy prevalence.

1164 | Eosinophilic sialodochitis: A rare comorbidity of severe asthma

Gonzalez Jimenez O. M.[1]; Picado C.[2,3]; Alobid I.[4]; Ramirez J.[5]; Arismendi E.[6,3]; Valero A.[2,3]; Bobolea I.[2,3]

[1]*Allergy section. General Hospital of Ciudad Real, Ciudad Real, Spain;* [2]*Allergy Section. Pneumology and Respiratory Allergy Service, Hospital Clinic, Barcelona, Spain;* [3]*Centro de Investigaciones Biomédicas en Red de Enfermedades Respiratorias (CIBERES) Instituto de Salud Carlos III, Madrid, Spain;* [4]*Otorhinolaryngology Service. Hospital Clinic. University of Barcelona, Barcelona, Spain;* [5]*Pathological Anatomy Service. Hospital Clinic, Barcelona, Spain;* [6]*Pneumology Service. Hospital Clínic., Barcelona, Spain*

Background: Recurrent parotid gland (PG) swelling can occur due to many causes, mainly obstruction of ducts by mucus plugs, salivary stones, or anatomic anomalies.

Kussmaul et al reported the relation between repetead swelling and mucus plugs containing eosinophils and Charcot–Leyden crystals. Since then, similar cases associating allergies, eosinophilia or high serum IgE have been diagnosed as "Allergic Parotiditis" or "Eosinophilic sialodochitis (ES)"

Method: We herein report on an 80-year-old woman, non-smoker, with severe persistent Eosinophilic asthma, eosinophilic esophagitis, chronic rhinosinusitis with nasal polyps (CRSwNP), bronchiectasis, Allergic bronchopulmonary aspergillosis; treated with Omalizumab between 2009–2013 and from 2016 to present.

In this context, she presents numerous episodes of bilateral parotid swelling, initially mild and autolimited, then increasing in duration and intensity, requiring use of oral corticosteroids.

Evaluated by many specialists over the years, tests, who performed the following tests: Parotid Gland Tomography (CT), Autoimmune markers (ANA, Anti-Ro/La, Ro52, ANCAs), general atopy markers, Schirmer test, parotid scintigraphy, Parotid MRI, biopsy and cytology

Results: CT: No litiasis or lymphadenopathy. ANA, Anti-Ro/La, Ro52, ANCAs: all NEGATIVE. Schirmer test: Negative. Scintigraphy: moderate to severe disfunction, grade III.

MRI: moderate hypertrophy with fat infiltration in both glands with dilation of the intraparotid ducts, compatible with chronic parotitis.

Salivatory gland biopsy: Inespecific chronic sialoadenitis. No evidence of histologic changes of Sjogren, amyloid nor sarcoidosis. IgG4 negative.

Total IgE: 368-3017 KU/L throughout the years. Eosinophilia: 300-1400 cels/mm3.

Given the persistent suspicion of eosinophilic inflammation as responsible of the recurrent parotid gland (PG) swelling, we decided to complete the study with a salivary cytology, which demonstrated the presence of eosinophils as single inflammatory cells.

Conclusion: We present a case of ES, an infrequent pathology related to allergic/eosinophilic diseases. The patient has been switched to benralizumab, in the idea that suppression of eosinophils will imply consequent decrease/cessation of the PG swelling attacks.

This entity should be considered in atopic/T2 patients with suggestive symptoms, requiring compatible histology of the gland and /or saliva cytology for the definitive diagnosis.

TABLE 1 Diagnostic criteria proposed by Baer et al (4).

Number	Criteria	Fullfilled by our patient
1	Recurrent paroxysmal swelling of the major salivary glands	x
2	Salivary duct mucus plugs containing numerous eosinophils.	x
3	Peripheral blood eosinophilia and elevated IgE level.	x
4	Associated atopic disease	x
5	Ductal dilatation and occasional focal narrowing of the major salivary gland ducts.	x
6	Periductal eosinophil inflammation and fibrosis with associated reactive ductal epitelial cells	
7	Failure to satisfy the diagnostic criteria of IgG4-related disease.	x

Mandatory features of eosinophilic sialodochitis include criteria 1 and 2 or criteria 1,6 and 7.

1032 | Mapping the cytokine and clinical responses to nasal allergen challenge in birch pollen allergic individuals

Campion N. J.[1]; Villazala-Merino S.[1]; Thwaites R. S.[2]; Stanek V.[1]; Tu A.[1]; Killick H.[3]; Pertsinidou E.[4]; Nemethy C.[1]; Nemec L.[1]; Toth J.[1]; Fröschl R.[1]; Perkmann T.[1]; Gangl K.[1]; Schneider S.[1]; Ristl R.[1]; Scott I. C.[3]; Cohen S.[3]; Molin M.[4]; Focke-Tejkl M.[1]; Hansel T. T.[2]; Valenta R.[1]; Niederberger-Leppin V.[1]; Eckl-Dorna J.[1]

[1]*Medical University of Vienna, Vienna, Austria;* [2]*Imperial College of London, London, United Kingdom;* [3]*AstraZeneca, Cambridge, United Kingdom;* [4]*Thermo Fisher, Uppsala, Sweden*

Background: Nasal allergen provocation studies have shown biphasic nasal responses to grass pollen challenge where immediate inflammatory responses, within in the first hour of allergen exposure, are characterised by rapid release of mast cell proteases (PGD2 and Tryptase), complement and D-dimer. In some individuals these are followed after 4-8 hours by secondary "late phase responses" (LPR) characterised by release of IL-13, IL-5, IL-9 and MMP. However, it is not yet known how these responses are affected by repeated nasal challenge and how they correlate with clinical measures of inflammation.

Method: 30 eligible birch allergic patients were recruited into this double blinded, randomised placebo-controlled trial (birch pollen extract: n = 20, placebo: n = 10). Nasal challenge with birch extract was performed on 3 consecutive days and 24 hour nasal sampling

time courses took place on provocation days 1 and 3. Before, during and after nasal provocation; nasal secretions, total nasal symptom scores (TNSS), visual analogue scales (VAS) and peak nasal inspiratory flows (PNIF) were collected to assess clinical responses. A 34 cytokine panel was measured in nasal secretions.

Results: All 30 participants completed the study. Patients provoked with birch had significantly greater increases in TNSS and VAS in comparison to placebo accompanied by significantly impaired nasal breathing assessed by PNIF. In terms of cytokine responses all patients provoked with birch showed significant increases in tryptase and sST2 in comparison to placebo in the first hour of provocation which correlated well with reduced PNIF and the symptoms "Sneezing" and "Nasal Itch". 8/20 birch provoked patients displayed significant LPR which were characterised by large rises in Th2 cytokines, IL-6, sST2, EDN and TSLP. These rises also correlated with a reduced PNIF and the symptom of "Nasal Obstruction. Analysis of repeated allergen challenge showed that some cytokine responses (e.g. IL-4, TSLP) were diminished on challenge day 3 whereas others were unaffected (e.g. sST2, MCP-1). Interestingly some cytokines (e.g. Exotaxin, IL-16) showed purely mechanical responses to nasal sampling.

Conclusion: Cytokine responses in the nose correlate well with symptom and objective clinical markers. LPR occurred in 8 out of 20 patients provoked with allergen and were characterized by rises in cytokines associated with Th2 responses.

1265 | Cystatin from the helminth ascaris lumbricoides (aI-CPI) upregulates cholesterol biosynthesis pathways and several immunomodulatory genes in human monocyte-derived dendritic cells (moDC)

Acevedo N.[1]; Lozano A.[1]; Zakzuk J.[1]; Brodin D.[2]; Espinoza H.[3,4]; Nejsum P.[5]; Williams A. R.[6]; Caraballo L.[1]

[1]*Institute for Immunological Research, University of Cartagena, Cartagena, Colombia;* [2]*Bioinformatics and Expression Analysis Core Facility (BEA), Karolinska Institutet., Huddinge, Sweden;* [3]*Faculty of Engineering, University of Cartagena, Cartagena, Colombia;* [4]*Division de Informática, CIDIT, Grupo INMEDIT S.A.S, Cartagena, Colombia;* [5]*Department of Clinical Medicine. Aarhus University, Aarhus, Denmark;* [6]*Department of Veterinary and Animal Sciences. University of Copenhagen, Frederiksberg, Denmark*

Background: The *Ascaris lumbricoides* cystatin (AI-CPI) prevents development of allergic airway inflammation and dextran induced colitis in mice models. It has been suggested that helminth derived cystatins inhibit cathepsins in dendritic cells (DC), but their immunomodulatory mechanisms are unclear. We aimed to analyze the transcriptional profile of human monocyte derived dendritic cells (moDC) upon stimulation with AI-CPI to elucidate target genes and pathways of parasite immunomodulation.

Method: moDC were generated from peripheral blood monocytes from six healthy, non-parasited human donors of Denmark, stimulated with 1 µM of AI-CPI and cultured during 5 hours at 37°C. RNA was sequenced using TrueSeq RNA libraries and the NextSeq 500 v2.5 (75 cycles) sequencing kit (Illumina, Inc). After QC, reads were aligned to the human GRCh38 genome using STAR. Differential expression was calculated by DESEq2 and expressed in fold changes (FC) and *p* values. *p*-values were adjusted for multiple tests using the Benjamini-Hochberg correction. Gene Ontology and pathway analysis were performed with ConsensusPathDB.

Results: Compared to unstimulated cells, AI-CPI stimulated moDC showed gene expression differences in 4403 transcripts. The top significant differences were in kruppel like factor 10 (*KLF10*, FC -3.3, $P_{BH} = 3 \times 10^{-136}$), palladin (FC 2, $P_{BH} = 3 \times 10^{-41}$) and the low-density lipoprotein receptor (*LDLR*, FC 2.6, $P_{BH} = 5 \times 10^{-41}$). Upregulated genes were enriched in regulation of cholesterol biosynthesis by sterol regulatory element-binding proteins (SREBF) and transforming growth factor beta (TFGb) signaling pathways. AI-CPI also increased the expression of interleukin 24 (*IL24*, FC=4.1, $P_{BH} = 6 \times 10^{-9}$) and the downregulated *SLC9A7P1* (FC -3.1, $P_{BH} = 1 \times 10^{-11}$). AI-CPI also downregulated chemokine receptors including CX3CR1, CCR2, CXCR2 and upregulated CXCR4.

Conclusion: AI-CPI modifies the transcriptome of moDC, increasing several transcripts encoding chemokine receptors, members of the SMAD family, the TGF beta family and the IL-10 family, including the fibrosis-related cytokine IL-24. Overall, supporting the anti-inflammatory effects of AI-CPI previously observed in the experimental allergy model. AI-CPI also induces remarkable changes in the expression of several genes involved in cholesterol byosinthesis and metabolism, suggesting new mechanisms mediating the DC response to helminth immunomodulatory molecules.

1305 | Signs of positive selection in new rounds of affinity maturation during B cell memory reactivation

Alekseeva E.[1]; Mikelov A.[1,2,3]; Komech E.[2,3]; Turchaninova M.[3]; Shugay M.[3,2]; Zvyagin I.[2,3]; Bazykin G.[1,4]

[1]*Skolkovo Institute of Science and Technology, Moscow, Russia;* [2]*Pirogov Russian National Research Medical University, Moscow, Russia;* [3]*Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russia;* [4]*A.A. Kharkevich Institute for Information Transmission Problems of the Russian Academy of Sciences, Moscow, Russia*

Background: Naive/memory B cell activation and clonal expansion is accompanied by differentiation into antibody-producing plasmablasts and plasma cells and isotype switching of the antibody. To produce high-affinity antibodies B cells go through the evolutionary process, based on somatic hypermutations and selection. Altogether these processes form B cell lineages, consisting of closely related but diverse in somatic hypermutations B cells of different subpopulations and isotypes. Recent studies have shown the effect of positive selection in vaccine-responsive lineages or long-living lineages of

chronic HIV-infected patients, however for the best of our knowledge evolutionary forces, shaping phylogeny of B cell lineages in healthy individuals are poorly understood.

Method: Here we are presenting the analysis of longitudinal B cell repertoire tracking data obtained for three cellular fractions: memory B cells, plasmablasts, and plasma cells, sampled three times within a year from five individuals.

Results: We show that the clonal structure of IGH repertoires in memory B-cell subpopulation is stable over time, displaying higher number of public clonotypes than in naive, indicating functional convergence. We observe two types of B cell lineages: long-living persisting memory with Ig M/D isotype, and active antibody secreting lineages, composed mainly of plasmablasts and plasma cells with the predominance of switched isotope (Ig G, Ig A). Negative selection predominates in persisting memory, most probably maintaining the structure of B cell receptor, formed at previous rounds of affinity maturation. Nevertheless persisting lineages continue to accumulate somatic hypermutations, increasing its diversity. In contrast active antibody producing lineages show signs of positive selection and originate from highly hypermutated ancestors, which means that they expand from preexisting hypermutated cells and represent memory reactivation.

Conclusion: Taking together our work reveals that evolution of antibodies demonstrates signs of adaptation and affinity maturation at new rounds of memory reactivation.

1107 | Colostrum drives the development of successful anti-helminth immune defenses

Rekima A.[1]; Isnard C.[2]; Smyth D.[3]; Maizel R.[3]; Verhasselt V.[1]
[1]*School of Molecular Sciences, University of Western Australia, Perth, Australia;* [2]*Department of paediatrics Hopital de l'Archet II, Nice, France;* [3]*Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom*

Background: Early life is a critical time window for neonatal gut immunity development that heavily influences the susceptibility or resistance to various diseases later in life. During this critical period, the infant's nutrition as breastmilk can influence the gut development. Colostrum is produced during the first 2 -3 days by the mammary gland and profoundly differs both qualitatively and quantitatively from mature breast milk. It is enriched in antibodies, growth factors, vitamins, and oligosaccharides. Strikingly, among breastfeeding mothers, there is a worldwide lack of colostrum administration in more than 50% of cases. A recent large scale study in developing countries showed a major negative impact of delayed initiation of breastfeeding on neonatal mortality and morbidity up to 6 months of age.

Method: To elucidate by which mechanisms colostrum mediates health benefits, we addressed its impact on gut mucosal immune ontogeny in a mouse experimental setting. Mice were breastfed by mothers providing either physiological feeding, i.e. colostrum from followed by mature milk, or only mature milk from birth.

Results: At the time of weaning, we found that innate lymphoid group 2 and Th2 cells in the small intestine *lamina propria* are severely diminished in the mice fed with mature milk from birth compared to mice fed with colostrum. The lack of colostrum at birth also resulted in a dramatic increase of gut permeability and a decreased representation of goblet cells. This improper development of gut mucosal immunity resulted in an increased susceptibility to infection by the intestinal helminth parasite, Heligmosomoides polygyrus.

Conclusion: In conclusion, our data highlight that colostrum may be specifically designed to satisfy the needs of the developing newborn and be critical for type 2 immunity in early post-natal life.

1157 | The effect of IL-25 and IL-33 on the phenotypic and functional characteristics of ILC2s in patients with allergic rhinitis and donors

Pashkina E. A.; Makeeva A. O.; Shevchenko Y. A.; Tereschenko V. P.; Kozlov V. A.
Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia

Background: Group 2 innate lymphoid cells (ILC2s) are considered to be the most significant mediators during the orchestration of immune response in allergic diseases including allergic rhinitis. ILC2s consist of two cell populations depending on KLRG1 expression: inflammatory (KLRG1+) and natural (KLRG1-) ILC2 cells. These subsets substantially differ in their response to stimuli and range of cytokine production . Herein, we evaluate differences in phenotypic and functional characteristics of distinct ILC2s subsets.

Method: PBMCs were extracted from heparinized blood samples of patients with allergic rhinitis (n = 9) and healthy donors (n = 4) using standard technique. At the time of blood sampling all patients had remission of seasonal allergic rhinitis and were asymptomatic. Cells were used for cell culture and cultured for 72 hours in RPMI-1640 medium with 10% FCS in air with 5 % CO2 at 37°C and 95% humidity in presence or absence of IL-25 (50 ng/ml) and IL-33 (50 ng/ml). Then cells were fixed, stained and subjected to flow cytometry. ILC2s were identified as a Lin-CD127+CRTH2+ cell population. We also investigated expression of surface markers (PD-1, PD-L1, KLRG1) and intracellular cytokines (IL-4, IL-5) on ILC2 cells after cultivation. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Local Ethical Committee of Research Institute of Fundamental and Clinical Immunology.

Results: There weren't any significant differences in phenotypical and functional characteristics of ILC2s cultivated in absence of alarmins (IL-25, IL-33) between patients with allergic rhinitis and healthy donors. Amount of PD1+nILC2 cells and PD-L1+nILC2 cells significantly increased in presence of IL-25 and IL-33 in both groups. Interestingly, patient group had poor response to alarmins comparing

with healthy donors. Moreover, cultivating ILC2s with IL-33 resulted in increase of IL-4+ILC2s in donors , but not in patient group.

Conclusion: With the present study we observe that IL-25 and IL-33 affect to a lesser extent functional and phenotypical characteristics of ILC2s in patient with allergic rhinitis in comparison with healthy donors.

The reported study was funded by RFBR and Novosibirsk Oblast according to the research project no. 19-415-543004

1145 | Bone marrow-derived dendritic cells from muc2-/- mice have increased expression of DC-SIGN

Blinova E. A.[1,2]; Galdina V. A.[3]; Feofanova N. A.[1,2]; Barkovskaya M. S.[1,2]; Litvinova E. A.[2]

[1]Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia; [2]Scientific Research Institute of Neurosciences and Medicine, Novosibirsk, Russia; [3]Novosibirsk State University, Novosibirsk, Russia

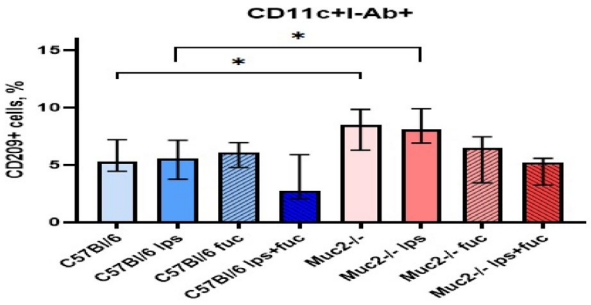
Background: Mucin 2-deficient mice - a model of inflammatory bowel disease. Bacterial contact with the intestinal epithelium resulted to inflammation and the elevation of colon macrophages and $CD103^{+}11b^{+}$ dendritic cells (DCs). One of the surface marker of DCs is DC-SIGN (CD209), which have adhesive, Ag-recognition properties, and can modulate immune responses. Induction of tolerance by immature DCs, recognized glycosylated self-antigens, may be the physiological function of DC-SIGN. The aim of this study was to investigate the proportion of $CD209^{+}$ DCs, generated in vitro from bone marrow of Muc2-/- mice.

Method: The experimental animals were C57BL/6 mice (n = 5) and Muc2-/- mice (n = 5), female, 8-12 weeks old, purchased from the Scientific Research Institute of Neurosciences and Medicine (Novosibirsk). Muc2-/- mice on the C57BL/6 background were bred as Muc2+/- x Muc2+/- and offspring were genotyped. Suspension of cells from bone marrow (from each mice separate) were cultured in the culture flask (25 cm2, TPP) in the RPMI-1640 (HyClone), supplemented with 10% FCS (Gibco), GM-CSF (20 ng/ml, PeproTech), IL-4 (20 ng/ml, PeproTech), during 7 days. Then cells were plated into 6-well plates for an additional incubation with LPS (2mkg/ml, Sigma) and 0,1% L-fucose for 48h. We used antibodies against CD11c and I-Ab (BioLegend) to phenotype DCs, and CD209 (BioLegend) to evaluate the expression of DC-SIGN by flow cytometer FACS Canto II.

Results: 70-80% of generated cells was $CD11c^{+}I\text{-}Ab^{+}$ DCs. Additional incubation with 0,1% L-fucose didn't affect on DCs phenotype in both C57Bl/6 and Muc2-/- mice. The number of $CD209^{+}$ among immature and mature DCs increased in Muc2-/- line compared to C57Bl/6. Under incubation with 0,1% L-fucose, it was a tendacy to decrease the proportion of $CD209^{+}$ DCs from Muc2-/- mice. Binding of soluble ligand to DC-SIGN induced internalization via clathrin-coated pits, so it is possible explanation for decreasing of $CD209^{+}$ DCs after incubation with fucose. DC-SIGN modulated TLR-induced activation of DCs. Interaction of particular pathogens with DC-SIGN can lead to the inhibition of Th1 response, and immune supression through induction of IL-10.

Conclusion: Altered expression of DC-SIGN on bone marrow-derived DCs from Muc2-/- mice suggested that generated in vitro DCs may have tolerogenic potential, and take a part in the prevention of acute intestinial inflamation in mice model with deffective mucus barrier.

The study is supported by RSF project No 20-64-47020.



1292 | SLAMF7 and CD38 as possible new therapeutic targets on NK cells for systemic lupus erythematosus

Humbel M.; Fluder N.; Horisberger A.; Fenwick C.; Ribi C.; Comte D.

CHUV, Lausanne, Switzerland

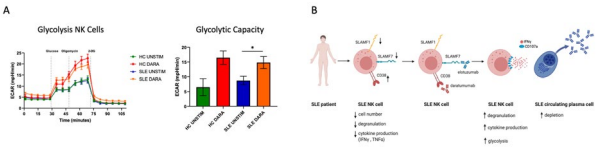
Background: Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology and poorly understood pathophysiology. The disease is currently managed with broad spectrum immunosuppressants, that have severe side effect. Therefore identification of novel therapies is mandatory. Natural killer (NK) cells are decreased in count and have an altered cytotoxic function in SLE. Here, we investigated the functional, phenotypic and immunometabolic alteration of SLE NK cells and how these abnormalities contribute to the production of autoantibodies. In addition, we propose innovative approaches to restore SLE NK cell function.

Method: Phenotype and function of cryopreserved NK cell from 40 SLE patients and 40 healthy controls (HC) matched by sex, age, and ethnicity were analyzed by single cell mass cytometry, flow cytometry and by Seahorse XFe96 Analyzer.

Results: NK cells of SLE patients exhibited impaired cytokine production, degranulation, cellular glycolysis and mitochondrial metabolism. Single cell mass cytometry showed that SLE NK cells displayed increased expression of CD38 and altered upregulation of SLAMF7 following activation compared to HC. Engagement of SLAMF7 and CD38 with monoclonal antibodies (mAb) restored NK function (cytokine production and degranulation) and promoted the killing of circulating plasma cells (cPC) in SLE and HC *in vitro*. Mechanically, we showed that anti-SLAMF7 primarily promotes mitochondrial respiration while anti-CD38 enhances glycolysis in HC NK cells.

Conclusion: SLAMF7 and CD38 are aberrantly expressed or regulated on SLE NK cells and ligation of these receptors with mAb

enhances NK cell function (cytokine production, degranulation), thus promoting the killing of cPC and potentially reducing the production of autoantibodies. Furthermore, using mAb against these receptors promotes mitochondrial metabolism and glycolysis, respectively. Targeting SLAMF7 or CD38 with mAbs could represent future therapeutic targets in patients with SLE.



1213 | Whole exome sequencing analysis detects association between SNP in FCGR2A, ITGAM, PTPN22, VDR genetic systems, and pediatric lupus nephritis in colombian children

Garavito-De Egea G.[1]; Fang L.[1]; De La Cruz-López F. R.[1,2]; Aroca-Martínez G.[2]; Iglesias-Gamarra A.[1,2]; Moreno-Woo S.[1]; López-Lluch G.[3]; Cabarcas F.[4]; Alzate J. F.[4]; Egea E.[1]
[1]*Universidad del Norte, Grupo de investigación de Inmunología y Biología Molecular, División Ciencias de la Salud, Barranquilla, Colombia;* [2]*Universidad Simón Bolívar, División Ciencias de la Salud, Barranquilla, Colombia;* [3]*Centro Andaluz de Biología del desarrollo, Universidad Pablo de Olavide, Sevilla, Spain;* [4]*Centro Nacional de Secuenciación Genómica - CNSG, Sede de Investigación Universitaria - SIU. Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia*

Background: Pediatric Systemic Lupus Erythematosus (pSLE) is an autoimmune disease that mainly affects the kidneys. Pediatric Lupus Nephritis (pLN) is the complication with the highest morbidity and mortality. Single nucleotide polymorphisms (SNPs) in *ITGAM*, *FCGR*, *IRF5*, *TNIP1*, *STAT4*, *TNFSF4*, *APOL1*, *PDGFRA*, *HAS2*, *PTPN22*, *VDR*, and *TNF* genetic systems have been described and associated with susceptibility to the development of pLN. The aim of this study was analyze the whole exome of 6 Colombian children with pLN not related familiarly and identify SNPs in *ITGAM*, *FCGR*, *IRF5*, *TNIP1*, *STAT4*, *TNFSF4*, *APOL1*, *PDGFRA*, *HAS2*, *PTPN22*, *VDR*, and *TNF* systems associated with pLN.
Method: Six whole exomes (WE) were sequenced by Novogene. This WES belonging to pLN class IV patients were analyzed. Genomic DNA extraction as obtained by Salting Out modified and purified with QIAamp DNA Kits (QIAGEN/R®). The data was analyzed with a pipeline from the National Center for Genomic Sequencing (CNSG) of the Universidad de Antioquia. wANNOVAR tool was used for functional annotation.
Results: Of the 12 genetic systems analyzed, we identified SNPs in *FCGR2A*, *ITGAM*, *PTPN22*, and *VDR*. Genetic variants reported in the literature as rs1143679, rs1801274, and rs2476601 in *ITGAM*, *FCGR2A*, and *PTPN22*; respectively were identified. For *VDR* the SNPs rs2228570 and rs731236 were recognized. These are in agreement with findings found in previous GWAS studies. Prioritization analysis in the four genetic systems suggests the *FRGR2A* gene is a possible candidate for pLN development.
Conclusion: This is the first study of exomes in pediatric patients with pLN in Colombia. Our results raise the need to increase the sample of exome studied and contrast it with exomes from healthy individuals; analysis that could allow obtaining more data to validate those found.

1020 | Effect of cucurbiturils on cytokine production

Pashkina E. A.; Aktanova A. A.; Boeva O. S.; Kozlov V. A.
Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia

Background: Cucurbiturils (CB[n]) are macrocyclic compounds used for drug delivery. Bioactive compounds should fulfill a number of requirements, including biological safety. Since the cells of the immune system are the most sensitive to the damaging effects of various factors, it is important to assess the immunomodulatory effect of cucurbiturils.
Method: Peripheral blood mononuclear cells (PBMCs) were isolated from the blood of healthy donors. PBMCs were cultured in RPMI-1640 medium with 10% FCS in air with 5 % CO2 at 37°C and 95% humidity. Cells were cultivated with cucurbiturils (0.3 mM CB[6], 0.3 mM CB[7], and 0.01 mM CB[8]) in the presence or absence of anti-CD3 antibody (1 μg/mL) for 72 hours. Levels of TNFα, IL-2, IL-4, IL-6, IFNγ and IL-10 in in the culture supernatants of PBMCs was evaluated by using enzyme immunoassay method.
Results: CB[n] had no effect on the production of TNFα, IL-2 and IL-6. Addition of CB[6] increases the level of IL-4 compared to control cells, both for unstimulated and antiCD3-stimulated IL-4 production. CB[7] increased the level of spontaneous IFNγ production and decreased the level of antiCD3-stimulated IFNγ production. Supression of IFNγ and IL-10 was obtained with CB[8], both for the spontaneous and stimulated productions.
This study was funded by the Russian Science Foundation according to research project No. 19-15-00192.
Conclusion: Therefore, the effect of CB[6], CB[7] and CB[8] on cytokine producing activity of PBMCs are different.

1162 | Neurocognitive evaluation of patients with Di George syndrome

Karali Z.; Karali Y.; Cekic S.; Kilic S. S.
Uludag University Faculty of Medicine, Pediatric Allergy and Clinical Immunology, Gorukle, Turkey

Background: We aimed to evaluate the clinical, laboratory, radiological and neuropsychological findings of our patients diagnosed with Di George Syndrome (DGS) in this study.

Method: Patients with DGS between June 2001 and March 2021 were included in the study. Clinical and laboratory data of the patients were evaluated retrospectively from electronic file records. Neuropsychological tests were applied to the patients to evaluate their neurocognitive findings.

Results: Forty six patients (25 boys and 21 girls) were included in the study, 13 of the patients died in the follow-up.

The median age of the patients was 15 years (2 months - 49 years 5 months), and the median age at the time of diagnosis was 2 months (intrauterine-8 years-one month). Thiry-five patients (76%) had heart disease, 21 had hypoparathyroidism, and 14 had epileptic seizures. Autoimmune diseases developed in 13 patients (39%) during follow-up (autoimmune thrombocytopenia in 2, Juvenile idiopathic arthritis in 2 cases and Hashimoto thyroiditis in 9 cases). Two patients had cancer (Non-Hodkin lymphoma and mycosis fungoides).

Bilateral conduction deceleration in the anterior visual pathways in 5 (20%) of 25 patients was determined by the VEP (Visual Evoked Potentials). The auditory brainstem evoked potential test (BAEP) showed sensorineural hearing loss in 4 out of 10 patients. Cranial MRI disclosed developmental brain abnormalities in 10 out of 15 patients.

Impairments were noted in executive functions, visual-spatial functions, expressive language, verbal memory in fourteen patients who were neuropsychologically assessed.

Immunological investigation showed serum IgM level was low in 28 (66.6%) patients and the absolute number of CD3 was <1500/mm^3 in 20 patients.

Conclusion: Awareness of the potential for underlying neurologic disorders is key to anticipatory guidance, optimization of therapies, and maximizing life quality.

1330 | Assessment of the change in immunoglobulin G and M levels in relation to the tacrolimus level in patients attending transplant clinic-ibn sina hospital (2019)

Abdallah S. E.Y.

Sudan Medical Specialization Board, Khartoum, Sudan

Background: Tacrolimus is a commonly used immunosuppressant post kidney transplantation. the trough level is the gold standard test to follow the drug effects. Recently the published data showed a contradiction between the tacrolimus level and the drug effect. With an increase in the drug complication burden. we tried to explore the relationship between Tacrolimus dose and level in relation to Immunoglobulins levels were explored and described.

Method: It was a cross-sectional, centre-based study conducted at Ibn-Sina Hospital. The study included 45 patients out of 73 who had their renal transplantation in Ibn-Sina Hospital in the period from September 2018 – September 2019. Data were obtained and extracted from direct interviews and patient`s records respectively. the immunoglobulin levels were measurement by turbidimetry.

The reference mean of immunoglobulins level was obtained from 25 control patients with end-stage renal disease and candidate for renal transplant. Control was free from infection with male to female ratio of 60% and 40% respectively and an estimated mean age of 45 ± 2.5 the immunoglobulin mean references were 0.87 ± 0.09 for IgM and 14.7 ± 0.84 for IgG

Results: Forty-five kidney transplanted patients with a mean age of 37 ± 11 years were included in the study. Thirty-one (68.9%) males and 14 (31.1%) females. The mean level of Tacrolimus was 8.18 ± 2.71 ng/ml. IgM level mean was 0.88 ± 0.50 g/l, while that of IgG was1.07 ± 0.52 g/l distribution of the immunoglobulin values around the reference range means were shown in (Table 1). The regression test shows a very poor relation between Tacrolimus and IgM levels (Table 2), which expected due to the indirect effect of the drug on B cell via suppression of T cell cytokines and activity. While there is a very weak relationship between the Tacrolimus dose and Igg level the regression statistic define a very poor relationship between the IgG level and the drug level (Table 3).

Conclusion: Tacrolimus is tended to affect more the production of IgG but the study data showed great reduction in IgM level from the references mean of the population with poor relationship to drug level and dose there is a relationship between the increase in Tacarolimus dose and reduction in the IgG level and the study need to be carried on a large number of population to define the correlation. The drug level is not a good predictor for its effect on IgG level.

1135 | Portuguese immunoallergology clinical experience in patients with severe atopic dermatitis under dupilumab treatment

Lopes C.[1,2]; Neto M.[3]; Fernandes R.[1]; Santos N.[4]; Campina S.[5]; Ferreira A.[6]; Ciobanu A.[7]; Almeida E.[7]; Rosmaninho I.[8]; Araújo M.[9]; Leiria Pinto P.[9]; Lopes A.[10]

[1]Immunoallergollogy Unit, Hospital Pedro Hispano, Unidade de Saúde Local, Matosinhos, Portugal; [2]Immunology Department, Faculdade de Medicina da Universidade do Porto, Porto, Portugal; [3]Immunoallergollogy Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal; [4]Immunoallergology Department, Hospital de Portimão, Centro Hospitalar Universitário do Algarve, Portimão, Portugal; [5]Immunoallergology Unit, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal; [6]Immunoallergology Department, Hospital das Forças Armadas, Lisboa, Portugal; [7]Immunoallergology Department, Centro Hospitalar Tondela-Viseu, Viseu, Portugal; [8]Immunoallergology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova De Gaia, Portugal; [9]Immunoallergology Department, Hospital D. Estefânia, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal; [10]Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal

Background: Dupilumab has been recently approved for treatment in patients with severe AD in Portugal - until now there is no published data regarding Portuguese experience in Allergy centers.

Method: Cross sectional clinical and laboratory assessment of 33 patients (pts) with moderate to severe AD treated with dupilumab (dupi) for at least 16 weeks (W): prospective evaluation of severity scores (SCORAD-Scoring Atopic Dermatitis, EASI-Eczema Area and Severity Index, P-VAS-Pruritus Visual Analogic Scale), report of adverse events up to 52 weeks of treatment. SCORAD and EASI were assessed in 23 pts at W52, P-VAS in 21 pts at W52.

Results: Of the 33 pts, 18 were female (55%) with a mean age (SD, range) of 35.3 years (13.2, 15-60). In 16 pts the age of onset was before 2 years old, mean (SD) disease duration 28.1 years (12); 94% patients had a diffuse pattern of skin lesions; 97% of pts had allergic rhinitis, 82% asthma, 52% conjunctivitis and 30% food allergy. Median total IgE at baseline was of 6313 U/ml (P25-P75: 2842-12491) with a 76% reduction at W52 in 16 pts. Median eosinophil count at baseline was 520 eosinophils/mm^3 (P25-P75: 270-740). Before starting dupi 29 pts had been treated with cyclosporine. At the beginning, 15 pts were under oral corticosteroids, 14 under oral systemic immunosuppressive drugs (all pts but two stopped both until W12 of dupi) and 5 switched from omalizumab. At baseline, median SCORAD and EASI were 69.3 and 24.2 points. At W16, W36 and W52, median SCORAD was 27.4, 22.3 and 21.5, and median EASI 5.3, 4.1 and 2.1. At W16, the EASI-50, EASI-75 and EASI-90 were achieved by 91%, 61% and 18% pts, and at W52, by 87%, 70% and 52% pts. The mean percentage of SCORAD reduction at W16 and W52 was 55% and 73%; and of EASI was 76% and 82%. At W16 and W52, an improvement of ≥4 points in P-VAS was achieved by 77% and 95% pts. There was a mean reduction of P-VAS at W2, W4, W16 and W52 of 2.6; 3.6; 4.7 and 6.3 points, respectively. Conjunctivitis was reported in 10 (30%) pts, two of them with keratoconjunctivitis and blepharitis, without needing to interrupt treatment; two pts also had facial erythema. One patient had COVID, and dupilumab scheme treatment was maintained.

Conclusion: The majority of AD patients had a significant and consistent improvement in all the severity scores, after one year of treatment with dupilumab. No relevant adverse events were reported.

1050 | A case of protracted eosinopenia after a single subcutaneous dose of benralizumab

Miranda J.; Plácido J.; Amaral L.
Serviço de Imunoalergologia, Centro Hospitalar Universitário de São João, Porto, Portugal

Benralizumab is a humanized, afucosylated IgG1k monoclonal antibody directed against the α subunit of IL-5R. It inhibits IL-5, the main regulator of the biology of eosinophils, from binding to its specific receptor. Moreover, it directly targets and depletes eosinophils and other IL-5R + cells by inducing antibody-dependent cell-mediated cytotoxicity, differentiating it from the other IL-5 ligand targeted therapies.

We report a case of a 61-year-old woman with severe eosinophilic asthma and rhinosinusitis, referred to our department in 2014. Blood eosinophilia (560 cells/μL) and normal total IgE levels (57 kU/L) were present. She was on GINA step-5 treatment with additional aminophylline 225mg twice daily. Control was not achieved despite good compliance with frequent asthma exacerbations requiring emergency department visits, multiple systemic corticosteroid courses and hospitalizations.

Maintenance therapy with prednisolone 5mg daily was attempted with only a slight improvement. Although no more hospitalizations were required, she continued to have several asthma exacerbations. Treatment with subcutaneous Benralizumab 30mg was started in October 2020. The subsequent administration was skipped because the patient had COVID-19. An interval of approximately 3 months (82 days) separated the first 2 administrations. Regardless of our recommendation, the patient decided to discontinue systemic corticosteroids and aminophiline. Evaluation before the 2nd administration showed that blood eosinophils decreased to 0 cells/μL and clinical improvement that was established by disease control and health-related quality of life questionnaires (see table I)

Although maintained eosinopenia after an isolated intravenous administration of Benralizumab has been reported, to our knowledge this is the first case related to a single subcutaneous administration in a previously eosinophilic patient. Additionally, clinical improvement was sustained in spite of stepping down her maintenance therapy. This case raises questions regarding the possibility and success of patient-oriented scheduling of Benralizumab administration as an alternative to the current treatment regimen.

Questionnaire	1st evaluation	2nd evaluation
CARAT	10 (4 + 6)	20 (4 + 16)
ACT	12	22
EQ5D	21222 – 65%	11111 – 85%

CARAT, Control of Allergic Rhinitis and Asthma Test; ACT, Asthma Control Test; EQ5D, EuroQol-5D; 1st evaluation, before 1stBenralizumab administration; 2nd evaluation, before 2ndBenralizumab administration.

1080 | Potential cancer risk with omalizumab: a disproportionality analysis of the WHO's vigibase pharmacovigilance database

Mota D.[1]; Rama T. A.[1,2]; Severo M.[3]; Moreira A.[1,2,3]
[1]*Serviço de Imunoalergologia, Centro Hospitalar Universitário de São João, Porto, Portugal;* [2]*Serviço de Imunologia Básica e Clínica, Faculdade de Medicina da Universidade do Porto, Porto, Portugal;* [3]*EpiUnit, Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal*

Background: Immunoglobulin E (IgE) may play a key role in cancer immune surveillance and very low or absent IgE levels have been associated with malignancy. Studies have failed to show that omalizumab induces the development or progression of malignancy.

This study aims to define an association between cancer and omalizumab in a wide pharmacovigilance database.

Method: Disproportionality analysis (case/non-case study) within VigiBase, the global database of individual case safety reports of the World Health Organization, to identify a signal of cancer, expressed as the reporting odds-ratio [ROR] and its 95% confidence interval [CI] for omalizumab. Cases were defined as Adverse Drug Reactions (ADR) coded as Neoplasms according to the Medical Dictionary for Regulatory Activities terminology reported between 2000 and 2020. Non-cases were defined as all other ADRs during the same period.

Results: A total of 1380 reports mentioned neoplasms associated with omalizumab. The disproportionality signal was significant and positive: ROR [95%CI] = 1.65 [1.56 to 1.74]. This association was particularly strong in breast cancer, with 232 cases and 4.12 [3.61-4.69], and in lung cancer with 85 cases and 3.04 [2.45-3.76] (Table 1).

Conclusion: Omalizumab may be associated with a significantly higher risk of malignancies, as shown by a ROR of 1.65, using real-world data mining. However, these results should be interpreted with caution, since signal detection does not allow true risk quantification. Still and until further studies confirm the long-term safety of omalizumab, a benefit-risk assessment should be performed before considering it for the treatment of allergic diseases.

TABLE 1 Disproportionality analysis (reporting odds ratio [ROR] and its 95% confidence interval [CI]) of selected cancers and total neoplasms for omalizumab in VigiBase for the period between 2000 and 2020.

Neoplasm	Cases associated with Omalizumab, *n*	Total cases, *n*	ROR	95% CI
Breast cancer	232	34449	4.12	3.61–4.69
Lung cancer	85	17012	3.04	2.45–3.76
Prostate cancer	57	13625	2.54	1.96–3.30
Colon cancer	46	7595	3.68	2.76–4.92
Malignant melanoma	45	8258	3.31	2.47–4.44
Thyroid cancer	22	3841	3.48	2.29–5.30
Leukemia	21	4604	2.77	1.80–4.25
Neoplasms (total)	1380	515120	1.65	1.56–1.74

1110 | Potential sex differences in human milk leptin and their association with asthma and wheeze phenotypes: Results of the ulm birth cohorts

Siziba L. P.[1]; Brenner H.[2]; Amitay E. L.[2]; Koenig W.[3]; Rothenbacher D.[3]; Genuneit J.[1,3]

[1]*Pediatric Epidemiology, Department of Pediatrics, Medical Faculty, Leipzig University, Leipzig, Germany*; [2]*Division of Clinical Epidemiology and Aging Research, German Cancer Research Centre (DKFZ), Heidelberg, Germany*; [3]*Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany*

Background: The hormone leptin is suggested to play an important role in the immune system and inflammation. Evidence on sex-specific concentrations of leptin in human milk and sex-specific associations with the development of asthma and wheeze has been put forward but is still scarce. The objective of this study was to investigate whether male and female infants receive different levels of leptin through human milk and whether leptin is associated with the development of asthma and wheeze in a sex-dependent manner using data from the two Ulm birth cohort studies.

Method: Human milk samples collected at 6 weeks [Ulm Birth Cohort Study (UBCS, *n* = 678; Ulm SPATZ Health Study, *n* = 587)], and, in SPATZ only, at 6 months (*n* = 377) and 12 months (*n* = 66) were analysed. Crude and adjusted logistic regression models were used to investigate sex-specific associations.

Results: At 6 weeks, human milk leptin concentrations (median [min, max], in ng/l) were higher in the milk for girls (197 [0.100, 4120]) than in milk for boys (159 [1.02, 3280], $p = 0.045$) in UBCS. There were no statistically significant sex differences in SPATZ ($p = 0.152$). No statistically significant sex-specific associations of leptin with asthma or wheeze were observed in both studies ($p>0.05$).

Conclusion: It is suggested that male and female infants receive different amounts of leptin through human milk. However, these results suggest that human milk leptin may not be associated with asthma and wheeze in a sex-specific manner.

1092 | Is it possible to complete treatment with omalizumab in patients with chronic urticaria? real life experience in Ecuador

Cherrez-Ojeda I.[1,2]; Robles-Velasco K.[2]; Osorio M. F.[2]; Tinoco I.[3]; Muñoz N.[4]; Cherrez A.[5,2]; Cherrez S.[6,2]

[1]*Universidad Espíritu Santo, Samborondón, Ecuador*; [2]*Respiralab Research Group, Guayaquil, Ecuador*; [3]*Centro de Investigaciones Alérgicas del Sur, El Oro, Ecuador*; [4]*Centro de Asma y Alergias Instituto Pediátrico Muñoz, Riobamba, Ecuador*; [5]*Clinic and Policlinic for Dermatology and Venereology, University Medical Center Rostock, Rostock, Germany*; [6]*Department of Dermatology, SRH, Zentralklinikum Suhl, Germany*

Background: The purpose of the study is to describe the real experience of using omalizumab at a dose of 150 mg in chronic spontaneous urticaria (CSU). CSU is a skin disorder characterized by hives and/or angioedema for at least 6 weeks. In severe refractory

patients, the application of OMA 300 mg every 4 weeks is recommended. In Ecuador, the cost per vial is $ 400, being a limitation to continue treatment.

Method: This is a retrospective observational study about the experience of using OMA in CSU according to the EAACI/GA2LEN/EDF/WAO guideline and at least one application of omalizumab of 150 mg dividing into two groups (pre- and post- application of OMA) and CSU clinical improvement, using patient-reported outcomes (UAS7, UCT and CU-Q2oL). The primary endpoint analyzed was total response, defined as an Urticaria Activity Score summed over 7 days (UAS7) ≤6 and/or Urticaria Control Test (UCT) ≥12 at any point during the treatment. For quality of life improvement response, a change in the minimal clinical important difference (MCID) of 15 points in the total CU-Q2oL score from the baseline measurement was considered meaningful.

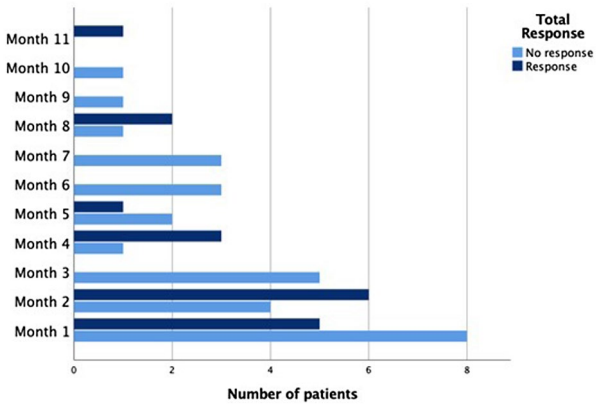
Results: A total of 13 patients were included, the mean age was 37.63 ± 12.16 and 84.61% were female. The mean treatment duration was 3.62 ± 3.25 months and 61% of participants abandoned the treatment after the third month. UAS7, UCT and CU-Q2oL total response distribution post application of 150 mg of OMA was statistically significant compared to pre-OMA (Figure and Table 1). Although the use of medication was reduced, the values were not significant.

Conclusion: Despite using a low dose, omalizumab allowed a better quality of life, response to treatment, and control of CSU at the end of follow-up. However, its use must be individualized because the high cost of this agent prevents patients from completing at least 3 months of treatment, as happened in our experience. Therefore it is concluded that future research is needed where it can be established whether a low dose of omalizumab (150 mg) could be an option in low/middle income countries.

TABLE 1 Comparison of the patient-reported outcomes before and after application of omalizumab at a dose of 150 mg

	Pre-omalizumab Mean ± SD *N* (%)	Post-omalizumab Mean ± SD *N* (%)	*p* value
CU-Q2oL	40.42 ± 17.53	21.33 ± 17.26	0.009**
UCT	5.64 ± 3.88	10.18 ± 3.60	0.006**
No control	11 (84.6)	5 (38.5)*	
Control	1 (7.7)	6 (46.2)	0.016**
UAS7	24.75 ± 9.41	14.42 ± 10.96	0.019**
No activity	0	2 (15.4)	
Well controlled	1 (7.7)	3 (23.1)	
Mild	1 (7.7)	2 (15.4)	
Moderate	6 (46.2)	4 (30.8)	0.306
Severe	5 (38.5)	2 (15.4)	
Treatment			
Antihistamine			
FG	1 (7.7)	0	
SG	5 (38.5)	3 (23.1)	0.264
Corticosteroids	3 (23.1)	1 (7.7)	
Autologous serum therapy	0	2 (15.38)	

*1 patient did not complete UCT; ** *p* value statistically significant; Urticaria Activity Score summed over 7 days (UAS7), Urticaria Control Test (UCT), Chronic Urticaria Quality of Life (CU-Q2oL), First Generation antihistamine (FG), Second Generation antihistamine (SG).



1003 | Terrific improvement of refractory atopic dermatitis with benralizumab (anti-IL5 receptor) therapy

Lanciarotta A.[1]; Favero E.[2]; Agostini C.[1]
[1]*Allergology and Clinical Immunology Unit, Internal Medicine, Ca' Foncello Hospital, University of Padua, Treviso-Padua, Italy;*
[2]*Allergology and Clinical Immunology Unit, Ca' Foncello Hospital, Treviso, Italy*

In 2012 a 25-year-old man presented to our outpatient clinic for severe atopic dermatitis (AD) and severe allergic eosinophilic asthma in polisensitivity (house dust mite, cat, gramineous plants, birch, milk protein and, in particular, Alternaria).

His clinical history was also characterized by gastro-esophageal reflux disease and chronic rhinitis without polyposis, with septal deviation and turbinate hypertrophy, worthy of surgical intervention.

History taking revealed egg and cow milk protein allergy and severe asthma since the first months of life, with frequent hospital admissions due to exacerbations.

AD was severe and diffuse, involving especially face, neck, back and superior limbs, often complicated by impetigo. The esthetic, social and psychological impact led him to quit his job as a barman.

At presentation, the Eczema Area and Severity Index (EASI) score was 72/72.

Laboratory tests showed eosinophilic count ranging between 1.060 and 2.140/mm3, and high serum levels of total Immunoglobulin E (5.939 kUI/L). Tryptase levels were normal and autoantibody analysis was negative.

Parasite stool examination was negative. Nasal swab tested positive for Staphylococcus aureus, which was treated with Sulfamethoxazole-Trimethoprim.

Asthma Control Test was 15/25, pulmonary function tests (PFTs) showed mild obstruction (FEV1 4.43 L, 103%, FEV1/FVC 69%), with positive bronchodilator testing (FEV1 5.12 L, + 670 mL, + 16%).

Firstly, he was treated with topical steroids and sometimes with oral corticosteroids, with poor response. Then, in July 2019, he initiated therapy with cyclosporine 3-5 mg/kg. Soon, the drug had to be discontinued due to adverse effects (gastrointestinal symptoms and infections).

In November 2019, at the age of 32 years, he started therapy with monoclonal antibody anti-IL-5 receptor alpha (benralizumab 30 mg 1 subcutaneous vial every 4 weeks for the first three administrations and then every 8 weeks), with a terrific clinical improvement of AD since the first administrations and with benefit on asthma control (ACT after the first administration increased up to 25/25; PFTs could not be performed, due to SARS-CoV-2 pandemic). This therapy has always been well tolerated.

The eosinophilic count decreased to 0/mm3 after the first administration.

At the moment, after one year of therapy, AD is almost fully disappeared (EASI SCORE 4/72), despite being in free diet, and the quality of life of the patient has definitely improved.

982 | Inflammatory markers in patients with different vitamin D status having allergic airway diseases

Tamasauskiene L.; Gintauskiene V.M.; Sitkauskiene B.

Lithuanian University of Health Sciences, Kaunas, Lithuania

Background: Prevalence of allergic rhinitis and allergic asthma is growing in the world. The etiology and pathogenesis of these diseases are not fully investigated yet. One of the theories is that lack of vitamin D can be associated with higher risk and poorer outcomes of allergic airway diseases. Experimental studies show that vitamin D increases interleukin (IL) 10 and reduces proinflammatory cytokine production. The aim of this study was to investigate inflammatory markers in patients with different vitamin D status having allergic airway diseases.

Method: Patients with persistent allergic rhinitis (diagnosed according to ARIA) with or without allergic asthma (diagnosed according to GINA) were involved into the study. Nasal smear and peripheral blood test for eosinophil detection were performed. 25(OH)D and total immunoglobulin (Ig) E in serum were investigated. Measurements of IL-22, IL-13 and IL-10 in serum and nasal lavage was performed by ELISA. Patients were divided into groups according to 25(OH)D level: <50 nmol/l, 50-75 and ≥75 nmol/l.

Results: Forty-two patients with allergic rhinitis only and 21 with allergic rhinitis and asthma were involved into the study. The mean level of vitamin D was 51.33 ± 23.00 nmol/l in patients with allergic rhinitis only and 45.85 ± 22.70 nmol/l in patients with allergic rhinitis and asthma. Only 8 patients had serum 25(OH)D level ≥75 nmol/l. These patients had significantly lower eosinophil count in nasal smear when comparing to patients with vitamin D level 50-75 and <50 nmol/l (0.00 ± 0.00% vs. 14.85 ± 24.19% vs.14.03 ± 21.80%, $p < 0.05$). IL-10 level in nasal lavage was statistically significantly higher in patients with serum vitamin D level ≥75 nmol/l in comparison to patients with vitamin D level <75 nmol/l (1.67 ± 0.82 pg/ml vs. 1.04 ± 0.75 pg/ml, $p < 0.05$). Moreover, IL-10 in nasal lavage was significantly higher in patients with allergic rhinitis only who had serum vitamin D level >75 nmol/l compared to those with serum vitamin D level 50-75 nmol/l (1.47 ± 0.71 pg/ml vs. 0.66 ± 0.60 pg/ml, $p < 0.05$). Levels of total IgE, blood eosinophil, IL-22 and IL-13 did not significantly differ between studied groups.

Conclusion: Our study argues that vitamin D plays an important role in the regulation of immune response in allergic airway diseases, because higher levels of serum vitamin D, especially ≥75 nmol/l, are associated with decrease of inflammatory cells and increase of anti-inflammatory cytokines in nasal secretion.

1234 | Combined prenatal lactobacillus reuteri and ω-3 supplementation synergistically modulates DNA methylation in neonatal T helper cells

Huoman J.[1]; Martínez-Enguita D.[2]; Olsson E.[2]; Ernerudh J.[3]; Nilsson L. J.[4]; Duchén K.[4]; Gustafsson M.[2]; Jenmalm M. C.[1]

[1]Division of Inflammation and Infection, Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden; [2]Department of Physics, Chemistry and Biology, Linköping University, Linköping, Sweden; [3]Department of Clinical Immunology and Transfusion Medicine, Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden; [4]Allergy Center, Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

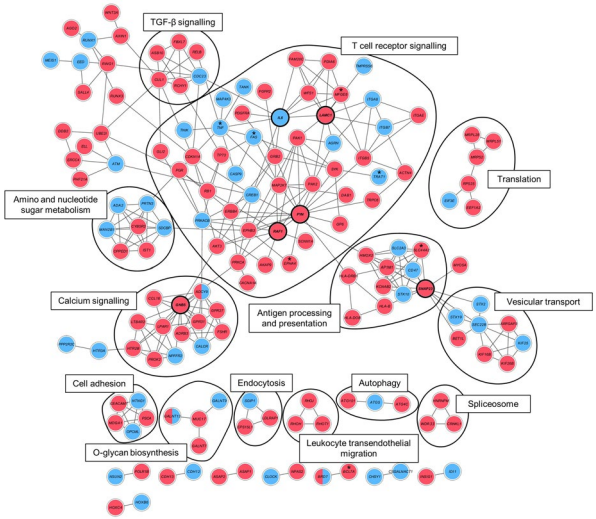
Background: Environmental exposures may alter T helper cell DNA methylation patterning. As T helper cells are instrumental for allergy development, changes in methylation patterns may constitute a mechanism for allergy preventive interventions. While epigenetic

effects of separate perinatal probiotic or ω-3 fatty acid supplementation have been studied previously, combined treatment has not been assessed.

Method: We investigated epigenome-wide DNA methylation patterns in cord blood samples from children in a randomised double-blind placebo-controlled allergy prevention trial using pre- and postnatal combined *Lactobacillus reuteri* and ω-3 fatty acid treatment. To this end, >866 000 CpG sites in cord blood CD4+ T cells were examined in samples from all four study arms (double-treatment: n = 18, single treatments: probiotics n = 16, ω-3 n = 15, and double-placebo: n = 14). Statistical and bioinformatic analyses identified treatment-associated differentially methylated CpGs and genes, which were used to identify treatment-induced network modules. Pathway analyses inferred biological relevance, and comparisons were made to an independent allergy data set.

Results: Comparing active treatments to the double-placebo group, most differentially methylated CpGs were hypermethylated, suggesting induction of transcriptional inhibition. The double-treated group showed the largest number of differentially methylated CpGs, of which many were unique, suggesting synergy between interventions. Clusters within the double-treated network module consisted of immune-related pathways, incl. T cell receptor signalling, and antigen presentation, with similar pathways revealed for the single-treatment modules. CpGs derived from differential methylation and network module analyses were enriched in an independent allergy data set, particularly in the double-treatment group, proposing treatment-induced DNA methylation changes as relevant for allergy development.

Conclusion: Prenatal *L. reuteri* and/or ω-3 fatty acid treatment results in hypermethylation and affects immune- and allergy-related pathways in neonatal T helper cells, with potentially synergistic effects and relevance for allergic disease. Further studies need to address these findings on a transcriptional level, and whether the results associate to allergy development in the children. Understanding how DNA methylation regulates effects of perinatal probiotic and ω-3 interventions may provide essential knowledge in the development of efficacious allergy preventive strategies.



1279 | Atypical memory B cells defined by CD21^{-}CD27^{-} as a biomarker of clinical disease activity in patients with systemic lupus erythematosus

Horisberger A.; Humbel M.; Fluder N.; Fenwick C.; Ribi C.; Comte D.

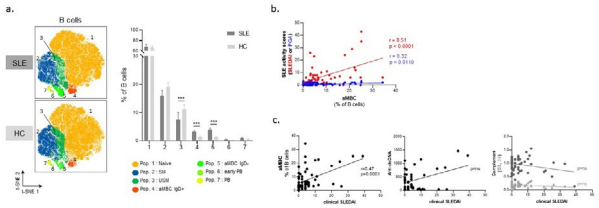
Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background: Systemic lupus erythematosus (SLE) is a protean, chronic autoimmune disease characterized by periods of remission and flares. Determining disease activity in SLE remains a challenge given the heterogeneity and multisystemic nature of the disease. The lack of reliable, non-invasive and broadly available biomarkers is an important limitation. The altered distribution of B cells in the peripheral blood of patients with SLE represents great potential for assessing disease activity, but previous studies are limited by inconsistent classifications and definitions of B subsets. Here, we performed a systematic study of peripheral B cells in 93 SLE patients to identify accurate biomarker of disease activity.

Method: B cells were studied in two separate cohorts of patients included in the Swiss SLE Cohort Study. In cohort A, cryopreserved PBMCs from 30 SLE patients and 30 age-, sex- and ethnicity-matched healthy controls (HC) were analyzed by mass cytometry (CyTOF). In cohort B, fresh blood from 63 other SLE patients, 14 Sjoegren's patients (pSS), 14 Sarcoidosis patients (Sarc) and 39 age-matched HC were analyzed by flow cytometry.

Results: In cohort A, using an unbiased exploratory approach with mass cytometry, we identified 7 subsets of B cells which were further confirmed by manual gating. Two of these B subsets, both lacking the expression of CD21 and CD27, exhibited a similar phenotype than the atypical memory B cells (aMBC) : CD11c^{hi}, CXCR3^{+}, CXCR5^{-}. These aMBC were significantly increased in SLE patients compared to HC (Figure 1a). We confirmed the increase in aMBC in SLE patients from cohort B, compared to HC, pSS and Sarc. In both cohorts, aMBC were positively correlated with disease activity using two separate validated scales (results from cohort B are shown in Figure 1b). Compared to anti-dsDNA and complement, aMBC frequency showed better correlation with SLE disease activity (results from cohort B are shown in Figure 1c).

Conclusion: aMBC were significantly increased in SLE patients and the increase was strongly correlated with disease activity. aMBC frequency may be a useful biomarker for the assessment of disease activity. Longitudinal study would be needed to define their correlation with response to treatment and their potential use as a predictive biomarker.



1263 | Asthma-COPD overlap (ACO) patients have altered levels in three plasma chemokines (CXCL1, CXCL9 and MCP-3) and the cleaved glycoprotein CDCP1

Escamilla Gil J. M.[1]; Espinoza H.[2]; Regino R.[1]; Ramirez J.[1]; Zelaya B.[1]; Florez De Arco L.[3]; Dennis R.[4]; González-García M.[5]; Torres-Duque C.[5]; Caraballo L.[1]; Acevedo N.[1]

[1]*Institute for Immunological Research, University of Cartagena, Cartagena, Colombia;* [2]*Faculty of Engineering, University of Cartagena, Cartagena, Colombia;* [3]*Clínica Respiratoria y de Alergias, Cartagena, Colombia;* [4]*Fundación Cardioinfantil, Bogota, Colombia;* [5]*Fundación Neumológica Colombiana, Bogota, Colombia*

Background: It is estimated that one in five individuals with asthma or chronic obstructive pulmonary disease (COPD) has Asthma-COPD overlap (ACO). These patients have more exacerbations and worse prognosis. Diagnosing ACO is a challenge and there is great interest in identifying its biomarkers. Here, we compared biomarkers levels among patients with asthma, COPD, ACO and healthy controls (HC) to identify those associated with ACO.

Method: We analyzed 397 adult participants (age 40-90 years) recruited in two Colombian cities (Cartagena and Bogotá): 123 with asthma, 100 with COPD, 74 with ACO and 100 HC. Eosinophil counts were analyzed by hemocytometry. Total and specific IgE levels (d1, d201, p1) were determined by ImmunoCAP. Periostin was measured by quantitative ELISA (Periostin/OSF-2 DuoSet ELISA, R&D). Fractional Exhaled Nitric Oxide (FeNO) was measured by NOBreath (Bedfont Scientific); 67 plasma protein levels were measured by Proximity Extension Assay (Olink Inflammation Panel). Statistical analyses were performed in SPSS and R. A p value < 0.05 after correction for multiple testing was considered statistically significant.

Results: There was no difference in eosinophil counts, periostin and FeNO levels in ACO patients compared to asthma or COPD patients. Total IgE and specific IgE levels were increased in ACO compared to COPD albeit the levels were similar to those in asthmatics. In ACO patients, FeNO levels were directly correlated with total IgE levels (rho 0.4, p = 0.007) and with the ACQ-5 score (rho 0.62, p < 0.0001). Ten plasma proteins showed significant differences between ACO patients and HC (p < 0.05, fold change >0.2). In addition, levels of CXCL1 and CXCL9 were increased in ACO compared to asthma. Levels of monocyte chemotactic protein 3 (MCP-3) and CUB domain-containing protein 1 (CDCP1) were increased in COPD compared to ACO and asthma. Of these, MCP-3 was also increased in ACO compared to asthma.

Conclusion: None of the type 2 biomarkers had differences between asthma and ACO, but total and specific IgE measurements could aid in the differentiation of ACO- from COPD especially if combined with other biomarkers and the clinical history. No marker was exclusively altered in ACO but CXCL1, CXCL9, MCP-3 and CDCP1 were associated to this overlap condition.

974 | Successful allergological risk-assessment protocol and SARS-coV-2 vaccination: The experience of a large italian university hospital

Heffler E.[1]; Paoletti G.[1]; Racca F.[1]; Piona A.[2]; Melone G.[1]; Merigo M.[1]; Puggioni F.[1]; Ferri S.[1]; Azzolini E.[3]; Lagioia M.[3]; Lamacchia D.[1]; Cataldo G.[1]; Cecconi M.[4]; Canonica G. W.[1]

[1]*Personalized Medicine, Asthma and Allergy – IRCCS Humanitas Research Hospital, Rozzano (mi), Italy;* [2]*Allergy Service – Humanitas San Pio X Hospital, Milano, Italy;* [3]*Clinical Quality Department - IRCCS Humanitas Research Hospital, Rozzano (mi), Italy;* [4]*Department of Anesthesiology and Intensive Care - IRCCS Humanitas Research Hospital, Rozzano (mi), Italy*

Background: Novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) vaccines have been recently approved, and public concern regarding the risk of anaphylactic reactions arised after few cases during the first days of mass-vaccination. Polyethylene glycol (PEG) has been suggested as the most probable culprit agent for allergic reactions.

We describe the allergy work-up protocol implemented for the vaccination campaign in our Center, aiming to allow the greatest number of people to be vaccinated safely.

Method: The protocol included the self-report of a history of suspected drug or vaccine allergies, and subsequent teleconsultation and allergometric tests for PEG and Polysorbate 80 (PS80). A desensitizing protocol of vaccine administration was applied to patients sensitized only to PS80, and to those with a suspect allergic reaction after the first vaccine dose.

Results: 10.2% (414 out of 4042) of the entire vaccine population have been screened: only one patient resulted allergic to PEG and therefore excluded from the vaccination. Another patient was sensitized to PS80 only and safely vaccinated applying the desensitizing protocol. Seven subjects without a previous history of allergic disease experienced suspect hypersensitivity reactions to the first administered dose: one of them resulted allergic to PEG and was excluded from the second dose, while the others safely completed the vaccination with the desensitizing protocol.

Conclusion: A careful allergological risk-assessment protocol significantly reduces the number of patients who would have avoided SARS-CoV-2 vaccination for their allergies and to effectively identify and manage those rare patients with sensitization to PEGs and/or PS80.

1089 | Immediate adverse events and allergy work-up to a SARS-coV-2 vaccine – A prospective study in a vaccination center of a tertiary hospital

Pasali M.[1]; Papapostolou N.[1]; Vrana M.[1]; Fokoloros C.[1]; Aggelides X.[1]; Taka S.[2]; Makris M.[1]

[1]*Allergy Unit "D. Kalogeromitros", 2nd Dpt. Dermatology and Venereology, National and Kapodistrian University of Athens, "Attikon" University Hospital, Athens, Greece, Athens, Greece;* [2]*Allergy and Clinical Immunology Unit, 2nd Dpt. Pediatrics, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece*

Background: With the launch of COVID-19 vaccination, cases of allergic reactions to tozinameran were soon reported, with excipient polyethylene glycol (PEG) 2000 becoming the principal suspect. We present the immediate reactions recorded in our Vaccination Center, the allergological workup performed and the outcome of the second dose whenever administered.

Method: This is a prospective study among people working in public health care facilities and armed and security forces who received the first dose between 27/12/2020 and 17/01/2021. Reactions with at least one objective sign observed within 6 hours after vaccination were recorded. Allergological investigation was carried out 14-20 days later as follows: 1/ skin prick tests to tozinameran 100%, PEG 6000 (100mg/ml) 10% and 100%, polysorbate 80 (50mg/ml) 10% and 100%, intradermal tests with PEG 6000 up to 1% and polysorbate 80 up to 0.1% both in three consecutive 10-fold dilutions, 2/ serum tryptase (reaction's and basal), 3/ basophil activation test (BAT) to PEG 2000. The same work-up was followed for patients who had received their shot in other vaccination centers but were referred for investigation.

Results: From a total of 1755 immunizations, 14 reactions (0.8%) were recorded in our unit and extra 8 referred reactions were included in the work-up. Median age was 43.5 years (range 28-59) and 72.7% were female. Mean time of onset was 14 min (range 3-40) with a broad duration frame (1-72h). Hypertension and tachycardia were the most prevalent symptoms (86.4% and 77.3% respectively); flushing (63.6%), nausea/eructation or intestinal hyperperistalsis (36.4%), tremor (22.7%) were also recorded. Reaction's serum tryptase was measured in 8/20 patients; elevated compared to baseline was detected only in a 32ys old female treated with IM adrenaline. Skin tests were performed in 17/22 patients, none turned positive. BAT results were positive in 1/5 reactors. Finally, 13/22 already received the second dose, with 10/13 (77%) not reacting at all, while the rest experienced a much milder similar reaction.

Conclusion: Female predominated and a special pattern of reaction with elevated blood pressure/ heart rate along with flushing and/ or increase in gastrointestinal motility, resembling the acute stress response ("fight-or-flight") was observed. PEG does not seem to be the offending "allergic" agent. Polysorbate 80 can be tested before administration of other SARS-CoV-2 vaccine in case of suspended PEG allergy.

Patient	Tryptase		Skin tests		BAT	
	Reaction	Baseline	Performed	Result	Performed	Result
1						
2	2.4	2.5	Y	N	Y	N
3						
4	4.3	4.6	Y	N		
5			Y	N		
6			Y	N		
7	2	3	Y	N		
8			Y	N		
9						
10	5.2	4.16	Y	N		
11	3.9	5.4	Y	N		
12	6.7	5.7				
13						
14	**9.8**	**3.7**	Y	N		
15			Y	N	Y	N
16	9.8	7.3	Y	N	Y	N
17		11.7	Y	N	Y	N
18			**SPT-only**	*	**Y**	**Y**
19		6.7	Y	N		
20			Y	N		
21			Y	N		
22			Y	N		

blank=N/A; Y=yes, N=negative; SPT=skin prick test.

*reaction observed without positivity of tests

Patient	Demographics		Vac. Unit	Onset (min)	Signs & Symptoms					Investigation performed	Second dose	
	Gender	Age (y)			Skin	G/I	C/V	Resp.	Neur./ Other		Performed	Result
1	F	45	ATTIKON	40	F,B		P				Y	N
2	F	48	ATTIKON	13	F,B,I	N,P	P			Y	Y	P
3	F	39	ATTIKON	10		N	P,T		D		Y	N
4	M	54	ATTIKON	5		H	P,T		F,T	Y		
5	F	35	ATTIKON	10	F,B		T			Y	Y	N
6	F	54	ATTIKON	5			P,T			Y	Y	N
7	F	38	ATTIKON	5	F,I		P		T	Y		
8	F	40	ATTIKON	5		E	P,T			Y	Y	N
9	F	59	ATTIKON	10			P		F		Y	N
10	F	44	ATTIKON	20	F,B		P,T		T	Y		
11	F	37	ATTIKON	20	F,I		P,T		T	Y	Y	P
12	M	43	ATTIKON	5		E	P,T				Y	N
13	F	28	ATTIKON	5			T		D		Y	N
14	F	32	ATTIKON	15	F,B	H	P,T			Y		
15	F	47	OTHER	5	F,B & A		T	U	F	Y		
16	M	51	OTHER	30	F,B		P			Y	Y	P
17	F	49	OTHER	3	F,B	N	P,T		F,D	Y		
18	F	46	OTHER	15	F,I		P,T	L & U		Y		
19	M	41	OTHER	15	F		P,T		T	Y		
20	F	56	OTHER	20			P,T		H	Y	Y	P
21	M	42	OTHER	40	F,B		P,T			Y	Y	N
22	F	38	OTHER	15	F,B		P,T	U	F	Y		

Skin: F=flushing, B=burning sensation, I=itch, A=angioedema
G/I: N=nausea, P=epigastric pain, H=hyperperistalsis, E=eructations
C/V: P=high blood pressure, T=tachycardia
Resp.: U=upper respiratory (throat itching or tightness), L=lower respiratory (cough)
Neur./Other: F=faint feeling, D=dizziness, T=tremor, H=headache
Performed: Y=yes – Result: P=positive, N=negative
blank=N/A

1128 | Early efficacy results of montelukast as add on treatment of hospitalized patient with COVID-19 pneumonia: an investigator-initiated open labelled randomized controlled ongoing clinical trial

Tavares M.[1,2,3], Farraia M.[1,3], Silva S.[2,3], Ribeiro A.M.[2,3], Severo M.[1], Paciência I.[1,3], Ribeiro R.[2], Hespanhol V.[1,3], Guimarães J.T.[1,2,3], Almeida J.[2,3], Magro F.[2,3], Sarmento A.[2,3], Oliveira A.M.[2], Moreira A.[1,2,3]

[1]*EPIUnit - Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal;* [2]*Centro Hospitalar Universitário São João EPE, Porto, Portugal;* [3]*Faculdade de Medicina da Universidade do Porto, Porto, Portugal*

Background: Leukotriene receptor antagonists might have a role in viral infections, either by improving lung injury and inflammation, or by acting on 3CL proteinase of the HCoV-19. Thus, we hypothesised that montelukast may be an adjuvant drug in HCoV-19 infection treatment.

This study aims to evaluate the efficacy and safety of montelukast in the adjuvant treatment of COVID-19 pneumonia.

Method: We are conducting a randomized, controlled, parallel, open-label trial involving hospitalized adult patients with confirmed COVID-19. Patients were randomly assigned in a 1:1 ratio to receive either montelukast 10 mg, once a day for 14 days, in addition to standard of care (SoC), or SoC alone. SoC follows the best practice for treating these patients, according to updated recommendations. The primary outcome is time to recovery. Participants are assessed using diary cards to capture data on treatment-related improvements in an 8-point ordinal scale (COVID-19 scale). Secondary endpoints include changes in NEWS (National Early Warning Score), respiratory and inflammatory parameters. Mann-Whitney U test for continuous variables and Ficher's exact test for categorical variables were used to compare differences between groups. This phase IV clinical trial takes place at the University Hospital of São João, Porto. EudraCT number: 2020-001747-21.

Results: Eighteen patients (11 males, mean age 60 years, age range 42–89, table 1) enrolled and completed the trial. The trial is still open for the recruitment of participants. The participants from the active group spent less time hospitalized than control group [median (P25-75): 3.0 (3-6) vs 7.5 (4.75-17.75) days, $p = 0.03$]. The number of days to achieve 7 (not hospitalized, limitation on activities) or 8 points (not hospitalized, no limitations) in the COVID-19 scale was also statistically significant. The number of patients in need of supplemental high flux oxygen and the NEWS score followed the same trend (table 1).

Conclusion: In conclusion, early efficacy results from this ongoing clinical trial suggest montelukast may have a role in treating COVID-19 patients as an adjuvant treatment by diminishing hospitalization days until discharge.

TABLE 1 Characteristics of the included participants and clinical endpoints

Variables	Control group, SoC (*N* = 9)	Active group, Montelukast + SoC (*N* = 9)	*p*-value
Baseline characteristics			
Sex, Male, *N* (%)	4 (44)	7 (78)	0.34
Age, mean (min-max)	63 (42-89)	57 (46-71)	0.56
Smoker, *N* (%)	1 (11)	3 (33)	0.58
Chronic cardiac disease, *N* (%)	3 (33)	1 (11)	0.58
Hypertension, *N* (%)	5 (56)	1 (11)	0.13
Asthma, *N* (%)	1 (11)	0 (0)	1
Excess weight, *N* (%)	1 (11)	5 (56)	0.13
Obesity, *N* (%)	3 (33)	2 (22)	1
Diabetes, *N* (%)	2 (22)	1 (11)	1
NEWS Score (ordinal)	5 (4-9)	4 (4-6)	0.28
COVID-19 Scale (ordinal)	4 (3-4)	4 (4-4)	0.30
Number of days since first symptom(s) until randomization	9.00 (7.00-13.00)	9.00 (8.00-11.50)	0.80
Systolic blood pressure (mmHg)	118 (108-125)	120 (104-140)	0.72

Variables	Control group, SoC (*N* = 9)	Active group, Montelukast + SoC (*N* = 9)	*p*-value
Diastolic blood pressure (mmHg)	72 (63-84)	78 (67-86)	0.65
Temperature (°C)	36 (35-37)	36 (35-37)	0.73
Pulse rate (bpm)	84 (69-97)	76 (68-87)	0.54
Respiratory rate (cpm)	22 (20-32)	22 (19-24)	0.38
Saturation O_2 (%)	93 (93-97)	95 (94-96)	0.26
Clinical endpoints			
Number of days since randomization until hospital discharge	7.50 (4.75-17.75)	3.00 (3.00-6.00)	**0.03**
Number of days until COVID-19 Scale increases to 7 or 8 points	6.50 (3.75-16.00)	3.00 (2.00-5.00)	**0.04**
Number of days until NEWS score decreases to 2 or less points	6.00 (2.25-16.00)	2.00 (2.00-5.00)	0.14
In need of supplemental High Flux Oxygen (any time during study), *N* (%)	4 (44)	1 (11)	0.13

Data were presented as median (25th percentile – 75th percentile) unless otherwise states.

Bpm: beats per minute; cpm: cycles per minute; NEWS: National Early Warning Score); SoC: standard of care.

NEWS is based on 7 clinical parameters (respiration rate, oxygen saturation, any supplemental oxygen, temperature, systolic blood pressure, heart rate, level of consciousness), and is being used as an efficacy measure. Higher points represent higher risk of poor outcomes. COVID-19 scale is as follows: (1) Death; (2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); (3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; (4) Hospitalized, requiring supplemental oxygen; (5) Hospitalized, not requiring supplemental oxygen—requiring ongoing medical care (COVID-19 related or otherwise); (6) Hospitalized, not requiring supplemental oxygen—no longer requires ongoing medical care; (7) Not hospitalized, limitation on activities and/or requiring home oxygen; (8) Not hospitalized, no limitations on activities.

1144 | Biomarkers of cytokine storm in critically ill hospitalized COVID patients

Fodor B.[1,2]; Braun M.[1]; Zemlényi G.[1]; Gilányi I.[1]

[1]*BAZ County's Central Hospital and University Teaching Hospital, Miskolc, Hungary*; [2]*Faculty of Health Care, University of Miskolc, Miskolc, Hungary*

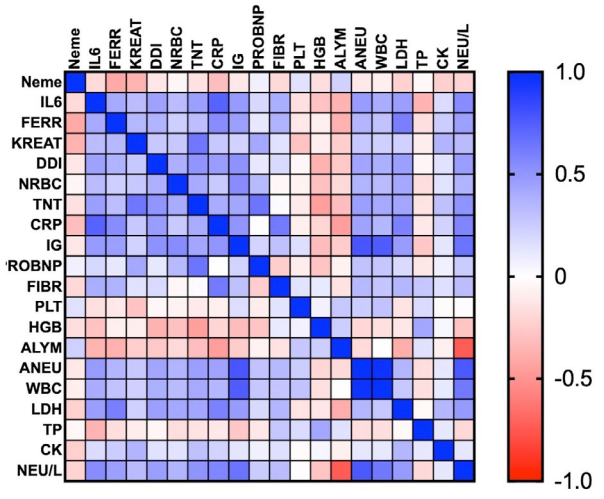
Background: In COVID pandemic - began in 2019 - millions of people became seriously ill or lost their lives. One of a critical, life-threatening complication of this infection is the cytokine storm, which means releasing of large amounts of TNF alpha and other cytokines, producing a severe systemic inflammation. Laboratory analysis of serum IL-6 levels is crucial in predicting and monitoring of cytokine storm. In addition, a number of biomarkers are being routinely investigated in this case. However, their diagnostic applicability and usefulness are not fully known.

Method: In our work, we investigated the development of inflammatory biomarker levels and their correlation with IL6 concentrations in patients hospitalized with COVID infection retrospectively. We compared the levels of these biomarkers in recovered and died patients. Our study included 667 patients with a mean age of 61 years. Serum IL-6 levels was determined by Roche Cobas IL-6 test. The results were compared to the level of ferritin, creatine, D-dimer, Troponin-T, NT-proBNP, CRP, fibrinogen, Hgb, PLT, WBC, ANeu/Aly, IG, NRBC, LDH, CPK, total protein levels. (Table 1.) The statistical analysis was done by Mann-Whitney and Spemann's rank correlation test.

Results: The mean level of IL-6 was significantly higher in patients who died, than in the surviving population (103.2 pg/ml vs. 25.38 pg/ml; p <0.0001). LDH, ferritin, D-dimer, CRP, creatinine, troponin-T, WBC, IG, Aneu/Aly were also significantly elevated (p <0.0001) in died population. In parallel the hemoglobin concentration was significantly lower (114.5 g/l vs. 129.6 g/l), and the NRBC count was higher (0.06 vs. 0.006). We did not find any significant difference in NT-proBNP, fibrinogen, PLT, total protein, and CPK values between the two populations. A very close correlation was observed for several parameters: IL-6 and CRP (r = 0.73; p <0.0001), ferritin and LDH (r = 0.6; p <0.0001), CRP and fibrinogen (r = 0.63; p <0.0001) WBC and IG and Aneu /Aly and so on. (Table 1.)

Conclusion: Our data supports that the levels of most important inflammatory biomarkers correlate well with the level of IL-6 which is the key parameter of cytokine storm. We observed that elevated IL-6 levels may predict a worse outcome of COVID infection.

	Ferritin (D)	Ferritin (A)	Creat (D)	Creat (A)	D-dimer (D)	D-dimer (A)	Trop-T (D)	Trop-T (A)	CRP (D)	CRP (A)	IG (D)	IG (A)	NT-proNP (D)	NT-proBNP (A)	WBC (D)	WBC (A)	LDH (D)	LDH (A)	ANEU/ALY (D)	ANEU/ALY (A)
Number of values	233	367	107	173	202	320	171	179	155	259	203	315	156	76	215	338	217	354	215	338
Minimum	24,92	0,9	40,8	32,3	220	220	3,82	3	1,1	0,2	0,01	0,01	16,43	21,93	1,74	2	186	141	1,543	0,08448
Maximum	35738	60520	1027	947	23400	16000	3069	8083	630,8	430,1	3,27	3,65	70000	70000	53,74	89,82	49820	5826	152,5	54,9
Range	35713	60519	986,4	914,7	23180	15780	3065	8080	629,7	429,9	3,26	3,64	69984	69978	52	87,82	49634	5685	151	54,82
Mean	1956	1042	181,3	89,31	5516	1740	125,8	121,8	157,8	78,28	0,2723	0,09251	10876	6026	14,01	9,458	1557	663	21,24	7,549
Std. Deviation	3591	4185	181,5	88,69	5795	3174	326,9	720,8	106,1	82,19	0,4161	0,2391	17489	12201	7,437	6,715	3963	539,4	19,87	7,797
Std. Error of Mean	235,3	218,5	17,54	6,743	407,8	177,4	25	53,87	8,524	5,107	0,0292	0,01347	1400	1400	0,5072	0,3652	269	28,67	1,355	0,4241



1184 | Pfizer-biontech covid-19 vaccine: suspected allergic reactions to the first dose

Valente C.[1]; Miranda G.[2]; Aguiar A.[2]; Silva P.[2]; Santa C.[1]; Mesquita M.[1]; Presa A.R.[1]; Ferreira C.[1]; Garcia S.[1]; Malheiro D.[1]; Cadinha S.[1]; Cruz L.[1,2]

[1]*Allergy Department, CHVNG/E, Portugal, Porto, Portugal;*

[2]*Occupational Health department, CHVNG/E, Portugal, Porto, Portugal*

Background: The coronavirus disease 2019 (COVID-19) was first identified in December 2019 in Wuhan, China. The WHO declared the outbreak a Public Health Emergency of International Concern in January 2020 and a pandemic in March 2020. Until March 28 2021, more than 125 million cases have been confirmed, with more than 2.7 million deaths attributed to COVID-19. On December 21, 2020, the EMA issued an Emergency Use Authorization for Pfizer-BioNTech COVID-19 vaccine to prevent COVID-19, to be administered in 2 separate doses 21 days apart.

The aim of this study was to identify and describe the suspected allergic reactions to first dose of Pfizer-BioNTech COVID-19 vaccine in health care professionals of our center. We also aimed to know if these reactions interfered with the compliance of vaccination protocol.

Method: All health care professionals that receipt the vaccine were included. A prospective study was carried out using an online questionnaire to access the demographic data, personal allergic history and description of reaction to the vaccine.

Results: In our hospital, the vaccination began on December 29, 2020. A total of 3040 first doses were administered. A total of 2095 (69%) questionnaire responses were collected. It was reported 1649 (79%) adverse events. Among these, 16 (1%) were identified as suggestive allergic reaction. These reactions occurred in professionals, 13 cases (81%) female, with a median age of 41 years (28-52y). The median interval from vaccine administration to symptom onset was 6 hours (5 min-48h). Eight professionals had late cutaneous reactions: 6 had mild reactions and tolerated the second dose; and 2 had severe reactions and it was decided not to administer the vaccine. The other 8 professionals had immediate

reactions: 7 performed allergological study that was negative. The second dose vaccine was administered with vigilance and it was observed cutaneous reaction similar to prior reaction in only one case.

Conclusion: In our study population, only 0.8% (16 of 2095) had a suggestive allergic reaction to first dose of the Pfizer-BioNTech COVID-19 vaccine. Half of them had immediate reactions and only 1 professional had a reproducible episode with the second dose; the other had late reactions and only 2 (0.1%) professionals did not complete the vaccination protocol. We can conclude that this vaccine has a good safety profile. and that mild reactions do not interfere with compliance with vaccination schedule.

1194 | The effect of human anti-SARS-coV-2 convalescent plasma for the treatment of COVID-19

Sematonyte J.[1]; Bajoriuniene I.[1]; Remeikiene D.[2]; Vaguliene N.[3]; Sitkauskiene B.[1]

[1]*Department of Immunology and Allergology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Department of Oncology and Hematology, Lithuanian University of Health Sciences, Kaunas, Lithuania, Kaunas, Lithuania;* [3]*Department of Pulmonology, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Background: Human anti-SARS-CoV-2 convalescent plasma is used for the treatment of patients with coronavirus disease 2019 (COVID-19) who are at risk of severe illness. There is currently a lack of evidence about effectiveness of the human anti-SARS-CoV-2 convalescent plasma in the COVID-19 treatment.

Method: The retrospective analysis was consisted of data from 40 patients (19 men and 21 women; mean age 64.97 ± 15.78) who were treated from COVID-19 in the hospital of the Lithuanian University of Health Sciences, Kaunas, Lithuania. The diagnosis of severe COVID-19 was confirmed by clinical symptoms and positive PCR test of nasopharyngeal swab. The participants treated with standard COVID-19 treatment (antiviral, immunomodulatory and antithrombotic therapy) combined with anti-SARS-CoV-2 convalescent plasma (250–500ml) with anti-spike (S) antibody titers of at least 1:600. Clinical outcomes were compared by 8-point disease severity scale (ranging from 0 [not infected] to 8 [death]), value of saturation (SpO_2), the flow of oxygen therapy (O_2), count of leucocytes (LEU) and lymphocytes (LY), c-reactive protein (CRP), prognostic laboratory markers (lactate dehydrogenase (LDH), ferritin, D-dimer) before and after 7-10 days of convalescent plasma transfusion.

Results: The flow of oxygen therapy decreased and the value of SpO_2 improved significantly after 7-10 days ($p < 0.05$). The count of LY, CRP and prognostic markers differed significantly ($p < 0.05$). The score of disease severity scale did not differ before and after 7-10 days of convalescent plasma transfusion ($p < 0.05$).

Conclusion: Treatment of severe coronavirus disease 2019 by adding convalescent plasma for treatment may remarkably improve clinical outcomes of these subjects.

1205 | Asthma may influence long-term consequences of COVID-19 in hospitalised adult

Bobkova P.[1]; Spiridonova E.[1]; Shihaleva A.[1]; Gamirova A.[1]; Blyuss O.[1,2]; Nekliudov N.[1]; Bugaeva P.[1,3]; Andreeva M.[1]; Dunngalvin A.[1,4]; Comberiati P.[5]; Apfelbacher C.[6]; Genuneit J.[7]; Avdeev S.[8]; Kapustina V.[9]; Guekht A.[10]; Fomin V.[11]; Svistunov A. A.[11]; Timashev P.[12]; Drake T. M.[13]; Hanson S. W.[14]; Merson L.[15]; Horby P.[15]; Sigfrid L.[15]; Scott J. T.[16]; Semple M. G.[17,18]; Warner J. O.[19]; Vos T.[14]; Olliaro P.[15]; Glybochko P.[11]; Butnaru D.[11]; Munblit D.[1,19]

[1]*Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [2]*School of Physics, Astronomy and Mathematics, University of Hertfordshire, College Lane, Hatfield, United Kingdom;* [3]*Julius-Maximilian Universität Würzburg, Würzburg, Germany;* [4]*School of Applied Psychology, University College Cork, Cork, Ireland;* [5]*Department of Clinical and Experimental Medicine, Section of Pediatrics, University of Pisa, Pisa, Italy;* [6]*Institute of Social Medicine and Health Systems Research, Faculty of Medicine, Otto von Guericke University Magdeburg, Magdeburg, Germany;* [7]*Pediatric Epidemiology, Department of Pediatrics, Medical Faculty, Leipzig University, Leipzig, Germany;* [8]*Clinic of Pulmonology, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [9]*Department of Internal Medicine ?1, Institute of Clinical Medicine, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [10]*Research and Clinical Center for Neuropsychiatry, Moscow, Russia;* [11]*Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [12]*Institute for Regenerative Medicine, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [13]*Centre for Medical Informatics, University of Edinburgh, Edinburgh, United Kingdom;* [14]*Institute for Health Metrics and Evaluation, University of Washington, Seattle, United States;* [15]*ISARIC Global Support Centre, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom;* [16]*MRC-University of Glasgow Centre for Virus Research, Glasgow, United Kingdom;* [17]*Health Protection Research Unit in Emerging and Zoonotic Infections, Institute of Infection, Veterinary and Ecological Sciences, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, United Kingdom;* [18]*Department of Respiratory Medicine, Alder Hey Children's Hospital, Liverpool, United Kingdom;* [19]*Inflammation, Repair and Development Section, National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, United Kingdom*

Background: The symptoms of the COVID-19 acute phase are well studied, but the long-term sequelae (post-COVID condition) are still poorly characterised. The aim of this study was to evaluate the prevalence of persistent symptoms in previously hospitalised adult patients with COVID-19 and assess risk factors for the post-COVID condition

Method: Ambidirectional cohort study of patients over 18 years hospitalised to Sechenov University Hospital Network, Moscow, Russia with clinically diagnosed or laboratory-confirmed COVID-19

between April 8 and July 10, 2020. Study participants were interviewed 6-8 months after discharge via telephone using a follow-up case report form (CRF) developed by ISARIC in collaboration with WHO. Identified symptoms were categorised according to organ systems. Risk factors were assessed by multivariate logistic regression.

Results: Among 4,755 patients discharged from the hospitals, 2,649 were subsequently interviewed. The median age of patients was 56 years (46-66), and 1,353 patients (51.1%) were female. The follow-up median time was 217.5 days (200.4-235.5).

1,247 (47.1%) participants reported persistent symptoms (since discharge). The most frequent symptoms were fatigue (21.2%, 551/2599), shortness of breath (14.5%, 378/2614) and forgetfulness (9.1%, 237/2597). Female gender was associated with chronic fatigue with an odds ratio of 1.67 (95% confidence interval 1.39-2.02), neurological 2.03 (1.60-2.58), mental 1.83 (1.41-2.40), respiratory 1.31 (1.06-1.62) and dermatological symptoms 3.26 (2.36-4.57), GI disturbances 2.50 (1.64-3.89) and sensory problems 1.73 (2.06-2.89).

Pre-existing asthma was associated with a higher risk of neurological 1.95 (1.25-2.98) and mood and behavioural changes 2.02 (1.24-3.18).

Conclusion: Six to eight months after COVID-19 nearly half of patients have symptoms lasting since discharge. The main risk factor for the majority of the development of long-term symptoms was female sex. Asthma may also serve as a risk factor for the post-COVID condition. Further follow-up of patients reporting the persistence of COVID-19 symptoms and the development of interventional approaches for the prevention of post-COVID manifestations are needed.

1297 | Low percentages of eosinophils after the 4th dose of mepolizumab may be an independent risk factor for sarscoV-2 transmission in patients with severe asthma

Atayik E.

University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

Background: In the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, patients with severe asthma require particular attention not only due to the underlying airway disease but also in regard to the biological treatments received. Mepolizumab has negative effect on the number and development of eosinophils, and the assertion that eosinopenia is a poor prognostic factor for Coronavirus disease 2019 (COVID19) lead to confusion in the impact of mepolizumab on the course of COVID-19. Therefore, in this study, we aimed to demonstrate potential risk factors for SARS-CoV-2 infection transmission of the patients who were using mepolizumab for treatment of severe asthma and had SARS-CoV-2 infection during their follow-up.

Method: Medical records of 27 adult patients who were being followed-up with a diagnosis of severe asthma and using mepolizumab (Female (F): 17, Male (M): 10) were reviewed and whether they had SARS-CoV-2 infection within 1 year after March 2020 (between March 2020 and March 2021)

Results: After 1 year of follow-up, Sars-Cov-2 PCR (+) was detected in 6 patients. As a result of univariate analysis, eosinophil count and percentage after the 4th dose of mepolizumab treatment were found to be independent predictors of SARS-CoV PCR positivity (p: 0.046 and p: 0. 0.046, respectively). As a result of multivariate analysis, eosinophil percentage after the 4th dose of mepolizumab treatment was found to be an independent predictor of SARSCoV-2 PCR positivity (p: 0.046, Odd ratio: 6488.72, 95% of confidence interval: (1.157- 36389529.84)).

Conclusion: Eosinophil percentages that reduced after mepolizumab treatment were found to be a risk factor for SARS-CoV-2 transmission. However, the need for more extensive studies on the effect of this on the course of the disease is obvious. Clinicians caring for this patient group need to follow-up patients with low eosinophil percentage carefully for SARS-CoV-2 transmission.

969 | Immune paralysis in paediatric patients with multisystem inflammatory syndrome associated with COVID-19

Petrovicova O.; Jesenak M.; Kapustova L.; Banovcin P.

Centre for the primary immunodeficiencies, Department of Paediatrics, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, University Teaching Hospital in Martin, Martin, Slovakia

Background: Paediatric SARS-CoV-2 infection is usually mild and often asymptomatic. **Multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19** is a complication that occurs 4 to 6 weeks after primary infection. Typical symptoms are high fever, organ dysfunction and strongly elevated markers of inflammation. The immunopathology includes **T-lymphocyte paralysis** that is characterised by **severely reduced circulating T-cells** that have **dysregulated activation and differentiation** mechanisms, mainly **$CD4^+$ T-lymphocytes**. Immune paralysis is defined as **increased expression of PD-1 and TIM-3**. The pathogenesis is unclear but has overlapping features with Kawasaki disease suggestive of vasculitis and a likely autoimmune etiology.

Method: We present **3 paediatric patients** (2 males, 1 female) with **MIS-C** aged 11 to 13 years admitted to paediatric intensive care unit in our University teaching hospital in Martin. Immunological parameters were measured after the admission to the hospital and continuously evaluated during the treatment.

Results: In all patients we detected in immunological profile significant signs of **immune paralysis of T-lymphocytes,** both **$CD4^+$** and **$CD8^+$ T-lymphocytes.** One patient had **increased expression of PD-1 and TIM-3**, other two patients had **increased expression of PD-1**. In two patients we detected **depletion of NK cells**. All patients had **lymphopenia** (moderate to severe) and highly elevated inflammatory markers (CRP, IL-6, ferritin) and procoagulant factors (fibrinogen, D-dimers). They were treated according to the protocol with combined immunomodulatory and anti-inflammatory therapies (intravenous

immunoglobulins, corticosteroids, one patient with anakinra) with positive effect on immune profile and also on clinical condition.

Conclusion: Children with MIS-C show various immunological abnormalities including **T-cell reduction and cytokine release syndrome**, which can be fatal. It is poorly understood how T-cell dysregulation can contribute to the pathogenesis, but **hyperactivation of CD4$^+$ T-lymphocytes and immune paralysis** that promote further viral infection can drive pulmonary damage, cardiorenal syndrome and organ failure. Understanding of the immunopathology in MIS-C can help in development of better immune intervention therapies to prevent serious long-term effect of COVID-19 infection also in paediatric patients.

1200 | Multisystem inflammatory syndrome in children (MIS-C) temporarily associated with the new coronavirus infection COVID-2019 and its short- and long-term consequence

Spiridonova E.[1]; Bobkova P.[1]; Krasnaya E.[1]; Kovygina K.[1]; Romanova O.[1]; Zholobova E.[1]; Glazyrina A.[2]; Blyuss O.[1,3]; Munblit D.[1,4]

[1]*Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;* [2]*Morozovskaya Children's City Clinical Hospital, Moscow, Russia;* [3]*School of Physics, Astronomy and Mathematics, University of Hertfordshire, College Lane, Hatfield, United Kingdom;* [4]*Inflammation, Repair and Development Section, National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, United Kingdom*

Background: Children develop severe COVID-19 much less often than adults. However, a small proportion of children present with a complication, known as a multisystem inflammatory syndrome (MIS-C) sometimes associated with admission to an intensive care unit or death. Clinical presentation and consequences of MIS-C are still unclear. The aim of our study is to assess the features of MIS-C and its consequences on a child's health.

Method: An observational longitudinal study of children and adolescents hospitalised from May 17 to October 26, 2020, with MIS-C to Morozovskaya Children's City Clinical Hospital, Moscow Department of Health Care, Moscow, Russia.

Results: 37 children with MIS-C (meeting WHO, CDC, or RCPCH criteria) were hospitalised. The median age was 6 years (interquartile range 3.3-9.9 years), and 22 patients (59.5%) were male. The most common symptoms on admission were fever (97.3%), fatigue (86.5%), scleritis (85%), oral mucosal inflammation (83.8%), rash (70.3%), tachycardia (51.4%), nausea (51.4%), bilateral conjunctivitis (43.2%), cervical lymphadenopathy (43.2%). The most common laboratory abnormalities detected during hospitalization were elevated CRP (100%), ferritin (100%), D-dimer (89.19%), CRP (86.49%), platelets (85.49%), hypoalbuminemia (100%) and anemia (95.59%). EchoCG abnormalities were present in 6 (16.2%) children with evidence of myocardial dysfunction, 5 (13.5%)-pericarditis, and 3 (8.1%) with a coronary anomaly.

The median time from discharge to the first follow-up was 15 days (interquartile range, 14-18 days) to the second follow-up was 47 days (interquartile range, 41-52 days). At the first follow-up, 7/33 (21.21%) children had at least 1 symptom, of whom 5 (15.15%) reported fatigue. At the second follow-up, only 1 child reported a symptom (rash). The normalisation of laboratory values and EchoCG findings was noted in all the children.

Conclusion: In spite of the MIS-C severity, the tendency to fast regression of symptoms and laboratory and instrumental indexes is traced, which suggests recovery of children and adolescents from MIS-C without long-term consequences. Further long-term follow-up of patients with MIS-C is necessary since data on long-term health outcomes are limited.

1238 | Lessons from a big COVID-19 project with focus on diagnosis and hospitalized patients management

Grenfell R. F.Q.

Oswaldo Cruz Foundation - Fiocruz, Belo Horizonte, Brazil

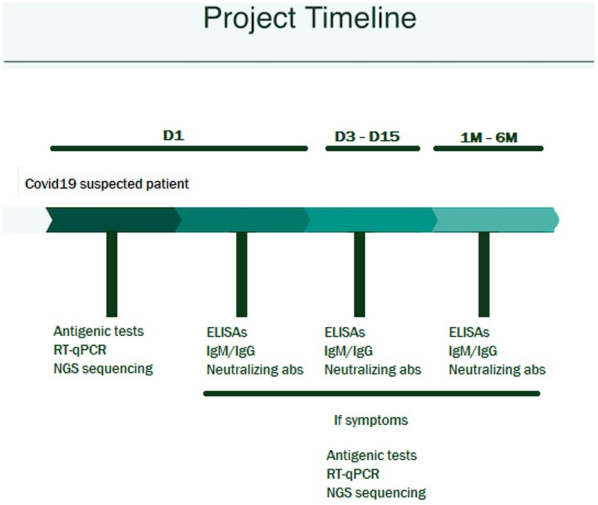
Background: More than a 1000 patients has been monitored by us since the first day of symptomatology and up to 6 months under Hospital da Baleia and Fiocruz cooperation in Brazil.

Method: Patients are monitored on day 1 when samples are collected for molecular and antigenic analysis. With diagnosis, patients are isolated when positive for Covid19. Blood and nasopharynge samples are collected every 3 days from day 1 to 15 of hospitalization and once a month during 6 months after hospital discharge. Blood samples are used for antibodies tests by ELISA, IgM/IgG kits, neutralization kits and neutralization assays in virus culture.

Results: Comparison between the rapid antigen test and RT-qPCR revealed an overall PPV of 97%, extended to 100% when performed between 4 and 15 days of symptoms, with an accuracy of 90-91% from days 1 to 7 and 'Substantial' agreement. Our data support that rapid diagnosis upon patient admission is critical to reduce mortality of Covid19 patients, hospital internal costs and inhospital transmission, especially because the median time to obtain RT-qPCR results has been 83.6 hours, a precious time for deciding on patient isolation and management. ELISA analysis showed that antibodies specific for SARS-CoV-2 S1 portion start to be detected on day 3 of symptoms onset and remain increasing for 30 days. A decrease is observed for the next 10 days when a plateau is established and remains for 6 months. IgM/IgG kits start to identify antibodies after 10 days of symptoms onset in a few patients with a 'moderate' agreement with RT-qPCR. Most of the patients presented detectable antibodies on these kits after 15 days of symptoms revealing 'substantial' agreement with RT-qPCR. Neutralization assays are under evaluation and data will be presented at the conference. Nasopharynge samples are directed to NGS sequencing and, so far, revealed no variants

among our patients, only B.1.1.7 and B.1.351 lineages, although this may change suddenly. Some reinfections cases have been detected. Demographics, baseline comorbidities, symptoms and outcomes are considered and prediction analysis revealed that previous stroke, chronic obstructive pulmonary disease, desaturation and tachypnea were the most relevant determinants of the death of COVID-19 patients.

Conclusion: It is crucial to associate new variants and reinfection cases with molecular and immunological analyzes to understand how the virus is acting on patients in order to control the spread of the disease.



1327 | The first year of COVID-19 outbreak from PID patients' perspectives

Cekic S.; Kose H.; Karali Z.; Kilic S. S.

Uludag University Faculty of Medicine, Pediatric Allergy and Immunology, Bursa, Turkey

Background: We aimed to evaluate the effect of the COVID-19 outbreak in our patients diagnosed with PID.

Method: This is the first year of results investigating the effect of the Covid-19 pandemic on patients with primary immunodeficiency in Turkey.COVID-19 The online questionnaires prepared by us were sent to the patients via e-mail and mobile communication tools. The data obtained from filled the online questionnaire were evaluated.

Results: One hundred fifty-six patients diagnosed with PID participated in the study. The median age of the patients was 15.7 years (0.24-77.2 years), and the female-to-male ratio was 0.6 (60/96). The largest group of patients included in the study was predominantly antibody deficiency (*n* =96, 61.5%). Most of the COVID-19 infected patients were in the PAD group, but when sorted by the number of patients in the subgroups, the highest rate of COVID-19 was in the "Congenital defects of phagocyte number or function" group (12.5%) (Table 1). The general frequency of COVID-19 infection in our PID patients was 15%. The most common symptom in COVID-19 infected patients was fever (*n* = 6, 40%). Symptoms according to their frequency were given in figure 1. Ninety-seven cases (62.2%) thought they had a higher risk for COVID 19 infection. In the COVID-19 pandemic, 78 cases (50%) stated that their economic situation deteriorated and 14 cases (9%) lost their jobs. Complete recovery was achieved in 12 cases and partial in 3 cases.

Conclusion: It has been observed that the COVID-19 pandemic significantly affects both the health and social status of patients diagnosed with PID. New policies should be developed to improve patient's well-being, taking into account the health, social and economic effects.

953 | The impact of the COVID-19 pandemic on antiallergics' prescription trends

Cunha I. M.[1]; Silva T. M.[2]; Herdeiro M. T.[2]; Gomes E.[1]

[1]*Immunoallergology Department, Centro Hospitalar Universitário do Porto, Porto, Portugal;* [2]*iBIMED- Institute of Biomedicine, Department of Medical Sciences, University of Aveiro, Aveiro, Portugal*

Background: During the COVID-19 pandemic, the Portuguese government implemented several stringent measures and all the health care sectors were reorganized.

The goal of this study was to assess the antiallergic prescription tendency in outpatient settings in Portugal, including in public primary health care (PC) and hospital care (HC) centers, and to evaluate potential changes during the COVID-19 pandemic.

Method: The data on antiallergic prescription, in the form of monthly Defined Daily Doses (DDD), prescribed by physicians of the public health sector, were retrieved from the System of Information and Monitoring of the Portuguese National Health System (SIM@SNS) public-access platform, from January 2018 to October 2020. We used the student's t-test with 95% confidence level to compare antiallergics' prescription between the analyzed years.

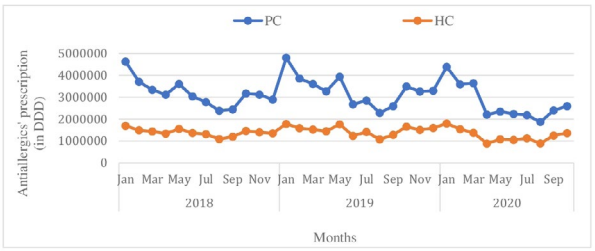
Results: Antiallergics` prescription in outpatient settings of PC/HC (Figure 1) presented a seasonal pattern: with increased peaks being observed throughout autumn and winter and decreased peaks in summer, with the exception of an usual spike occurring in May.

In 2020, the monthly average prescription (PC= 2 747 409 ± 824 538; HC= 1 237 395 ± 289 133) was found to be lower than in 2018 (PC= 3 185 220 ± 605 702; HC =1 392 217 ± 159 337) and 2019 (PC= 3 327 975 ± 688 781; HC=1 489 159 ± 213 014), $p>0.05$ (in PC and HC when comparing with 2018 and 2019).

In 2020, upon COVID-19 emergence, an overall decrease on antiallergics' prescription was observed, being particularly noticeable and statistically significant ($p>0.05$) on PC (p = 0,028) and HC (p = 0,037) centers after May.

Conclusion: A significant decline on antiallergics' prescription was detected in 2020, mainly over the spring/summer months following COVID-19 emergence, probably due to the reduction in all non-essential health care activity, especially in HC. Another interesting outcome is the absence of the usual spike in May 2020**, as** this period

was coincident with the home confinement and routine mask use, which may have reduced patients contact with outdoor allergens.



996 | Venom immunotherapy during COVID-19 pandemic: Experience from a university allergy center in northern Italy

Dell'Edera A.; Borghesan F.; Agostini C.
Internal Medicine, University of Padua, Padua, Italy

Background: During the ongoing pandemic of Coronavirus Disease 2019 (COVID-19) allergic patients need to continue their constant and proper treatment, including allergen-specific immunotherapy. These patients are expected to be at a higher risk for exacerbation of lung inflammation during viral infection. We investigated the putative interplay existing between allergen-specific immunotherapy and COVID-19 infection in Hymenoptera venom-allergic population.
Method: We evaluated the frequency and severity of COVID-19 infection in a cohort of 211 Hymenoptera venom–allergic patients referring to our Center from the end of February till May 20th 2020 for the regular administration of venom immunotherapy (VIT). Each patient completed a form with information regarding symptoms (fever, cough, dyspnoea, sore throat, anosmia and/or ageusia) and eventual close COVID-19 contacts in the previous 14 days.
Results: Our result showed that the median age of our cohort is similar to the one that in our region has been associated with a high incidence of COVID-19 infection, increased hospitalization and mortality rates. We reported only an isolated positivity of COVID-19 in the overall group, whereas none suffered from upper airway symptoms associated with COVID-19 (fever, cough, dyspnoea, sore throat, anosmia and/or ageusia). In our cohort 24 patients were in monotherapy with ACE-i, but none of these patients developed COVID-19 disease. In our cohort the median serum tryptase level at baseline was 8.13 ± 11.49: no correlations were found between tryptase levels and COVID-19 infection.
Conclusion: Even though the demographic characteristics pose a substantial risk for such a population, we suggest that a regular administration of VIT may help to the development of an immunological milieu able to down modulate the Th1/Th17 environment that has been linked to inflammatory manifestations of COVID-19. To the best of our knowledge, this is the first description of the incidence of COVID-19 infection in Hymenoptera venom allergic patients treated with VIT, suggesting indirectly that venom immune tolerance-inducing treatment may be capable of reducing the aberrant inflammatory response induced by the virus in this specific population.
Characteristics of the 211 patients referred to our Allergy center for VIT

Total subjects	*n* = 211
Vespa crabro	16
Polistes	63
Vespula	72
Apis mellifera	44
Polistes and *Vespula*	15
Apis and *Vespa crabro*	1
Average age	64.85 ± 10.05 y
Contact with a positive subject	53 (25%)
ACE-i therapy	24
Median serum tryptase level	8.13 ± 11.49 ug/L
Health care professionals	5

Total subjects of 211 patients referred to our Allergy center for VIT in the aforementioned frame of time, 16 of which are allergic to *Vespa crabro*, 63 to *Polistes*, 72 to *Vespula*, 44 to *Apis mellifera*, 15 to both *Polistes* and *Vespula* and one patient to both *Apis* and *Vespa crabro*. The average age was 64.85 ± 10.05 years. 24 patients are in mono-therapy with angiotensin-converting enzyme inhibitors (ACE-i). 5 subjects work as health care professionals.

1023 | Delayed local reactions to mRNA vaccines against COVID-19

Juárez Guerrero A.; Domínguez Estirado A.; Crespo J.; Rojas Pérez- Ezquerra P.
Gregorio Marañón University General Hospital, Madrid, Spain

Background: Vaccines represent an efficient means to control the pandemic of Coronavirus Disease 2019 (COVID-19). Two mRNA-based emergency vaccines have recently been licensed for mass administration: BNT162b2 and mRNA-1273 COVID-19 vaccine.
Delayed hypersensitivity reactions these new vaccines can range widely from localized skin symptoms to disseminated exanthemas. Locally confined reactions can be caused by the active component or the excipients in the vaccine.
Both mRNA vaccines contain polyethylene glycol (PEG) 2000 lipid conjugate as excipient. PEG and its derivatives with clinical cross-reactivity (polysorbates, laureth-9) are ubiquitous in many drugs. The mRNA-1273 COVID-19 vaccine also contains trometamol, an organic amine used extensively.
Method: We reported a series of 14 patients referred to our Allergy Department with suspected delayed large local reactions (DLLR): erythematous and edematous plaques ≥10 cm in diameter accompanied by pain or pruritus, after the administration of BNT162b2 or mRNA-1273 COVID-19 vaccine between January to February 2021.

We describe cutaneous manifestations,latency time, treatment and duration of the lesions.

We performed patch test in the upper back with PEG 400 1% in petrolatum (pet), PEG 3350 10% pet, PEG 3350 in aqueous solution (aq), PEG 4000 10% pet, polysorbate 80 1% pet, polysorbate 80 10% pet, laureth-9/sodium lauril sulphate 1%, trometamol 0.50% aq (only in mRNA-1273 vaccinated patients), with readings at day 2 and day 4.

Results: We collected 14 patients: 13 received mRNA-1273 and only one BNT162b2 COVID-19 vaccine. Most patients (13/14) reacted to the first dose. 42.9% had detectable serum specific IgG antibodies against SARS-CoV-2 in the last 3 months.

The mean size of DLLR was 11.9 ± 1.6 cm and the latency time was 4.4 ± 1.8 days.

Ten patients (71.4%) not receive any treatment, and four (28.6%) received topical corticosteroids. The mean duration of the reactions was 4.75 ± 2.7 days when treated and 4.5 ± 0.60 days without treatment, with no significant differences (p = 0.79). All patients completed vaccination with the second dose and 69.2% developed DLLR again.

PT were negative in the 100% cases

Conclusion: We didn't found any sensitization to excipients in our 14 cases series. We thought that DLLR may occur due to a non-specific inflammatory response or represent the normal immune response to the vaccination, and in our experience, this should not be a contraindication to receive further doses of mRNA vaccines.

1039 | The safety of mRNA vaccine in patients with common variable immunodeficiency

Milota T.; Smetanova J.; Sediva A.

Motol University Hospital, Prague, Czech Republic

Background: Common variable immunodeficiency (CVID) is a heterogeneous group of disorders characterized by the disturbed production of immunoglobulin and specific antibodies. CVID usually manifests with recurrent bacterial respiratory tract infections, although broad spectrum of non-infectious complications affecting lungs and many other vital organ systems may develop. Therefore, CVID patients may be recognized as a risk group for Covid-19 infection and the vaccination should be considered despite of the terrain of humoral immunodeficiency. However, only limited data are available on the safety of mRNA vaccine in CVID patients

Method: A single-center prospective observational study focused on the safety of mRNA vaccine Comirnaty administration in a cohort of CVID patients. Only patients who had met inclusion and exclusion criteria were enrolled upon signed written informed consent. Total blood count with differential, coagulation, biochemistry and immunologic parameters were assessed before a first dose of the vaccine (Day 0), then at Day 21 (before a second dose) and at Day 51. The study was approved by Motol University Hospital Ethic Committee.

Results: Together 25 CVID patients were included into the study. The most reported adverse events were local pain, fatigue, myalgia, arthralgia or increased body temperature. Neither severe adverse events nor anaphylaxis were reported. No safety concern were also revealed in the evaluated laboratory parameters.

Conclusion: The administration of mRNA vaccine Comirnaty in the terrain of CVID – severely impaired humoral immunity is safe. However, there is an open question of its efficacy, particularly from the point of view of T cell response that plays crucial role in antiviral immunity.

1056 | Anxiety disorder in allergic patients during COVID-19 pandemic

De La Cruz Martínez C. A.[1]; Suárez Lorenzo I.[1]; Castaño Santos A.[2]; Pena Pérez X.[3]; González Núñez V.[1]; Valero Santiago A.[1]; Rueda García M.[1]

[1]*Allergy Department, Hospital Quironsalud Barcelona, Barcelona, Spain;* [2]*Faculty of Psychology, Universitat de Barcelona, Barcelona, Spain;* [3]*Internal Medicine Department, Hospital Germans Trias I Pujols, Barcelona, Spain*

Background: Since the beginning of the spread of COVID-19, a lot of studies have been published describing the disease, its impact on other medical conditions, and the psychological consequences derived from the state of alarm and the confinement. However, no literature has been published regarding the impact of the pandemic situation on allergic patients.

Objective: Assess and describe the appearance and development of an anxiety disorder in allergic patients during COVID-19 confinement measures due to the pandemic situation.

Method: A descriptive observational study of patients aged 18-65 years attended by phone appointment at the Allergy department of Hospital Quironsalud Barcelona between March and May 2020. Those who had been diagnosed with any mental illness or psychological disorder, were excluded. All individuals gave their consent. The Goldberg scale was used for the diagnose of anxiety disorder. All analysis were performed using the Statistical software package SPSS version 20. A p value <0.05 was considered significant.

Results: A total of 104 allergic patients were included (51.9% males, 50% females). Mean age was 39.1 years (20-66). The allergic history included 81.7% rhinitis, 51% asthma, 9.6% food allergy and 8.7% chronic urticaria. The 81.7% were under allergen specific immunotherapy treatment. During the observation period, 72.1% of the patients presented new symptoms: 46.2% attributed them to their allergy condition, 10.6% to COVID-19 and 15.4% to anxiety. Only one patient was truly diagnosed with COVID-19. According to Goldberg Scale, 49% presented anxiety disorder. This group developed more symptoms during confinement (88%) than those who were not diagnosed with anxiety (56%) (p < 0.001). The perception of allergic symptoms was similar in both groups (47% and 45% respectively, p = 0.92), while the perception of anxiety symptoms was different between groups (25.5% vs. 5.6%, p = 0.028). The presence of asthma was not correlated with higher diagnosed anxiety (p = 0.11).

Conclusion: It is well known that allergic and respiratory infectious symptoms have similar characteristics and, therefore, it could be difficult for allergic patients to make the difference between Covid-19 infection and allergic reaction. To our knowledge, this is the first study to document a clear diagnosis of anxiety among allergic patients during the COVID-19 state of alarm. It is extremely important to take this condition into account to achieve a global good control of our patients.

1063 | Systemic skin delayed reactions after the administration of BNT162b2 and mRNA-1273 COVID-19 vaccines

Domínguez-Estirado A.; Juárez-Guerrero A.; Crespo-Quirós J.; Skrabski F.; Pérez-Pallisé E.; Rojas-Pérez-Ezquerra P.
University Hospital Gregorio Marañon, Madrid, Spain

Background: Vaccination has become increasingly relevant to prevent the global pandemic from coronavirus disease 2019 (COVID-19). Two mRNA-based emergency vaccines have recently been licensed for mass administration: BNT162b2 and mRNA-1273 COVID-19 vaccine.

Delayed vaccines hypersensitivity reactions can be caused by residual proteins, or most frequently by excipients. Both mRNA vaccines contain polyethylene glycol (PEG) 2000 lipid conjugate as excipient. PEG and its derivatives with clinical cross-reactivity (polysorbates, laureth-9) are ubiquitous in many drugs. mRNA-1273 COVID-19 vaccine also contains trometamol, an organic amine used extensively.

Method: We collected the patients referred to our Allergy Department with systemic skin delayed reaction after the administration of BNT162b2 or mRNA-1273 COVID-19 vaccine between January to February 2021.

We recorded age, sex, personal history of allergies and previous SARS-CoV-2 infection. We describe cutaneous manifestations, latency time, treatment, and duration.

We performed patch test (PT) in the upper back with PEG 400 1% in petrolatum (pet), PEG 3350 10% pet, PEG 3350 in aqueous solution (aq), PEG 4000 10% pet, polysorbate 80 1% pet, polysorbate 80 10% pet, laureth-9/sodium lauril sulphate 1%, trometamol 0.50% aq (only in mRNA-1273 vaccinated patients), with readings at day 2 and day 4.

Results: The study population comprised 11 patients: 6 (54.5%) received BNT162b2 and the rest received mRNA-1273 COVID-19 vaccine. Most patients (10/11, 90.9%) reacted to the first dose. Almost half of them (5/11, 45.4%) had detectable serum specific IgG antibodies against SARS-CoV-2 in the last 3 months.

The most frequent manifestation was generalized maculopapular exanthema (6/11, 54.5%), 2 flaking palms, 1 acute generalized exanthematous pustulosis (AGEP), 1 micropapular exanthema accompanied by a 7-centimeter blister, and 1 multiple fixed drug eruption (MFDE).

PT were negative in the 100% cases. We contraindicate the second dose of the vaccine in patients with severe skin reactions (MFDE, AGEP) after the first dose (2/10, 20%). The remaining patients received the second dose, reappearing systemic skin lesions in 1/8 (12.5%), having a maculopapular exanthema again.

Conclusion: In our experience, mild exanthemas should not be a contraindication to receive further doses of mRNA vaccines. However, we recommended an exhaustive allergy workout in all patients with systemic skin delayed reaction.

1166 | Whole blood-based cytokine release assay identifies IL-2 as a biomarker for rapid determination of vaccine-induced SARS-coV-2-specific T cell immune responses

Smith B. R.[1]; Brackett N. F.[1]; Agah S.[1]; Chapman M. D.[1]; Oliver M. A.[2]
[1]*Indoor Biotechnologies, Inc, Charlottesville, United States;* [2]*Indoor Biotechnologies, Ltd, Cardiff, United Kingdom*

Background: A simple, accurate and rapid whole blood-based T cell test was previously developed to determine SARS-CoV-2-specific T cell immunity. The test was established by comparing cytokine production from naturally infected convalescent donors with covid-19 negative donors. The data revealed IL-2 production to be the most indicative of prior SARS-CoV-2 infection. However, accurately identifying vaccine-induced SARS-CoV-2-specific T cell immunity via this method was still to be confirmed. Herein, we sort to address if this was possible.

Method: A cohort of unvaccinated healthy individuals was recruited to donate a single blood sample for an overnight *in vitro* stimulation with peptides spanning immunodominant regions specific for SARS-CoV-2. Blood plasma samples were harvested and analysed for a broad panel of cytokines using ELISA for IFN-g and Luminex xMAP cytokine arrays for IL-2 and other T_H1/T_H2 cytokines. The same cohort were then asked to donate a second blood sample following SARS-CoV-2 vaccinations, and the same stimulations and analyses were performed. In addition, plasma anti-SARS-CoV-2 IgG levels were assessed in both pre- and post-vaccination samples by direct ELISA against the whole spike protein.

Results: A multiplex cytokine array revealed IL-2 to be the most reliable biomarker in indicating a vaccine-induced SARS-CoV-2-specific T cell response, with 100% of post-vaccinated donors mounting a significant IL-2 response above a pre-determined cut off level for positivity of 19.91pg/ml. All donors demonstrated a considerable increase in magnitude of IL-2 responses from pre-vaccination to post-vaccination, with results ranging from ~125% change to >36,000% change. In addition, IFN-g and plasma IgG ELISAs revealed both to be reliable biomarkers, with post-vaccination levels of each being significantly raised above pre-vaccination levels. However, the magnitude of these responses was not as greatly increased as those observed with IL-2, nor did they achieve an increase in 100% of donors assessed.

Conclusion: This standardisable, rapid, and accurate T cell test approach can be utilised to make accurate and comparable assessments

of vaccine-induced T cell immunity across multiple population cohorts. This could provide valuable insight into the extremely important question of how long vaccine-induced immunity may last, and aid decision making around if and when vaccine boosters should be administered.

1211 | Pilot study of acute allergic reactions to mRNA-BNT162b2 vaccine in an ecuadorian cohort

Cherrez-Ojeda I.[1,2]; Robles-Velasco K.[2]; Osorio M. F.[2]; Fernández-Cadena J. C.[1]; Andrade-Molina D. M.[1]; Vanegas E.[1,2]; Felix M.[1,2]; Cherrez A.[3,2]; Cherrez S.[4,2]; Panchana M.[2]

[1]Universidad Espíritu Santo, Samborondon, Ecuador; [2]Respiralab Research Group, Guayaquil, Ecuador; [3]Clinic and Policlinic for Dermatology and Venereology, University Medical Center Rostock, Rostock, Germany; [4]Department of Dermatology, SRH, Zentralklinikum Suhl, Germany

Background: Allergic reactions to vaccines are rare, occurring at 1 per 1'000.000 to 30 per 100.000; BNT162b2 vaccine excipients include polyethylene glycol/macrogol (PEG), rarely cause of allergy. Contact sensitivity to PEG is more frequent than anaphylaxis. CDC reported an estimated rate of 11.1 cases of anaphylaxis per million doses administered in patients with a history of allergies.

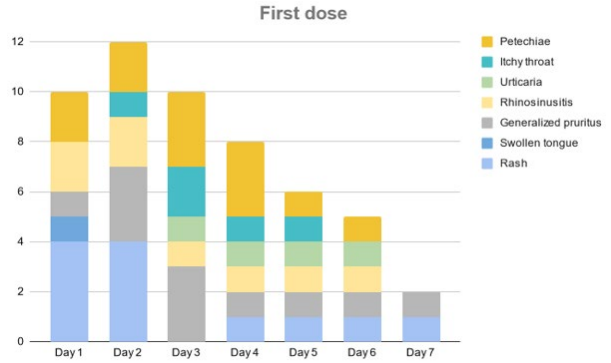
Method: We prospectively assessed the early allergic reactions of Phase 0 COVID-19 vaccination plan in Guayaquil, Ecuador. Participants received two 30-µg doses, administered intramuscularly 21 days apart. Phase 0 included first line health care workers who were healthy or had stable chronic medical conditions. Participants were observed for 30 minutes after vaccination for any acute reactions; we used Brighton scale for anaphylaxis definition criteria. The primary endpoint was to measure any allergic reaction, anaphylaxis and use of medication within 14 days after the receipt of each dose of vaccine; day 1 referred to the vaccination day. Participants reported their symptoms on weekly telephonic follow-up made by the pollsters team.

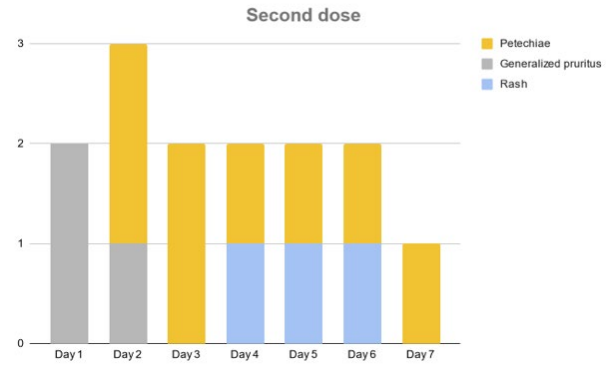
Results: 187 subjects were enrolled, the mean age was 41.11 ± 17.78, 61% were female and 27.3% patients presented with an allergic past history, 15% had allergic rhinitis (Table 1). Allergic symptom onset was 2.2 ± 3.63 minutes compared to 30 minutes of another study. We did not report any anaphylaxis case. On the first day, 5.35% presented an allergic reaction including generalized rash, injection site rash and petechiae. On second dose, 3.7% presented injection site rash, generalized pruritus and petechiae (Figure 1).

Conclusion: Our study found a similar prevalence of allergic reaction according to previous reports. The majority of patients, 94.65%, did not report any allergic symptoms after BNT162b2, similar to previous studies (98%). Anaphylaxis with COVID-19 vaccination is extremely rare, we did not find any case similarly to other reports (0.027%). To our knowledge, this is the first study to report acute allergic reactions in South America. Further studies are needed in order to prove the allergic reactions differences with other populations.

TABLE 1 Demographic characteristics of participants that received mRNA-BNT162b2 vaccine

Variable	Mean ± SD *N* (%)
Age	41.11 ± 17.78
Gender	
Male	73 (39%)
Female	114 (61%)
Race	
Hispanic	187 (100%)
Comorbidities	
None	143 (76.5%)
Hypertension	21 (11.2%)
Diabetes Mellitus II	4 (2.1%)
Asthma	8 (4.3%)
Hypothyroidism	2 (1.1%)
Rheumatoid arthritis	1 (0.5%)
HIV	1 (0.5%)
Myocardial infarction	1 (0.5%)
Gastritis	2 (1.1%)
Hypertension+Diabetes Mellitus	3 (1.6%)
Psoriasis	1 (0.5%)
Stroke	1 (0.5%)
COVID-19 past infection	
No	157 (84%)
Yes	30 (16%)
History of allergy	
None	136 (72.7%)
Allergic rhinitis	28 (15%)
Food allergy	6 (3.2%)
Atopic dermatitis	2 (1.1%)
Drug allergy	15 (8%)
Dose 1	
Received medical attention	1 (0.5%)
First-generation antihistamine	1 (0.5%)
Second-generation antihistamine	1 (0.5%)
Antibiotics	1 (0.5%)
Non-steroidal anti-inflammatory drugs (NSAIDs)	3 (1.6%)
Acetaminophen	51 (27.3%)
Dose 2	
Received medical attention	2 (1.1%)
First-generation antihistamine	0
Second-generation antihistamine	1 (0.5%)
Antibiotics	1 (0.5%)
Non-steroidal anti-inflammatory drugs (NSAIDs)	7 (3.7%)
Acetaminophen	63 (33.7%)





1260 | COVID-19 pandemic and immunoglobulin shortages in Brazil

Sobrinho A. S.O.; Machado A. M.; Ramos B.C.; Teixeira L. N.; Fanti G. C.; Guimarães R. R.L.; Schmid L. S.; Rizzo M.C.; Aranda C. S.; Solé D.

Universidade Federal de São Paulo - UNIFESP, São Paulo, Brazil

Background: Immunoglobulin replacement has been revolutionized the treatment of inborn errors of immunity (IEI), ensuring greater survival and quality of life for these patients. Most IEI patients need to receive continuous and regular immunoglobulin replacement. In Brazil, unfortunately, there is no production of this biological or policies for plasma reuse and its importation becomes necessary. Immunoglobulin is distributed monthly by the Brazilian Public Health System (SUS), free of charge. Apart from the difficulty in importing, we had to face the worldwide decrease in blood donations related to COVID-19 pandemic. The aim of this study was to report the rate of lack of immunoglobulins and complications related to this event.

Method: This is a cross-sectional, retrospective study, based on the analysis of patient's medical charts at an IEI reference center in Brazil, from January to December 2020.

Results: During this period, 124 patients received intravenous immunoglobulin (IVIG) replacement, 62 patients are female (50%), 70 adults (18 to 84 years, median age: 38y) and 54 children (0 to 17 years, median 11y). The most prevalent diagnostic were Common Variable Immunodeficiency – CVID (28.2%), Hypogammaglobulinemia (19.3%), Specific Antibody Deficiency – SAD (11.2%), Ataxia-Telangiectasia (8.8%) and other diagnostics (32,5%: SCIDS, leaky SCID, XLP2, XHIGM, VEO-IBD). Indeed, 70 patients (56.4%) were affected by the lack of distribution of IVIG (56.4%) related to COVID-19 pandemic, remaining without IVIG from one to 12 months, 2.9 months on average. Of these, 48 patients (68.5%) had at least one infection (total 125), all of whom needed to use antibiotics for the treatment of infections and 12 patients required hospitalization.

Conclusion: In 2020, 70 (56.4%) patients were affected by the lack of distribution of IVIG. It was possible to identify shortage of immunoglobulin replacement in Brazil due to COVID-19 pandemic led to more infections and increase of antibiotics use.

1278 | Allergy to COVID19 vaccine: the role of an allergist

Moura A. L.[1]; Marques J. G.[1,2]; Ribeiro A. R.[3]; Rodrigues E.[3]; Martinho T.[3]; Campina S.[1]

[1]*Immunoallergology Department, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal;* [2]*Integrated Pathophysiological Mechanisms, Comprehensive Health Research Centre, Nova Medical School, Lisboa, Portugal, Libsoa, Portugal;* [3]*Occupational Health Service, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal*

Background: COVID-19 vaccines are being administered all over the world, but information is lacking about the frequency and type of allergic reactions associated to these new vaccines.

Method: Retrospective study of health care professionals (HCP) from our hospital who received COVID 19 vaccine Comirnaty, between 29/12/2020 and 20/2/2021. We reviewed clinical data, particularly the immediate reactions after the administration (<6h), skin tests (ST) and graded vaccine administration. Following national guidelines, all HCP with previous history of food, drug or hymenoptera venom allergy or idiopathic anaphylaxis (IA) were first evaluated by an allergist. Vaccination was postponed if HCP had previous history of IA and/or recurrent anaphylaxis (RA), severe allergic reactions to vaccines and mast cell activation syndromes. ST to the vaccine (prick and intradermal) were performed in HCP with IA and/or RA, severe allergic reactions to vaccines and HCP with immediate reactions to the 1st dose. Graded administration of the vaccine (0.1+0.2cc after 30') was performed in the postponed HCP and the ones with immediate reactions to the 1st dose.

Results: From 3073 HCP who received the vaccine, 74.2% were female, mean age 40.2 years-old ± 13.4, 316 (10.3%) were evaluated by an allergist and 4 (1.3%) postponed the administration and performed allergy investigation. 2955 HCP (97%) were able to receive the 2 doses of the vaccine. 118 employees received only one dose: 98 had COVID-19 meanwhile, 7 got pregnant, 13 due to other conditions. Adverse reactions to the vaccine with possible hypersensitivity mechanisms, occurred in 17 (0.6%) HCP, 12 on the 1st dose and 5 on the 2nd dose. Observed reactions were 6 (0.2%) urticaria, 5 (0.16%) pruritus with or without *flushing*, 2 (0.07%) anaphylaxis (mild), 2 (0.07%) *flushing* and hoarseness, 1 (0.03%) *flushing* and nausea and 1 (0.03%) asthma exacerbation. ST with the vaccine were performed in 4 HCP, all negative in the immediate reading and

1 positive in non-immediate reading. 7 HCP undertook the graded administration with the vaccine: 6 tolerated, but one reproduced the immediate urticaria with 0.1cc of the vaccine (0.03% vaccine allergy).
Conclusion: In the evaluated sample, suspicious allergic reactions to COVID19 vaccine Commirnaty were rare and allergy was only confirmed in one HCP. The allergist initial evaluation was essential for a safe risk stratification and permitted the non-exclusion of a considerable number of HCP from the vaccination program.

1296 | Effect of COVID-19 pandemic on the treatment process and adherence to treatment of the patients receiving allergen-specific immunotherapy

Atayik E.; Aytekin G.
University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

Background: During the COVID-19 pandemic, the number of hospital admissions has significantly decreased, due to both the risk of transmission and the restrictions imposed. The most adversely affected ones are patients who need to admit to a hospital due to their chronic diseases, such as those receiving allergen immunotherapy. We aimed to investigate the effect of the SARS-CoV-2 pandemic on adherence to treatment of the patients receiving AIT due to allergic diseases in our clinic, to determine the reasons why patients are coming late/not coming for treatment and to reveal the effect of SARS-CoV-2 pandemic on the anxiety of this patient group.
Method: Files of the patients who were administered subcutaneous immunotherapy (SCIT) regularly, were retrospectively reviewed. At first outpatient clinic visits during the period of so-called normalization process (June-July-August 2020), the patients were asked to fill a mini questionnaire and validated coronavirus anxiety questionnaire.
Results: A total of 151 patients receiving SCIT were included in the study. The most common government-related factors hindering outpatient clinic visits of the patients were travel restrictions (40.6%) and the most common patient-related factors were fear of contracting SARS-CoV-2 (39.7%). Overall adherence to treatment during the 3-month period from March to April-May 2020 was determined to be 54.3%. The duration of immunotherapy, increased allergic symptoms, the need for additional treatment and treatment switch in SCIT because of the pandemic were significantly higher in patients non-adherent to SCIT treatment compared to adherent ones (p: 0.031, p: 0.001, p: 0.001 and p: 0.001, respectively).
Conclusion: Access to allergen immunotherapy, applicability, and maintenance of the immunotherapy should be a priority during the COVID-19 pandemic. Considering both patient-related and government-related factors in the administration of immunotherapy, the process of immunotherapy should be continued, minimizing the risk of SARS-CoV-2 transmission. Furthermore, patients' worry and anxiety levels may be reduced with these measures and their adherence to treatment may be promoted.

1298 | The effect of COVID-19 pandemic on treatment compliance and process of chronic urticaria patients receiving omalizumab treatment

Aytekin G.; Atayik E.
University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

Background: Social distancing, curfew restrictions, travel restrictions and quarantines were imposed in order to reduce the risk of transmission of SARS-CoV-2. These restrictions have caused a severe reduction in admissions to hospitals. Therefore, with this study, we aimed to investigate effect of the COVID-19 pandemic on treatment processes and adherence to therapy of the patients that require to receive omalizumab due to chronic urticaria and to address effect of the pandemic on anxiety level of this patient group.
Method: Among the patients who were being followed-up for chronic urticaria and receiving omalizumab for this, files of the patients were examined retrospectively. These patients were applied a mini survey and a validated coronavirus anxiety index.
Results: Ninety-eight patients (Female: 65; Male: 33) were recruited in the study. The patients' 3-month adherence to therapy during March-April-May 2020 was 42.9%. It was the lowest during April (56.1%). The curfew (51%) and the fear of contracting SARS-CoV-2 (50%) were the most common reasons. Although rates of admissions to emergency department, an increase in symptoms of urticaria and need for an additional treatment were higher in the patients with chronic urticaria who were nonadherent to omalizumab therapy, this difference was not statistically significant (p: 0.113, p: 0.216, p: 0.141, respectively).
Conclusion: During the pandemic, patients' adherence to therapy has reduced due to both government-related and patient-related reasons. For patients with chronic urticaria, their adherence to therapy should be ensured by minimizing the risk of transmission of SARS- CoV-2. Furthermore, in order to enhance adherence to therapy of this patient group and make access to health institutions easier, it should be considered for these patients to provide some tolerances and privileges in pandemic-related restrictions.
Keywords: COVID-19, omalizumab, chronic urticaria

1307 | A call for action: Understanding mental health impact of COVID-19 in the referred allergic population

Lopera Hernandez G.; Bhatt V.; Dales M. S.; Ohayon J.
Hamilton Allergy, Hamilton, Canada

Background: With the rise of the COVID-19 pandemic, feelings of fear and anxiety have increased across the world. Extended isolation has led to mental health implications requiring immediate efforts to address the impact of the pandemic, especially in individuals who present with respiratory allergies given that the symptoms are

similar to those experienced in the COVID-19 virus (Gonzalez-Diaz et al., 2021).

Method: A retrospective, 16 point questionnaire evaluating the mental health of adult patients with allergic rhinitis (AR) or allergic rhinoconjunctivitis (ARC) aged 18 to 30 years and 31 years to 70 years was conducted. The COVID-19 Impact on Mental Health Questionnaire (CIMhQ) focusing on mood behaviours was based on a 1-7 scoring system with 1 being not affected and 7 being extremely affected. Additionally, all patients were asked about interest in mental health support programs through professionals including TV live streams, applicable social media content, Zoom webinars, question and answer sessions, nutrition help along with positive COVID-19 stories and successes.

Results: Data was collected from January - March 2021 in a community allergy clinic. Fifty- nine people aged 18- 30 years (younger group) and thirty-seven people aged 31 to 70 (older group) answered the CIMhQ. Mean scores between both groups were compared with an analysis of variances (ANOVA) and a two-tailed t-test. A significant difference in mean CIMhQ scores was identified in the younger group (M= 78.12) versus the older group (M= 67.92), t (94) = 3.26, $p = 0.0016$. The younger group displayed higher mean CIMhQ scores. Twenty- seven percent of the younger group showed interest in receiving mental health support compared to 41% in the older group.

Conclusion: The younger group showed higher levels of anxiety based on average CIMhQ results in comparison to the older group. Paradoxically, the older population was more willing to receive mental health support than the younger group. Awareness of the impact of mental health during a pandemic in referred patients for allergy assessments can help physicians direct appropriate counsel.

T-Test: Two-Sample Assuming Unequal Variances

T statistic	Degrees of freedom	*p* value
3.26	94	0.0016

Mean Scores of COVID-19 Impact on Mental Health Questionnaire

Age group	Mean score
18–30 years	78.12
30–70 years	67.92

1320 | The association of cytokine profiles and SARS-coV-2 viral load with COVID-19 severity and mortality

Neumann A.[1]; Gökkaya M.[1]; Dorgham K.[2]; Quentric P.[2]; Yssel H.[2]; Traidl-Hoffmann C.[1]; Gorochov G.[2]

[1]*University of Augsburg, Augsburg, Germany*; [2]*Sorbonne Université, Paris, France*

Background: Markedly elevated levels of pro-inflammatory cytokines and defective type-I interferon responses were reported in COVID-19 patients. This study aimed to determine whether particular profiles of cytokine combinations and SARS-CoV-2 viral loads are associated with COVID-19 severity and mortality.

Method: Cytokine concentrations and SARS-CoV-2 antigen were measured at hospital admission in serum of symptomatic COVID-19 patients ($N = 115$), classified at hospitalization into three respiratory severity groups: moderate severity with no need for mechanical ventilatory support (No-MVS), intermediate severity requiring mechanical ventilatory support (MVS) and critical severity requiring extracorporeal membrane oxygenation (ECMO). Principal component analysis was used to characterize cytokine profiles associated with severity and mortality. The results were thereafter confirmed in an independent validation cohort ($N = 86$).

Results: At time of hospitalization, moderately severe No-MVS patients presented an elevated type-I interferon response involving IFN-α and IFN-β, with relatively low levels of pro-inflammatory cytokines. In contrast, critically severe ECMO patients presented a dominant pro-inflammatory response and relatively low type-I interferon response. Intermediate severity MVS patients exhibited a mix of the above cytokine combination profiles. SARS-CoV-2 antigen levels correlated with type-I interferon levels, but not with pro-inflammatory response.

Mortality at one month after hospitalization was accurately (87%) predicted by higher levels of IFN-α, IFN-β, and Il-10 in combination with higher SARS-CoV-2 antigenemia and older patients' age, irrespectively of the oxygen support modality.

Conclusion: Different levels of two distinct cytokine profiles are observed in different patients in association with COVID-19 severity. Furthermore, by measuring three cytokines and SARS-CoV-2 antigen at time of hospital admission, mortality one month later can be accurately predicted. These results warrant personalized treatment of COVID-19 patients based on cytokine profiling and viral load measurement.

986 | Flare-up phenomenon of SARS-COV2 vaccine secondary to epicutaneous test with polyethylene glycol

Torrado Español I.[1]; Peña Arellano M.I.[1]; Tsopana A.[1]; Vega Castro A.[1]; Mateo Borrega M.B.[1]; Rordriguez Fernandez A.[2]; Beitia Mazuecos J.M.[1]

[1]*Hospital Universitario Guadalajara, Guadalajara, Spain*; [2]*Complejo Hospitalario Universitario de Vigo, Vigo, Spain*

Background: A 41 y/o woman diagnosed with betalactam hypersensitivity without any other medical condition or treatment was referred to our Allergy Service because of a large local reaction after the application of an Influenza vaccine.

She showed a large local reaction, from elbow to shoulder, some hours after the inoculation of an Influenza vaccine in 2005. The

reaction disappeared after a week treatment with oral and topical corticosteroids.

As a consequence of the present pandemic situation she asked about (the possibility of) getting the SARS-CoV-2 vaccine administered.

Methods and results: We performed the prick and intradermal (ID) tests with the available Influenza vaccine and prick and ID (1/100, 1/10 and 1/1) tests with the available SARS-CoV-2 vaccine. Tests with Influenza vaccine were negative and positive 1/10 ID with SARS-CoV-2 vaccine. 1/1 ID test was also positive but in later studies this concentration seemed to be irritating and it wasn't taken into account.

Some of the Influenza vaccines commercialized in Spain contain polysorbate 80 and it has shown cross reactivity with other preservatives as polyethylene glycol (PEG), used in the latest SARS-CoV-2 vaccines. As we didn't know the exact Influenza vaccine administered to our patient, and being suspicious that it could have contained polysorbate 80, we performed epicutaneous tests with both polysorbate 80 and PEG-400 7 days after the neutralization of the first tests. Polysorbate 80 was negative but PEG-400 was positive 96 hours later and it reactivated the 1/10 and 1/1 ID tests of the SARS-CoV-2 vaccine, which is known as a flare-up phenomenon.

Conclusions: We present a singular case of a flare-up phenomenon of intradermal tests to SARS-CoV-2 vaccine after an epicutaneous test with PEG-400.

According to our present experience, this is the first documented report of this type involving PEG and SARS-CoV-2 vaccine.

1290 | Tocilizumab-induced anaphylaxis in two patients with COVID-19-induced cytokine storm

Atayik E.; Aytekin G.

University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a zoonotic virus which was first discovered in Wuhan, the People's Republic of China in December 2019 and has led to one of the greatest pandemics of world history in a short period of time1 . SARS-CoV-2 is a rapidly spreading infectious disease with a high mortality rate. The disease has a moderate and severe course in approximately 20% of the patients and mortality reaches up to 62% among these patients2 . The majority of the patients develop SARS-CoV-2-induced pneumonia and manifestations of pneumonia rapidly progress to respiratory failure. In severe Covid pneumonia, it has been demonstrated that increased plasma concentrations of cytokines including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and IL-12 are involved in immune response and in cytokine storm caused by the increase in these cytokines lead to mortality1, 3. Tocilizumab (TCZ) is a promising agent that is used for the treatment of cytokine storm. TCZ is an IgG1 class recombinant humanized monoclonal antibody against IL-6 receptor3 . It has then been used for the treatment of rheumatic diseases. Due to its mechanism of action, TCZ treatment comes to the forefront particularly in cases of severe COVID-19-induced cytokine pneumonia presenting with cytokine storm3 . However, potential IgE-mediated immunological reactions against this drug, especially anaphylaxis, may deprive these patients of an important treatment option for the treatment of COVID-19-induced cytokine storm. Although TCZ-induced anaphylaxis has been reported as case reports of indicated rheumatic diseases, TCZ-induced anaphylaxis has not yet been reported in patients using TCZ for SARS-CoV-2-induced cytokine storms4 . In this case series, we aimed to represent cases of anaphylaxis which developed in two different patients using TCZ for SARS-CoV-2-induced cytokine storm.

Keywords: anaphylaxis, COVID-19, cytokine storm, drug allergy, Tocilizumab

1081 | Changes in asthma control after administration of COVID-19 mRNA vaccines

Crespo Quirós J.; Juárez Guerrero A.; Rodríguez Hermida S.; Domínguez Estirado A.; Rojas-Pérez-Ezquerra P.

Hospital General Universitario Gregorio Marañón, Madrid, Spain

Background: Rapid development of vaccines to prevent coronavirus disease 2019 (COVID-19) has become a global imperative. Two mRNA vaccines have been recently approved by European Medicines Agency: BNT162b2 and mRNA-1273 COVID-19 vaccine. They have demonstrated safety in 1-3 phase clinical trials but data in asthmatics vaccinated in real-life is scarce.

We sought to assess the change in asthma control before and 4 weeks after the administration of mRNA vaccine against COVID-19 in adults diagnosed with mild to severe asthma.

Method: We performed an observational descriptive study of asthmatic healthcare workers who were vaccinated in our Allergy Department. Asthma severity were measured following Spanish Guideline on the Management of Asthma (GEMA) criteria. Asthma control was evaluated prior to vaccination and 4 weeks after vaccination using Asthma Control Test (ACT) questionnaire. The mRNA vaccines were administered under medical supervision and 30 minutes observation.

Results: We recorded a total of 52 asthmatic healthcare workers who receive COVID-19 vaccination in our Allergy Department. The mean age was 52.3 years (range 21-66) and 46 (88.5%) were female. Ten (19.2%) and 42 (80.8%) subjects received BNT162b2 and mRNA-1273 COVID-19 vaccine, respectively.

Twenty patients (38.5%) had intermittent asthma, 8 (15.4%) mild, 18 (34.6%) moderate, and 6 (11.5%) severe asthma. One patient was receiving oral corticosteroids and one biologic treatment. Coexisting allergic diseases were common: 26 (50%) had allergic rhinitis, 5 (9.6%) atopic dermatitis, 18 (34.6%) food allergy, 19 (36.5%) drug allergy. Other comorbidities were cardiovascular disease (23.1%), obesity (21.2%), autoimmunity (19.2%) and nasal polyposis (5.8%).

The ACT before vaccination was 24.2 (range 21-25, SD 1.4). We detected 2 (3.8%) patients with ACT<20 who were vaccinated once ACT was ≥20. Four weeks after the first and second dose of mRNA vaccine, ACT was 23.4 (range 10-25, SD 2.6) and 23.8 (range 12-25, SD 2.5), respectively. We found no statistical significant differences in ACT changes among intermittent, mild, moderate, and severe asthma.

Conclusion: In our experience, asthma exacerbation after mRNA vaccination is infrequent and not related to asthma severity. Asthmatic population can safely receive mRNA vaccines against COVID-19.

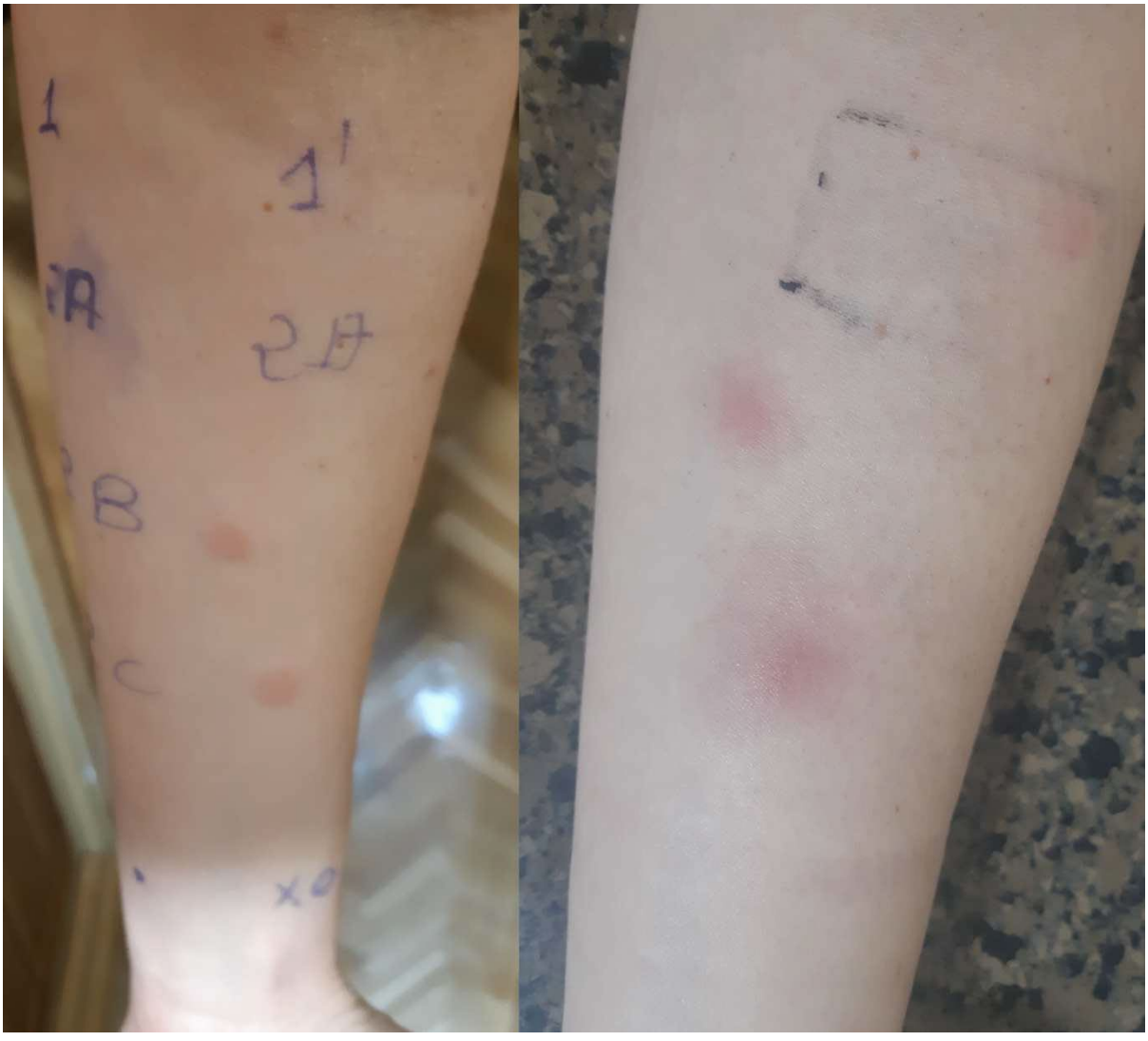
1105 | The clinical and cost effectiveness of telemedicine consultation in tertiary paediatric allergy during the COVID-19 pandemic: A comparative study

Lee R.; Vance G.

The Great North Children Hospital, Newcastle, United Kingdom

Background: The COVID-19 pandemic has enhanced the growth of telemedicine in an unexpected speed. Our study compares the service and cost effectiveness of telephone clinics (TC) to standard face to face clinics (FTFC) in the paediatric allergy service.

Method: This retrospective study looked into paediatric allergy clinic activities from April 1- October 1, 2020 in the Great North Children Hospital, Newcastle. We also collected data from standard FTFCs in the pre-COVID period as comparative group. Clinic activities were reviewed by looking into patients' clinic notes and letters.



Results: Clinic attendance rate in both groups was similar (91%, 94%). 9% of the patients were not available at the time of TC appointment. Majority did not answer but 4 consultations were discontinued due to language barrier.

Up to 73% of patients did not have allergy tests after TC, despite being clinically indicated in half of them. Serum IgEs (sIgE) has become the preferable diagnostic option in TC. The median of sIgEs ordered per patient is 7 in TCs, as compared to 6 in control ($p < 0.05$). This has resulted in a 20% increase in laboratory cost.

Clinic discharge rate is higher in FTFC (41%) as compared to TC (25%). The average follow-up time interval after TC is shorter than FTFC, 7.6 months and 9.4 months respectively ($p < 0.05$). More regular follow-ups in TC group has led to an increase of average clinician follow-up cost per patient by 32%.

Conclusion: A telemedicine-based allergy service model can be more time-effective and improve patient access to specialist care, only with well-designed framework and planning. Screening criteria for selecting suitable TC patients can be the key to success. We present an example of recommended screening criteria based on patients' diagnosis and certain special circumstances.

	FTFC	TC	Depends
Food allergies			
New	♦		
FU			♦
Eczema			
New	♦		
FU			♦
Severe Allergic Rhinitis			
New	♦		
FU		♦	
Urticaria/Angioedema			
New		♦	
FU		♦	
Eosinophilic Oesophagitis			
New			♦
FU		♦	
Drug Allergy			
New		♦	
FU		♦	
Family history/parental anxiety			
New	♦		
FU		♦	
Non-specific reactions			
New		♦	
FU		♦	
Special circumstances			
Language barrier	♦		
Existing CPP/previous safeguarding concerns	♦		
Multiple missed appointments	♦		
Geographical location	♦		

1148 | COVID-19 vaccines: An allergological study

Bartha I.; Las Heras P.; Mugica V.; Belver M.; Vega F.; Ramos T.; Valls A.; Frutos C.; Lopez-Raigada A.; Mamula J.; Catala M.; Blanco C.

Allergy Department. Hospital Universitario de La Princesa and Instituto Princesa (IP), Madrid, Spain

Background: In order to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) an active approach is necessary. On December 2020 the commercialization of the COVID-19 vaccines was made. In Spain the first one to arrive was Pfizer-BioNtech vaccine. Initially, several reports of anaphylactic reactions due to the vaccine in the USA and in the UK were reported, which lead to an early recommendation to avoid the administration in patients with allergic history.

The objective of this study is to describe and characterize the allergenic profiles of patients attended in our clinic for allergy testing to prevent reactions with the COVID-19 vaccine.

Method: The allergological profile of 85 patients diagnosed with previous history of allergic disorders was analysed between January 18th and March 16th 2021. The allergological study included skin-prick test with polyethylene glycol (PEG), Tween 20, Tween 80, and COVID-19 vaccine (Pfizerâ), together with latex and other allergens when necessary. After the double dose of vaccine was completed, a follow up was done by telephone.

Results: Risk stratification and approach is exposed in figure 1. Clinical and allergological characteristics of 85 patients are shown in table 1. Out of them, 88.2% had an allergic comorbidity and 48.2% had drug allergy. The reason for consultation was in 92.9% due to their allergic history, 76.5% were referred from the Occupational Health Service, and 80.6% of the patients have had previous vaccination with other anti-infective vaccines without reactions.

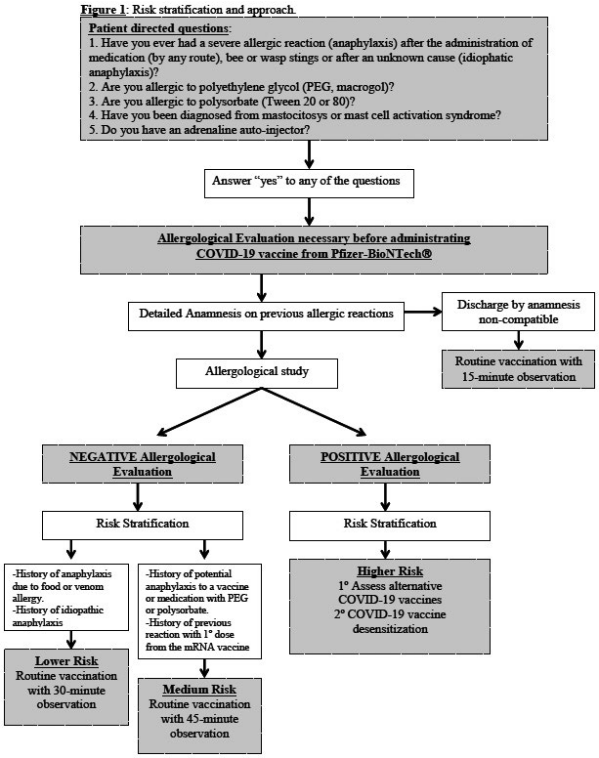
Also, table 1 shows the prick-test results with COVID vaccine an its excipients, without any positive result. 70.7% of our population has completed the vaccination. Only 9 patients had a possible allergic reaction to the first dose, 8 of them had cutaneous and the remaining had respiratory symptoms. Out of these 9 patients, 6 had their second dose without any symptoms.

Conclusion: None of the patients studied showed a positive test for neither the components of the vaccine nor the vaccine itself. More studies are required with a larger sample size to reach final conclusions.

TABLE 1 Clinical and allergological characteristics of the patients included in the study (*N* = 85)

Variable	Mean	SD
Age (years)	47.1	13.9
Variable	***N***	**%**
Sex (F)	69	81.2
Work: Health worker	81	95.3
Allergic Comorbidities	75	88.2
Rhinoconjunctivitis	39	45.9
Asthma	21	24.7
Food allergy	31	36.5
Drug allergy	41	48.2
Venom allergy	7	8.2
Contact dermatitis	12	14.1
Urticaria/Angioedema	21	24.7
Anaphylaxis	36	42.4
Reason for consultation		
Previous to vaccination	79	92.9
Reaction to first dose	6	7.1
Derivation		
Occupational Health	65	76.5
Primary Care Physician	6	7.1
Patients decision	14	16.5
Vaccines History (*n*)	36	
No reactions to other vaccines	29	80.6
Vaccines History (*n*)	29	
Previous Influenza vaccination	24	82.8
Allergy study		
Pfizer BioNTech vaccineâ	51	89.5
Polyethylene glycol	52	91.2
Polisorbate 20 (Tween 20)	23	40.4
Polisorbate 80 (Tween 80)	52	91.2
Latex	6	10.5
Other allergens	7	12.3
Local Anaesthetics	1	1.8

* SD: standard deviation.



1154 | Impact of allergen immunotherapy in COVID-19: An italian survey

Sánchez-López J.[1]; Heffler E.[2]; Czarlewski W.[3]; Canonica G.W.[2]
[1]*Stallergenes Greer, Barcelona, Spain*; [2]*Humanitas University & Research Hospital, Milano, Italy*; [3]*Stallergenes Greer, Antony, France*

Background: COVID-19 may present with many different clinical manifestations and a wide severity range. Common signs are respiratory disorders, that could be similar in some cases to those observed in allergic rhinitis or asthma.

Respiratory allergies may be treated with allergen immunotherapy (AIT). It is assumed that AIT reduces the tendency to produce IgE, modulates the Th2-polarized immune system, increases IFN-γ production and reduces allergic inflammation. On the other hand, it is described that severe forms of COVID-19 are related to the secretion of type-I cytokines.

The main purpose of the following survey was to evaluate, from the physician's perspective, if COVID-19 could have an impact in allergic diseases, and specially in patients treated with AIT.

Method: A web-based survey (SurveyMonkey®) of 18 questions was defined to evaluate, from the clinician's perspective, the impact of COVID-19 in allergic diseases and patients under AIT based in their clinical practice. It was shared with a pool of 855 Italian physicians.

Results: A total of 62 respondents answered the survey. 93% asked to their patients regularly about COVID-19. They estimated that 1/100 have had COVID-19, being mild in the 88% of cases, with no severe or fatal cases to their knowledge. 16% observed higher incidence of COVID-19 in patients with rhinitis, but most of them considered that disease was equal to other patients (71%) or less severe (24%). Similar was observed for asthma. None of the responders considered that COVID-19 was more severe in patients with AIT, however, 48% prescribed AIT less frequently. Most doctors (75%) maintained their prescription habits, while 22% increased SLIT vs SCIT.

Conclusion: Among the 62 Italian doctors answering the survey, doctors reduced AIT prescription during COVID-19 pandemic, switching to SLIT in some cases. They did not consider that AIT could affect COVID-19 severity. In addition, some doctors believed that COVID-19 is less severe in allergic rhinitis or asthma patients.

1171 | MRNA vaccine and reported allergic reactions in employees from the health area of Puertollano (spain)

Extremera Ortega A. M.[1]; Mur Gimeno P.[1]; Rodríguez Soler M.[2]; Giner González J.R.[2]

[1]*Allergy Unit. Santa Bárbara Hospital, Puertollano, Ciudad Real., Spain;* [2]*Occupational Risk Prevention Service. Santa Bárbara Hospital, Puertollano, Ciudad Real., Spain*

Background: Vaccines are a well know public health intervention that can modify the spread of some infectious diseases. They have demonstrated more benefits than risks.

The aim of our study was to describe the adverse reactions (AR) reported by the employees belonging to the Health Area of Puertollano who received two doses of the mRNA COVID-19 Pfizer-BioNTech vaccine from January to March 2021. We also compared these data with pharmacovigilance reports issued monthly by Spanish Agency of Medicines and Medical Devices.

Method: We collected data about self-reported AR sent for any health employee by email after receiving Pfizer-BioNTech vaccine. In suggestive reactions of hypersensitivity, we performed patch test (PT), skin prick test (SPT) and intradermal reaction test (IDT) with several molecular weights (400, 1500 and 4000) of polyethyleneglycol (PEG) and with polysorbate 80.

Results: A total of 1491 out of 1550 workers, received both doses of the mRNA COVID 19 Pfizer-BioNTech vaccine 1046/445 (female/male). We collected 35 (2%) AR, mainly in women (89%). The distribution of the AR notified were: General disorders (fever, shiver, dyspnea, wheeze, cough…) in 27 employees (77%). Neurological symptoms in 14/35 (40%). Musculoskeletal pain in 16/35 (46%). Gastrointestinal illness in 2/35 (6%). Skin lesions as generalized itching or maculopapular rush in 2/35 (6%). These results were similar to those compared with National Data (Table 1). The allergy study was negative in those two workers.

Conclusion: mRNA COVID-19 Pfizer-BioNTech vaccine has been safe, since few adverse reactions have been reported in the Health Area of Puertollano.

The number of reported AR in this Health Area is greater than the Nacional Data, probably due to the awareness of this health care group.

Our results were similar to those reported by National Data, being the most common symptoms general disorders, followed by neurological symptoms and musculoskeletal pain.

We could not prove hypersensitivity mechanism involved in the two cutaneous reactions suggestive of allergy.

A Limitation of our study was the use of email self-reported data in a specific group including health care workers.

Further studies are needed in order to improve safety in vaccines.

TABLE 1 Data of mRNA COVID 19 Pfizer-BioNTech vaccine administered

	Health Area of Puertollano No. (%)	National Data No. (%)
No.	1491	1631448
Women	1046 (70%)	72%
Men	445 (30%)	28%
Age (18-64)	100%	72%
Self-reported adverse reactions	35 (2%)	5736 (0.3%)
Women	31 (89%)	83%
Men	4 (11%)	17%
General disorders	27 (77%)	3848 (67%)
Neurological symtoms	14 (40%)	2282 (40%)
Musculoeskeletical pain	16 (46%)	1733 (30%)
Gastrointestinal illness	2 (6%)	1262 (22%)
Maculopapular rush/itching	2 (6%)	529 (9%)

1183 | Type I hypersensitivity to mRNA-vaccines against SARS-coV-2

Audicana M.T.; Martinez-Arcediano A.; Longo N.; Ollo P.; Girao I.

Hospital Universitario Araba, Vitoria, Spain

Background: To describe anaphylactic/anaphylactoid reactions induced by mRNA-vaccines against SARS-CoV-2 and immune-allergic studies carried out.

Method: Twenty two patients were referred prior to the administration of the second dose of vaccine.

Skin tests were performed to both mRNA vaccines (Pfizer and Moderna1/1), different sources of poliethylenglycol (PEG), Polysorbate 80 and Trometamol. Total IgE, specific IgE to ethylene oxide, tryptase and Basophile activation test (BAT) were performed to the same reactives including both Pfizer and Moderna vaccines adding PEG2000.

Results: Four anaphylaxis/anaphylactoid reactions are documented. One of them with the entire study negative. The remaining three cases were non-severe anaphylaxis.

PEG 1.500 0,1%, 1% and 10%, Polysorbate 80 (0,04mg/ml) and Trometamol (1 mg/ml) were negative in all cases. TAB was positive only to Pfizer and Moderna vaccines but not to PEG or other excipients.

Four additional woman with positive skin test were observed in the same period of time related to the first exposition to vaccines and only positive test were obtained with vaccines but not to PEG or other excipients studied. All of them sanitary workers affected by urticaria and/or angioedema and adenitis associated with cutaneous delayed reaction.

More than 20 skin tests were negative as the same concentrations in other patients with suspected adverse reactions to vaccines or other drugs containing PEG. All negative patients were encouraged to receive the second dose and 10 did not have a recurrence of reaction. More than 10 BAT were also performed in cases and controls with negative results to PEG.

A positive specific IgE to ethylene oxide was obtained.

Conclusion: Different mechanisms of anaphylactic/anaphylactoid reaction are inferred from the results.

In the most severe case, it was not possible to demonstrate an IgE mechanism involved.

Skin test to vaccines involved were the most useful tool to diagnose hypersensitivity reactions.

PEG was positive in one case, Ethylene oxide was positive in other case (associated with positive ID test to vaccines) and BAT in other two patients.

1216 | Role of antihistamines in the management of COVID-19 infection

Sepiashvili R.[1]; Chikhladze M.[2]; Slavyanskaya T.[3]; Gamkredlidze S.[4]; Khachapuridze D.[5]

[1]Peopels Friendship University of Russia, Moscow, Russia; [2]National Institute of Allergy,Astma and Clinical Immunology of Georgian Academy of Sciednce, Tskhaltubo, Georgia; [3]Peopels Friendship University of Russia, Moscows, Russia; [4]National Institute of Allergy,Astma and Clinical Immunology of Georgian Academy of Sciednces, Tskhaltubo, Georgia; [5]Akaki Tsereteli UIniverrsity, Kutaisi, Georgia

Background: The Covid-19 pandemic is considered as the biggest challenge not only to modern medicine but to all mankind. The situation is exacerbated by the lack of specific effective medications/drugs against the virus. Coronavirus disease management is a continuous process of constant updating.

Method: Common symptoms of the novel coronavirus include dry and lingering cough, and less common symptoms - a skin rash, respectively. During the course of infection an active involvement of allergic mechanisms type can be observed, leading to the need for including anti-allergic medications in the management of Covid infection.

Results: During the course of infection an active involvement of allergic mechanisms of pathogenic type can be observed, leading to the need for including anti-allergic medications in the management of Covid infection. This clinical symptom persisted in the post-covid period. The above-mentioned aroused our interest and the study of post-covid patients experiencing post-covid symptoms such as lingering cough and a prolonged feeling of respiratory failure was conducted. It is noteworthy to emphasize that according to the results of clinical and laboratory studies, no sharp changes in allergic diagnostic parameters in the blood of these patients were revealed. Therefore, the empirical prescription of antiallergic drugs based on symptoms was chosen as a research tactic. 56 patients involved in the study (18 to 65 years of age, 33 women, 23 men) with dry and lingering cough symptoms were prescribed an inhaled form of local glucocorticosteroid -Budesond with generic active substance, leukotriene receptor antagonist, and antihistamines. Follow-up showed that the clinical effect was more pronounced in patients administering montelukast/desloratadine or levocetirizine in combination than in patients who were taking montelukast and/or desloratadine or levocetirizine separately. Monitoring of the patients revealed that 45 (80%) patients receiving above complex treatment had sooth in cough as a symptom, however, the clinical effect was obtained after nearly 10 days of treatment while 11 (20%) patients failed to achieve clinical efficacy with this treatment regimen

Conclusion: Research monitoring has confirmed the ancillary effect of antiallergic drugs, however, the issue of Covid infection management still remains open and research in this direction still continues to be active around the world.

The publication was prepared with the support of the «RUDN University Program 5-100».

1217 | Monitoring of vitamin D index in COVID-19 patients among georgian population

Sepiashvili R.[1]; Chikhladze M.[2]; Slavyanskaya T.[3]; Gamkrelidze S.[2]; Khachapuridze D.[4]

[1]Peopedls Friendship University of Russia (RUDN Univedrsity), Moscow, Russia; [2]National Institute of Allergy,Asthma and Clinical Immunology of Georgian Academy of Sciences, Tskhaltubo, Georgia; [3]Peopels Friendship Univerrsity of Russia (RUDN University), Moscow, Russia; [4]Akaki Tsereteli University, Kutaisi, Georgia

Background: COVID 19 pandemic, undoubtedly, is a challenge of the 21st century. Due to its urgency, the issue can be considered

as a problem of medicine. According to the researchers around the world, a strong correlation between vitamin D deficiency and severity and mortality rate of the disease caused by novel coronavirus (Covid-19) has been established.

Method: Based on the above-mentioned, the aim of the study was to determine the correlation between Vitamin D plasma level and serum markers of disease in patients with covid-positive among Georgian population confirmed by the PCR method.

Results: 135 COVID positive patients (74 females, 61 males) of mild and moderate severity who applied to the our Institute of Allergy in Tskaltubo, (Georgia) have been involved in the study to monitor Covid markers in the blood. Patients underwent the following examinations/tests: complete blood count (CBC), C-reactive protein, coagulogram, D-dimer. In parallel, Vitamin D level in the blood was determined. Analysis of the results obtained showed that 113 (84%) of 135 patients involved in the study had severe leukopenia, 13 (9%) - leukocytosis, and only 9 (7%) – white blood cell level within the norm, respectively. It is noteworthy to emphasize that erythrocyte sedimentation rate (ESR) was elevated in 39 (28%) cases and C-reactive protein - in 95 (70%), respectively, while increase in D-dimer level was observed in only 65 (48%) of the patients. Coagulogram analysis revealed a sharp increase in fibrinogen concentration (FB) in 125 (92%) patients. In parallel, vitamin D deficiency was detected in 76 (56%) of Covid- patients in Georgian population, and acute deficiency in 37 (27%), respectively. Vitamin D level was found to be in norm only in 22 (17%) cases. According to the analysis of the results obtained, the greater vitamin D level deficiency, the more pronounced change in other blood Covid markers. Statistical analysis showed a high degree of correlation between vitamin D level and fibrinogen concentration (r = 0.8), C-reactive protein (r = 0.6), D-dimer (r = 0.5) blood levels. It is also worth noting that vitamin D deficiency correlates to a high degree with the severity of Covid infection clinical course.

Conclusion: The results obtained allowed make conclusion: Vitamin D deficiency is directly related to the infection course degree, thus explaining the recommendations on necessity to include in disease management,

The publication has been prepared with the support of the «RUDN University Program 5-100».

1249 | In COVID-19 times, can remote rapid drug desensitization (RDD) be possible?

Medeiros L. C.M.d.; Oliveira B. R.d.; Ramos B. C.F.; Lima A. O.d.A.; Schimid L. S.; Guimarães R. R.L.; Martins A. M.; Aranda C. S.; Solé D.

Federal University of São Paulo, São Paulo, Brazil

Background: Since 2019, we have experienced a terrible pandemic, COVID-19. Emerging countries, like Brazil, with logistical difficulties and lack of public policies, face a generalized collapse in health system. Rare Diseases Reference Centers are located distant from patients' houses. Thus, patients with lysosomal diseases, unable to travel and need to receive their recombinant enzyme replacement therapy (ERT) close to their homes. Infusion-related reactions (IRR) are uncommon; however, they can impair the treatment. Therefore, due to the impossibility of locomotion and unavailability of teams of allergists, RDD protocol were accomplished. The study aimed to describe remote points of training and protocols execution.

Method: After appointments from treating lysosomal centers (TLC) diseases about adverse reactions, the following strategy was adopted: three online meetings between metabolic team and allergists to present the clinical case; lectures about adverse reactions to medications and RDD: video demonstrations off how to perform skin tests and nursing training for the use of. Two meetings were held with the families, terms of consent were applied, and a communication group was created on WhatsApp® with team leaders. Afterwards, the RDD was formulated and applied remotely, by Google Meet®. Finally, three infusions were followed up under the supervision of our center.

Results:: Six patients presented immediate IRR to different recombinant enzymes: three patients with Fabry disease, one with MPS I, one with MPS II and one with MPS IV. The Allergy Center located in São Paulo, was composed of a team of allergology and health professionals with expertise in inborn errors of metabolism. The (TLC) were in the interior of São Paulo, Bahia, Pernambuco and Piauí, 300 to 1,800 miles apart. The protocols were carried out respecting the Standard 12 -16 steps according to risk stratification. One of the patients, developed urticaria on the 11th step, despite the addition of premedication.

Conclusion: The new Coronavirus' pandemic imposed a new reality, which include much more telecommunication. Barriers have been overcome, such as offering remote alternatives to the treatment of incurable diseases in countries with continental dimensions.

1262 | The epicenter of COVID-19 outbreak and quality of life (qoL) of patients with inborn errors of immunity (IEI): A sad reality

Schmid L. S., Teixeira L. N., Aranda C. S., Guimarães R.R. L., Pimentel M. G.P., Fanti G. C., Rizzo M. C., Solé D., Wandalsen G. F.
Federal University of Sao Paulo (UNIFESP), São Paulo, Brazil

Background: *The world is facing one of the worst pandemics in history. Its social, economic and psychological consequences will leave profound marks on society. This study evaluated the QoL of patients with IEI at an immunology referral centre, during the SARS-CoV-2 pandemic.*

Method: A prospective, single-center study with an adapted questionnaire was applied in two moments of the pandemic: from April to June 2020, and again in March 2021. IEI patients over 18 years old and the caregivers of children under this age answered it online. This questionnaire was adapted from the Portuguese version of the shortened WHO QoL-brief QoL assessment instrument (questions 1,2,4,5 e 26) and the 10-item version of the Perceived Stress Scale (questions 1,2 e 3), taking into account the past four weeks.
Results: In the first three months analyzed (April to June/2020), 123/160 questionnaires were answered: 44.7% by caregivers and 55.3% by patients themselves. The children were 12-18 years old and adults were 18-45 years old. 91.1% of the patients have been receiving intravenous immunoglobulin replacement. 84.5% of the patients have already been hospitalized, and 38.2% of them in the intensive care unit at least once. All participants have heard of SARS-CoV-2 and 91% were afraid of being infected with the new virus. 81 patients (66%) reported good QoL prior to the pandemic and, after its onset, this percentage dropped to 27%. In March 2021, with the exponential increase in cases and deaths in Brazil, the questionnaire was reapplied, and 99/160 were answered, 52.4% by patients. The majority (72.6%) are between 18-45 years old, and only 8% of the responders reported good QoL. Everyone fears the coronavirus.
Conclusion: Currently, Brazil is the epicenter of COVID-19 outbreak on the planet. In recent weeks, the number of new cases and deaths has grown wildly. Furthermore, IEI patients in Brazil had to deal with the lack of immunoglobulin supply throughout 2020, and until now. In the face of so much adversity, there is an urgent need to think about strategies to improve the QoL of these patients. This is one of the alerts of World primary immunodeficiencies (PI) Week 2021.

1274 | PASC, reinfections and variants: COVID-19 in patients with inborn errors of immunity in São paulo - Brazil

Guimarães R. R.L.[1]; Aranda C. S.[1]; Schmid L. S.[1]; Ramos B. C.F.[1]; Machado L. M.O.[1]; Gouveia-Pimentel M.[1]; Rizzo M. C.[1]; Goudouris E. S.[2]; Solé D.[1]
[1]*UNIFESP, São Paulo, Brazil;* [2]*UFRJ, Rio De Janeiro, Brazil*

Background: Inborn Errors of Immunity (IEI) are a heterogeneous group of diseases which immune defect may be related to a complications by COVID 19. Although there are few studies on the evolution and the real clinical impact of infection by SARS-CoV 2 in this group of patients. The aim of the study was to describe the clinical evolution of COVID-19 in patients with different IEI, in a reference center in Brazil.
Method: Retrospective and longitudinal study, with analysis of electronic medical charts of patients with IEI and diagnosis of suspected/confirmed COVID-19 from March 2020 until now.
Results: Eighteen patients (61% male), with a median age of 26.6 years (range 12,3-53,4 y), were included in the study. Four X-linked agammaglobulinemia (XLA), 7 common variable immunodeficiency (CVID), 1 specific antibody deficiency, one Good Syndrome - GS, 2 STAT1-GOF, 2 MSMD and one AT. Ten patients (55,5%) had mild flu syndrome and only one patient was asymptomatic. Hospitalization was necessary for 7 patients (38,8%) due to respiratory complications and 3 (16.6%) deceased (2 XLA and 1 GS). Two patients were reinfected (STAT1-GOF and MSMD), with no need for hospitalizations or long-term complications. One of the XLA patients remains hospitalized, with fever for more than 90 days. Five patients experience coughing and tiredness after more than three months of the disease, one also persists with anosmia.
Conclusion: Almost 40% of our sample required hospitalization and 16% died. This rate is worrying and reveals how much immunological competence is required by SARS-CoV-2 as well as the fact that Brazil has increasing death rates from COVID-19. Post-acute COVID-19 syndrome (PASC) has presented in more than 25% of IEI patients infected with SARS-CoV-2.

1332 | The effect of atmospheric pollutants on the grass pollen allergenicity

Ščevková J.; Vašková Z.; Sepšiová R.; Kovác J.
Comenius University in Bratislava, Bratislava, Slovakia

Background: Grass pollen is one of the most important allergen sources inducing respiratory allergies and Phl p 5 allergen of timothy pollen is considered one of the major parts of the allergenic activity of grass pollen. In this study, we evaluated seasonal variation in the concentration of both grass pollen and Phl p 5 allergens as well as the ratio allergen/pollen (pollen potency) in the air of Bratislava, Slovakia during two consecutive years, 2019–2020. These two years differed in terms of air pollution, as COVID-19 lockdown in 2020 improved air quality in a very emphatic manner in the study area. Therefore, the goal of this research was also to determine how environmental factors affect airborne pollen and aeroallergen levels and pollen potency.
Method: Pollen sampling was performed using a Hirst-type sampler, while a cyclone sampler was used for the aeroallergen capturing. Allergenic molecules were quantified by ELISA assay.
Results: In 2020, the year characterised by a less polluted atmosphere due to COVID-19 lockdown, we observed significantly higher

Seasonal Poaceae Pollen Integral, the mean daily pollen value and even peak pollen value, while the mean daily pollen potency, the mean daily allergen concentration and peak allergen value were significantly lower than in 2019. Raised pollen concentrations were accompanied by increased ozone and carbon monoxide levels in 2020, whereas increased rainfall or relative humidity led to the reduction of pollen in the atmosphere. In 2020, the aeroallergen levels were associated mainly with pollen, but nitrogen dioxide in the air could increase the number of allergens per pollen. In contrast, the aeroallergen levels were associated with carbon monoxide in 2019.

Conclusion: Based on our results it is evident that air pollutants can influence grass plants to produce pollen with altered allergenic content.

988 | Anti-COVID-19 vaccine late hypersensitivity reaction

Completo S.[1]; Geraldo A.[2]; Sokolova A.[2]

[1]*Pediatrics Department, Hospital Prof. Doutor Fernando Fonseca, EPE, Amadora, Portugal;* [2]*Pneumology Department, Hospital Prof. Doutor Fernando Fonseca, EPE, Amadora, Portugal*

Background: First approved anti-COVID vaccines brought a new experience of hypersensitivity reactions into clinical practice. This experience and knowledge of mechanisms are important for further safer and wider use of these immunizations.

Methods: Clinical and laboratory data collected in immunoallergology outpatient evaluation and consultation of informatic process. Written consent was obtained.

Results: We report a case of a 33-year-old woman, a laboratory worker, who received the first dose of mRNA-based anti-COVID-19 vaccine. After 48-72h she presented with extensive generalized urticaria lesions and pruritus. She was admitted to the emergency department, treated with endovenous corticosteroid and antihistaminic, attenuating skin lesions. However, 12-24h later, urticaria exacerbated, with labial and bilateral ear swelling. She was medicated with oral prednisolone, gradually resolving symptoms. She had no concomitant alcohol/ drug consumption nor practiced physical exercise.

She had antecedents of persistent allergic rhinitis and allergic bronchial asthma in the first step of treatment. She had no prior history of drug allergy nor adverse reactions to vaccines. Skin prick tests performed with commercial extracts of aeroallergens were positive for D. *pteronyssinus*, D. *farinae*, *lepidoglyphus*, olive tree pollen, grass pollen, and cat and dog dander. Skin prick test with latex was negative. Basal tryptase was 6.4 and total IgE 154.0 UI/mL. Spirometry was normal at basal condition.

Prick test with anti-COVID-19 vaccine was negative. Intradermal test with 1/100 and 1/10 dilutions of anti-COVID-19 vaccine was also negative at 20-30 minutes. However, after 4h she showed hyperemia and swelling of about 7-8cm, localized at the place of both dilutions of intradermal test vaccine administration. PATCH tests performed with anti-COVID-19 vaccine were negative at 48h and 72h readings.

She was diagnosed with anti-COVID-19 vaccine late hypersensitivity and, therefore, was not able to take the second dose.

Discussion: We report a clinical case of late hypersensitivity to mRNA-based anti-COVID-19 vaccine in a patient without prior history of drug allergy. The reaction was documented with positive intradermal tests performed with 1/100 and 1/10 vaccine dilutions. According to EAACI indications, she did not receive the second dose of the vaccine. Extracts of vaccine components will help to understand adverse reactions and choosing an alternative vaccine, when available.

1266 | Pre-hospital care for a patient with moderate severity of COVID-19

Sargsyan A.[1]; Sargsyan V.[2]

[1]*Izmirlian MC, Yerevan, Armenia;* [2]*Best Life MC, Yerevan, Armenia*

Patient 60 years old, a teacher working from home, got infected from her husband. The husband was an asymptomatic. Symptoms were loss of taste and smell, fever, weakness, nausea, vomiting, diarrhea, blurred vision. Hemodynamic parameters - BP 90/60 mm Hg, HR - 99 bpm. Her regular HR was 55-60 bpm. Due to the overloading of hospitals, there was a queue for hospitalization at home. She was receiving the treatment of a family doctor. On the 9th day, her condition became worst. CT-scan picture showed 20% of lung lesions. Hemodynamic parameters were - BP 80/50 mm Hg, HR -115 beats. Due to of progressive dehydration, the high temperature lasted for 12 days. In anamnesis she has a drug allergy, chronic hypertension with left anterior bundle branch block because of suffering with rheumatic heart disease from the childhood. Any kind of liquid per oral caused immediate nausea and vomiting. Saturation was 74. We had to start i/v therapy at home in order to stop severe dehydration and high fever. Mobile oxygen delivery devices were used to monitor saturation. With that treatment during the day, the saturation indicator was 92. But at night, when the saturation went down below 86, the device, by means of an audible alert, gave a signal to connect oxygen. BP dropped to 70/50 mm Hg, HR -120 bpm. The patient also received factor XA inhibitor, antibiotic therapy, antiviral therapy, vitamins C and D. After these measures, she felt better, but could not take liquid on her own, as it still caused nausea. On the 14th day, a place was vacated in one of the hospitals and she was hospitalized. In the hospital, she spent another 10 days, the hemodynamics returned to normal and the second CT-scan showed 5% of the lungs damage. She was discharged of her own free will. For 1.5 months after that, she still felt severe weakness and was unable to work.

1289 | First SARS-coV-2 infection in patients with severe asthma receiving mepolizumab

Atayik E., Aytekin G.
University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

Severe acute respiratory syndrome coronavirus (SARS-CoV)-2 is a zoonotic viral pathogen belonging to the same family as SARS-CoV. To the best of our knowledge, no case that received mepolizumab for severe asthma and developed COVID-19 has been reported to date in the literature. In September 2020, a 61-year-old male patient who was receiving monthly mepolizumab treatment for the last 6 months in addition to his current asthma treatment, was admitted to our clinic with complaints of high fever (38-38.50C), loss of senses of taste for 3-4 days, as well as nonproductive cough and shortness of breath. Patchy ground-glass densities were observed in basal parts of lower lobes of both lungs and the patient had a positive nasopharyngeal real-time PCR SARS-CoV-2 test. The patient was initiated the treatment of hydroxychloroquine, favipiravir, and an anticoagulant and home quarantine was recommended. The patient's complaints were significantly relieved on day 5 of the treatment. Need for larger and more extensive studies on the effect of the medications used for the treatment of patients with severe asthma on COVID-19 infection is obvious and, due to its antiviral effects, the potential favorable contribution of mepolizumab to the treatment of COVID-19 infection in this patient group should be monitored.

Keywords: severe asthma, mepolizumab SARS-CoV-2

1155 | Reality of allergists during the COVID-19 pandemic in Argentina 2020

Cavallo M. C.[1]; Irastorza M. J.[2]; Baillieau F.[3]; Borghello M. C.[4]; Indiveri M.[5]; Cavallo A.[6]; Villa L.[7]; Fernandez L.[8]; Ritche C.[9]; Ramon G.[10]; Strass M.[11]
[1]*Hospital San Martin, Paraná, Argentina;* [2]*Insituto IMGO, Córdoba, Argentina;* [3]*Clínica de Alergia, Mar Del Plata, Argentina;* [4]*Hospital de la Baxada, Parana, Argentina;* [5]*Hospital T.J.Shestakow, San Rafael, Argentina;* [6]*Consultorios Medicos Paraná, Parana, Argentina;* [7]*Sanatorio San Roque, Marco Juarez, Argentina;* [8]*Clínica del Valle,, Santa Fe, Argentina;* [9]*Hospital Italiano, Buenos Aires, Argentina;* [10]*Hospital Regional Italiano del Sur, Bahia Blanca, Argentina;* [11]*Sanatorio Boratti, Posadas, Argentina*

Background: The COVID-19 pandemic modified the way of practicing medicine, causing a changes in medical actions in the health professional and in their habits in relation to daily practices. Accelerated changes have taken place, which have led to the development and implementation of telemedicine as a very useful tool that allows professional contact with their patients, and on the other hand, access to up-to-date scientific training.

Objetive: Evaluate the impact of the COVID-19 pandemic on the activity of the allergist in Argentina during phase 1 of preventive and mandatory social isolation (april and may 2020). Determine the impact of the pandemic on allergic diseases. Analyze the use of telemedicine in daily practice.

Method: It is a prospective, observational and cross-sectional study. A questionnaire was made to specialist doctors in Allergy and Immunology during april and may 2020 of preventive and compulsory social isolation, for subsequent statistical study..

Results: 113 surveys were carried out, 72.9% showed a decrease in work practice by 50%, 20.7% between 25-50% and 6.3% less than 25%. The most frequent consultations were request for prescriptions in 67%, medical history certificates in 48%, rhinitis and urticaria in 46%, atopic dermatitis and asthma attack in 23%, and contact dermatitis in 5.3%. 94% implemented telemedicine, the most used tools were whatsapp/webcam (61%) followed by telephone assistance (38%).

Conclusion: The COVID-19 pandemic affected the practice of the specialty in terms of the decrease in medical consultation, the way of working, interacting with patients, the need for protective equipment, with an emotional and economic cost. On the other hand, it gave the possibility of having other care alternatives such as telemedicine.

1293 | SARS-coV-2 in a patient with persistent asthma taking omalizumab: The first case in turkey

Atayik E.; Aytekin G.
University of Health Science Konya City Hospital Department of Allergy and Clinical Immunology, Konya, Turkey

Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China, it has been one of the largest pandemics in the history which has been aggressively spreading all over the world and affected more than 6 percent of world's population. In SARS-CoV-2 pandemics, patients with severe asthma require particular attention due to not only the underlying airway disease, but also immunomodulatory treatments used. Although it is known that viruses infecting the respiratory mucosa are risk factors for asthma attacks and that viral infections at early stage of the life are risk factors for development of asthma, and patients with a chronic disease have been declared as the risk group for severe SARS-CoV-2 infection by The Centers for Disease Control and Prevention (CDC), some studies reported that ratio of patients with asthma is relatively lower among the patients hospitalized for SARSCoV-2. This suggests that treatments used for asthma may be protective against SARS-CoV-2. In addition, our knowledge regarding effect of omalizumab on mortality and morbidity in patients with asthma using omalizumab in SARS-CoV-2 infection is limited. In this case report, through reporting this first case of accompanying SARS-CoV-2 case in a patient with severe persistent asthma using omalizumab from Turkey, we aimed to discuss potential effects of

omalizumab treatment on accompanying SARS-CoV-2 pneumonia in these patients.

Keywords: SARS-CoV-2, omalizumab, severe asthma

1096 | Methylchloroisothiazolinone/methylisothiazolinone and methylisothiazolinone sensitization: An 11-year single center experience

Presa A. R.; Mesquita M.; Valente C.; Ferreira J.; Guilherme A.; Cadinha S.; Rosmaninho I.

Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova De Gaia, Portugal

Background: Allergic contact dermatitis (ACD) is a common problem confronted in clinical practice. Several authors have started to point to methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI) and methylisothiazolinone (MI) as emerging allergens, primary present in many daily cosmetics.

The aim of this study was to characterize patients referred to our Allergy Department with suspected ACD in whom sensitization to MCI/MI and/or MI was found, between 2010-2020.

Method: A retrospective study was carried out were data related to patch tests, demography, occupational history, atopy, body area affected and products suspected were reviewed.

Results: ACD was diagnosed in 987 patients (80.9% female, median age of 42 years IQR 25), between 2010 and 2020. A total of 36 (3.8%) patients had positive reactions to MI, MCI/MI or both (n = 19, n = 9, n = 8, respectively). Of these, 20 (55.6%) patients had positive reactions to other sensitizers, being nickel the most frequent one. Atopy and allergic disease were found, respectively, in 15 (41.7%) and 12 (33.3%) patients, with no statistically significant difference between MCI/MI and MI sensitization (p =1.000 and p = 0.224, respectively). Onset of dermatitis was between 1-5 years in 19 (52.8%) patients. Clinical relevance of contact dermatitis was considered current in 26 (72.7%) patients. The main sources of sensitization were the workplace (n = 12) and daily cosmetics (n = 11). The more commonly affected occupations were beauticians (25%), hairdressers (16.7%) and painters (16,7%). Nine patients were exposed to one product and 2 patients were exposed to three products. Sixty percent of suspected cosmetics were leave-on products, mostly corresponding to MCI/MI sensitization. MI was the most frequent sensitizer in rinse off products. Hands were the most frequent body area affected, followed by face, arms, neck and trunk. Over the years, MCI/MI and/or MI sensitization has become increasingly frequent. In 2019 and 2020 they were the second most identified allergens, 11.1% and 16.7% respectively, after nickel.

Conclusion: Among the total population with suspected ACD who underwent patch tests, almost 4% had positive reactions to MI and/or MCI/MI. In most of these patients, the onset of dermatitis was between 1-5 years. Leave-on products were suspected more frequent than the rinse-off type. Current clinical significance was considered in 73% of patients. In the last two years analysed, MCI/MI and/or MI have become the most frequent allergens identified, after nickel.

1021 | Eosinophilic fasciitis, an unusual presentation

Ferrando Anaut P.[1]; López San Martín M.G.[1]; Blanco Ramos M.T.[1]; Villalón García A.L.[1]; Durán Del Campo P.[2]; Bilbao Garay J.[2]

[1]*Allergy Department. Puerta de Hierro Majadahonda University Hospital, Madrid, Spain;* [2]*Internal Medicine Department. Puerta de Hierro Majadahonda University Hospital, Madrid, Spain*

Eosinophilic fasciitis (EF) is characterized in its early phase by limb or trunk erythema and non-pitting edema of the skin and later by symmetrical induration of the skin and deeper perimuscular fascial planes, accompanied by a peripheral blood eosinophilia. The onset is typically acute.

A 52 year old man, presented during his last months, recurrent generalized episodes of pruritus and evanescent hives, sometimes associated with peripheral angioedema. Oral corticosteroid pulses and daily antihistaminics intake acheive a good clinical control. An exhaustive study, just detected a slight peripheral eosinophilia and tiroid autoimmunity with normal tiroid function. 6 months later, pruritus and hives stopped but he started complaining of muscle pain, muscle weakness and weight loss. A new study was conducted.

Results:

- Laboratory findings:

- Peripheral eosinophilia 3.09 10E3/microL. Hypoalbuminemia. Normal complement and immunoglobulin levels.
- Autoimmunity Test: elevated antithyroglobulin antibodies (493.50 U/mL) and antimicrosomal antibodies (756 U/mL) levels but normal tiroid hormones. Negative for ANA, ENA and ANCA
- Microbiological analysis: negative serum serology for parasites, virus and bacterias, but Chlamydia pneumoniae IgM(+). Negative fecal parasites studies

- Radiological studies:

- Eco-Doppler-lower limbs: symmetrical generalized lymphedema
- CAT Scan- thoracoabdominal: bilateral inflammatory changes in obliquus abdominis muscles
- Magnetic resonance imaging- pelvis&lower limbs: symmetric thickening, wihout muscle afectation, interpreted as consistent with fascial inflammation present in EF

-Biopsy: full thickness biopsy of skin and subcutaneous tissues down to the muscle surface found EF compatible changes in the deep dermis and fascia

-Hematologic disorders associated with EF and hipereosinophilic syndrome were discarded by molecular and genetical studies along with a bone marrow biopsy

Oral corticosteroid therapy was started at 60 mg/day, acheiving clinical improvement and peripheral eosinophilia resolution.

Corticosteroids were tapered slowly to 10 mg/day, but withdrawal was not be possible because of myalgias and muscle weakness recurrence. Low-dose methotrexate 15 mg once weekly reach clinical control.

Conclusions

A case of an uncommon disorder is presented, to emphasize that a close follow up is mandatory in clinical cases presenting pruritus and hives, in order to rule out or to diagnose other entities apart from chronic urticaria

1047 | The impact of the presence and eradication of different subtypes of blastocystis spp on the clinical course of chronic spontaneous urticaria

Tuzer C.[1]; Sonmez N.[2]; Yegit O. O.[1]; Demir S.[1]; Ertek B.[1]; Demirpek U.[3]; Boral O.[2]; Buyukozturk S.[1]; Gelincik A.[1]; Colakoglu B.[1]

[1]*Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Immunology and Allergic Diseases, Istanbul, Turkey;* [2]*Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Division of Medical Parasitology, Istanbul, Turkey;* [3]*Bursa City Hospital, Department of Medical Microbiology, Istanbul, Turkey*

Background: The impact of the presence of different subtypes of *Blastocystis spp* on the clinical course of chronic spontaneous urticaria (CSU) has not been precisely determined. The purpose of this study was to investigate the presence of *Blastocystis spp*. subtypes in CSU and the role of their eradication in disease activity.

Method: Stool samples from 295 adult CSU patients and 38 healthy controls (HCs) were microscopically examined. The samples having parasites were cultured in Dulbecco' s Modified Eagle Medium (DMEM) and Jones media. After the DNA isolation from the cultures, samples were evaluated by real-time (RT)-PCR. Subsequently, DNA sequences were analyzed by "Sequencing Analysis 5.3.1" software. Subtype results were obtained by analyzing megablasts of "NCBI Blast" database. Medication scores (MS), Urticaria Activity Score-7 (UAS-7) and laboratory values were compared at the beginning and six months after anti-parasitic treatment between the patient groups having various *Blastocystis spp*. subtypes. The demographic and laboratory data were also compared between the patients and HCs. Written informed consent was taken from the study participants.

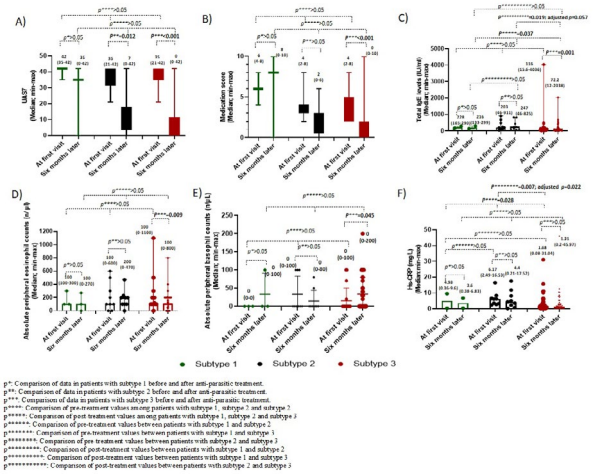
Results: The parasite was detected in 45.8% (n = 135) of the patients and %34.2 (n = 13) of HCs (p>0.05). 57 (85.1%) of 67 samples in the patient group and 12 (92.3%) of 13 samples in HCs revealed a positive RT-PCR. Serum total IgE levels were higher in the patient group (p < 0.001). Subtype 3 was significantly higher in the patient group (p < 0.001) whereas subtype 1 was higher in HCs (p < 0.001). The remission rate of the disease was higher (p = 0.031) while UAS-7, MC and total IgE levels were lower in the patients having subtype 3 than in the patients with other subtypes at the end of sixth month of anti-parasitic treatment (p = 0.028, p = 0.044, p = 0.01) (Table-1). MS, UAS-7, total IgE levels, eosinophil counts decreased (p < 0.001, p < 0.001, p = 0.001, p = 0.009) and basophil counts increased significantly in patients with subtype 3 (p = 0.045) whereas only UAS-7 decreased in those with subtype 2 after anti-parasitic treatment (p = 0.012) (Figure-1).

Conclusion: The presence and eradication of *Blastocystis spp* subtype 3 seem to be related to CSU clinical course. *Blastocystis spp*. sequencing analysis can be helpful in determining the patients in need of Blastocystis eradication to control CSU activity.

	Patients with subtype 3 (n = 45, 79%) N (%)	Patients with other subtypes (n = 12, 21%) N (%)	p
Gender			
Female	30 (67%)	7 (58%)	>0.05
Male	15 (33%)	5 (42%)	>0.05
Non allergic comorbidities	23 (51%)	7 (58%)	>0.05
Hypertension	10 (22%)	3 (25%)	>0.05
Diabetes Mellitus	4 (9%)	0 (0%)	>0.05
Coronary artery disease	3 (7%)	0 (0%)	>0.05
Gastritis	7 (16%)	1 (8%)	>0.05
Hypothyroidism	9 (20%)	2 (17%)	>0.05
Depression	4 (9%)	1 (8%)	>0.05
Allergic comorbidities	26 (58%)	9 (75%)	>0.05

	Patients with subtype 3 (*n* = 45, 79%) *N* (%)	Patients with other subtypes (*n* = 12, 21%) *N* (%)	*p*
Rhinitis	18 (40%)	4 (33%)	>0.05
Asthma	2 (4%)	2 (%17)	>0.05
Food hypersensitivity	14 (31%)	7 (58%)	>0.05
Drug hypersensitivity	8 (18%)	5 (42%)	>0.05
Presence of physical urticaria	13 (29%)	3 (25%)	>0.05
Accompanying angioedema	25 (56%)	9 (75%)	>0.05
Autoimmunity*	25 (56%)	8 (67%)	>0.05
Anti-nuclear antibody positivity	4 (9%)	2 (17%)	>0.05
Thyroid autoantibody positivity	14 (31%)	5 (42%)	>0.05
Autologous serum skin test positivity	9 (20%)	4 (33%)	>0.05
Presence of Helicobacter pylori	16 (36%)	3 (25%)	>0.05
Remission of the disease after antiparasitic treatment	27 (60%)	3 (25%)	**0.031**
	Median (IQR 25-75)	**Median (IQR 25-75)**	***p***
Age (year) (Mean ± SD)	40.2 ± 13.3	47.5 (17.1)	>0.05
Body Mass Index (BMI) (Mean ± SD)	27.2 ± 4.8	29.9 ± 5.3	>0.05
Duration of urticaria (months)	24 (13.5-120)	24 (12-45)	>0.05
UAS7 (at first visit)	35 (35-42)	35 (35-42)	>0.05
ÜAS7 (at sixth month visit)	0 (0-12)	8 (2-32)	**0.028**
MC (at first visit)	4 (2-5)	4 (4-6)	>0.05
MC (at sixth month visit)	0 (0-2)	2 (0-6)	**0.044**
Total IgE (at first visit) (IU/mL)	116.00 (44.24-200.71)	203.00 (125.92-485.19)	**0.024**
Total IgE (at sixth month visit) (IU/mL)	72.19 (36.13-185.42)	246.59 (93.49-429.22)	**0.01**
Absolute peripheral eosinophil count (at first visit) (*n*/ µl)	100 (100-200)	100 (100-300)	>0.05
Absolute peripheral eosinophil count (at sixth month visit) (*n*/ µl)	100 (85-200)	150 (100-223)	>0.05
Absolute peripheral basophil count (at first visit) (*n*/ µl)	0 (0-0)	0 (0-75)	>0.05
Absolute peripheral basophil count (at sixth month visit) (*n*/ µl)	0 (0-60)	0 (0-38)	>0.05
High sensitive C reactive protein (at first visit) (mg/L)	1.68 (0.69-3.87)	6.17 (2.76-8.4)	**0.013**
High sensitive C reactive protein (at sixth month visit) (mg/L)	1.31 (0.47-3.55)	4.40 (0.81-8.18)	>0.05
Tryptase level (ug/L)	4.48 (1.78-7.31)	2.29 (1.5-6.03)	>0.05
Peripheral leukocyte count (*n*/µl)	7.100 (6.500-8.050)	7.550 (6.525-10.800)	>0.05
Absolute peripheral neutrophil count (*n*/µL)	4.200 (3.600-5.200)	4.650 (3.700-6.475)	>0.05
Thyroid-stimulating hormone (mIU/L)	2.14 (1.58-3.12)	1.54 (0.94-3.01)	>0.05
Alanine transferase (U/L)	18 (14-25)	19 (13.5-26.8)	>0.05
Aspartate transferase (U/L)	18 (15.8-23)	17 (15-27)	>0.05
Creatinine (mg/dl)	0.7 (0.6-0.8)	0.8 (0.7-0.94)	>0.05

*Thyroid autoantibody, anti-nuclear antibody, autologous serum skin test positivity and co-existence of autoimmune diseases.



1094 | Angioedema is associated with severity in patients with chronic urticaria

Argolo P. N.; Kalil J.; Motta A. A.; Agondi R. C.
University of São Paulo, São Paulo, Brazil

Background: Approximately half of the patients with chronic spontaneous urticaria (CSU) and, less frequently, patients with chronic inducible urticaria (CIndU) report angioedema (AE). Several markers may indicate a worse prognosis for chronic urticaria, such as AE. The objective of this study was to classify CU patients according to the presence of AE, and characterize both groups according to biomarkers anti-TPO and total IgE.

Method: This was a retrospective study with data collected from electronic medical records of patients with CU followed up in a tertiary service. All patients were at outpatient follow-up for more than 6 months. Demographic data, CU classification, exacerbation by nonsteroidal anti-inflammatory drug (NSAID), refractoriness to H1-antihistamines, total serum IgE and anti-TPO were evaluated.

Results: There were 161 sequentially selected patients. Of them, 139 (86.3%) were female, the mean current age was 48.4 years, and mean duration of urticaria was 9.4 years. Of them, 116 patients (72%) had only CSU and 45 (28%) had CIndU, associated or not with CSU. AE was reported by 103 patients (64%). CSU was more frequently observed in patients with AE than those patients without AE (98.1% vs 86.2%, $p = 0.027$), on the other hand, CIndU was lesser diagnosed in patients with AE (18.4%) than those without AE (44.8%), $p < .001$. Refractoriness to H1-antihistamines was observed more frequently in patients with AE than those without AE, 35% *vs* 10.3%, $p < 0.001$), as well as and NSAID-exacerbated chronic urticaria, 47.6% *vs* 29.3%, $p = 0.02$. Positive anti-TPO was more frequent in patients with AE ($p = 0.048$) and total serum IgE was similar in both groups ($p>0.05$), although, in a high value, mean 362 IU/mL.

Conclusion: AE was a frequent manifestation and it was associated with a worse prognosis for CU, as observed by the lower response to antihistamines. Those patients had more often chronic urticaria exacerbated by NSAID and positive anti-TPO. Total IgE was high and similar in both groups.

950 | Dietary fiber and the SCFA butyrate protect against atopic dermatitis and subsequent allergic airway inflammation

Trompette A.[1,2]; Pernot J.[1,2]; Ubags N. D.[1,2]; Nicod L. P.[2]; Von Garnier C.[1,2]; Marsland B. J.[1,3]
[1]CHUV_service de pneumologie, Epalinges, Switzerland; [2]Faculty of Biology and Medicine, UNIL, Lausanne, Switzerland; [3]Department of Immunology and Pathology, Monash University, Melbourne, Australia

Background: Atopic dermatitis (AD) is a chronic skin disease typically manifesting during the first years of life and affecting up to 20% of children in Westernized countries. Currently no cure exists. Novel therapeutic strategies are thereby desperately needed.

One main risk factor for AD is a decreased skin barrier function, which can lead to increased allergen ingress and consequently, establishment of a Th2-polarized milieu driving initiation and progression of allergic skin inflammation. Recently, it became evident that AD is not an isolated disease but rather an early inflammatory trigger. Early allergic skin sensitization can indeed predispose children to develop other allergic disorders later in life, such as allergic asthma, a succession of events known as the "atopic march".

Interestingly, products of the fermentation of dietary fiber, the metabolites short-chain fatty acids (SCFA), have been shown to alleviate various allergic diseases.

Method: Here, using a mouse model and the common house dust mite (HDM) allergen, we report that high-fiber diet and SCFA (butyrate) supplementation protect against the development of AD, and subsequent allergic airway inflammation (AAI).

Results: Indeed, fiber-rich diet or oral SCFA ameliorated transepidermal water loss and AD severity. Sensitization to HDM was blunted as indicated by lower levels of circulating IgE antibodies. These beneficial cutaneous and systemic effects translated into an improved AAI once mice were subsequently exposed intranasally with HDM. We found that the beneficial effects of SCFA were mediated by their ability to strengthen and preserve skin barrier integrity during repeated allergen exposure. Ultimately, we unraveled that SCFA alter mitochondrial metabolism, promoting keratinocyte differentiation and the production of key structural components responsible for maintaining the architecture of the cornified envelope, the outermost layer of the epidermis.

Conclusion: Overall, our results show that dietary fiber and SCFA prevent the development of AD by improving skin barrier function, ultimately halting the dire "atopic march" sequelae.

984 | Provocation testing in chronic inducible urticaria: Experience of a Brazilian urticaria center of reference and excellence - UCARE

Azizi G. G.; Dortas Junior S. D.; Valle S. O.R.

Serviço de Imunologia, Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ), Rio De Janeiro, Brazil

Background: Chronic Urticaria (CU) is a common condition, determined by the activation of mast cells that presents with erythematous, swollen, itchy, and sometimes painful hives (wheals), angioedema, or both and occur repeatedly for more than 6 weeks.However, it is highly complex when considering etiology and therapies. The current guidelines classify CU as spontaneous (chronic spontaneous urticaria [CSU], with no specified eliciting factor involved) or inducible (chronic inducible urticaria [CIndU], with a specific eliciting factor involved). The diagnosis of CIndUrelies on a thorough history and provocation testing. In all patients with a history suggestive of CIndU, provocation testing should be performed if possible, to confirm the diagnosis.

We aim to describe CIndU relevant triggers by positivity provocation tests performed in an Urticaria Center of Reference and Excellence (GA2LEN UCARE) in Rio de Janeiro, Brazil.

Method: We retrospectively reviewed the records of 111 patients who had suspicion of CIndU and were submitted to provocation tests, from December 2017 to February 2021. We analyzed CIndU report and its confirmation or not throughout provocation tests.

Results: Eighty-eight patients were female, and 23 were male with age between 12-85 years old. Patients had the following CindUs confirmed by tests: Symptomatic Dermographism (65/60%), Delayed Pressure Urticaria (23/21%), Cold Urticaria (12/11%), Heat Urticaria (3/2,7%), Cholinergic Urticaria (1/0,9%) and Vibratory Urticaria (1/0,9%). Aquagenic and Solar Urticarias were not reported. Multiple UCInd were found in 15% of subjects.

Conclusion: Our data are similar to those previously reported and confirm that clinical history as well as a precise indication of provocation tests can exclude or confirm the diagnosis of CIndU, which is essential for specialists management of the disease and patient's quality of life improvement.

1018 | Are hereditary angioedema patients satisfied with on-demand therapy with icatibant?

Beyaz S.; Demir S.; Öztop N.; Çolakoglu B.; Büyüköztürk S.; Gelincik A.

Division of Immunology and Allergic Diseases, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Background: The satisfaction level of hereditary angioedema (HAE) patients upon on-demand treatment with icatibant has not been addressed before.

The aim of this study was to evaluate the opinions and satisfaction levels of the HAE patients about icatibant.

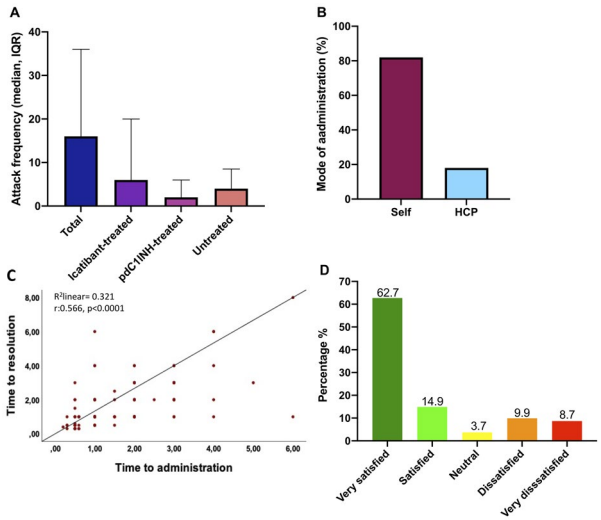
Method: 161 HAE patients were prospectively evaluated with a questionnaire including several questions about their icatibant-treated attacks. Details of demographic and clinical features were collected from their medical records and attack diaries.

Results: A total of 161 HAE-C1INH patients were included in the study. Patients reported a median of 2 (IQR:0.5-3) attacks per month and 16 (IQR:4.5-36) attacks per year (Table 1). Median frequency of attacks treated with icatibant was 6 (IQR:0-20) per year (Figure 1A). Mean duration of treatment with icatibant was 3 ± 2.3 years. Self-administration rate was 91.3% (Figure 1B). Mean time to administration and time to resolution were 1.6 ± 1.1 and 1.7 ± 1.3 hours, respectively. There was a correlation between the time to administration and time to resolution (r:0.566, $p < 0.0001$) (Figure 1C). A total of 125 (77%) patients reported that they were very satisfied or satisfied with icatibant (Figure 1D). A total of 52 patients reported 74 mild local reactions (Table 1). No moderate or severe adverse events (AEs) related to icatibant treatment were reported.

Conclusion: The current real-life study shows that icatibant is safe and effective. Moreover, patients' satisfaction level with icatibant in on-demand treatment, is high. We believe that availability of icatibant should be encouraged during the HAE attacks since patients are more involved in their disease management.

Characteristics	Patients (*n* = 161)
Age (year), mean ± SD	40.3 ± 13.3
Gender, *n* (%)	
Male	58 (36)
Female	103 (64)
HAE type, *n* (%)	
Type I	146 (91)
Type II	15 (9)
Age at onset of symptoms (year), mean ± SD	17.6 ± 11.9
Age at diagnosis (year), mean ± SD	30.8 ± 13.3
Delay in diagnosis (year), mean ± SD	13.3 ± 10.7
Disease duration (year), mean ± SD	9.49 ± 6.84
Long term prophylaxis, *n* (%)	87 (54)
Danazol	75 (86)
Tranexamic acid	12 (14)
Number of attacks, median (IQR)	
Per/months	2 (0.5-3)
Per/year	16 (4.5-36)
Site of attacks, *n* (%)	
Face	54 (33.5)
Abdominal	148 (91.9)
Oropharolarynx	60 (37.3)
Extremities	122 (75.8)
Genitalia	16 (9.9)
Prodromal symptoms, *n* (%)	84 (52)
Tiredness	45 (54)

Characteristics	Patients (*n* = 161)
Nausea/vomiting	23 (27)
Pain	41 (49)
Prickling	16 (19)
Irritability	24 (29)
Rash	5 (6)
Triggering factors, *n* (%)	104 (65)
Emotional distress	84 (80)
Physical trauma	78 (75)
Prolonged sitting or standing	23 (22)
Changes in estrogen levels	14 (13)
Surgery (minor or major)	27 (26)
Medications	3 (2.8)
Attack treatment, *n* (%)	
Icatibant (one or two injections)	135 (84)
pdC1INH (after icatibant injection)	20 (12)
Increasing danazol dose with icatibant injection	6 (4)
Injection-site reaction, *n* (%)	52 (32)
Erythema	27 (52)
Swelling	9 (17)
Burning/warm sensation	21 (40)
Pain	14 (27)
Prickling	3 (6)



1114 | Relationship between EASI, SCORAD, and QOL in atopic dermatitis in children

Jeon Y.H.[1]; Kim J.H.[2]

[1]*Department of Pediatrics, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, South Korea;* [2]*Department of Pediatrics, Inha University Hospital, Incheon, South Korea*

Background: The quality of life (QOL), itching numeric rating system (NRS), and sleep disturbance NRS are separately evaluated in pediatric atopic dermatitis (AD), where deterioration in QOL of a child affects the entire family. The Eczema Area and Severity Index (EASI) consists of only objective scores without subjective items, and it is doubtful whether it will reflect the QOL, itching, and sleep disturbances in children. In this study, we want to find out how EASI, Scoring Atopic Dermatitis (SCORAD), children's dermatology life quality index (CDLQI), itching NRS, and sleep disturbance NRS are correlated with each other in AD in children aged 6 and older.

Method: AD patients aged 6-18, who visited 23 secondary and tertiary hospitals nationwide were surveyed EASI, SCORAD, oSCORAD (objective SCORAD), itching NRS, sleep disturbance NRS, and CDLQI by pediatric allergy specialists. The correlation between the methods of measuring severity and the relationship between skin care, treatment, and laboratory test results were analyzed.

Results: A total of 248 pediatric AD patients were analyzed. EASI showed strong correlation with SCORAD (r=0.797) and significant correlation with CDLQI (r=0.405), itching NRS (r=0.261) and sleep disturbance (r=0.279). SCORAD as well as oSCORAD showed significant correlations with itching NRS (r=0.185), sleep disturbance NRS (r=0.267), and CDLQI (r=0.347). Onset age of AD was negatively correlated with itching NRS, sleep disturbance NRS and CDLQI (r=-0.153, -0.139 and -0.161, respectively). The number of oral antihistamines was correlated with SCORAD, EASI and CDLQI. (r=0.193, 0.228, 0.201) Total IgE levels showed positive correlation with SCORAD (r=0.155), EASI (r=0.161), and CDLQI (r=0.224).

Conclusion: In pediatric AD, EASI and SCORAD showed strong correlation. EASI consists of only objective scores, but it is also thought to reflect some of the quality of life, including itching and sleep disturbance.

1178 | Factors associated with the severity of allergic contact dermatitis

Sridi C.[1,2]; Kacem I.[1,2]; Chouchene A.[1,2]; Chelly F.[1,2]; Aloui A.[1,2]; Maoua M.[1,2]; Brahem A.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Occupational Medicine Department, Teaching Hospital "Farhat Hached", Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine "Ibn El Jazzar", Sousse, Tunisia*

Background: Allergic contact dermatitis (ACD) is a frequent reason for consulting in dermatology. The severe forms are responsible for a major physical and mental handicap.

Objective: To study the sociodemographic and occupational factors associated with the severity of ACD.

Method: This is a cross-sectional study conducted among active patients referred to the Dermato-Allergology Unit of the Teaching Hospital "Farhat Hached" of Sousse (Tunisia) as part of an etiological assessment of their ACD during the period from May 2017 to December 2018. The evaluation of the severity of the ACD was based on the POEM (Patient-Oriented Eczema Measure) score. Severe ACD was defined as a POEM score ≥17.

Results: A total of 101 cases of ACD were enrolled. The mean age was 40.1 ± 9.9 years. The population was predominantly female (sex ratio= 0.87). Average job seniority was 14.12 ± 10.37 years. The sector of activity most represented was healthcare (15% of cases). The majority of patients (92%) complained of itching. Severe forms were reported in 23.8% of cases. The severity of ACD was significantly associated with the duration of symptom progression (p = 0.046). However, no occupational factors were correlated with the severity of ACD.

Conclusion: ACD is a multifactorial recurrent disease that has significant socioeconomic and occupational repercussions and a real impact on patients' quality of life. Therefore, effective means of prevention must be applied.

1030 | Eyelid contact dermatitis: clinical and etiological particularities

Sridi C.[1,2]; Brahem A.[1,2]; Chelly F.[1,2]; Athimni Z.[1,2]; Aloui A.[1,2]; Choachane A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Occupational Medicine Department, Teaching Hospital "Farhat Hached", Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine "Ibn El Jazzar", Sousse, Tunisia*

Background: Contact dermatitis (CD) is a public health problem. Allergic CD is the most common cause of eyelid dermatitis.

Objectives: To determine the clinical and occupational characteristics of patients with eyelid contact dermatitis (ECD) and to identify the allergens causing allergic ECD.

Method: This is a retrospective descriptive study carried out on all patients with ECD who attended the Dermato-Allergology Unit of the Occupational Medicine Department of the Teaching Hospital "Farhat Hached" of Sousse (Tunisia) over a period of 31 years from January 1989 to December 2019. The data collection was conducted using a synoptic sheet which included the socio-professional and medical characteristics of the patients as well as the results of patch tests performed with allergens from the European Baseline Series.

Results: A total of 188 cases of ECD were enrolled. Our population was predominantly female (55.3%) with a mean age of 37.2 ± 12.2 years. The majority of patients were active (87.2%). The most represented sector of activity was the Textile sector (17.7%). The appearance of the lesions was mostly erythematosquamous (68.8%) in cases of isolated palpebral injury. The most frequently associated localization was on the hands. Allergic CD was the most common diagnosis (51.6%). The most frequently found allergen was nickel (16.5%). After multivariate analysis by binary logistic regression, the allergic origin of ECD was significantly correlated with occupational etiology. Isolated palpebral injury was independently correlated with colophony sensitization.

Conclusion: As for any allergic contact dermatitis, avoidance of the allergens involved remains the privileged therapeutic approach. Close collaboration between the occupational physician and the dermatologist is necessary to fight against contact dermatitis in the workplace.

978 | Effectiveness of immediate and delayed moisturizing after bathing/washing on the improvement of SCH and TEWL

Nguyen H. H.K.[1]; Nguyen T. T.T.[2]; Chu H. T.M.[2]; Nguyen D. T.[2]; Ngo K. T.D.[2]; Pham D. L.[2]

[1]*VinUniversity, Ha Noi, Vietnam;* [2]*University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam*

Background: Moisturizers play an essential role in maintaining the integrity of skin barrier by increasing stratum corneum hydration (SCH) and reducing transepidermal water loss (TEWL). According to dermatology and allergy guidelines, moisturizers should be applied on the skin within 3 minutes after bathing or showering. However, there were very few evidence supporting that recommendation. This study aimed to investigate the effectiveness of immediate and delayed moisturizing after bathing/washing on the improvement of SCH and TEWL.

Method: This was a crossover study on 60 healthy Vietnamese volunteers aged 18-25 year-old. In each subject, the left volar forearm was left non-moisturized while the lower right volar forearm was moisturized within 3 min after washing (immediate moisturizing) and the upper right volar forearm was moisturized 30 min after washing (delayed moisturizing). SCH and TEWL levels were measured by a GPskin® (GPower, Korea) at 30, 60, 120 and 180 min after moisturizing.

Results: SCH levels of males were higher than females (p < 0.05), while TEWL levels were not different by gender. Both non-moisturized and moisturized skins had time-dependent increases in SCH and decrease in TEWL levels compared to baseline. In non-moisturized skins, SCH and TEWL levels were significantly increased compared to baseline at 60 min after washing, while significantly increased TEWL levels were observed immediately after moisturizing. In addition, moisturized skins had significantly higher SCH and lower TEWL levels compared to non-moisturized area at every time point (p < 0.05). Interestingly, the % changes of SCH and TEWL levels from baseline were not different between immediate and delayed moisturized skins.

Conclusion: Moisturizing helped increase skin hydration and decrease TEWL; however, there was no difference in moisturizing effectiveness between immediate and delayed moisturizing in healthy

skins. The recommendation of immediate application of moisturizers after bath/washing should be reconsidered and more studies are needed to establish a stronger recommendation.

1010 | Etiological causes of angioedema with or without urticaria

Luku D.[1]; Lekli E.[1]; Lazri E.[2]; Zhabjaku E.[1]; Nushi V.[1]; Bakiri A.[3]; Mingomataj E.[1]

[1]*University Medical Center of Tirana, Tirana, Albania;* [2]*Regional Hospital of Gjirokastra, Gjirokastra, Albania;* [3]*American Hospital, Tirana, Albania*

Background: Angioedema manifests clinically with bouts of asymmetric nondependent swelling involving cutaneous or mucosal surfaces. It is most commonly mast cell-mediated, often accompanied by urticaria. Although non–mast cell-mediated forms of angioedema manifest as recurrent angioedema not associated with urticaria. This study aims to figure out the etiological causes of angioedema, as well as their association with the presence or absence of concomitant urticaria.

Method: This is a retrospective-descriptive study and consists of 178 cases with angioedema. Cases were grouped into nine categories according to the probable cause and the association of angioedema with or without urticaria (Tab. 1). The ANOVA test is used, the level of significance is set at $p \leq 0.05$ (Tab. 2; 3).

Results: In this study is observed a predominance of Idiopathic Angioedema (IAE) with 31% of cases, Type I hypersensitivity reactions from drugs in 13% of cases, Pseudo-allergic reactions from NSAIDs 12.3% of the cases, immediate hypersensitivity reactions from Hymenoptera stings in 10.1% of cases. Food Allergy resulted in 7.8% of cases, foods causing the allergic reaction were milk (2 cases), eggs (2 cases), fish (2 cases), seafood (2 cases), peaches (2 cases), and kiwi (2 cases); where half of the cases with peach and kiwi had angioedema with urticaria, while all cases with milk, eggs, fish and seafood angioedema were associated with urticaria. Autoimmune angioedema, mainly associated with thyroid involvement was found in 9% of cases. We detected only one case (0.5%) with angioedema and physical urticaria from the cold. Of the non-allergic reactions, all cases caused by ACEI (ACEI-AAE) in 9% of patients and cases with Hereditary Angioedema (HAE) in 7.3% of cases presented only angioedema. Other cases presented different percentages of angioedema associated with urticaria (Tab. 1). Using the ANOVA test resulted that F < F crit (1.1 < 4.4) with a *p*-value = 0.29, therefore, the means of the groups with and without urticaria are equal (Tab. 2). In Table 3, F < F crit (0.9 < 3.2) with a *p*-value = 0.51, therefore, the means of the nine groups are equal.

Conclusion: The association with urticaria represents the largest number of cases and idiopathic angioedema is the most common cause. There is no statistically significant difference between the number of patients according to the etiology of any significant difference between the presence or absence of urticaria.

Table 1

ETIOLOGY	With urticaria		Without urticaria		Total	
IDIOPATIC	43	78%	12	22%	55	100%
OTHER DRUGS	21	91%	2	9%	23	100%
NSAIDs	16	73%	6	27%	22	100%
HYMENOPTERA VENO	8	44%	10	56%	18	100%
ACEI-AAE	0	0%	16	100%	16	100%
AUTOIMUNE	12	75%	4	25%	16	100%
FOOD ALLERGY	12	86%	2	14%	14	100%
HAE	0	0%	13	100%	13	100%
PHYSICAL	1	100%	0	0%	1	100%
Total	113		65		178	100%

Table 2

Anova: Single Factor

SUMMARY

Groups	Count	Sum	Average	Variance
With urticaria	9	113	12.55556	185.0278
Without urticaria	9	65	7.222222	32.44444

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	128	1	128	1.177162	0.294012	4.493998
Within Groups	1739.778	16	108.7361			
Total	1867.778	17				

Table 3

Anova: Single Factor

SUMMARY

Groups	Count	Sum	Average	Variance
Column 1	2	55	27.5	480.5
Column 2	2	23	11.5	180.5
Column 3	2	22	11	50
Column 4	2	18	9	2
Column 5	2	16	8	128
Column 6	2	16	8	32
Column 7	2	14	7	50
Column 8	2	13	6.5	84.5
Column 9	2	1	0.5	0.5

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	859.7778	8	107.4722	0.959573	0.517792	3.229583
Within Groups	1008	9	112			
Total	1867.778	17				

1029 | Contact dermatitis in woodworks: clinical and etiological particularities

Sridi C.[1,2]; Brahem A.[1,2]; Drira A.[2]; Chelly F.[1,2]; Aloui A.[1,2]; Chouchane A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Occupational Medicine Department, Teaching Hospital "Farhat Hached", Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine "Ibn El Jazzar", Sousse, Tunisia*

Background: Occupational dermatitis represents an important occupational health problem. The wood industry is one of the sectors at risk of contact dermatitis due to the exposure of workers to numerous irritants and allergens.

Objectives: To determine the clinical characteristics of patients with occupational dermatitis and to identify the allergens responsible for allergic contact dermatitis in the wood industry.

Method: This is a retrospective descriptive study carried out on cases of contact dermatitis in woodworking professionals who attended the Occupational Medicine Department of the Teaching Hospital "Farhat Hached" of Sousse (Tunisia), over a period of 12 years. The data collection was conducted using a synoptic sheet containing the socio-professional and medical characteristics of the patients as well as the results of patch tests performed with allergens from the European Baseline Series (EBS).

Results: Our population was composed of 42 subjects with a mean age of 41.6 ± 8.72 years and a clear male predominance (91.1 %). The most frequent localization of dermatitis was on the hands (45.5%). The aspect of the lesions was predominantly erythematovesicular (28.9% of cases). The most frequent diagnosis was allergic contact dermatitis (42.2%), followed by irritative contact dermatitis (24.5%). Patch tests were positive in 42.2% of cases. Cobalt and chrome

were the most frequently found allergens (24.4% and 13.3% of cases respectively).

Conclusion: Allergic contact dermatitis is common in the workplace, especially among woodworkers. Therefore, it is important to develop a preventive strategy to reduce the incidence of this dermatitis.

1060 | Acquired C1 inhibitor deficiency; not everything is as it seems

Blanco Ramos M.T.[1]; López San Martín M.G.[1]; Ferrando Anaut P.[1]; Barrios Albajar M.[1]; Navarro Matilla M.B.[2]; Mellor Pita S.[3]

[1]*Allergy Department, Hospital Universitario Puerta de Hierro, Madrid, Spain;* [2]*Hematology Department, Hospital Universitario Puerta de Hierro, Madrid, Spain;* [3]*Internal Medicine Department, Hospital Universitario Puerta de Hierro, Madrid, Spain*

Background: Acquired angioedema due to C1 inhibitor deficiency (AAE-C1INH) is characterized by low levels and/or function of C1 inhibitor without inheritance pattern. It is usually associated with underlying pathology.

Method: We present a 54 years old woman with recurrent episodes over the last three years of abdominal pain (1-2 monthly) lasting 48 hours. She required multiple visits to the emergency department with poor response to analgesia. An unnecessary appendicectomy was performed at the debut. Cervical lymphadenopathies were associated in the last 2 years. Neither wheals nor cutaneous or upper airway angioedema were present.

Results: C4 and CH50 hypocomplementemia with normal C3 values, quantitative and functional C1 inhibitor deficiency and autoantibodies to C1 inhibitor were documented. Autoimmunity was ruled out. Additional studies led to the diagnosis of B-cell malignant lymphoma (low-grade follicular lymphoma with marginal differentiation. Ann Arbor stage IIIB. FLIPI 4). She achieved complete remission (confirmed by PET/TC) after first line schedule Rituximab-Bendamustine x 6 cycles (Rituximab 375 mg/m^2, 1^{rt} cycle day + Bendamustine 90 mg/m^2, 1st and 2nd cycle day). Afterwards, maintenance treatment with Rituximab every 2 months for 2 years was administered. Hematologic remission remained throughout the treatment and to date (1 year later). Bradykinergic angioedema attacks stopped one month later the lymphoma treatment started, so long-term angioedema prophylaxis was not needed.

Normal values of C1q, IgG, IgM and Ig A were always present.

Complement analysis evolution is detailed below.

Previous treatment:

C1 inhibitor level: 4.88 mg/dl (16-33)

C1 inhibitor function: 9.19% (>50%)

C4: <1.5 mg/dl (10-40)

C3: 114 mg/dl (90-180)

Anti-C1 inhibitor Ac: IgG, IgA, IgM Negative

Completed immunochemotherapy Rituximab-Bendamustine:

C1 inhibitor level: 19.8 mg/dl

C1 inhibitor function: 63%.

C4: 6.46 mg/dl

C3: 90.3 mg/dl

Anti-C1 inhibitor Ac: IgG and IgM positive. IgA, Negative.

Completed maintenance Rituximab therapy:

C1 inhibitor level: 30.3 mg/dl

C1 inhibitor function: 88.79

C4: 6.23 mg/dl

C3: 109 mg/dl

Anti-C1 inhibitor Ac: IgG, IgA, IgM Negative.

Conclusion: This case of AAE-C1-INH demonstrates the importance of:

-Quantifying complement in suspected cases of bradykinergic angioedema so as to avoid diagnostic errors.

-Identify the underlying cause whose effective treatment has been successful in eradicating the C1 inhibitor alteration and in resolving angioedema attacks.

1083 | Early and sustained response to dupilumab in adults patients with atopic dermatitis: a prospective study

Ciotta D.; Parente R.; Cardamone C.; Carrieri I.; Triggiani M.

[1]*Department of Medicine, Division of Allergy and Clinical Immunology, University of Salerno, Salerno, Italy*

Background: Dupilumab is a monoclonal antibody targeting IL4/13 pathways and inhibits eosinophilic homing in tissues. Dupilumab is approved for treatment of refractory atopic dermatitis (AD). We present our experience with Dupilumab in adult patients with AD.

Method: We enrolled 7 patients (5 males; median age 35 years) with diagnosis of AD. We evaluated the severity of AD using Eczema Area and Severity Index (EASI), SCORing Atopic Dermatitis (SCORAD), numerical rating scale for pruritus (NRSp) and sleep disturbances (NRSs). These types of assessment were performed at baseline and after 4 and 10 weeks of treatment. We investigated the impact of Dupilumab on quality of life (QoL) of patients using Patient-Oriented Eczema Measure (POEM) and Dermatology Life Quality Index (DLQI). These questionnaires were administered at baseline and after 10 weeks of therapy. We evaluated eosinophils (Eos) levels at baseline and after 10 weeks of treatment. We investigated the changes in EASI, SCORAD, NRSp, NRSs, DLQI, POEMS and the variations of Eos levels during treatment. The Student unpaired *t* test was used for analysis.

Results: At the time of the enrollment, all patients were treated with topical steroids and four patients (57.1%) with cyclosporine A (CysA, 3 mg/kg). Table 1 shows the median values of clinical scores ± standard deviation (SD) during treatment. We observed a statistically significant reduction of all variables after 4 and 10 weeks of therapy ($p < 0.05$). These reductions were maintained until 64 weeks of treatment.

The median Eos levels (cells/mm^3) at baseline were 286.5 (160-957; IQ: 562) and 430.0 (164-1428; IQ: 983) at 10wks. There was no correlation between the entity of Eos elevation and all these scores, except for a strong negative correlation with NRSs (-0.949; p = 0.014). All patients dropped topical steroids and three of them (75%) dropped CysA.

Conclusion: In our patients with AD, Dupilumab has proved effective very early in the course of therapy (already at 4 weeks) and the effectiveness remained until week 64.
Dupilumab improves the QoL, as demonstrated by the reduction of POEM and DLQI. These data indicate that Dupilumab induces a strong and durable improvement in disease activity and QoL.

Scores	Baseline	4wks	*pvalue*	10wks	*pvalue*
EASI	26.2 ± 9.7	12.2 ± 8.1	*0.029*	4.7 ± 4.1	*0.006*
SCORAD	62.0 ± 20.4	35.0 ± 23.5	*0.031*	21.5 ± 11.5	*0.019*
NRSp	8.0 ± 1.8	3.4 ± 1.5	*0.023*	3.0 ± 2.1	*0.003*
NRSs	6.7 ± 1.8	3.2 ± 2.6	*0.003*	2.0 ± 1.0	*<0.0001*
DLQI	14.8 ± 7.5			4.5 ± 4.0	*0.015*
POEM	22.0 ± 5.3			11.5 ± 4.9	*0.008*

1088 | The importance of differential diagnosis in chronic urticaria

Moreno Lozano L.[1]; De Aramburu Mera T.[1]; Albéndiz Gutierrez V. J.[1]; Mota Burgos A. M.[1]; Torres Casanova E. A.[2]; Sánchez Alonso M.[3]; García Rodríguez R. M.[4]; Joyanes Romo J. B.[4]
[1]Vithas Hospital Xanit International. Allergy Department, Malaga, Spain; [2]Hospital General de Ciudad Real. Emergency department, Ciudad Real, Spain; [3]Hospital Santa Bárbara de Puertollano. Gastroenterology department, Puertollano, Spain; [4]Hospital General de Ciudad Real. Allergy department, Ciudad Real, Spain

Background: Erythematous-papular skin rashes of short duration suggest the clinical diagnosis of urticaria. However, a non-negligible percentage of cases may occur due to another type of dermatitis. This case requires complementary tests, such as skin biopsy for diagnosis.
Method: A 53-year-old female patient was diagnosed in 2016 with Diffuse Large B-cell Lymphoma with complete remission after a treatment with R-CHOP, Methotrexate and prophylactic intrathecal therapy.
She evidenced since 2010 daily episodes of erythematous-papular lesions of about 24-36 hours duration, especially in extensor areas. In accordance to this situation, she also reported impairment of quality of life.
Without total control of the symptoms, she was prescribed a treatment with antihistamines, cycles of oral corticosteroids and Omalizumab. Furthermore, her case and treatment with Omalizumab showed evidences and symptoms compatible with serum sickness.
The following method was performed:

1. CBC: blood count, serum immunoglobulins, thyroid hormones, complement, cryoglobulins, proteinogram, autoimmunity markers.
2. Skin biopsy (x2).
3. After results, we expanded analytical analysis with celiac disease antibodies and HLA DQA1and DQB1 locus.

Results:

1. IgM: 43.3 mg/dL; ANA positive 1/320 nuclear mitotic pattern. Rest within normality.
2. Compatible with dermatitis herpetiformis.
3. Negative IgA antibodies (transglutaminase, endomysial and gliadin). HLA-DQ2 positive DQ2.5 in heterozygosis

Conclusion: The skin lesions, the results of the immunological study and the biopsy confirm the diagnosis of dermatitis herpetiformis.
Dermatitis herpetiformis is a rare and underdiagnosed autoimmune disease. It is characterized by a pruritic, pruritic, papulovesicular rash, usually located symmetrically on the extensor surfaces.
Its diagnosis is sometimes difficult to reach due to its association to other dermatological diseases.
Treatment consists of a strict gluten-free diet and dapsone.
To conclude, we highlight the importance of differential diagnosis of papular exanthema, focusing on it when the patient does not respond adequately to the usual treatments. Furthermore, we emphasize the importance of an interdisciplinary follow-up for the correct diagnosis.

1090 | How to study inducible urticaria? development of diagnostic circuits for more than one stimulus

Catalán Cáceres N.; Landaveri Sánchez L.; Stein Coronado C.; Domingo González C.; Alamar Martínez R.; Díaz Palacios M.
Hospital Universitari i Politecnic La Fe, Valencia, Spain

Background: Inducible Urticaria (IU) is a type of Chronic Urticaria (CU) that occurs after exposure to physical and non-physical stimuli.

The diagnosis is based on patient history and provocation tests, which reproduce the symptoms after exposure to an appropriate triggering stimulus.

IU may be present in patients with history of Chronic Spontaneous Urticaria (CSU)

Our objective was to establish standardized protocols through diagnostic circuits that included tests for different stimuli in the same visit, reduce consultation time and evaluate their effectiveness and safety.

Method: We designed 4 circuits where different test instruments for IU were included: Temptest, Fric-Test, Calibrated Dermographometer, Standard laboratory vortex and suspension of weights (7 kg.) over the shoulder. The circuits were:

- Basic Circuit (BC): Dermographism, Temperature (cold and heat), Pressure (delayed an acute) and Vibratory Urticaria **(Diagram 1)**
- Cold Urticaria Circuit (CUC): CB plus Ice Cube Test
- Aquagenic Urticaria Circuit (AqUC): CB plus Aquagenic test
- Autoimmune Urticaria Circuit (AuUC): CB plus Autologous Serum Skin Test (ASST)

Cholinergic Urticaria tests were not included due to COVID pandemic restrictions, nor tests for Solar Urticaria as the necessary technical means were not available.

For 6 months, we selected 51 patients with urticaria history lasting for more than 6 weeks. The circuit chosen for the study depended on the initial clinical suspicion. If there was no clear triggering stimulus, the BC was performed which includes the most frequent causes of IU.

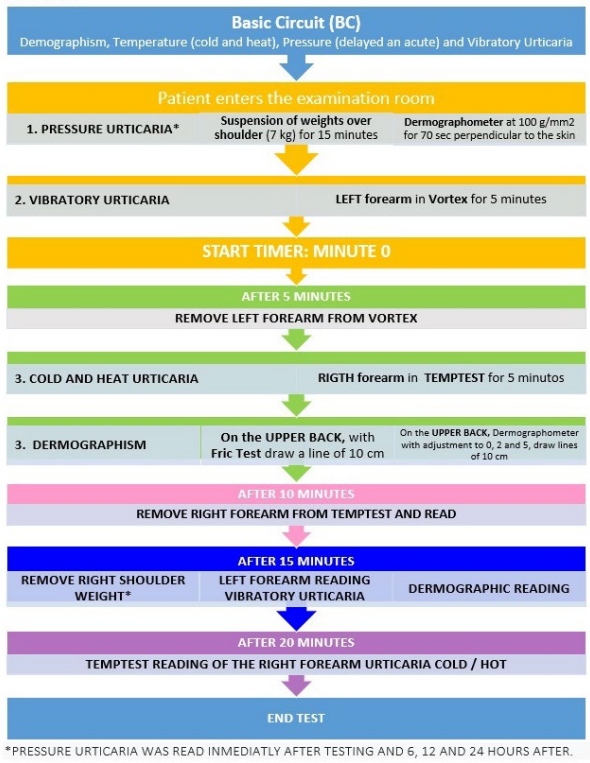
Results: Of the total number of patients studied, BC was applied to 82.4%, CUC to 7.8%, AqUC to 7.8% and AuUC to 2%. The most frequent diagnosis was Dermographism in 47.05% of the patients. This diagnosis was also present in some patients with CSU.

The maximum time to perform these circuits was 30 minutes.

None of the patients studied presented systemic reactions, anaphylaxis or other unexpected reactions.

Conclusion: We observed that the use of standardized circuits in patients with suspected UI makes it possible to study more than one stimulus and to give the appropriate recommendations in each case. These tests are easy to apply and help to optimize study time. Besides, they allow the detection of physical or non-physical stimuli associated with SCU. Given that no patient presented adverse reactions, it appears to be a safe test.

DIAGRAM 1



1091 | Presentation, subtypes and severity of chronic urticaria in different ages

De Souza A.C. M.C.F.F.; Dortas Junior S. D.; Lupi O.; Valle S. O.R.

Serviço de Imunologia, Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ), Rio De Janeiro, Brazil

Background: Chronic spontaneous urticaria (CU) is defined by the occurrence of wheals, angioedema or both for more than 6 weeks. It predominantly occurs in adults, but it can also be present in children or elder.

We aim to compare the presentations of CU between adults and older patients.

Method: Observational, cross-sectional study, with prospective data collection of 180 patients with CU followed up at a Reference Center, from June to December/2018. The patients were divided into two groups according to age group: (1) <65 years (adults) and (2) ≥ 65 years (elderly).

Results: One hundred and fifty-five patients (86.1%) were females and 25 (13.9%) males, were included. The mean disease duration was 10.3 years. The average age of the patients was 46.2 +16.1 years. The average age of onset of symptoms between 20 and 49 years (62.7%).

There were 25 (13.9%) patients aged ≥ 65 years and 155 (86.1%) <65 years. Among the elderly, 64% had angioedema while 78.7% in <65 years old group presented angioedema ($p = 0.54$). Regarding the type of CU: 84% of the elderly had Chronic Spontaneous Urticaria (CSU) and 91.6% of <65 years of age did it ($p = 0.19$); 76.2% of the elderly had Chronic Inducible Urticaria (CIndU). As for the CIndU subtype, Symptomatic Dermographism was the most frequent subtype

in both age groups, 57.1% in patients in < 65 years and 63.9% in ≥ 65 years. In elderly patients, the second most frequent subtype was Cholinergic Urticaria (14.3%), followed by Heat Urticaria (9.5%) and Delayed Pressure Urticaria (DPU) [4.8%]. In < 65 years patients, DPU was the second most frequent CIndU (26.1%), followed by Heat Urticaria (7%), Cold Urticaria (4.3%), Solar Urticaria (1.7%) and Vibratory Urticaria (0.9%). As for the activity of the CSU (UAS7), the elderly group had a median 9 (IIQ 5-15) and <65 years old median 8 (IIQ 0-19), *p* value = 0.66. As for the quality of life related to CU, elderly patients had a median of 28.5 in CU-Q2oL (IIQ- 24-38) and those with <65 years of age, a median of 39.5 in CU-Q2oL (IIQ- 27-58), *p* value = 0.072.

Conclusion: Our data are in accordance with literature with a higher prevalence of CU in adults. Presentation and severity of CU in this sample patients studied showed no difference between the age groups.

1098 | Pruritus burden characterization in a portuguese cohort of severe atopic dermatitis patients treated with dupilumab

Brás R.[1]; Limão R.[1]; Neto M.[1]; Cosme J.[1]; Costa C.[1]; Duarte F.[1]; Mendes A.[1]; Spínola-Santos A.[1]; Branco-Ferreira M.[1,2]; Pedro E.[1]; Lopes A.[1]

[1]*Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte EPE, Lisbon, Portugal;* [2]*University Clinic of Immunoallergology, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

Background: Chronic pruritus is an important driver of quality of life (QoL) impairment in atopic dermatitis (AD) and its true burden has been underestimated. Dupilumab significantly reduced pruritus in clinical trials. We aimed to characterize pruritus burden in a Portuguese cohort of patients (pts) with severe AD treated with dupilumab (DUP) for 52 weeks(w).

Method: Prospective observational study of pts who completed at least 52w of DUP by March 2021 in our Department. Itch Severity Scale (ISS) and Pruritus Numerical Rating Scale (NRS-P) were applied at 6 time-points: 0, 2, 4, 16, 24 and 52w. Correlations with severity indexes SCORAD/EASI, QoL scale DLQI, NRS for sleep disturbance (NRS-SD) and biomarkers total serum IgE (TIgE) and eosinophils (Eos) were assessed.

Results: 16 pts were included, 11(69%) female, mean age 36.5years (SD12.2;range17-60), mean duration of AD 31.5years (SD10.2;range14-48). Regarding baseline pruritus evaluation, the majority of pts (*n* = 15;94%) reported a worsening by night, describing their itch mostly as "annoying" *n* = 15;94%), "unbearable" (*n* = 14,88%) and "worrisome" (*n* = 13;81%). All body surface areas were implicated. Pruritus was considered strong/very strong in its average and worst states by 10pts (63%) and 15 pts (94%), respectively. Mood (*n* = 15; 94%), sex (*n* = 9;56%) and sleep (*n* = 16;100%) disturbances were reported. DUP treatment significantly reduced pruritus severity since w2 ($p < 0.05$) [(median;IQR) w0: ISS15.3(4.7), NRS-P7.5(3); w2: ISS10.8(5.4), NRS-P6(2.8); w16: ISS4.3(4.4), NRS-P3.5(3.5); w52: ISS3.4(3.4), NRS-P2(2)], and in all ISS items (frequency, description, extension, intensity, effects on mood, sex and sleep). Sub-group analyses of pts reaching EASI-50 at w4 vs not, and pts reaching EASI-75 at w16 vs not, didn't show a significant difference ($p>0.05$) concerning median ISS and NRS-P improvement. Regarding ISS, we found positive moderate correlations with NRS-P (r0.555,p0.026) and DLQI (r0.655,p0.045). Considering NRS-P, a positive strong correlation with DLQI and a positive moderate correlation with Eos (r0.550,p0.042) were documented. Correlation of both pruritus scales with NRS-SD didn't reach statistical significance, as well as with severity indexes and TIgE.

Conclusion: DUP significantly reduced pruritus severity in our cohort, from w2 to w52, with positive impact on mood, sex, sleep and QoL, regardless of the severity of AD. Pruritus burden should be assessed as it may contribute to identify treatment responders, especially in pts with low severity indexes improvement.

1120 | Sleep impact of dupilumab treatment in portuguese patients with severe atopic dermatitis

Limão R.; Brás R.; Neto M.; Costa C.; Cosme J.; Duarte F.; Mendes A.; Spínola Santos A.; Branco Ferreira M.; Pedro E.; Lopes A.

Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universita'rio Lisboa Norte, Lisbon, Portugal

Background: Current published data demonstrate that sleep disturbance (SD) is reported in 47% to 80% of children and in 33% to 90% of adults with Atopic Dermatitis (AD), being a major factor leading to impaired quality of life (QoL). This study aims to evaluate the effectiveness of Dupilumab treatment in increasing the duration and quality of sleep in patients with severe AD in Portugal.

Method: Prospective observational study carried out in our Immunoallergology Department, which included patients with severe AD who completed at least 52 weeks (w) of Dupilumab by March 2021. SD were assessed using self-reported Athens Insomnia Scale (AIS) and Numeric Rating Scale (NRS)-sleep at 6 time-points: baseline, 2, 4, 16, 24 and 52w. Correlations with severity indexes SCORAD and EASI, QoL scale DLQI and NRS-pruritus were assessed.

Results: A total of 16 patients were included, 68.8% females, mean age 36.5 years (SD 12.2; range 17-60), with mean duration of AD of 31.5 years (SD 10.2; range 14-48). Median baseline score for AIS was 18 (IQR 14), reflecting considerable sleep impairment, with 13 patients experiencing insomnia (AIS >=6). Patients who received Dupilumab showed significant improvement since w4 to w52, with median AIS 1 (IQR 3) ($p < 0.05$). The median AIS score for all eight items was 0 at w52, corresponding to "no problema at all". Significant improvement was observed at w2 with respect to awakenings during the night, final awakening earlier and quality of sleep ($p < 0.05$),

and at w4 with respect to sleep induction, total sleep duration, well-being, functioning capacity and sleepiness during day, with further improvement until w52 ($p < 0.05$). Regarding NRS-sleep, median baseline score was 7 (IQR 2). There was a significantly lower total score as early as w2 and at the end of the treatment ($p < 0.05$), with median score of 1 (IQR 2). There was a positive moderate correlation between AIS and DLQI (r=0.688; $p = 0.041$), and a strong correlation between AIS and NRS-sleep at w4 (r=0.712; $p = 0.009$) but not at w52. No correlation was observed between AIS and EASI, SCORAD or NRS-pruritus.

Conclusion: Our experience with Dupilumab showed a significant positive impact in the intensity of perceived sleep-related problems as early as w2 that was sustained through w52. These results were reflected in improvements in the duration and quality of sleep and QoL and emphasize the need for assessing SD in patients with AD.

1137 | Determinants of poly-sensitization to contact allergens: Study conducted at the dermato-allergology unit of the university hospital farhat hached of Sousse-Tunisia

Sridi C.[1,2]; Belhadj N.[1,2]; Brahem A.[1,2]; Belhadj Chabbah N.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]*Department of occupational Medicine, Teaching Hospital Farhat Hached, Sousse, Tunisia;* [2]*University of Sousse, Faculty of Medicine Ibn El Jazzar, Sousse, Tunisia*

Background: Allergic contact dermatitis (ACD) is a frequent reason for consultation in dermatology. Its diagnosis is based on the relevance of the clinical history and a positive reaction to the patch test. It is common to observe multiple positive reactions to the initial series, even with three or more different allergens. This phenomenon, called poly-sensitization, is considered as a phenotypic marker of increased susceptibility to contact sensitization. The objective of this study is to determine the factors associated with polysensitization to allergens in the patch test.

Method: This is a retrospective descriptive study conducted among patients referred to the Dermato-Allergology Unit of the Occupational Medicine Department of the University Hospital « Farhat Hached » of Sousse - Tunisia during the period from January 2009 to December 2018 for the exploration of ACD. Only patients who presented positive reactions to the patch test were included in the study. The data collection was based on a synoptic sheet including the socio-professional and medical characteristics of the patients as well as the data of the patch test realized.

Results: A total of 464 cases of contact dermatitis were enrolled. The mean age of our population was 38.9 ± 12.5 years with a slight predominance of females (sex-ratio= 0.89). The sectors of activity most concerned were the building and public works sector (14.4% of cases) followed by the health sector (10.6%). Average job seniority was 13 ± 10 years. Hands were the most frequent location of the ACD (71.1%). About 16% of patients had positive reactions to 3 or more allergens. The most frequently reported allergen combinations were those of the triplet (chromium, cobalt, and nickel). A statistically significant association was found between poly-sensitization on the one hand and personal history of leg ulcer; the location of the lesions in the chest and the erythema squamous and dyshidrotic aspect of the lesions on the other hand.

Conclusion: Considering this frequent phenomenon of poly-sensitization, a close collaboration between dermatologists and occupational physicians is necessary to prevent this type of allergy through a better management of personal and professional risk factors.

1227 | Effectiveness and safety of dupilumab in adults with moderate-to-severe atopic dermatitis: A real-world study in Colombia

Londoño J.[1]; Perez L.[1]; Moreno S.[1]; Chapman E.[1,2]; García M. B.[1,2]; Celis A. M.[1]; Muñoz M. A.[1]; Castillo D.[3]; Lozano A.[4]; Alvis N. J.[4,5]; García E.[1,2,6]

[1]*Unidad Médico Quirúrgica de Otorrinolaringología (UNIMEQ-ORL), Bogotá, Colombia;* [2]*Allergology Section, Fundación Santa Fe de Bogotá, Bogotá, Colombia;* [3]*Funinderma, Bogotá, Colombia;* [4]*ALZAK Consulting & Research, Cartagena, Colombia;* [5]*Universidad de la Costa-CUC, Barranquilla, Colombia;* [6]*Faculty of Medicine, Universidad de Los Andes, Bogotá, Colombia*

Background: Dupilumab is a fully human recombinant monoclonal antibody available to treat moderate-to-severe atopic dermatitis (AD). Its efficacy and safety have been demonstrated in clinical trials and real-life cohorts from North America, Europe, and Asia. However, there is a lack of information in Latin American countries. In that sense, we aimed to describe the effectiveness and safety of dupilumab in adults with moderate-to-severe AD in a retrospective Colombian multicenter cohort.

Method: We included patients treated for at least six months during March 2018-May 2020 at four specialized centers. Efficacy outcomes, including Scoring Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI), and Patient-Oriented Eczema Measure (POEM) were collected at baseline and 3–5 months, 6–12 months, and over 12 months when available. Days of sick leave, hospital admission, and AD exacerbations before and after initiating dupilumab were reported. Adverse events (AE) were recorded at follow-up.

Results: We included 57 patients; median ±IQR age, 32 ±17 years; 36(63.2%) males; and median disease duration, 24 ±27 years. Most patients (93%) had comorbid type 2 diseases (asthma, 27[47.4%]; food allergies, 24.6%; allergic rhinitis, 82,5%). An improvement of at least 75% on the EASI (EASI-75) was reported in 6 of 13 (46.2%) patients at 3-5 months, 13 of 18 (72.2%) at 6-12 months, and 6 of 8 (75.0%) over 12 months. For the same time periods, the median ±IQR percent change from baseline in SCORAD was -73.4 ±19.4 ($n = 13$), -82.9 ±18.3 ($n = 20$), and -66.7 ±26.3 ($n = 9$); and POEM, -58.6 ±10.8 ($n = 4$), -73.0 ±19.8 ($n = 16$), and -87.3 ±23.8 ($n = 8$), respectively. Most

patients (89.5%) patients reported at least one exacerbation of AD in the last 12 months before initiating dupilumab treatment and after, only 11(9.3%) patients reported at least one exacerbation of AD during the follow-up period. Three patients (5.3%) had an AE.

Conclusion: The effectiveness and safety of dupilumab treated patients in this real-life cohort are similar to previous clinical trials and real-world data, showing most patients benefit from the treatment and confirm the favorable benefit/risk profile of dupilumab.

1243 | The prevalence of contact hypersensitivity in patients with oral lichen planus - Preliminary study

Olejnik M.[1]; Jenerowicz D.[2]; Adamski Z.[2]; Czarnecka-Operacz M.[2]; Dorocka-Bobkowska B.[1]

[1]*Department of Gerodontology and Oral Pathology, Poznan University of Medical Sciences, Poznan, Poland;* [2]*Department of Dermatology, Poznan University of Medical Sciences, Poznan, Poland*

Background: Oral lichen planus (OLP) is a chronic autoimmune inflammatory disease with an unknown etiology and a higher prevalence in women. Oral lichenoid lesions both clinically and histologically resemble oral lichen planus and are often associated with contact allergy to dental materials.

This study was designed to investigate the prevalence of delayed hypersensitivity reactions in patients with OLP and to identify the most common allergens that may exacerbate the disease.

Method: Twenty patients diagnosed with OLP and undergoing treatment in the Gerodontology and Oral Pathology Department of Poznan University of Medical Sciences were enrolled in the study. The subjects underwent a detailed oral examination consisting of anamnesis and a clinical evaluation by a qualified dentist, while an assessment of the skin and skin appendages was carried out by a dermatologist. Patch testing was performed using the Polish Baseline Series and Dental Screening Series.

Results: Fifty percent of the examined patients displayed positive patch test reactions. A total of 18 allergic reactions were revealed, but only four appeared during the first test. The most common allergens were found to be nickel, gold, and a fragrance mix. Only one patient had a positive reaction to more than three allergens.

Conclusion: There seems to be a high contact reaction rate in patients with oral lichen planus which is not related to contact with synthetic dental materials. However, further investigations on a larger population with the introduction of additional tests administered seven days after exposure are required to confirm the effects of delayed hypersensitivity reaction on patients with OLP exacerbation.

1250 | Atopy assessment in patients with chronic spontaneous urticaria

Argolo P. N.; Fernandes M. M.; Batalha A. P.; Oliveira I. F.A.; Motta A. A.; Kalil J.; Agondi R. C.

Division of Clinical Immunology and Allergy, University of São Paulo, São Paulo, Brazil

Background: Classify chronic spontaneous urticaria (CSU) by endotypes is important to predict the evolution and prognosis. The presence of atopy, chronic induced urticaria (CIndU) and high serum IgE were associated with a poor response to H1-antihistamine. The aim of this study was to classify and characterize CSU patients according to the presence of atopy evaluated through allergen-specific IgE.

Method: This was a retrospective study with data from CSU patient records who had allergen-specific IgE performed by *in vitro* assays or skin tests, followed up in a tertiary service. Demographic data, presence of CIndU, refractoriness to H1-antihistamines, total serum IgE, allergen-specific IgE, peripheral eosinophil number and antithyroid antibodies (anti-TPO/anti-TG) were analyzed.

Results: Seventy-one CSU patients were included, in which 68 patients (95.8%) were female, with an average age of 45.5 years and urticaria time of 12.1 years. Of the total, 22 patients (31%) had also CIndU and 16 (22.5%) were refractory to H1-antihistamines. Total serum IgE was 446.1IU/mL, peripheral eosinophilia 292.5 cel/mm3, and anti-TPO/anti-TG were positive in 16 patients (22.5%). Fifty-two patients (73.2%) had elevated serum IgE (>100; average of 616.3IU/mL). These patients had more positive allergen-specific IgE (77.3% *vs* 47.4%; $p = 0.04$), more CIndU (40.9% *vs* 15.8%; $p = 0.08$) and more refractoriness to antihistamines (25% *vs* 15.8%, $p>0,05$). Of the total, there were forty-six (64.8%) atopic patients. They were younger (43y *vs* 51y; $p = 0.03$), they had an earlier age at onset of symptoms (31y *vs* 38y; $p = 0.06$), higher frequency of CIndU (41.3% *vs* 12% $p = 0.01$) and a higher total serum IgE (540 *vs* 245 IU/mL; $p = 0.03$).

Conclusion: Atopic CSU patients were younger, with higher total serum IgE and a higher frequency of CIndU, which may be associated with a poor prognosis of the disease. High serum IgE were associated with atopy, high frequency of CIndU and high frequency of antihistamine refractoriness. This may indicated that higher IgE level was associated with a poor response to antihistamines, although literature have shown a better response to Omalizumab. Further studies for a better definition of the role of atopy in the CSU are needed.

1300 | Urticaria in endurance athletes

Borzova E.[1]; Popova C. Y.[1]; Nekliudov N.[1]; Zaborova V.[1]; Dunn-Galvin A.[2]; Munblit D.[3,1]; Kurowski M.[4]; Rukhadze M.[5]; Kurshev V.[1]; Bonini M.[6,3]

[1]*I.M.Sechenov First Moscow State Medical University, Moscow, Russia;* [2]*University College Cork, Cork, Ireland;* [3]*Imperial College London, London, United Kingdom;* [4]*Medical University of Lodz, Lodz, Poland;* [5]*Center of Allergy and Immunology, Tbilisi, Georgia;* [6]*Università Cattolica del Sacro Cuore, Rome, Italy*

Background: The data on the prevalence of urticaria in athletes is limited. Urticaria occurs in 1-3% of the general population, with a 14-17.3% rate in athletes (Shartanova, 2004, Mikhailov *et al*, 1977). However, urticaria was not reported among 201 runners participating in the 2010 London marathon (Robson-Ansley *et al*, 2012). Therefore, the prevalence of urticaria in endurance and ultra-endurance athletes warrants further research in view of the growing popularity of endurance/ultra-endurance events worldwide. In this study, we aimed to assess the prevalence of urticaria in athletes, with a special focus on endurance/ultra-endurance athletes, using the standardized AQUA questionnaire.

Method: The recruitment of athletes was carried out via distribution of flyers at the Moscow Marathon 2020 and via email announcements at the athlete groups/associations between September 2020 and February 2021. Inclusion criteria were age ≥ 18 years and a participation in a sports event for short, medium, long or ultra-long distances. All participants completed a web-based Allergy Questionnaire for Athletes (AQUA) questionnaire (Bonini *et al*, 2009). Prior to the survey, the AQUA questionnaire was translated from English to Russian and back by two independent translators. The permission from the copyright holders for using the AQUA questionnaire was obtained.

Results: Of 100 respondents, there were 27 females and 73 males. Participants were aged 31.6 ± 10.5 and 36.4 ± 9.9 for women (n = 26) and men (n = 70), respectively. Survey respondents (n = 100) included 38 endurance athletes and 23 ultra-endurance athletes. Of interest, 49 participants reported a history of itchy skin rashes. Five athletes (5%), including three endurance athletes (triathlon, skiing, cycling), had urticaria.

Limitations: This is a cross-sectional study based on self-reported survey data without clinical verification of the diagnosis.

Conclusion: Based on the AQUA survey, urticaria occurs in 5% of athletes, including endurance athletes. Further clinical research into urticaria characteristics, its impact on patient's quality of life and athletic performance in athletes is required. Strategies for increasing awareness and screening for urticaria in athletes participating in endurance events can be beneficial for early diagnosis and prompt treatment of urticaria.

1051 | Dress syndrome due to zolpidem in a patient with severe atopic dermatitis

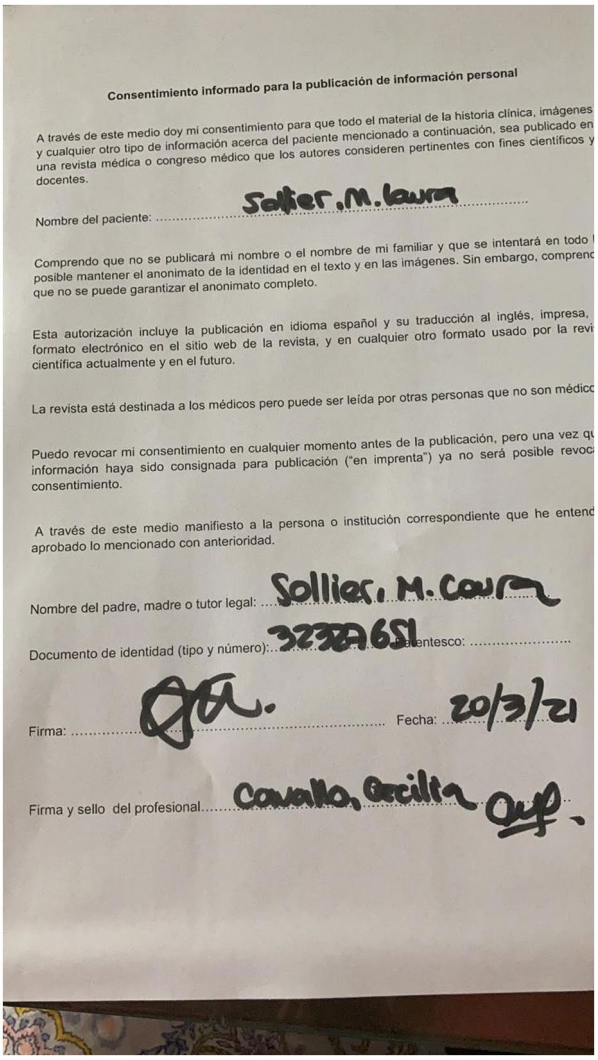
Cavallo M. C.[1]; Frenkel V.[2]; Venturini S. V.[3]

[1]*Hospital San Martin, Paraná, Argentina;* [2]*Hospital Materno Infantil San Roque, Paraná, Argentina;* [3]*Consultorios Médicos Parana, Paraná, Argentina*

Background: DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms) or drug reaction with eosinophilia and systemic symptoms due to severe drug reaction. The purpose is to present the clinical case of a patient with severe atopic dermatitis and DRESS syndrome associated with the sleep inducer, zolpidem

Case Report: A 34-year-old female patient, with a history of severe atopic dermatitis since childhood, who self-medicated during the last month by increasing the dose of zolpidem to 20 mg/day due to exacerbation of pruritus. she presented fever, generalized erythroderma, trembling limbs, altered blood count, eosinophilia, increased liver enzymes, and peritoneal and pleural serositis, requiring hospitalization with a DRESS diagnosis. Zolpidem patch skin test was performed: papula 8 mm erythema 10x15 mm.

Conclusion: The importance of early recognition and treatment of this entity lies in the incidence of mortality. The diagnosis is clinical and requires multidisciplinary work. It is a complication of severe atopic dermatitis and poor control of its disease.



Consentimiento informado para la publicación de información personal

A través de este medio doy mi consentimiento para que todo el material de la historia clínica, imágenes y cualquier otro tipo de información acerca del paciente mencionado a continuación, sea publicado en una revista médica o congreso médico que los autores consideren pertinentes con fines científicos y docentes.

Nombre del paciente: Salier. M. Laura

Comprendo que no se publicará mi nombre o el nombre de mi familiar y que se intentará en todo posible mantener el anonimato de la identidad en el texto y en las imágenes. Sin embargo, comprend que no se puede garantizar el anonimato completo.

Esta autorización incluye la publicación en idioma español y su traducción al inglés, impresa, formato electrónico en el sitio web de la revista, y en cualquier otro formato usado por la revi científica actualmente y en el futuro.

La revista está destinada a los médicos pero puede ser leída por otras personas que no son médicc

Puedo revocar mi consentimiento en cualquier momento antes de la publicación, pero una vez q información haya sido consignada para publicación ("en imprenta") ya no será posible revoc consentimiento.

A través de este medio manifiesto a la persona o institución correspondiente que he entenc aprobado lo mencionado con anterioridad.

Nombre del padre, madre o tutor legal: Sollier, M. Cour

Documento de identidad (tipo y número): 32329651 Parentesco: .....

Firma: ..... Fecha: 20/3/21

Firma y sello del profesional: Cavallo, Cecilia Quf.

1112 | Tranexamic acid still carry hope for females with HAE: A successful story from qatar

Aqel S.; Mohammed Ali R.; Purayil S. C.; Taha S.; Khalil S.; Al-Nesf M. A.; Mobayed H.

Adult Allergy and Immunology Section, Department of Medicine, Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar

Background: Hereditary Angioedema (HAE) is a rare disorder of periodic cutaneous and subcutaneous tissue swelling caused primarily by functional C1 esterase deficiency in genetically susceptible individuals. Therapeutic modalities vary but limited by their high cost, inaccessibility, and some adverse events. Herein we describe HAE cases successfully treated with tranexamic acid (TXA) being an alternative, safe, and affordable treatment option.

Patient 1: A 44-y-old lady presented with recurrent facial swelling, abdominal pain, and laryngeal involvement started at the age of 20. Lab workup revealed low C4, an elevated C1 esterase inhibitor level, and low C1 esterase function compatible with HAE type II diagnosis. She was started on danazol with no further attacks since initiation. However, the patient reported amenorrhea and hirsutism after a year and was switched to TXA 1gm BID. She has been on TXA for the last 1 year and was symptom free apart from a single episode of mild periorbital swelling following a missed dose. **Patient 2:** A 48-y-old female was diagnosed with HAE type II in 2000, presented with recurrent peripheral angioedema with abdominal and laryngeal attacks. Workup showed low C4, normal C1 esterase inhibitor level, and low C1 esterase function. She was started on danazol in 2014 but later developed amenorrhea, acne, and hirsutism and was switched to TXA in December 2020. No further attacks of angioedema were noted up to date. **Patient 3:** A 27-y-old female presented with a history of frequent peripheral angioedema, abdominal pain, and vomiting since the age of 10 with 2-3 attacks per month and had airway involvement twice in her life. Workup revealed a low C4 and C1 esterase inhibitor level suggesting HAE type I. She was started on TXA and reported a significant reduction in symptom frequency.

Discussion: Among the options used for prophylactic treatment of HAE, the efficacy of TXA varies widely between patients. Danazol is associated with virilization, weight gain, hepatotoxicity, risk of hepatocarcinoma and other adverse events, while C1-inhibitor concentrate has a high cost (above €2000 per week). Compared to these options, TXA is considerably well-tolerated, safe and low-priced, making TXA a good option for prophylaxis, especially when the accessibility to high-cost treatment is challenging.

Conclusion: TXA may be favorable than no treatment; however, more effective treatment should always be sought when feasible.

Demographic and clinical characteristics	Patient 1	Patient 2	Patient 3
Age (years)	44	48	27
Age of first symptoms (years)	20	38	10
C4	↓	↓	↓
C1 esterase level	↑	↔	↓
C1 esterase function	↓	↓	↓
Diagnosis	Type II HAE	Type II HAE	Type I HAE
TXA duration (months)	12	3	17

1095 | Response to alternative drugs in patients with chronic urticaria refractory to antihistamines

Fernandes M. M.; Gehlen B.; Argolo P. N.; Oliveira I. F.A.; Kalil J.; Motta A. A.; Agondi R. C.

University of São Paulo, São Paulo, Brazil

Background: Considered the first line of treatment for chronic urticaria (CU), the non-response to antihistamines favors a worse prognosis. In the current scenario in which an arsenal of biological medicines is available, we may eventually face the inaccessibility to these medicines, often consolidated as effective and safe. Such facts support the discussion about the use and the response to alternative therapies with other drugs.

Method: Retrospective study of electronic medical records of adult patients with CU refractory to antihistamines, being followed up in a tertiary service. Demographic data, therapeutic options used (hydroxychloroquine, dapsone or sulfasalazine), therapeutic response taking into account the causes of discontinuity, as well as the highest serum level of C-reactive protein (CRP) during outpatient follow-up were analyzed.

Results: Fifty-four patients were included, in which 51 patients (94.4%) were female, with an average age of 48 years and urticaria time of 13.3 years. The average CRP was 11.8 mg/L. Of the total, 41 patients (75.9%) had chronic spontaneous urticaria (CSU), 3 patients (5.6%) only chronic induced urticaria (CIndU). Eight patients (14.8%) initially diagnosed as CSU, were later diagnosed as urticarial vasculitis (UV) after a skin biopsy. The patients with CIndU were younger than the others; the patients with CSU had longer disease duration. The most widely used alternative medication was hydroxychloroquine (51.9%), with only 25% of the patients showing a good response to the medication. Dapsone was used by 18 patients (64.3%) and 27.8% of these patients had a good response. Sulfasalazine was used by 8 patients, with 50% of them showing a good response. The main reason for the discontinuity wasn't the side effects but the lack of response. The highest CRP was observed in UV group.

Conclusion: Hydroxychloroquine was the most used alternative drug in our service, but sulfasalazine was the one that showed the best response among the users evaluated. The replacement or the discontinuation of the alternative medication was mainly due to clinical refractoriness and not due to side effects. Further studies are needed to clarify the role of these drugs in the treatment of chronic urticaria, when other more effective drugs are unavailable.

1218 | Aquagenic palmar keratoderma: About a case

Barbosa De Pina R. C.; Lemus Calderon J. A.; Faba Lopez E.; Caligaris Cataldi H. S.; Guzman Rodriguez R.; Moro Moro M.D.M.; Senent Sanchez C. J.

Hospital Virgen del Valle, Toledo, Spain

Background: Aquagenic keratoderma is a rare variant of acquired and transient keratoderma on palms and soles, characterized by producing whitish or translucent papules immediately after contact with water and remitting after drying in a short time. The etiology is unknown, it is associated with neuronal dysfunction, eccrine gland abnormalities and aquaporins. The clinical suspicion and the semiological test "hand in the bucket" give the diagnosis, the histopathological findings can be nonspecific. Topical treatment includes barrier mechanisms and botulinum toxin.

Method: 18-year-old woman with no relevant medical--surgical history or family of interest. Referred to allergy consultation for presenting for several years, minutes after contact with water at any temperature and sometimes after profuse sweating, multiple whitis.

Results: After the initial suspicion of aquatic urticaria, an analysis was carried out, without alterations in the inflammation and autoimmunity parameters, the ice cube test was performed on the palmar area and on the forearm with a reading at 15 minutes with a negative result. And finally, the hands were immersed in warm water for 10 minutesand after 3 minutes, multiple small translucent whitish papules with little itching and intense burning sensation appeared, which disappeared in 30 minutes, drying after the hands. Due to the subsequent clinical suspicion and observation of the lesions after the application of the stimulus, he was diagnosed with aquagenic palmar keratoderma. It was recommended to apply aluminum salts and hydration, presenting subjective clinical improvement.

Conclusion: We present a case of aquagenic palmar keratoderma, with significant deterioration in the quality of life, diagnosed through the clinical history and observation of the lesions after the application of the stimulus. Although few cases have been described in the literature, we think that it may be underdiagnosed. And we highlight

the importance of making an adequate differential diagnosis with other related entities. (Aquagenic urtiary, aquagenic pruritus, translucent acrokeratoderma hereditary papule, ...).

1188 | Secondary acrocyanosis: Case report

Mur Gimeno P.[1]; Extremera Ortega A. M.[1]; Fariña Escondrillas M.[2]
[1]*Allergy Unit. Santa Bárbara Hospital, Puertollano, Ciudad Real., Spain;* [2]*Family Medicine. Santa Barbara Hospital., Puertollano, Ciudad Real., Spain*

Introduction: Acrocyanosis is a painless condition characterized by discoloration of different shades of blue in the distal parts of the body, marked by symmetry and persistence of color changes exacerbated by cold exposure. It is less common than other acrosyndromes (erythromelalgia, Raynaud's phenomenon, erythema pernio) According to its ethiology could be classified: a) Primary: mostly in young adults. B) Secundy: anorexia nervosa, mitochondrial diseases, neoplasms, connective tissue/rheumatologic disorders, cryoglobulinemia, exposure to drugs among others.

We describe a case of secondary acrocyanosis.

Clinical case: A 15-year-old boy with atopic dermatitis since childhood, was referred by Dermatology to rule out a possible contact eczema in hands, four months long. In the outpatient allergy office he showed painless cold symmetrical erythematous-violaceous macules affecting fingers and hands that aggravated by cold exposure. There was also local hyperhidrosis on a scaly-itchy base in distal areas of both hands without paroxysmal pallor or chilblains. These symptoms had been more evident a month ago and did not respond to topical corticosteroids and anti-H1.

Neurologist had prescribed four weeks before amitriptyline to treat headache.

Material and methods: Patch test with the standard series of the Spanish Contact Dermatitis and analysis for acrocyanosis screening were performed.

Results: Patch tests with the standard battery: negative.

Hemoglobin concentration: 16 g/dl, white blood cell count: 5.000/mm^3, platelet: 182.000/mm^3, erythrocyte sedimentation rate: < 10 mm/h. Coagulation, urinalysis, immunoglobulin concentrations, C3, C4: normal. Cryoagglutinins, rheumatoid factor, anti-double stranded DNA antibody (Anti-ds-DNA), anti-cardiolipin and anti-Scl 70 antibodies: absents. COVID-19 RT-PCR-test: negative. Lues, HIV and Hepatitis B, C serologies:negatives. Arterial blood gas: pH: 7.43, PaO_2: 113 mmHg, $PaCO_2$: 31 mmHg. Chest radiographs: normal.

Amitriptyline treatment was discontinued after suspicion of being the causal agent and 15 days later hands were pink and warm.

Conclusions: We report a case of secondary acrocyanosis due to amitriptyline, a serotonin reuptake inhibitor.

We emphasize the importance of a detailed clinical history to achieve the diagnosis and to verify the reversibility of acrocyanosis when its etiology is due to medication.

Physicians should be aware of this possible side effect of tricyclic antidepressants.

1270 | The use of essential oil lemon myrtle (backhousia citriodora) in the treatment of molluscum contagiosum in children with atopic dermatitis

Kakleas K.; Wilson D.; Stiefel G.
Leicester Royal Infirmary, Leicester, United Kingdom

Molluscum contagiosum virus (MCV) is a common skin infection especially in children with atopic dermatitis, caused by a poxvirus. It results in firm, smooth, round papules with central umbilication. Recommended medical treatments for lesion eradication include cryotherapy, podophyllotoxin, imiquimod, cantharidin, or no treatment since MCV lesions may resolve naturally over time in children with a normal immune system. However there are also some natural treatments, such as essential oils that may also result in symptom improvement. We describe the case of a 2 year old infant female with eczema and molluscum contagiosum widespread infection that was seen by the paediatric allergy team in Leicester Royal infirmary. The infection was covering most part of the torso and would result in pruritus and discomfort. The paediatric team has suggested initial treatment with local application of Molludab which contains 5% potassium hydroxide and also has referred the patient to the Dermatology team. The family has tried molludab for three weeks, however there was minimal clinical improvement. The family after having searched the internet have identified that the essential oil of lemon myrtle (Backhousia citriodora) has anti-inflammatory and anti-viral action against molluscum contagiosum virus and decided to use. Initially the family has done a patch test with this oil which was negative. Then they have used a 5% solution (2.5 ml of lemon myrtle in 50 ml of olive oil) twice daily for a week, with mild success. Then the concentration was changed to 10% (5 ml of lemon myrtle to 50 ml of olive oil) and this has resulted in resolution of molluscum lesions and improvement of eczema within three weeks. There is some evidence from the literature that the topical application of non-medicinal products such as lemon myrtle and Triticum aestivum (wheatgrass) can result in MCV and eczema improvement. No adverse events have been reported. This case reports emphasizes that other possible treatments based on natural herbal products can be used as adjuncts-alternatives to medicinal products under close supervision of a trained medical practitioner. However there is still a need for more studies to explore the role of lemon myrtle in MCV management.

1185 | Oral lichen planus and nickel sensitization: A case report

Chelly F.[1,2]; Kacem I.[1,2]; Ghariani Fetoui N.[3]; Sridi C.[1,2]; Maoua M.[1,2]; Brahem A.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Denguezli M.[3]; Mrizak N.[1,2]

[1]Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia; [2]Faculty Of Medicine Ibn El Jazzar, Sousse, Tunisia; [3]Department of dermatology - Teaching Hospital Farhat Hached, Sousse, Tunisia

Associations of oral lichen planus (OLP) with dental material contact, particularly metals have been attributed to allergic sensitization to mercury. It has been reported in the literature that removal of amalgam leads to gradual and spontaneous disappearance of the lesions. However, no case has been reported related to nickel sensitization. We report the case of a patient who developed an OLP due to nickel sensitization after amalgam placement.

Description: A 36-year-old woman with a history of allergy to pollens attended the dermatology consultation with small scleroatrophic pigmented plaques on the two axillary hollows and the left flank that had been evolving for several months. These lesions were associated with a tingling of the tongue. Interrogation revealed that these lesions appeared following the placement of a dental amalgam. The anatomopathological examination confirmed a lichen. Patch-tests to allergens of the European standard battery were performed. The reading at 48 h revealed a positive test to nickel with 2 crosses.

Conclusion: Contact allergies to mercury in patients with OLP have been reported in previous studies, but the current finding of contact allergy to nickel has not been reported previously.

965 | Blister – a rare skin manifestation of the hereditary angioedema attack – A case report

Bara N. A.[1]; Nadasan V.[1,2]

[1]Romanian Hereditary Angioedema Reference Center, Singeorgiu De Mures, Romania; [2]George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu-Mure?, Tg-Mures, Romania

Introduction: Hereditary angioedema due to C1-inhibitor deficiency is a rare autosomal dominant genetic disorder clinically characterised by recurrent episodes of skin swelling, abdominal pain and life-threatening upper airway obstruction. The skin edema, named peripheral attack, is nonpitting and non-erythematous and without treatment lasts 2-5 days. It typically affects the face, extremities, and genitals but any part of the body can be affected. Pain and dysfunction are the dominant symptoms but in case of severe swelling, blister formation is possible.

Aim: To describe the case of a patient with hereditary angioedema due to C1-inhibitor deficiency type1, who experienced blister formation.

Case report: A 57-year-old female patient presented to the angioedema center with a severe peripheral attack on her left leg where a blister was also seen. The attack started one day before and the blister appeared 10 hours after the swelling formation. She did not use any specific treatment for this attack. Her medical history revealed she had more than 30 similar bullous eruptions during the last 20 years. A single blister appeared at one given time, exclusively at the crook of the elbows or legs. The blister never occurred in the absence of edema and there was no clear timeframe of the appearance during the edema development. Since specific treatment was administered the patient had no more blister formation during an angioedema attacks.

Conclusions: Blister formation is a rare manifestation of skin edema in patients with hereditary angioedema caused by C1-inhibitor deficiency and has been reported solely in case of severe swelling. In our patient the blisters appeared only in case of untreated attacks emphasizing the importance of treating every skin swelling episode as early as possible to prevent this complication.

1005 | Effectiveness of beta-lactam allergy label withdrawal

Villamor Martín T.; Morales Campoverde K.G.; Bosepa Toraó M.W.; Garcés Sotillos M.; Colás Sanz C.

Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain

Background: In our setting,it is common for patients to be "labelled" as allergic in the presence of doubtful clinical signs of intolerance or allergic reaction.

Moreover,it is not uncommon that patients who have been ruled out allergy to beta-lactam antibiotics (BL-ATB) continue to be mislabelled allergologically in the electronic medical records.Unfortunately,this mistake means that they are sometimes deprived of the first therapeutic option.

Objective: The main objective of the study was to assess the correct labelling of patients(p) from an allergological point of view in Primary Care,in the Emergency Department and in visits to other specialists. The secondary objectives were:to determine the percentage of patients who received BL-ATB,the reason for the prescription and the drugs used.

Method: Prospective review of the medical records of 92 patients who have been ruled out allergy to BL-ATB in our department during the months of August 1st,2019, to March 31st,2020.All patients have been followed for at least 12 months.Data were collected by reviewing the electronic medical records.

Results: Of the 92 patients, only 64%(54p) were well identified in primary care.

Only 36%(33p) had attended the Emergency Department,of which 76%(25p) were correctly identified and the remaining 24%(8p) were not.

38%(35p) were visited by an specialist, in a total of 42 visits(v). In 74% of the visits (31v) the patients were correctly identified and in the remaining 26% they were not.Table 1 summarises the number of visits to each specialist and the correct or incorrect allergological identification.

Only 17%(16p) received BL-ATB, on a total of 20 occasions.Urinary tract infections were the most frequent reason for prescribing BL-ATB (4p), followed by H.Pilory infection(3p),skin infections(3p),respiratory infections(3p),sepsis (2p),acute otitis media(1p),pharyngitis(1p),sinusitis(1p),oral infections(1p) and bone fractures(1p).

Amoxicillin was the most commonly used drug(8p),followed by Amoxicillin/Clavulanic acid(5p),Cefuroxime(2p),Meropenem(2p),Ceftriaxone (1p) and Piperacillin/Tazobactam(1p).

Conclusion: Despite the efforts being made by Allergology services to correctly label patients with HS to BL, a high percentage remain misidentified.

In relation to the consumption of BL-ATB,we believe that the data are underestimated,given that during the months of follow-up of the study (year 2020) the use of masks and hand washing recommended by the COVID-19 pandemic have reduced both infections and access to health care.

Medical speciality	Well identification	Misidentified
Digestive	4	0
Gynaeology	2	0
Anaesthesia	2	1
Medical Oncology	3	0
Breast Unit	0	1
Urology	4	2
Dermatology	2	0
General Surgery	5	0
Cardiology	2	3
Otorhinolaryngology	1	2
Rheumatology	0	2
Pneumology	1	0
Internal Medicine	3	0
Traumatology	2	0

1048 | Hypersensitivity reactions to iodinated contrast media: Diagnostic workup

Gomes J. Q.; Malheiro D.; Lopes J. B.; Sousa M. J.; Cruz L.; Barreira P.; Lopes I.; Cadinha S.

Allergy Department, Centro Hospitalar Vila Nova de Gaia/Espinho, EPE, Vila Nova De Gaia, Portugal

Background: Iodinated Contrast Media (ICM) with low-osmolarity are increasingly used because of their safety profile. Despite the lower incidence of hypersensitivity reactions (HR) when compared to high-osmolarity contrasts, they still occur. Our aim was to characterize the diagnostic workup when HR to ICM are suspected.

Method: Retrospective analysis of patients referred to our department (1/2012-12/2020) with suspected ICM hypersensitivity. Diagnosis was confirmed based on a suggestive clinical history and positive skin tests (ST) [skin prick tests (SPT), intradermal tests (ID), patch tests (PT)] with or without positive basophil activation test (BAT)/lymphocytic transformation test (LTT) or positive intravenous drug provocation test (DPT); considered probable based on a suggestive clinical history and positive BAT/LTT; excluded based on a negative DPT.

Results: Sixty-seven patients were included: 55% female, medium age of 58 ± 14 years, 9% atopic. Iopromid was the culprit drug in 63%. Clinical manifestations were cutaneous in 62%, anaphylaxis in 21%, malaise in 6%. HR were immediate in 64% (*n* = 43), non-immediate in 36% (*n* = 24). Twenty-one patients didn't conclude study (15 immediate HR; 6 non-immediate HR): 10 still ongoing, 11 refuse.

Twenty-eight patients with immediate HR concluded study: all SPT were negative; ID were positive in 7 out of 28 patients, BAT in 1 out of 12 and DPT with suspected drug in 5 out of 21. Negative predictive value (NPV) of ID was 76.2%. Diagnosis was confirmed in12 patients (5 based on DPT, 6 on ID, 1 on ID/BAT), excluded in 16.

Eighteen patients with non-immediate HR concluded study: ID were positive in 2 out of 17 patients, PT in 2 out of 15, LTT in 5 out of 9 and DPT with suspected drug in 6 out of 11. Diagnosis was confirmed in 9 patients (6 based on DPT, 1 on ST/LTT, 2 on ST), considered probable in 4 (based on LTT), excluded in 5.

Conclusion: In our sample, if DPT had not been performed we would have missed diagnosis in 11 (5 with immediate and 6 with non-immediate HR) out of 21 patients with confirmed HR. Additionally, ID in immediate reactions showed medium/low NPV corresponding to a relevant percentage of false-negatives. These results reinforce the importance of DPT as the gold standard to establish diagnosis, also in these group of drugs.

1319 | Revaccination of persons with an immediate reaction after the first dose of mRNA COVID-19 vaccine

Stehlin F.[1]; Canton L.[1]; Girard C.[1]; Miauton A.[2]; Santos A.[1]; Genoud P.[1]; Ribi C.[1]; Meylan S.[1]; Muller Y. D.[1]

[1]*CHUV, Lausanne, Switzerland;* [2]*Unisanté, Lausanne, Switzerland*

Background: The newly developed mRNA-based COVID-19 vaccines can provoke anaphylaxis. Management of persons with an immediate reaction suggestive of an allergy after the first dose remains to be defined.

The newly developed mRNA-based COVID-19 vaccines can provoke anaphylaxis. Management of persons with an immediate reaction suggestive of an allergy after the first dose remains to be defined.

Method: Skin testing was performed with both mRNA-based vaccines. Upon a negative skin test, a 2-step (10 + 90%) revaccination protocol was performed. Positive skin tests were confirmed with a Basophil Activation Test (BAT).

Results: 25'162 first doses of COVID-19 vaccines (80% from Pfizer BioNTech) were administered at the university hospital of Lausanne. Respectively, 3.47 and 1.99 immediate reactions per 10'000 doses were observed with the vaccine of Pfizer BioNTech and Moderna. An allergy workup was performed in 18 persons among who 11 were

referred from external centers. 17/18 (94%) were females and 7/18 (39%) had criteria for anaphylaxis. 3/18 (17%), 2/3 with anaphylaxis, had positive intradermal reactivity after 20 minutes for both mRNA vaccines. BAT was positive in 2 persons and is pending in the third one. 14 patients had negative skin testing. Among those 8 received a 2-step re-vaccination protocol, 3 refused revaccination, and 3 wait for revaccination. 8/8 with negative tests tolerated the 2-step re-vaccination. One patient with suspicious skin tests but positive BAT developed again urticaria 7 minutes after the 90% dose.

Conclusion: Only 22% of patients, all females, with an immediate reaction to the first vaccination were sensitized to the vaccine. A two-step re-vaccination protocol could be safely administered upon negative skin testing.

956 | Trends in drug induced stevens johnson/toxic epidermal necrolysis: A 40 years study using vigibase, the WHO international database

Lebrun-Vignes B.[1,2]; Chinchilla Portillo C.[3]; Bettuzzi T.[4,2]; Sbidian E.[4,2,5]

[1]*Centre Régional de Pharmacovigilance, Service de Pharmacologie clinique, Hôpital Pitié-Salpétrière, AP-HP University, Paris, France;* [2]*EpiDermE, Univ Paris Est Créteil, F-94010 Créteil, France, Paris, France;* [3]*Sorbonne University, Paris, France;* [4]*Service de Dermatologie, AP-HP, Hôpital Henri Mondor, F-94010 Créteil, France, Paris, France;* [5]*INSERM, Centre d'Investigation Clinique 1430, F-94010 Créteil, France, Paris, France*

Background: Epidermal Necrolysis including Stevens Johnsons syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) is a rare and potentially life-threating delayed-type hypersensitivity reaction, which are mostly (70-90%) drug induced.

Method: In this retrospective pharmacovigilance study we used VigiBase, the WHO's global database collecting individual case safety reports (ICSR), to describe the evolution over time of the drugs most frequently involved in cases of SJS/TEN. We have selected drugs suspected in more than 0.5% of SJS/TEN cases and we compared these drugs between two 20 years periods (1st January 1980 to 31th December 1999 vs 1st January 2000- 31th December 2019). In addition, ICSR data quality was assessed by the completeness score.

Results: Preliminary results identified a total of 53,361 ICSR of SJS, TEN and Overlap Syndrome, including 7,678 ICSR for the first period and 45,683 for the second period. The overall ICSR data quality improved between the two periods. The most frequently involved drugs in both periods were antibiotics, antiepileptics, allopurinol and AINS. During the second period, some highly reported drugs emerged including IPP, antiretrovirals, new antiepileptics, COX-2 selective inhibitors and tramadol. A disproportionality analysis is now being assessed to compare the association between these drugs and SJS/TEN cases using the information component (IC) over time.

Conclusion: These results revealed a stability over time of the most frequently involved drugs in SJS/TEN cases, but also a wider spectrum of drugs as new drugs are being developed. We have also highlighted an improvement of reporting both in terms of quality and quantity.

957 | Polymorphisms of the lipoxygenase and prostaglandins pathways in malay patients with non-steroidal anti-inflammatory drug induced urticaria/angioedema: preliminary findings

Bakhtiar M.F.[1]; Nurul Aain A.F.[1]; Siti Aisyah A.A.[1]; Nur Aida Sabrina M.R.[1]; Haziqah Itqan A.[1]; Nadia R.[1]; Tan L.K.[1]; Tang M.M.[2]; Too C.L.[1]

[1]*Immunogenetic Unit, Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia. National Institutes of Health Complex, Bandar Setia Alam, Shah Alam, Malaysia;* [2]*Department of Dermatology, Ministry of Health Malaysia., Kuala Lumpur, Malaysia*

Background: Non-steroidal Anti-Inflammatory Drugs (NSAIDs) hypersensitivity is one of the commonly reported drug hypersensitivity reactions with NSAIDs induced urticaria/angioedema (NIUA) the predominantly associated clinical phenotype. Studies across different populations have shown that it is associated with the arachidonic acid metabolism pathways.

Method: Data source from 66 Malay patients with confirmed diagnosis of NIUA and 61 Malay NSAIDs-tolerant controls, were analyzed. Twenty-eight SNP markers were selected from seven lipoxygenase pathway-related genes namely ALOX5, ALOX5AP, ALOX12, ALOX15, LTC4S1, CYSLTR2, TBXAS1 and, seven prostaglandin-E2 pathway-related genes including PTGFR, PTGDR, PTGER1, PTGER2, PTGER3, PTGER4, and PTGS1 were genotyped using the TaqMan Allelic Discrimination SNP genotyping assay for all participants. The odds ratio (OR) and 95% confidence intervals (95% CI) of developing NIUA were calculated using logistic regression between the NUA cases and tolerant controls.

Results: All the investigated SNP variants were in Hardy Weinberg Equilibrium ($p>0.05$) except for the LTC4S1_rs730012, which was monomorphic in the Malay population. The single-point analyses of the prostaglandins-related variations demonstrated trend of associations with PTGER1_rs3810523_A variant (cases 33% versus controls 22%, OR = 1.76), PTGER1_rs3810255_C (OR = 1.61), PTGER3_rs7551789_A (OR = 1.42), PTGER4_rs4957341_A (OR = 1.74), PTGS1_rs1330344_C (OR = 1.22). The genotypic model analysis of both the lipoxygenase- and prostaglandins-related markers also showed trend of associations for ALOX5AP_rs11147439 (CC versus AA + AC, OR = 4.069), PTGDR_rs8004654 (TT versus CC+CT, OR = 1.88), PTGER1_rs3810523 (AA versus AC+CC, OR = 2.95), PTGER1_rs3810255 (CC versus CT+TT, OR = 2.47), PTGER3_rs7551789 (AA versus AT+TT, OR = 1.34), and PTGER4_rs4957341 (AA versus AG + GG, OR = 2.67), respectively.

Conclusion: Our data provide evidence for trend of associations between lipoxygenase and prostaglandins-related genetic variants and NIUA in the Malay population.

1075 | Management of patients with a history of perioperative hypersensitivity reaction; do skin tests and premedication work?

Tasyürek S.; Tepetam F. M.; Bulut I.
University of Health Sciences, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Immunology and Allergy, Istanbul, Turkey

Background: Incidence of perioperative hypersensitivity reaction (PHR) ranges from 1/1.500 to 1/10.000. Patients with a history of hypersensitivity reaction to drugs (DHR) other than general anesthetics are also at risk for PHR. In the management of these reactions, which are reported to be IgE-mediated up to 60%, skin tests, premedication and if necessary provocation tests are recommended
Method: Patients with a history of DHR were evaluated retrospectively. Before the allergy tests, the data including the list of medications and other agents that were used perioperatively; such as non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, neuromuscular blocking agents (NBA), hypnotics, opioids, atropine, antiseptics, latex and also the severity of the reaction were recorded. Skin tests were performed at recommended nonirritant doses. (Figure1) If the culprit agent responsible for the reaction is known and the antidote of this drug is available, oral or subcutaneous provocation tests were performed and the results were evaluated. In addition, a premedication protocol with methylprednisolone and chlorpheniramine was recommended to the patients before the operation. Patients were called and questioned in terms of postoperative reaction to evaluate the success of skin tests, provocation tests, and the recommended premedication protocol
Results: The average age of 60 patients we evaluated in terms of PHR was 46 ± 11.7 and 86.7% of them were women. 15 patients had a history of PHR and when the severity of the reaction was evaluated, 4 had mild , 3 had moderate , 8 had severe reactions. The majority of DHRs were with antibiotics (*n*:29) and NSAIDs (*n*:23). 17 patients had asthma, 10 had allergic rhinitis, and 19 had aeroallergen sensitivity. Oral provocation test was performed when skin tests were found to be negative in 2 patients who were known to have a reaction with Midazolam before and no reaction was observed. 56 patients, who underwent operation after the drug allergy tests were questioned and it was learned that PHR was not observed in any of them
Conclusion: PHRs can be life threatening, NBAs are most frequently responsible for allergic reactions. With the skin tests and premedication recommendations, the next perioperative processes of the patients can be successfully managed.

	SPT (+) *n*/%	IDT (+) *n*/%
NMBAs		
Rocuronium	1 (1.7)	4 (6.7)
Vecuronium	1 (1.7)	21 (35)
Hypnotics		
Propofol	2 (3.3)	4 (6.7)
Thiopental	0 (0)	0 (0)
Ketamine	0 (0)	4 (6.7)
Midazolam	1 (1.7)	5 (5.8)
Opioids		
Petidine	6 (10)	6 (10)
Fentanyl	1 (1.7)	2 (3.3)
Tramadol	12 (20)	6 (10)
Others		
Neostigmine	0 (0)	1 (1.7)
Atropine	0 (0)	1 (1.7)
Chlorhexidine	0 (0)	0 (0)
Povidone	0 (0)	2 (3.3)
Latex	3 (5.6)	-

Figure 1: Non-irritan doses of skin test

	Pharmaceutial drug concentration	Skin Prick Test (ratio)	Intradermal Test (ratio)
NMBAs			
Rocuronium	50 mg/ml	1/1	1/200
Vecuronium	10 mg/ml	4 mg/ml	1/10
Hypnotics			
Ketamine	50 mg/ml	2/10	1/10
Propofol	10 mg/ml	1/1	1/10
Thiopental	5 mg/ml	1/1	1/10
Midazolam	5 mg/ml	1/1	1/10
Opioids			
Morphine	10 mg/ml	1/10	1/1000
Fentanyl	0,05 mg/ml	1/1	1/10
Petidine	50 mg/ml	½	1/20.000 (2,5 microg/ml)
Antiseptics			
Chlorhexidine	5 mg/ml	5 mg/ml	4/10.000 (0.002 mg/ml)
Others			
Povidone	100 mg/ml	1/1	1/100
Atropine	100 mg/ml	1/10	1/10.000
Latex		1/1	

1259 | Psychological distress and drug provocation test related anxiety level of pediatric patients and their parent

Yilmaz Topal O.[1]; Turgay Yagmur I.[1]; Kulhas Celik I.[1]; Uneri O. S.[2]; Toyran M.[3]; Karaatmaca B.[1]; Civelek E.[3]; Dibek Misirlioglu E.[3]
[1]Ankara City Hospital, Division of Pediatric Allergy and Immunology, Ankara, Turkey; [2]Istanbul Gelisim University, Faculty Of Economics, Administrative And Social Sciences, Department of Psychology., Istanbul, Turkey; [3]University of Health Sciences, Ankara City Hospital, Division of Pediatric Allergy and Immunology, Ankara, Turkey

Background: Drug provocation tests (DPTs) are considered the "*gold standard*" to confirm of drug hypersensitivity reaction. To the best of our knowledge, anxiety of the children and parents related to the DPTs has not been reported before. It was aimed to determine the anxiety levels of parents and children before and after DPTs and also determine the relationship between psychological distress symptoms and anxiety levels.
Method: The study included patients who had undergone DPTs for diagnostic purposes or to detect alternative drugs and accepted

the questionnaires in our pediatric allergy clinic between July 1,2019 and February 29,2020. Age-appropriate State-Trait Anxiety Inventory (STAI-S/T) scales was used to assess the state and trait anxiety levels of the patients' and parents. The SCL-90-R (Symptom Check List-90 Revised) scale was used to screen for psychological symptoms of parents.

Results: Sixty-nine patients were tested with DPTs and their parents filled the inventories. Median age of the patients was 7.28 (IQR:4.52-10.06) years. The mean age of the parents was 35.28 ± 5.38 years. Before the DPT, the mean STAI-S score was found to be higher in parents and 21 children over 8 years old who accepted to fill out the questionnaires. Also while STAI-S were not different before and after the DPTs in the parents of 5 patients whose DPTs resulted with a reaction; the parents of 64 patients whose DPTs resulted without any reaction had significant decrease in anxiety scores after the DPTs. According to the STAI-S scores of parents of patients with history of anaphylaxis, state anxiety was higher than parents of patients with history of other symptoms. The scores of STAI-T in parents was also positively correlate with the STAI-S before the DPTs. In the SCL-90-R subscales, patients with a general symptom index score >1 were found to have higher STAI-T scores.

Conclusion: DPTs carry the risk of causing an allergic reaction and increase anxiety level of patients and their parents. Appropriate evaluation of patients before the test and providing detailed information may be important for reducing anxiety.

1313 | IgE-mediated hypersensitivity to carboxymethylcellulose confirmed by basophil activation test: Two case reports

Yastremska I.[1,2]; Morales Mateluna C. A.[1,2]; Hartmann K.[1,2]

[1]*Division of Allergy, Department of Dermatology, University Hospital Basel, Basel, Switzerland;* [2]*University of Basel, Basel, Switzerland*

Background: Carboxymethylcellulose (CMC) is a cellulose derivative widely used as an additive in cosmetics, food, tablets and injectable drugs. It has been reported as a rare cause of anaphylaxis after parenteral administration of corticosteroids (CCS). IgE-mediated sensitization to CMC has been confirmed by basophil activation test (BAT) in six previous cases. Here, we report two additional patients with anaphylaxis after intra-articular injection, in whom IgE-mediated sensitization to the additive CMC was confirmed by BAT.

Method: Two patients with a history of anaphylaxis after intra-articular injection were evaluated using skin tests and BAT.

Results: A 56-year-old female underwent a facet joint injection of triamcinolone acetonide (TAC) suspension that contained CMC, lidocain and bupivacaine. Within 5 minutes, she developed generalized urticaria, cough, angioedema of the foot and eyelids, which resolved after administration of levocetirizine and prednisone. She had tolerated well two previous injections using the same drugs in the previous year. Skin prick tests with a panel of steroids (with and without CMC), bupivacaine, lidocaine and various additives including CMC were negative. Intradermal tests with the same substances were positive to CMC, TAC suspension and betamethasone (containing CMC). The BAT was positive to TAC suspension and betamethasone (with CMC). It was negative to four steroid formulations devoid of CMC, including TAC solution and betamethasone. Challenges with lidocaine and CMC-free betamethasone were uneventful.

A 32-year-old female developed generalized urticaria, facial swelling and loss of consciousness after intramuscular administration of betamethasone (containing CMC). Skin prick tests to CMC and a panel of steroids were negative. Intradermal tests were positive to CMC and negative to the steroid panel. The BAT was positive to CMC.

Conclusion: IgE-mediated allergy to CCS occurs only rarely. Both our patients failed to show sensitization to CCS, but instead showed positive intradermal tests to CMC. Moreover, IgE-mediated sensitization to CMC could be confirmed by BAT in both patients. Thus, we demonstrate that IgE-mediated sensitization to CMC represents a rare, but important cause of anaphylaxis in patients with reactions to intra-articular injections and that the BAT is useful in confirming this sensitization.

955 | Drug interstitial granulomatous dermatitis caused by warfarin: A clinical case

Iandoli R.; Iandoli D.; Puca R.V.; Sarno O.

Sant G. Moscati Hospital, Avellino, Italy

Background: The cutaneous complications of warfarin therapy include ecchymosis and purpura due to an excessive anticoagulant effect, photosensitivity, maculopapular vesicular urticarial eruptions, purple toes syndrome, skin tissue necrosis, and vasculitis.

Reactive granulomatous dermatitis has been proposed as an inclusive term for 3 syndromes: interstitial granulomatous dermatitis (IGD), palisaded neutrophilic and granulomatous dermatitis (PNGD), and interstitial granulomatous drug reaction (IGDR).

IGDR is a rare, idiopathic disease with typical histopathological characteristics and with a variable clinical expression. Implicated drugs include calcium channel blockers, beta-blockers, lipid-lowering agents, and angiotensin-converting enzyme inhibitors, antihistamines, diuretics, anticonvulsants, ganciclovir, antidepressants, adalimumab and herbal medications.

We report a new case of IGDR triggered by warfarin.

Clinical case

A patient with a history of cardiac infarct who presented erythematous papules and acutely pruritic, in the upper regions of the thorax appeared during treatment with Warfarin.

The incisional biopsy showed a chronic granulomatous inflammatory infiltrate in the superficial dermis with the presence of multinucleated giant cells distributed between the collagen fibres, lymphocytes and a variable number of neutrophilic and eosinophilic granulocytes (Fig. 1).

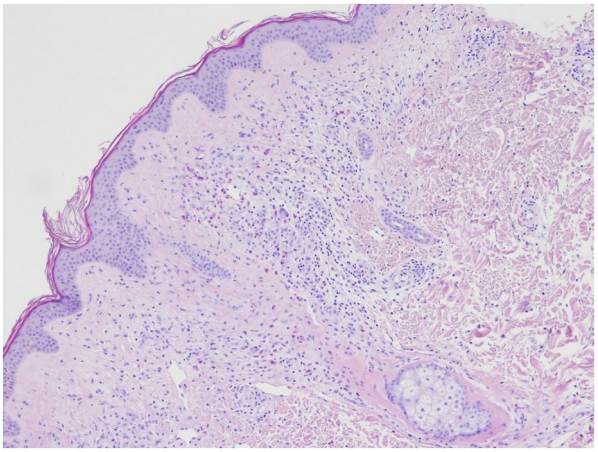
The symptoms failed to regress after a long period of topical steroid therapy. When the patient reduced the dosage of Warfarin until it

was stopped, the skin symptoms regressed. The conclusive diagnosis was IGDR induced by Warfarin.

The patient, after the disappearance of the symptoms, refused to undergo any drug exposure test.

Conclusions

We report a case of IGDR triggered by warfarin for the increased reports about this rare adverse drug reaction.



1328 | Semaglutide as alternative to liraglutide immediate hypersensitivity: A case report

Penella J.; Gomez M.; Gil J.; Ross A.; Quilez E.; Mendoza A.
Agrupació Mèdica i Quirurgica (AMiQ), Unidad Funcional de Otorrinolaringología y Alergia, Hospital Universitario Dexeus, Barcelona, Spain

Background: Current guidelines for the treatment of type 2 diabetes mellitus generally recommend metformin as first-line therapy in addition to lifestyle modifications, if not sufficet, is there a possibility to add other drugs to improve the effects.

Liraglutide is a glucagon-like peptide-1 receptor agonist (GLP-1 receptor agonist) also known as incretin mimetics. It works by increasing insulin release from the pancreas and decreases excessive glucagon release, used as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus, it should be use in increasing doses reaching the 300 mg plateau. Subcutaneous administration. Approved for medical use in the European Union in 2009.

We present a case of and 57 years old woman, with medical history of rhinoconjunctivitis due to cypress and olive pollens, and Diabetes Mellitus type II, that initiate a daily liraglutide. Asymptomatic during 3 months, 24 hours after receive the first 300mg dose, she started with erythema, pruritus and hives on the abdominal area. She repeated it during the subsequent daily doses, 24 hours after receive the GLP-1 receptor agonist. No other symptoms were described. She had no hives and 50% improve of the itching with cetirizine every 24 hours, and had no symptoms with 1 cetirizine every 12 hours. We recommend to discontinue the liraglutide treatment and her endocrinologist supports stop any GLP-1 receptor agonist treatment due to expensive treatment and possibility to have cross-reactivity allergy.

Methods: Performed a skin prick test (1/1) and intradermic (1/100 and 1/10) with liraglutide (6mg/ml) and semaglutide (1,34mg/ml), presenting an immediate positivity to liraglutide with 1/10. Tolerance with semaglutide was confirm, and no hypersensitivity symptoms during the treatment where observed, weekly doses completing 2 months,

Conclusion: We present the first case that shows a real alternative to liraglutide immediate hypersensitivity, confirmed after skin test and tolerance with and alternative treatment. It may be a real alternative to those patients that could avoid other GLP-1 agonist treatments due to possible allergy.

1016 | Cross-reactivity in non-immediate hypersensitivity reactions to iodinated contrast media: A case series

Sánchez J.[1]; Galán C.[2]; Gamboa P.M.[2]; Segurola A.[1]; Seras Y.[1]; Jauregui I.[1]; Martinez M.D.[2]; García E.[2]; Irazabal M.B.[2]
[1]HU CRUCES. Osakidetza, Getxo, Spain; [2]HU CRUCES. Osakidetza, Bilbao, Spain

Background: The diagnosis of non-immediate hypersensitivity reactions (NIHR) to iodinated contrast media (ICM) may require skin (prick and intradermal) tests; epicutaneous (patch) tests; and *in vitro* techniques (lymphocyte transformation test). Finally, the choice of an alternative ICM needs the assessment of previous tolerance through a challenge test. Cross-reactivity pattern is not well defined; hence, selecting a suitable ICM can be difficult.

We report a series of 45 patients with a suspicion of NIHR by ICM, whose study included skin tests to the causative ICM and challenge tests to the culprit and/or an alternative ICM.

Method: Forty-five patients with a suspicion of NIHR to ICM (onset of reaction more than 1 hour after administration) were included. Skin tests with undiluted ICMs (iomeprol, iopamidol, iopromide and iobitridol) were performed to all patients by means of prick-tests and, if negative, intradermal tests, with reading of results at 48 and 72 hours. Intravenous challenge test was performed with 100 mL of ICM administered over 30 minutes.

Results: 16 out of 45 patients had negative skin tests to the causal ICM (iomeprol). Of these, 10 patients had a negative challenge test to the same ICM, and 6 rejected iv challenge with the culprit agent.

Amongst the 29 remaining patients, the cause of ICM was:

Iomeprol (25)

Iodixanol (1)

Ioversol (1)

Unknown (2)

Skin tests were positive for some of the ICM used in 12 patients: 10 with Iomeprol, 1 with Iomeprol and Ioversol and 1 with Iomeprol, Iopamidol and Iopramide. Nine of them tolerated the challenge test

with Iopamidol, 1 with Iopramide and another with Iobitridol. A patient with positive skin tests to Iomeprol, Iopamidol and Iopramide did not tolerate Iobitridol, and refused to continue with the study.
IV challenge tests were performed in 17 patients with negative skin tests (16 with Iomeprol, 1 with Iodixanol), with positive results, *i.e.* repetition of the disease pattern that motivated their medical consultation. 13 out of them tolerated IV challenge with Iopamidol afterwards. Amongst the remaining four, one tolerated Iodixanol and three did not finalize the study, including the patient with a positive challenge to Iobitridol too.
Conclusion: Concerning NIHR, cross-reactivity between Iomeprol and Iopamidol (group A of ICM) is 16%. In these reactions, skin and challenge tests are necessary to establish the tolerance to alternative ICMs.

1086 | Anaphylaxis due to administration of filgrastim

De Aramburu Mera T.[1]; Moreno Lozano L.[1]; Albendiz Gutierrez V. J.[1]; Perez Padilla C. I.[1]; Torres Casanova E. A.[2]
[1]*Vithas Hospital Xanit International, allergy department, Malaga, Spain;* [2]*Hospital general de Ciudad rEAL, emergency department, Ciudad Real, Spain*

Background: Anaphylaxis is a severe, rapid-onset, life-threatening allergic reaction. The most common causes are food, drugs and hymenopters stings.
Granulocyte colony-stimulating factor (G-CSF) is a protein produced naturally by the body to increase white blood cell production. Filgrastim is a man-made version of G-CSF that stimulates white blood cell production and, in particular, neutrophil production.
Method: A 40-year-old woman with a history of breast cancer treated with lumpectomy, lymph node emptying, chemo-radiotherapy and subsequent hormone therapy. In relation to neutropenia in the context of chemotherapy, she underwent treatment with subcutaneous filgrastim (monocyte colony stimulating factors). After the second administration, she suffered immediate symptoms consisting of facial and neck rash, tachycardia, shortness of breath, vomiting of food content and sphincter incontinence. The symptoms resolved spontaneously after 4 hours. Concomitant administration of paracetamol, which was subsequently tolerated.
Skin tests against filgrastim (prick test and intradermal reaction (ID)), prick test and ID with paracetamol, as well as prick test against latex. Single-blind controlled exposure test with paracetamol.
Results:

- Prick test and ID with filgrastim: positive ID for filgrastim.
- Prick test and ID with paracetamol: negative.
- Prick test with latex: negative.
- Single blind controlled exposure test with paracetamol: Negative.
- Pending provocation with alternative (Neulasta) VS desensitisation.

*Skin tests with filgrastim (prick and ID) were performed on healthy controls with negative results.
Conclusion: We present a case of anaphylaxis due to monocyte colony stimulating factor with compatible clinical history and positive in vivo tests.
Published cases of anaphylactic reactions after administration of G-CSF are rare, so we stress the importance of the clinical history as a fundamental pillar of the diagnosis and the in vivo/in vitro study with the different drugs involved. We recommend the need to observe the patient after administration under medical supervision.

1245 | Drug intolerance: Clinical manifestations in elderly patients

Grakhova M.[1]; Rychkova O.[2]; Braun A.[3]; Sagitova A.[2]; Nesterova M.[4]
[1]*Regional Clinical Hospital No. 1, Tyumen, Russia;* [2]*Tyumen State Medical University, Tyumen, Russia;* [3]*INVITRO –Ural LLC, Tyumen, Russia;* [4]*Tyumen Region Infection Pathology Research Institute, Tyumen, Russia*

Background: Drug intolerance is an urgent public health problem due to the possibility of severe allergic reactions: 1 in 4,000 people are admitted to the emergency department with a life-threatening condition after taking medications. Currently, there are risk factors that aggravate the course of drug intolerance: genetic disposition, demographic factors and comorbid conditions. Older age, according to several authors, is the most unfavorable risk factor associated with the severity of drug intolerance.
Method: Over the period from 2017 to 2020, an observational single-center uncontrolled cohort study was conducted in outpatient practice (Tyumen, Regional Clinical Hospital No. 1). The study included 200 people diagnosed as having an unspecified pathological reaction to a drug or medication. All drug reactions are reported by patient's own statements and were allocated to dichotomous variables.Three groups of patients were identified: 18-44 years (n = 49); 45-60 years (n = 60); 61 and over (n = 91). The results were analyzed by nonparametric statistics (Pearson's chi-square).
Results: The odds of incomprehensible reactions were 2.2 times higher in patients in group 3 than in patients in the other groups (95% confidence interval:1.382-3.395; p = 0,001). Group 3 patients were 12 times more likely to have an itchy reaction to medications than patients in the other groups (95% confidence interval:1.553-94.391; p = 0,007). When comparing clinical manifestations of drug intolerance to penicillin- and cephalosporin-type antibiotics, no significant differences were found in elderly patients.
Conclusion: The aggravation of clinical manifestations and the occurrence of polypharmacy are not associated with age and comorbid background. It should be noted that correlation between age and non-life-threatening clinical manifestations of drug intolerance was revealed, which indicates the absence of reliable effect of age on the possibility of anaphylactic shock or angioedema.

1295 | Non-steroidal anti-inflammatory allergy in children – The experience of a tertiary center

Silva M. I.[1]; Lorenzo C.[2]; Virtuoso J.[2,3]; Gomes R.[2]; Cosme J.[1]; Pedro E.[1]; Neves A. M.[2]; Lopes A.[1]

[1]Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal; [2]Pediatric Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal; [3]Pediatric Department, Unidade Local de Saúde da Guarda, Hospital Sousa Martins, Guarda, Portugal

Background: Drug allergy is an important reason for referral to allergy departments in adults and also in children. About 10% of children referred to immunoallergologic outpatient clinics are suspected of drug allergy. The most common drugs involved are beta-lactam antibiotics, followed by non-steroidal anti-inflammatory drugs (NSAIDs). In general, preferential Cox-1 inhibitors seem to play a major role, mainly ibuprofen. Our aim is to describe the immunoallergological investigation, including clinical characteristics and diagnostic workup, of a pediatric population followed in an outpatient clinic for NSAIDs allergy.

Method: Retrospective observational study by consulting the medical records of patients evaluated in a pediatric outpatient clinic for NSAIDs allergy between 2016 and 2020.

Results: Among the 316 patients referred to our outpatient clinic for drug allergy, 24 have been evaluated for NSAIDs suspected allergy: 15 (62.5%) female, mean age in the reaction 7.8 ± 4.9 years old (4 months old – 15 years old), 50% with atopy.

The drugs evaluated were: 92% (22) ibuprofen; 4% (1) acetaminophen; and 4% (1) naproxen.

Clinical manifestations were: 16 (66.6%) urticaria/angioedema; 5 (20.8%) anaphylaxis; 2 (8.3%) maculopapular exanthema; and 1 (4.3%) gastrointestinal symptoms.

Skin tests were performed in 3 patients: 1 ibuprofen and dipyrone; 1 acetaminophen; and 1 naproxen. All skin tests were negative.

All the 24 patients underwent a drug provocation test: 14 (58%) patients with the culprit NSAID – 12 ibuprofen, 1 acetaminophen and 1 naproxen; and 10 (42%) patients with an alternative NSAID: 8 nimesulide, 1 etoricoxib and 1 acetaminophen.

In the culprit NSAID group, there were 3 positive reactions to ibuprofen: 1 immediate with periorbital angioedema and 2 delayed – one with lip edema with oropharyngeal tightness and the other with maculopapular exanthema.

In the alternative NSAID group, there were only 1 delayed reaction with nimesulide with lips angioedema. No anaphylactic reactions were described.

Conclusion: In our sample, the most common NSAID reported as the culprit was the Cox-1 inhibitor ibuprofen, as described in the literature. There were 4 (17%) reactions on drug provocation tests, being mostly urticaria/angioedema, also according to other studies. We could allow the use of the culprit NSAID in 11 patients and an alternative one in 9 patients. We concluded that drug provocation tests are safe and essential for a correct diagnosis and selection of an alternative drug.

1299 | Drug allergy in children – The experience of a tertiary center

Lorenzo C.[1]; Silva M.I.[2]; Virtuoso J.[1,3]; Gomes R.[1]; Cosme J.[2]; Pedro E.[2]; Neves A.M.[1]; Lopes A.[2]

[1]Paediatric Immunoallergology Unit, Department of Paediatrics, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, EPE, Lisbon, Portugal; [2]Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, EPE, Lisbon, Portugal; [3]Pediatric Department, Unidade Local de Saúde da Guarda, Hospital Sousa Martins, Guarda, Portugal

Background: Drug allergy is a public health problem for children. More than 10% of parents report drug allergy in their children. Immunoallergological investigation frequently confirms drug allergy in a lower percentage. Our aim is to describe the immunoallergological investigation of a pediatric population in an outpatient clinic for drug allergy.

Method: Retrospective observational study by consulting the medical records of patients evaluated in a pediatric outpatient clinic for drug allergy between 2016 and 2020.

Results: There were included 316 patients (55.1% male, mean age 5.8 ± 4.8 years old, 28.8% with atopy). The drugs evaluated were: 88.3% (279) beta-lactam antibiotics (amoxicillin 134; 48%); 7.6% (24) non-steroidal anti-inflammatory drugs (NSAIDs) (ibuprofen 22; 92%); 1.3% (4) non-beta-lactam antibiotics; 0.95% (3) local anesthetics; 0.3% (1) perioperative drugs; and 1.6 % (5) other drugs.

Delayed reactions (> 6 hours) occurred in 81%. Clinical manifestations were: urticaria/angioedema 74%; exanthema 47%; gastrointestinal symptoms 14%; and anaphylaxis 13%.

Specific IgE for beta-lactam antibiotics were requested in 216 patients with only 2 positive results.

Skin tests - prick, intradermal and/or patch tests were performed in 175 patients: beta-lactam antibiotics 163 patients (20 positive); NSAIDs 3 patients (0 positive); non-beta-lactam antibiotics 4 patients (1 positive); peri-operative drugs 1 patient (0 positive); and other drugs 4 patients (0 positive).

273 patients underwent a drug provocation test (DPT) with beta-lactam antibiotics: 261 patients with the culprit drug, being positive in 17. Among 24 DPT with NSAIDs: 14 with the culprit drug, 2 positive for the culprit drug and 2 positive for an alternative drug. 5 DPT with non-beta-lactam antibiotics: 4 with the culprit drug, all negative. 3 DPT with local anesthetics: all with the culprit drug and all negative. 4 DPT with other drugs: 3 with the culprit drug, with 1 positive. The reactions were all mild.

Conclusion: The most common reported drugs causing a reaction were beta-lactam antibiotics with amoxicillin being the most frequently identified, followed by NSAIDs, mainly ibuprofen, as described in the literature. The majority were delayed and mild

reactions, mostly cutaneous, being our results similar to other studies. We concluded that DPT are a safe procedure for a correct diagnostic investigation.

958 | Three cases of non-steroidal anti-inflammatory drugs (NSAIDs)-enhanced food allergy: relevance in the evaluation of nsaids hypersensitivity

Bakhtiar M.F.[1]; Nazatul Shima A.R.[2]; Sugina K.[3]; Roshnee Kaur J.S.[3]; Hema Presenaa C.K.[1]; Nadzirah J.[1]; Leecyous B.[1]; Zailatul Hani M.Y.[1]; Tang M.M.[3]

[1]*Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia. National Institutes of Health Complex, Bandar Setia Alam, Shah Alam, Malaysia;* [2]*Dermatology Unit, Department of Medicine, Putrajaya Hospital, Ministry of Health Malaysia, Putrajaya, Malaysia;* [3]*Department of Dermatology, Kuala Lumpur Hospital, Ministry of Health Malaysia., Kuala Lumpur, Malaysia*

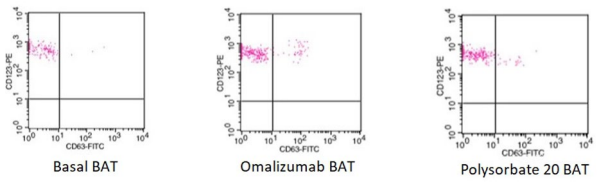
Background: Food-dependent cofactor-enhanced allergy is a unique form of allergy in that the food alone does not cause any symptoms. It is a cofactor-augmented reaction, with wheat as the frequently implicated food. The commonly incriminated cofactors include non-steroidal anti-inflammatory drugs (NSAIDs), exercise and/or alcohol.
Materials and methods: We report three patients with a history of chronic spontaneous urticaria (CSU) who were referred for investigation and management of suspected NSAIDs hypersensitivity. Two of these patients had an anaphylactic reaction following ingestion of ibuprofen while one allegedly had multiple NSAIDs intolerances. Two patients were unsure of any food allergies. One claimed exacerbation of symptoms after consumption of an unknown food following vigorous exercise. All patients were subjected to a graded aspirin and/or culprit NSAID provocation test. Skin prick test (SPT) was performed towards wheat, shrimp and dust mite. Total IgE, baseline tryptase and, specific IgE towards wheat and omega-5 gliadin were also performed. Subsequently, a five-step oral graded wheat provocation test with freshly prepared home-cooked high gluten flour fritter snack was performed, with immediate exercise of 30 minutes duration in all patients. In addition to exercise, a total of 1.5 g of aspirin was added as cofactor.
Results: All patients tolerated the graded aspirin provocation test. The two patients who reacted to ibuprofen gave a negative response following a graded ibuprofen challenge. The SPT gave positive responses to wheat and *Dermatophagoides pteronyssinus* for all patients. All patients had positive specific IgE towards wheat (range: 0.23 - 0.96 kUA/L) and omega-5 gliadin (range: 1.99 – 15.93 kUA/L). Total IgE ranged from 95.2 – 245 kU/L. Their baseline tryptase level was within normal limits (< 10 mcg/L). Two patients developed urticarial rash with hypotension while one patient only developed hypotension without any skin symptoms, after the last interval of exercise. These patients were treated and managed appropriately. They were discharged with an epi-pen prescription and advised on a gluten-free diet.
Conclusion: A high level of awareness and clinical suspicion of cofactor-enhanced food allergy is vital when provocation to aspirin and/or culprit NSAID is negative.

1208 | Allergy to omalizumab due to polysorbate 20, diagnosed by skin test and BAT

Ollo Morales P.; Audicana Berasategui M.T.; Longo Areso M.N.; Martinez Arcediano A.; Martel Martin C.

Hospital Universitario Araba, Vitoria, Spain

Purpose: We report a case of immediate reaction due to sensitization to polysorbate 20 following the administration of subcutaneous Omalizumab.
Method: A 59-year-old patient with chronic spontaneous urticaria in treatment with subcutaneous Omalizumab (300 mg/4 week) for a year now, who presents a good control of symptoms developed palpebral angioedema and exacerbation of the hives, 24h after the Omalizumab injection in the last three administration of the drug. These episodes were treated with oral corticosteroids and oral antihistaminic during one week. The patient achieved the control of the urticaria with oral antihistaminic in high doses after leave the treatment with Omalizumab. We performed prick test with Omalizumab, Movicol 55 mg/ml that contains polyethylene glycol (PEG) 3350, Casenlax 50 mg/ml that contains PEG 4000, PEG 1500, polysorbate 80 and polysorbate 20. We also performed intradermal test with Omalizumab, polysorbate 80 and polysorbate 20. A basophil activation test (BAT) was performed with Omalizumab in a 2.5 mg/ml concentration and with polysorbate 20 in a 1/50000 concentration.
Results: We detected a positive reaction with polysorbate 20 in intradermal test 1/10. The other prick and intradermal tests with Omalizumab, PEG and polysorbate 80 were negative. In BAT, the percentages obtained could not be properly evaluated because the stimulation response in presence of the anti-IgE antibody (positive control) was very low. Even that, we can see in the graphic of BAT that there is a mild positive stimulation response in presence of Omalizumab (2) and in presence off polysorbate 20 (3), compared to stimulation under baseline condition (1).
Conclusions: We report one case of immediate allergy to polysorbate 20 present in Omalizumab, demonstrated by skin testing and BAT. In addition, in this case we could not observe cross reactivity between polysorbate 20 and polysorbate 80 neither with PEG in different molecular weights.



1239 | Atrial fibrilation induced by teicoplanin: A case of perioperative anaphylactic reaction

Roa D.[1,2]
[1]Royal Surrey Hospital, Guilford, United Kingdom; [2]Oxford University Hospital, Oxford, United Kingdom

Background: Perioperative anaphylaxis is often severe and unpredictable and may lead to fatal outcome. Teicoplanin has been an emerging drug as a cause of perioperative anaphylactic reactions along with Beta lactams antibiotics. Atrial Fibrillation is frequent in perioperative care and has been described during anaphylactic reactions.

Methods: We present a case of 70-year-old man with a background of mitral valve replacement and high blood pressure, who underwent a total knee replacement on 2 March 2019. He had a spinal anaesthesia with Lidocaine to the skin, and 0.5 Bupivacaine and 400 mcg Diamorphine in a spinal block. In addition, he was given Gentamicin 160 mg and Teicoplanin 400 mg. After 5 minutes, he developed cough and complained of nausea and feeling unwell. He became sweaty and clammy and developed extreme bradycardia with low blood pressure (50mmHg systolic) and went into atrial fibrillation with 150 bpm. He also developed spread urticaria and there was no evidence of respiratory symptoms.

He was treated with Atropine, Metaraminol, Chlorpheniramine, Dexamethasone, Hydrocortisone and Phenylephrine infusion. In addition, he received Amiodarone and two DC cardioversions. After 12 hours he went back to sinus rhythm. The curve of tryptase after one hour showed values of 35 ng/L, 12 hours - 24 ng/L and the baseline was 6.8 ng/L.

He is currently treated with Atorvastatin, Rivaroxaban and Bisoprolol. The patient told us that he was treated prophylactically with Teicoplanin previously during his mitral valve replacement procedure.

Results: We performed skin prick test and intradermal test in standard concentrations with Lidocaine, Bupivacaine, Gentamicin, Teicoplanin, chlorhexidine and latex and he tested positive for Teicoplanin by intradermal test (13mm x 9mm).

He underwent another knee replacement procedure and was able to tolerate Lidocaine, Bupivacaine and Gentamicin.

Conclusions: We present a case of an atrial fibrillation and perioperative anaphylaxis due to allergy to Teicoplanin, which was confirmed with intradermal test and tryptase levels curve.

1055 | Anaphylactic shock by racecadotril

De La Cruz Martínez C. A.; Suárez Lorenzo I.; González Núñez V.; Lázaro López L.; Valero Santiago A.; Rueda García M.
Allergy Department, Hospital Quironsalud Barcelona, Barcelona, Spain

Background: Racecadotril is a drug used to treat acute diarrhea and it is usually administered orally in combination with rehydration measures. This medication works by inhibiting the intestinal enkephalinase enzyme, maximixing its antisecretory properties. In this vein, it reduces the secretion of water and electrolytes to the intestinal lumen, but without having an effect on intestinal motility. Thus, rapid activity is achieved, without modifying the bowel transit time.

Objective: To present a case of severe systemic IgE-mediated reaction after administration of racecadotril.

Method: A 41-year-old man, ex-smoker, with a history of arterial hypertension, and mitral valve replacement, antiaggregated with *acetylsalicylic acid* (ASA).

After the diagnosis of acute gastroenteritis, the patient was treated with racecadotril 100mg every 8 hours. The third day of therapy, he began with itchy palms, generalized itchy papuloerythematous rash, and poor general condition 2 hours after intake. Upon arrival at the emergency room, hypotension, decreased saturation and dyspnea were objectified. Epinephrine, dexchlorpheniramine, and methylprednisolone were administered, as well as fluid replacement, recovering vital signs in a short time. The skin lesions disappeared within 24 hours with no residual lesions. At that time he was on a strict diet for diarrhea but he had subsequently tolerated possibly implicated foods and drugs, including his usual treatment with ASA. The allergological study was performed 8 weeks after the condition by skin testing with the drug and food involved. The racecadotril skin prick test was performed using a 100mg capsule. The content was dissolved in saline solution at a concentration of 0.9% and applied on the forearm surface of the patient. The same skin test with the same concentration was performed on two controls in order to discard false positive results. Sensitization to food and recombinant food proteins was ruled out by in vitro study.

Results: Skin prick test with racecadotril was positive in our patient, while it was negative in the controls. Food allergy was dismissed.

Conclusion: We present the first case described in the literature of a severe IgE-mediated reaction to racecadotril.

1152 | Does the presence of cross-reactivity affect spirometric measurements in patients with non-steroidal anti-inflammatory drug hypersensitivity?

Koç E. N.; Tepetam F. M.
Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

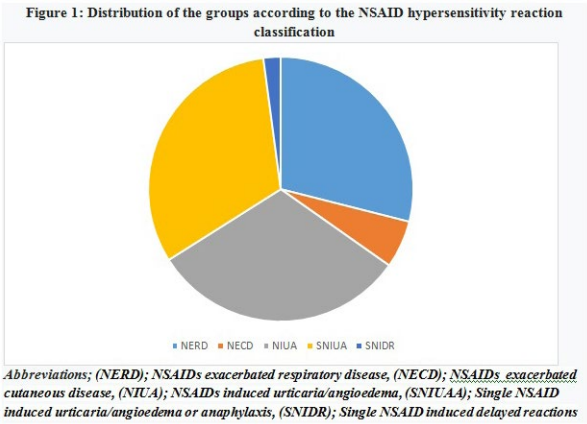
Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used drug groups which are also one of the most frequent causes of drug hypersensitivity reactions (DHRs). DHRs against more than one NSAID, which are not chemically similar, are called cross reactions. It was observed that in the presence of cross-reactivity, low spirometric parameters and airway reversibility could be possible without restriction of airflow. We aimed to investigate the effect of cross reactivity on spirometric measurements and bronchodilator reversibility in patients with a history of NSAID allergy.

Method: 201 patients who applied to our outpatient clinic due to NSAID hypersensitivity (HS) were evaluated retrospectively. 25 patients who were using other drugs concurrently with NSAIDs and 38 patients whose PFT results could not be reached were excluded from the study. Patients were divided into 5 classes according to EAACI's 2013 NSAID HS classification. Groups are defined as NSAIDs-exacerbated respiratory disease (NERD), NSAIDs-exacerbated cutaneous disease (NECD), NSAIDs-induced urticaria/angioedema (NIUA), Single-NSAID-induced urticaria/angioedema or anaphylaxis (SNIUAA) and Single-NSAID-induced delayed reactions (SNIDR). Spirometric measurement values and post-bronchodilator reversibility levels were compared between cross-reactive and noncross-reactive groups.

Results: %28.9 of 138 patients were NERD, %5.8 were NECD, %31.2 were NIUA, (In NECD and NIUA group, there were also 10 patients who had respiratory symptoms), %31.8 were SNIUAA and finally 2.1% of the patients were classified as SNIDR (Figure.1). When NERD was excluded, approximately half (51%) of the reactions in remaining 98 patients (68.4% female and mean age 42.5 ± 12.7) were mediated by cross reaction. 16 patients were newly diagnosed with asthma (NECD: 1, NIUA: 9, SNIUAA: 6). Baseline FEV1 levels was found to be higher in the cross-reactive group. In addition, post-bronchodilator reversibility level was 1.5 times higher in the cross reactive group. (140ml ,210ml; p = 0,35) (Table.1)

Conclusion: Although it is not statistically significant, the presence of NSAID HS due to cross-reactivity that is seen in patients without clinically diagnosed asthma, may affect the level of post-bronchodilator reversibility. Even further, as in our study, these patients can be newly diagnosed with asthma. Hence, this may be predictive for future airflow restriction, and asthma development should be monitored closely in these patient.

	Non-cross reactive (single) group (n = 48)	Cross reactive (multiple) group (n = 50)	p value
Baseline FEV1; ml (median ± SD)	2.76 (0.88)	2.83 (0.82)	0.87
Baseline FEV1/FVC; %(± SD)	94.5 (14.5)	94 (15.8)	0.68
Post-bronchodilator FEV1 variability; ml (median, %25-75 percentile)	140 (100-200)	210 (100-290)	0.35
Post-bronchodilator FEF25-75 variability; %(median, %25-75 percentile)	8.5 (4-12)	12.5 (2-17)	0.35
PEF percent variation%;(median, %25-75 percentile)	4 (2-9)	2.5 (1-10)	0.7



Abbreviations; (NERD); NSAIDs exacerbated respiratory disease, (NECD); NSAIDs exacerbated cutaneous disease, (NIUA); NSAIDs induced urticaria/angioedema, (SNIUAA); Single NSAID induced urticaria/angioedema or anaphylaxis, (SNIDR); Single NSAID induced delayed reactions

1115 | 10-year-maintenance of drug tolerance to nebulized colomycin

Sieber J.[1,2]; Renner S.[1]; Lakatos-Krepcik A.[3]; Szépfalusi Z.[1]

[1]*Medizinische Universität Wien, Vienna, Austria;* [2]*Wroclaw Medical University, Wroclaw, Poland;* [3]*Department of Pulmonology, Klinik Hietzing, Vienna, Austria*

Adverse drug reactions can be considered as important public health problem. Desensitization protocols have been successfully developed to prevent from withholding of first line therapy in allergic patients. However, most protocols are designed to obtain temporal tolerance. With recurrent need of treatments desensitization procedures have to be repeated. The data on long-term maintenance of drug tolerance is scarce. Thus, upon an IgE-mediated colomycin allergy we describe the maintenance of tolerance to nebulized drug for the period of 10 years in a 15-year-old cystic fibrosis patient, proceeded by successful rush intravenous desensitization protocol. Despite of mechanisms being largely speculative, the long-term maintenance of drug tolerance seems achievable by continuous local drug application.

1242 | How useful is our alert registration system?

Mediavilla M. M.[1]; Monteserin I.[1]; Lopez De Torre A.[1]; Blanco C.[1]; Urbina O.[1]; Audicana M. T.[2]; Llorens Y.[1]; Martin P.[1]; Martinez M. D.[1]

[1]*Osakidetza Basque Health Service, Araba University Hospital, Pharmacy Department. BIOARABA., Vitoria, Spain;* [2]*Osakidetza Basque Health Service, Araba University Hospital, Allergy and Clinical Immunology Department. BIOARABA., Vitoria, Spain*

Background: The aim of this report is to analyze and adapt the electronic drug allergy alert systems used both, in the Electronic Health Record (EHR) and the Electronic Prescribing Program (EPP) in our hospital setting.

Method: An alert software for pharmaceutical validation was used by clinical pharmacists to analyze alerts about allergies between 06/23/2020 and 12/23/2020.

Data collected were: drug, record in EPP, type of record in EHR ["Confirmed allergy", "Probable allergy", "No allergies/Allergies not consulted", "Adverse Drug Reaction (ADR)"], existence of Allergy Department (AD) report and pharmaceutical intervention (PI) carried out.

Results: A total of 136 drug allergy alerts were reviewed. Alerts related to 58 different drugs were identified, being Non-steroidal Anti-inflammatory Drugs (NSAIDs) the most prevalent therapeutic group. Record types in EHR were: "Confirmed Allergy" in 77.21% of the records; "No allergies/Allergies not consulted" in 14.71%; "Probable allergy" in 3.68%; and "ADR" in 1.47%. 2.94% of the alerts did not contain a record in the EHR.

Only 36.19% of the "Confirmed allergy" records, were endorsed by an AD report. 52.63% of these, however, were not registered in the EPP. The remaining 63.81% of the "Confirmed allergy" records, were not studied by the AD and 52.24% of these had the allergy registered in the EPP.

Of the 136 alerts analyzed, 101 required PI. 71 were modifications in the EHR (from "Confirmed allergy" to "Probable allergy") due to the lack of an AD report. 25 PI consisted in registering the allergy in the EPP, when an AD report was available and confirmed the allergy.

Conclusion:

- NSAIDs were the most involved drugs in alerts.
- Near half of the patients with AD report confirming an allergy did not have a record in the EPP, which could compromise patients safety.
- Around sixty percent of the "Confirmed Allergies" in EHR, were not previously studied by AD. Moreover, in near half of these the allergy was registered in the PEE, which could limit therapeutic options.
- In order to improve patient safety and therapeutic management, an interdisciplinary working group made up of Pharmacists, Primary Care Physicians, Emergencies and AD should be constituted. It is necessary to train professionals who record allergies in our hospital setting.

1264 | Paclitaxel (taxol) desensitization in a child with testicular cancer and anaphylaxis

Felix M. M.R.; Abdala J. d.S.; Miranda A. C.d.M.R.T.; Crespo C. G.; Fleury L. G.d.S.; Vianna J. C.; Grinapel R.; Avila R. S.A.; Nascimento R. C.; Souza M. S.d.

Federal Hospital of Servidores do Estado, Rio De Janeiro, Brazil

Case Report

Background: Testicular cancer is relatively uncommon and accounts for less than 1% of all male tumors. Testicular germ cell tumors comprise 95% of malignant tumors and radical orchiectomy is the primary treatment for most of these patients. Treatment options for postorchiectomy management includes systemic therapy such as paclitaxel (taxol). Taxol is a taxane antineoplastic agent that is used in the treatment of various types of cancers. However, it causes immediate hypersensitivity reactions (HSRs) in around 10% of patients despite premedication. Three mechanisms could account for immediate HSRs to taxanes: complement activation caused by the emulsifying agents (Cremophor EL and polysorbate 80); histamine release through a direct effect of paclitaxel on basophils; and an IgE/IgG-mediated reaction.

Method: We report a case of a 2-year-old boy, with testicular cancer and no personal history of atopic disease, that was referred to our unit after one episode of anaphylaxis (facial angioedema and hypotension) minutes after infusion of taxol. He received premedication with corticosteroid and antihistamine. It was the first cycle of his treatment after a relapse. The infusion was immediately stopped, and he was treated with epinephrine and saline infusion with good recovery. No tryptase level was available during the acute reaction. We evaluated the patient using the ENDA questionnaire. He has already been submitted to orchiectomy and other systemic treatments. Given the severity of the initial HSR (grade 3) and the failed response to standard treatments, taxol was restarted using a desensitization protocol. His mother gave informed consent before desensitization.

Results: In March 2021, he underwent successful desensitization which was completed in around 6 hours and 30 minutes. Premedication consisted of montelukast 4mg, diphenhydramine 10mg, dexamethasone 3,2mg and omeprazole 10mg, the day before and on the day of administration of taxol. Desensitization protocol commenced with an initial intravenous dose of 0.0006 mg, which was gradually increased to a cumulative dose of 82 mg, with 15-minute intervals between 16 steps. During the procedure, he did not experience any reaction. He was submitted to another desensitization without breakthrough reactions.

Conclusion: Desensitization to taxol-induced anaphylaxis was safe and effective in this child with testicular cancer and few options for treatment.

951 | Drug hypersensitivity reactions in patients with sjögren's syndrome

Oštric Pavlovic I.[1]; Bolpacic J.[1]; Raškovic S.[1]; Tomic-Spiric V.[1]; Peric-Popadic A.[1]; Savic N.[1]; Jovicic Ž.[1]; Arandelovic S.[1]; Stefanovic L.[1]; Dimitrijevic M.[1]; Plavšic A.[1]; Stojanovic M.[1]; Miškovic R.[1]; Velickovic A.[1]; Pavlovic A.[2]; Bogic M.[1]

[1]*Clinic of Allergology and Immunology, Clinical Center of Serbia, Belgrade, Serbia*; [2]*University Children's Hospital Tiršova, Belgrade, Serbia*

Background: It has been observed that drug hypersensitivity reactions are more common among patients with Sjögren's syndrome (SS) than the general population, yet data is very scarce.

Aim: The objective of this study was to examine the frequency of drug hypersensitivity reactions in our patients with SS.

Method: A retrospective cross-sectional monocentric study that included 100 consecutive patients with Sjögren's syndrome hospitalized in the Clinic of Allergology and Immunology of the Clinical Center of Serbia from 2014. to 2018. was conducted in February of 2018.

Results: The majority of patients were female (87 to 13 male patients). Primary SS (PSS) was the predominant diagnosis (74%) compared to 26% of patients with secondary SS (SSS) ($p < 0.001$). Almost half of the patients (49%) reported a drug reaction, which was respectively more common in the group of patients with PSS (38%) in comparison to 11% of patients with SSS. An allergic reaction to one drug was reported in 22% of patients compared to 27% of patients who had an allergic reaction to several drugs. Most patients reported drug reactions to antibiotics (36%), followed by analgesics (10%), while others reported reactions to other groups of medications. Among antibiotics, penicillins were most prominent (24%), then sulfonamides (11%), quinolones (6%), aminoglycosides (5%) and tetracyclines (4%) with solitary cases of reactions to cephalosporins and macrolides. Among analgesics, most of the hypersensitivity reactions were attributed to the metamizole group (11%), followed by the nonsteroidal anti-inflammatory drugs (NSAIDs) (8%). There were no reported reactions to acetaminophen. Adverse effects were also linked to the use of immunosuppressive drugs (mostly corticosteroids and antimalarials), vitamins, antihistamines, warfarin, iodine contrast agents, and intravenous immunoglobulins. Reported clinical manifestations included urticaria, angioedema, maculopapular rash, erythema. Anaphylactic shock (associated with penicillin and aminoglycoside administration) has been reported in three patients. Other adverse effects were rare.

Conclusion: Allergic reactions to various medications tend to be common in patients with SS and require a thorough history taking and observation following the drug administration, especially when it comes to antibiotics and over-the-counter medications.

Therefore, we have continued our research during the past years and we are looking forward to presenting our further results in the near future.

1191 | Evaluation of adverse reactions and hypersensitivity reactions with leuprolide acetate and triptorelin acetate in children

Metbulut A.P.; Toksoy Adigüzel K.; Islamoglu C.; Boyraz M.; Dibek Misirlioglu E.

Ankara City Hospital, Child Hospital, Ankara, Turkey

Background: GnRHa is commonly used to treat central precocious puberty (CPP). Generally, they are well-tolerated; however adverse reactions have been reported. Local adverse events occur in 10-15% of the patients who were treated with GnRHa. Anaphylactoid reactions with GnRHa are very rarely seen.

The aim of this study is to report our clinical experience with hypersensitivity reactions seen in pediatric patients receiving leuprolide acetate (LA) and triptorelin acetate (TA) in CPP at the single pediatric tertiary medical center and to evaluate the prevalence rate of adverse reactions.

Method: This retrospective study included children with CPP who were treated with GnRHa (LA and TA) at our hospital between January 2013 and December 2020. We analyzed clinical characteristics of patients who experienced adverse reactions and analyzed the prevalence rate.

Results: Seven side effects (0.69%) were observed among total of 1010 CPP patients who were treated with TA and LA. Sterile abscesses were observed in three patients (0.29%). In four patients, tremors at both hands, vomiting, an urticarial rash, and musculoskeletal stiffness were observed respectively. None of the patients had an anaphylaxis.

Conclusion: In our study, mild reactions were seen in 7 patients. GnRHa is safely used and well-tolerated medications; but exceedingly rare, severe reactions can be developed. All patients receiving GnRHa treatment should be carefully monitored for hypersensitivity reactions.

TABLE 1 Characteristics of the patients with precocious puberty developing adverse reaction

Patient Number	Age AT THE BEGINNING OF THE TREATMENT (years)	Gender	ADDITIONAL Chronic Disease	GnRHa depot	Dose of GnRHa	Number of the injection at the time of reaction AND INTERVAL BETWEEN THE REACTION	Symptoms	Continuation of the treatment
1	8.5	F	-	TA	3.75 mg/month	20th and 21st Immediately after	Tremor at both hands	Discontinued
2	9	F	-	TA	3.75 mg/month	11th Immediately after	Vomiting	Discontinued
3	7.5	F	-	TA	3.75 mg/month	1st 72 hour after	Urticarial rash	Discontinued
4	8	M	Bipolar disease, Autism spectrum disorder, hypothyroidism	LA	3.75 mg/month	9th 1 week later	Sterile abscess	Switched to TA treatment
5	8 years 9 month	F	-	LA	3.75 mg/month	4th 10 days later	Sterile abscess	Switched to TA treatment
6	7 years 11 month	F	-	LA	3.75 mg/month	3rd 1 week later	Sterile abscess	Switched to 11.25mg per 3 month
7	10 years 1 month	M	-	TA	3.75 mg/month	5th Immediately after	Musculoskeletal stiffness	Discontinued

959 | Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) post-intravenous co-amoxiclav provocation test: a case report

Bakhtiar M.F.[1]; Tang M.M.[2]

[1]*Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia. National Institutes of Health Complex, Bandar Setia Alam, Shah Alam, Malaysia;* [2]*Department of Dermatology, Kuala Lumpur Hospital, Ministry of Health Malaysia., Kuala Lumpur, Malaysia*

Case Report

Background: Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is an uncommon form of cutaneous drug reaction. It affects the intertriginous or flexural areas symmetrically in the absence systemic symptoms following systemic administration of a drug. Many drugs have been implicated for this reaction with beta lactams antibiotics commonly being reported.

Materials and methods: We describe a 42-year old man with post-traumatic stress disorder (PTSD) who gave a very vague history of non-steroidal anti-inflammatory drugs (NSAIDs), amoxicillin and cloxacillin hypersensitivities. He was referred for possible de-labeling of an alleged anaphylactic shock following intravenous cefuroxime administration in 2015, given for lower limb cellulitis. Baseline tryptase level, total IgE and specific IgE for penicilloyl G and V were taken. Subsequent to the in vitro test, skin testing (skin prick [SPT] and intradermal test [IDT]) was performed with an array of beta lactam (BL) antibiotics. A placebo-controlled graded intravenous (IV) co-amoxiclav provocation was performed following a negative skin test. Full blood count (FBC), renal profile, liver function, erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA) and urine spot tests were subsequently taken when the patient reported erythemathous rash 48-hours post IV challenge. The rash started from the groin area spreading to the umbilicus, trunk and upper limbs without systemic symptoms.

Results: The total IgE result was slightly raised (235 kU/L). Specific IgE to penicilloyl G and V were undetectable (0.00 kUA/L) and baseline tryptase level was within normal limits (< 10 mcg/L). Skin testing was negative for all BL tested. FBC did not show any eosinophilia, ANA was non-reactive, renal profile, liver function and ESR tests were within normal limits. There was no haematuria on the urine spot test. On examination, there was no fever or lymph nodes palpable. After consultation with dermatology, a diagnosis of SDRIFE was made and the patient was started on corticosteroid cream and a short course of oral prednisolone. He recovered well one week later.

Conclusion: SDRIFE is a rare delayed-type hypersensitivity drug reaction, confirmed by the negative IgE and immediate-type skin testing devoid of any systemic symptoms.

1324 | Cefepime induced steven jonson syndrome: A case report

Fouad S.[1]; El-Korashi L. A.[2]; Nagib E.[1]; Obeid D. F.[1]; Elmahdi A. R.[1]; Elmazaly A. Y.[1]; Elshayeb M. A.[1]

[1]Faculty of Medicine- Ain Shams University, Cairo, Egypt; [2]Faculty of Medicine- Zagazig University, Zagazig, Egypt

Case Report

Introduction: Steven Jonson syndrome (SJS) was first described in 1922 by Stevens and Johnson as a febrile illness with purulent conjunctivitis, stomatitis, and skin lesions. Together with toxic epidermal necrolysis (TEN) and Stevens–Johnson/toxic epidermal necrolysis (SJS/TEN), it forms a spectrum of disease, with SJS being less severe.[1]

Case Presentation: A 22-yr-old female, receiving lamotrigine and Felosac for psychic disorders, presented to the Emergency department complaining of erythematous maculo-vesicular rash extending from the trunk toward the extremities with skin sloughing and small vesicles on the nasal and oral mucosa as well as ocular drainage. The patient was hospitalized in the Allergy and Clinical Immunology department for the monitoring of epidermal sloughing. On examination she had a generalized symmetrical, blisters on the face, upper limbs, chest and back, associated with target-like lesions, and positive Nikolsky sign. She had an associated buccal ulceration with haemorrhagic crusting of the lips and conjunctival injection. Her temperature was 37°C, with SpO2 of 98%, a blood pressure recording of 120/80 mmHg and a regular pulse of 100 beats/min. Random blood glucose was high (178 mg/dl) and CRP was positive (4.5 mg/l). Lactic dehydrogenase was 223 IU/l. The severity of illness was evaluated according to the SCORE of Toxic Epidermal Necrosis (SCORTEN) score on day 1 (a score of 2). Using the Algorithm of Drug causality for Epidermal Necrolysis (ALDEN) Stevens– Johnson Syndrome/toxic epidermal necrolysis (SJS/TEN) drug causality scoring system, cefepime was the most probable drug. The patient received intravenous fluid resuscitation and urinary catheter was inserted. Supportive treatment was formed. A regimen of dexamethasone given intravenously twice daily was also started. The skin lesions were treated twice daily with a mixture of urea and triamcinolone. Immunosuppressive treatment was initiated on the second day of admission; IVIG 0.6 gm/kg divided by three days by infusion over 4 hours. The patient fully recovered after three weeks of hospitalization.

Conclusion: Early recognition of Steven Jonson syndrome and proper management decreased the rate of mortality among these patients.

Keywords: Steven-Johnson syndrome, toxic epidermal necrolysis, IVIG.

References

Stevens AM, and Johnson FC. A new eruptive fever associated with stomatitis and ophthalmia: report of two cases in children. Am J Dis Child 1922; 24: 526-533.

970 | Lamotrigine induced generalized fixed drug eruption

Kendirci N.[1]; Yakici N.[1]; Ersöz S.[2]; Kati B.[2]; Yildiz N.[3]; Kot H.[1]; Cansu A.[3]; Orhan F.[1]

[1]Department of Pediatrics, Division of Pediatric Allergy and Immunology, Karadeniz Technical University Medical School, Trabzon, Turkey; [2]Department of Pathology, Karadeniz Technical University Medical School, Trabzon, Turkey; [3]Department of Pediatrics, Division of Pediatric Neurology, Karadeniz Technical University Medical School, Trabzon, Turkey

Case Report

Fixed drug eruption (FDE) is a delayed immunologically mediated cutaneous adverse drug reaction, characterized by the abrupt appearance of one or numerous round edematous erythematoviolaceous patches with well-defined borders. In generalized fixed drug eruption, the typical lesions are multiple and disseminated and involve the trunk and extremities, sparing the mucosal and the semimucosal areas (1). Lamotrigine is a triazin derivative antiepileptic drug that blocks voltage depended sodium channels, thereby preventing excitatory neurotransmitter release (2). It has been used for many years for treating epilepsy. Although a small number, lamotrigine induced FDE cases have been reported in the literature (3). This report presents a case of generalized fixed drug reaction induced by lamotrigine use.

Case: An 11-year-old patient, who has been followed up with a diagnosis of epilepsy for four years, was admitted to our hospital because of rashes which was occurred three days after the initiation of lamotrigine. On his examination, we detected multiple violaceous patches on patient's trunk, back and legs. It was learned that the patient had no history of trauma and fever, and 1 year ago, he used lamotrigine for 2 weeks without any problem, but was discontinued by his neurologist during follow-up. Lamotrigine has been discontinued as it was suspected to be responsible for the eruptions and lesions were resolved within a few days with remaining hyperpigmented macular areas. The clinical findings, course and a skin biopsy that revealed a lymphocytic infiltration covering the basal layer and necrotic keratinocytes in epidermis and vacuolar degeneration in the basal layer (Figure 1) confirmed the diagnosis of lamotrigine induced fixed drug eruption.

References

1. Andrade P, Brinca A, Gonçalo M. Patch testing in fixed drug eruptions-a 20- year review. Contact Dermatitis 2011;65:195-201.
2. Fitton A, Goa KL. Lamotrigine. An update of its pharmacology and therapeutic use in epilepsy. Drugs 1995;50:691-713.
3. Hsiao CJ, Lee JY, Wong TW, Sheu HM. Extensive fixed drug eruption due to lamotrigine Br J Dermatol 2001;144:1289-1291

1141 | The association between chronic rhinosinusitis and proton pump inhibitor use: A nested case-control study using a health screening cohort

Choi H.G.[1], Kong I.[2]
[1]*Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University College of Medicine, Anyang, South Korea;* [2]*Department of Otorhinolaryngology-Head and Neck Surgery, Hospital Medicine Center, Seoul National University Hospital, Seoul, South Korea*

Background: The purpose of this study was to evaluate the relationship between chronic rhinosinusitis (CRS) and proton pump inhibitor usage in a Korean population.
Method: The Korean National Health Insurance Service-National Sample Cohort was assessed from 2002 to 2013. In total, 7,194 CRS patients were matched with 28,776 control participants at a ratio of 1:4 with respect to age, sex, income group, the region of residence, and index date using random order. We analyzed previous histories of PPI use in the CRS patients and control groups. CRS and previous PPI use were included using ICD-10 codes, and claim codes. Crude and adjusted odds ratios (ORs) were analyzed using conditional logistic regression analyses. 95% confidence intervals (CI) were calculated. Subgroup analyses were performed according to age and sex.
Results: A total of 7,194 cases were identified, and 28,776 controls were matched to the cases. The adjusted OR of CRS with/without nasal polyp was 1.71 (95% CI = 1.46-2.02, $p < 0.001$) and 1.28 (95% CI = 1.16-1.41, $p < 0.001$) in the current and past PPI users, respectively. Irrespective of PPI prescription days (<30, ≥ 30 days & < 90 days, ≥ 90 days), PPI use was associated with a higher occurrence of CRS, showing the adjusted OR as high as 1.46 (95% CI = 1.26-1.69, $p < 0.001$) at the group of 30-60 day PPI users. The results of the subgroup analyses were consistent.
Conclusion: The risk of CRS was increased in PPI users. This relation was consistent in all age and sex groups.

977 | Changes in nasal resistance and quality of life after endoscopic microdebrider-assisted inferior turbinoplasty in patients with persistent allergic rhinitis

Sagar D.M.
MGM medical college, Indore, India

Background: Objective: To assess objective and subjective outcomes in patients with persistent allergic rhinitis who had undergone endoscopic microdebrider-assisted inferior turbinoplasty.
Method: A prospective study of patients undergoing turbinate with or without septoplasty surgery for nasal obstruction or other features of allergic rhinitis was performed. Patient reported outcomes were: nasal obstruction, global nasal function (GNF), and sino-nasal outcome test (SNOT-22) with rhinitis, facial symptom, sleep and psychological sub-scores. Results were obtained preoperatively and 3 months postoperatively.
Results: 75 patients were assessed. AR had worse obstruction . All outcomes improved post-surgery; nasal obstruction, SNOT-22, rhinitis-symptoms, facial-symptoms, sleep- function, psychological-function and NPIF. GNF improvement was greater in AR.
Conclusion: Our results suggest that endoscopic microdebrider-assisted inferior turbinoplasty is effective for decreasing nasal resistance and improving quality of life in patients with persistent allergic rhinitis who have substantial nasal congestion.

1151 | Validation of different criteria for eosinophilic polyp? From pre-operative clinical and immunological point of view

Cho S.; Won T.; Kim J.; Rhee C.
Seoul National University Bundang Hospital, Seongnam, South Korea

Background: Bilateral chronic rhinosinusitis with nasal polyp (crswNP) can be classified into eosinophilic and non-eosiniphilic polyp. However, the definition of eosinophilic polyp has not been established. In this study, we tried to validate several criteria from preoperative clinical and immunological perspective.
Method: A cohort of 73 patients with crswNP and 11 negative control patients without CRS was retrospectively analyzed. Preoperative clinical characteristics including age, gender, CT score, comorbid asthma, and JESREC scores were reviewed. Tissues were harvested from ethmoid sinus and underwent histological and immunological analysis. Patients were divided into eosinophilic and non-eosinophilic polyps based on five different criteria; 1) eosinophils (EOS) accounted more than 20% of total inflammatory cell, 2) >70 EOS per high power filed (HPF) 3) > 55 EOS/HPF, 4) >10 EOS/HPF, and 5) JESREC score ≥ 11. Clinical characteristics were than compared among control, eosinophilic polyp, and non-eosinophilic polyp defined by the criteria. this classification was immunologically validated by predicting the performance of tissue eosinophilia using a random forest model based on 15 cytokine levels from nasal tissues.
Results: Preoperative clinical features showing significant differences between groups tended to differ according to various criteria. JESREC score was significantly higher in eosinophilic polyp compared to non-eosinophilic polyp when all criteria had been used except for >70 EOS per HPF. Only when >10 eos/HPF was used, the mean age of non-eosionphilic polyp was significantly lower than that of eosinophilic polyp. From an immunological perspective as represented by the levels 15 cytokines, EOS accounting more than 20% of total inflammatory cells resulted the highest accuracy (85.71%), F-measure (0.86), and area under curve (AUC) (0.93).
Conclusion: Clinical characteristics were different when various criteria for eosinophilic polyp was used. Therefore, when choosing the criteria for eosinophilic polyps, the purpose of the study should be taken into account. From immunological perspective, tissue eosinophilia can be best classified when tissue eosinophil comprise more than 20% of total inflammatory cells.

1038 | Risk factors and management of paediatric rhinosinusitis patients

Subha S.

Universiti Putra Malaysia, Serdang, Malaysia

Background: Paediatric rhinosinusitis is generally underdiagnosed by the general practitioner. It could cause many substantial physical symptoms and has a detrimental influence on the children's quality of life. This research is to evaluate the risk factors and management of paediatric rhinosinusitis patients at our institute.

Method: A cross-sectional study using retrospective data of paediatric rhinosinusitis patients who attended the ENT clinic for a period of 5 years was collected. A total of 324 patients' data were obtained from the medical records. The age group of the affected patients varying from a month to 18 years, of these 50.3%were between six years and eleven years old. We retrospectively studied the risk factors or any form of associated diseases, upper respiratory tract infection, asthma, allergic rhinitis, adenoid hypertrophy, GERD, established immunodeficiency, tonsillitis, epistaxis or eczema.

Results: Among our study population, 97.2% had allergic rhinitis, 27.2 % had asthma and 24.4 % had upper respiratory tract infections. Meanwhile, only 0.6% of affected children revealed to have GERD and none of them found with immunodeficiency as their risk factor.

We evaluated the association between these risk factors and demographic characteristics of these paediatric rhinosinusitis patients. It is revealed that there is a significant association between age group with URTI as a risk factor in paediatric rhinosinusitis. Based on the result, URTI has commonly occurred in patients aged around 6 to 11 years (51.4%).

Regarding the management,99.7 % of our paediatric rhinosinusitis patients obtained medical management. The majority of the medical management includes oral anti-histamine, while the least number of paediatric rhinosinusitis patients were given oral steroids.

Conclusion: Our study demonstrated that allergic rhinitis is the most established risk factor among paediatric rhinosinusitis patients, followed by asthma, upper respiratory tract infection (URTI) and adenoid hypertrophy. Furthermore, most of the pediatric patients who suffered from rhinosinusitis were given conservative medical management and only a few of them had undergone surgical management. Adenotonsillectomy is the most frequently used surgical management for rhinosinusitis among pediatric patients. It can be concluded that conservative medical care was the mainstay for management in pediatric rhinosinusitis.

1066 | Associations between short-term grass pollen exposure, food sensitisation and allergy in a paediatric cohort

Idrose N.S.[1,2]; Lodge C. J.[1]; Peters R. L.[1,2]; Douglass J. A.[1,3]; Koplin J. J.[1,2]; Lowe A. J.[1,2]; Perrett K. P.[1,2]; Tang M. L.[1,2]; Newbigin E. J.[1]; Abramson M. J.[4]; Erbas B.[5]; Vicendese D.[1,5]; Dharmage S. C.[1,2]

[1]University of Melbourne, Melbourne, Australia; [2]Murdoch Children's Research Institute, Melbourne, Australia; [3]Royal Melbourne Hospital, Melbourne, Australia; [4]Monash University, Melbourne, Australia; [5]La Trobe University, Melbourne, Australia

Background: The relationship between short-term pollen exposure and respiratory allergies is well researched. We hypothesised that short-term pollen exposure may contribute to increased food sensitisation, food allergy and reaction threshold to oral food challenge (OFC).

Method: Data come from the HealthNuts population-based cohort of 5276 children recruited at 12 months and followed up at age 6 years. Of these, n = 1108 (12 months) and n = 675 (age 6 years) underwent examination during the grass pollen season and were included in the study. Grass pollen levels were measured by volumetric spore trap (grains/m^3) located 15m above ground. Pollen exposure was considered on the day of testing (lag 0), up to three days before (lag 1-lag 3) and cumulatively (lag 0-3). Outcomes were sensitisation to specific foods (skin-prick test (SPT) >= ≥ 2 mm at 12 months and >= ≥ 3mm at age 6 years), challenge-confirmed food allergy, reaction threshold to OFC (cumulative dose given before a reaction occurred) and serum food-specific IgE levels. Associations were analysed using either logistic or quantile regression models depending on the outcome variable.

Results: Grass pollen levels at lag 0-3 was associated with up to 25% higher probability of sensitisation to all food allergens in 6-year-olds but not in 12-month-olds. At 12-months, grass pollen levels were only associated with peanut sensitisation and in those with a family history of food allergy (up to 60% higher probability) or severe eczema (up to 75% higher probability). There was no evidence of an association between grass pollen levels and the probability of challenge-confirmed food allergy in both age groups. However, grass pollen levels were associated with a lower median reaction threshold to OFC (at lag 0) and higher median serum-specific IgE levels (at lag 1 and lag 0-3) in peanut-allergic 12-month-olds.

Conclusion: Persistently high ambient grass pollen exposure over three days may be associated with an increased risk of food sensitisation but not necessarily food allergy in children. The associations in peanut-allergic infants may be related to immune activation or peanut and grass pollen cross-reactivity leading to a lower reaction threshold. Further research is required to confirm the findings of this study.

1099 | Aerobiological and allergenic analysis of amaranthaceae pollen in alentejo region (south portugal)

Caeiro E.[1,2]; Almeida J.[3]; Penedos C.[1]; Carreiro-Martins P.[1,4,5]; Tavares B.[1,6]; Fonseca J.[1,7,8,9]; Rodrigues-Alves R.[1,10]; Ferreira M. B.[1,11,12]

[1]*Sociedade Portuguesa de Alergologia e Imunologia Clínica - SPAIC, Lisbon, Portugal;* [2]*Instituto Mediterrâneo para a Agricultura, Ambiente e Desenvolvimento - MED, Instituto de Investigação e Formação Avançada- IIFA, Universidade de Évora, Évora, Portugal;* [3]*Universidade de Évora, Évora, Portugal;* [4]*Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal;* [5]*NOVA Medical School/Comprehensive Health Research Center - CHRC, Lisbon, Portugal;* [6]*Serviço de Imunoalergologia, Hospitais da Universidade de Coimbra, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal;* [7]*Departamento Medicina da Comunidade, Informação e Decisão em Saúde - MEDCIDS, Faculdade de Medicina, Universidade do Porto, Oporto, Portugal;* [8]*Centro de Investigação em Tecnologias e Serviços de Saúde - CINTESIS, Oporto, Portugal;* [9]*Unidade de Alergia, Instituto & Hospital CUF Porto, Oporto, Portugal;* [10]*Hospital do Divino Espírito Santo - HDES, Ponta Delgada, Portugal;* [11]*Clinica Universitária de Imunoalergologia - Faculdade de Medicina, Universidade de Lisboa, Açores, Portugal;* [12]*Serviço de Imunoalergologia, Centro Hospitalar e Universitário Lisboa Norte, Lisbon, Portugal*

Background: Inhaling pollen of the Amaranthaceae plants is a major cause of respiratory allergy in the Mediterranean area, particularly in summer allergies. This pollen type is becoming increasingly important in those regions where climate change is extending the desertification process. The rapid spread of these plants and their adaptation to hydric stress, to adverse conditions may explain this trend. The objectives of this study were: (1) To analyze the prevalence and aerobiological behavior of Amaranthaceae pollen in the Alentejo region; (2) to analyze the influence of meteorological factors on atmospheric pollen concentrations; and 3) to assess the pollen levels of exposition.

Method: For the study, Amaranthaceae pollen data from the Évora monitoring station of the Portuguese Aerobiology Network, from 2001 to 2019, were used.

Results: Amaranthaceae pollen showed a low representativeness in the pollen spectrum of the atmosphere, always < 1%. Amaranthaceae pollen season occurred between April and October, with an average duration of 161 ± 16 days, and with two distinct peaks periods, one in the spring and the other in the summer. Correlations between daily pollen counts and meteorological parameters were obtained. During the year, days with pollen levels that surpassed the threshold daily values which provoke allergy symptoms were detected.

Conclusion: Despite the low representativeness in the pollen spectrum of the atmosphere, its presence in the air in low concentrations, this pollen type may be an important cause of pollen allergy in region. Amaranthaceae pollen occurs in the air with other pollens with high allergological capacity simultaneously, with grasses and olive trees pollens, with which it presents cross-reactivity.

So, this study show the importance of Amaranthaceae pollen monitoring and the usefulness of the aerobiological information for the allergologists and patients with pollinosis of the region of study.

1315 | Pollen aeroallergens in Asuncion-Paraguay and metropolitan area: a 3 years survey

Alcaraz Duarte P. R.[1]; Piraino P.[2]; Perez C.[1]; Stanley R.[2]; Espinola S.[2]; Paredes K.[3]; Barrionuevo L.[4]; Ramon G. D.[4]

[1]*Hospital de Clinicas, Facultad de Ciencias Medicas, Universidad Nacional de Asuncion, Asuncion, Paraguay;* [2]*Instituto de Prevision Social. Hospital Central. Departamento de Neumologia y Alergia, Asuncion, Paraguay;* [3]*Facultad de Ciencias Exactas y Naturales. FACEN. UNA., Asuncion, Paraguay;* [4]*Instituto de Alergia e Inmunologia del Sur, Bahia Blanca, Argentina*

Background: Local aeroallergen surveys identify and establish patterns of prevalence for tree, grass, and weed species that enable the clinician to more effectively select allergens for skin testing and therapy.

Objectives: To determine peak pollination periods, atmospheric concentrations, and year-to-year variation for identified tree, weed, and grass aeroallergens.

Method: The sampling period is between January 2018 and December 2020. Atmospheric sampling for pollen aeroallergens was performed using a Hirst type suction sampler. The data are daily and are expressed in pollen grains/m3 of air.

Results: We could observe in the pollination curves, that the three categories are present throughout the calendar year. The period of highest concentration grain/m3 for trees starts at the beginning of July and ends in mid-November, although a second peak is found from mid-February to the end of March. The grasses are present mainly from the end of September to the end of February. Finally, weeds show the highest concentration between the end of September and the middle of July. The most important peaks were observed on September-october for the trees. In the case of grasses, it was recorded on February. Finally, the weeds presented their highest pollination peak on January- February. Observing the pollen curves, we can say that there is an overlap between the grasses, while the trees begin to pollinate since the beginning of July-August, having the highest prevalence in the city's atmosphere in these time. It is important to note that during the month of February there was a high concentration of pollen from the three categories in the air of Asunción.

Predominant pollen types include Cecropia, Poaceae, Moráceas, Cyperaceae, Urticaceae, Asterácea, Myrtaceae

Tree pollen accounts for 10-16%, weeds 76-73%, and grasses 18-9%% of total annual pollen yield. Variation in overall pollen production is evident from year to year. High production years for some species are low for others..

Conclusion: Asuncion-Paraguay and metropolitan area is host to a variety of tree, weed, and grass species that produce important

amounts of pollen. Further investigation into year-to-year variation with respect to inherent cycling and meteorological influences is warranted.

1322 | The role of pathogenic Th2 cells in the eosinophilic esophagitis

Lozano-Ojalvo D.; Chen X.; Dunkin D.; Berin C.
Department of Pediatrics. Icahn School of Medicine at Mount Sinai, New York, United States

Background: Eosinophilic esophagitis (EoE) is a non-IgE-mediated allergy triggered by foods characterized by allergic inflammation of the esophagus, eosinophil infiltration, and dysphagia. Although EoE is dominated by allergic type 2 cytokines, the phenotype of the cells producing these cytokines and their specificity is poorly understood. Our hypothesis is that tissue resident CD4+ Th2 cells are likely central to the pathophysiology of EoE and they may underly the local restriction of this allergic disease, that only affects the esophagus.
Method: Spectral flow cytometry was applied to investigate the frequency and phenotype of the main immune cell types in esophageal biopsies obtained from children with active or resolved EoE, and non-EoE controls (n = 10 per group). Furthermore, functional properties and cytokine expression patterns of T cells were studied upon tissue stimulation.
Results: EoE patients showed an increased infiltration of CD4+ T cells compared to resolved EoE ($p < 0.05$) and non-EoE control children ($p < 0.0001$). They were mainly characterized as Th2 cells and categorized in two major subsets: CCR3+ and CRTH2+CCR8+ Th2 cells. Functional characterization of CRTH2+ Th2 cells in EoE patients revealed a significantly increased expression of IL-2, IL-4, IL-10, and IL-13 that was suppressed upon exclusion of the main food allergens from the diet. Finally, tissue resident CRTH2+ Th2 cells found in active EoE patients were characterized by an increased expression of receptors for two major Th2-related cytokine released by epithelial cells, IL-33 and TSLP.
Conclusion: We have identified a unique subset of Th2 cells (CRTH2+) with a marked pathogenic polyfunctional profile that may be responsible for the development and maintenance of the EoE.

1158 | Eosinophilic esophagitis: Alternative personalized therapy according to phenotype

Bartha I.[1]; Belver M.[1]; Casabona-Francés S.[2]; Fernández-Pacheco J.[2]; Vega F.[1]; Argiz L.[1]; Santander C.[2]; Blanco C.[1]
[1]*Allergy Department. Hospital Universitario de La Princesa and Instituto Princesa (IP), Madrid, Spain;* [2]*Gastroenterology Department. Hospital Universitario de La Princesa and Instituto Princesa (IP), Madrid, Spain*

Background: Eosinophilic esophagitis (EEo) is a chronic inflammatory disease with an immunoallergic basis. The prevalence and diagnosis of EEo has increased exponentially in recent years. In the literature the successful rates of the 2-4-6 food elimination diets (2FED,4FEDor 6FED)are approximately 40%,50% and75%,respectively.
Objetives: The objective of this study is to describe and characterize the allergenic profiles of patients with EEo,to study their phenotypes and try to avoid excessively exclusive diets that can deteriorate their quality of life.
Method: Retrospective study in which the allergological profile of patients diagnosed with EEo and suspected allergy included between 2014-2021 in the multidisciplinary protocol of Allergy and Gastroenterology Departments was analysed. Patients were offered three alternative treatments:high-dose PPIs (proton pump inhibitors),2-4-6FED or swallowed corticosteroids for 8 weeks. Non-responders were offered the other alternative treatment. Results are expressed as number and percentages. Comparisons were done with chi squared and Fisher's exact tests. Statistical significance was set at 95% level ($p < 0.05$).
Results: A total of 126 patients were enrolled: 120had allergic comorbidities (Table1).
Figure1 shows the alternative treatment associated with allergological profile in patients with clinical remission.

- 59 patients underwent a food elimination diet: 24responded to a 2FED,1 responded to a 4FED and 3responded to a 6FED. Of these 28responders: 8patients were sensitized to LTP,5 to profilin and 4 to both.
- 101 patients who tried PPI therapy: 33responded and of those 9were sensitized to LTP, 11 to profilin and 6 to both.
- 55 patients underwent swallowed topical steroids: 40responded, and 13were sensitized to LTP, 10 to profilin and 4 to both.

Analysing the sensitization profile of the patients with remission compared to the rest, statistically significant difference was detected with a higher sensitization rate to profilin in the 2FED subgroup as compared with the rest (p = 0,024).
Conclusion: In our patients, the response to 2FED has been similar to the results reported in other series, although with 4-6FED it has been clearly lower.
Patients sensitized to panallergens could conform a different phenotype, in which the elimination diet could be a less effective strategy than the pharmacological one. This could be related to the difficulty of carrying out a panallergens elimination diet.

TABLE 1: Clinical, allergological profile and alternative treatment of patients enrolled in the study (n = 126)

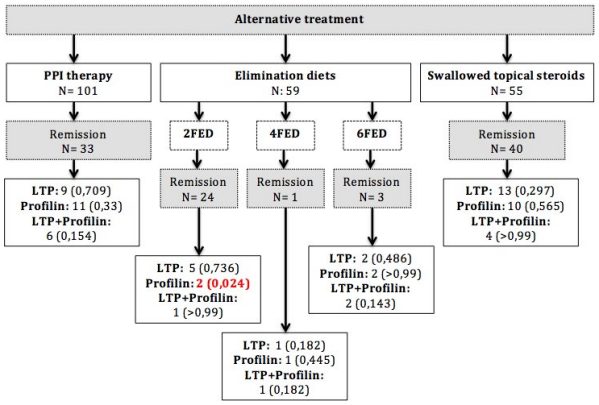
Variable	Mean	SD
Age (years)	31.5	12.8

Variable	N	%
Sex (M)	98	77.8
Allergic Comorbidities	120	95.2
Rhinoconjunctivitis	102	81

Variable	N	%
Asthma	48	38.1
Atopic Dermatitis	24	19
Food allergy	79	62.7
Allergy study		
Aeroallergens	107	84.9
LTP	32	25.4
Profilin	30	23.8
LTP+Profilin	13	10.3
Alternative treatment		
PPI therapy	101	80.2
Remission	33	32.7
Elimination diet	59	46.8
2FED	57	45.2
Remission	24	42.1
4FED	12	9.5
Remission	1	8.3
6FED	9	7.1
Remission	3	33.3
Swallowed topical steroids	55	43.7
Remission	40	72.7

* SD: standard deviation, PPI therapy: proton pump inhibitors; 2FED: two food elimination diet, 4FED: four food elimination diet; 6FED: six food elimination diet.

Figure 1: Alternative treatment associated with allergological profile in patients with clinical remission (N= 126).



1117 | Ex vivo food antigen stimulation of esophageal biopsies from adults with eosinophilic esophagitis: A potential guide for elimination diets?

Kleuskens M. T.[1]; Haasnoot M.L.[2]; Diks M. A.[1]; Akkerdaas J. H.[3]; Van Ree R.[3]; Van Ampting M. T.[4]; Garssen J.[1,4]; Bredenoord A. J.[2]; Redegeld F. A.[1]; Van Esch B. C.[1,4]

[1]*Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands;* [2]*Department of Gastroenterology & Hepatology, Amsterdam UMC, location AMC, Amsterdam, The Netherlands;* [3]*Department of Experimental Immunology, Amsterdam UMC, location AMC, Amsterdam, The Netherlands;* [4]*Danone Nutricia Research, Immunology Platform, Utrecht, The Netherlands*

Background: Food allergens are presumed to induce a local type 2 immune response in eosinophilic esophagitis (EoE). However, there are major gaps in knowledge on immune mechanisms that drive the persistence of EoE. Dietary elimination can be an effective and drug-free solution to induce clinical and histological remission in EoE patients, but skin prick tests and serum allergen-specific IgE measurements do not reliably identify food components for elimination from the diets. We hypothesize that challenge of esophageal tissue is needed for a better prediction of the offending food. Therefore, we investigated cytokine profiles of *ex vivo* food antigen-challenged esophageal biopsies to study the food-induced immune response and its potential to better identify culprit foods.

Method: Twelve EoE patients with active disease and six controls (non-EoE) underwent upper endoscopy. Four biopsies were collected from the proximal esophagus into culture medium, divided in two and subsequently stimulated with one of 6 food protein extracts or saline for baseline measurements. Extracts from three empiric foods (apple, cow's milk and wheat) and three foods based on patient's clinical history were included. Histamine concentrations were measured in 1-h culture supernatants, and an inflammatory profile of 10 different cytokines and IgE were measured in 24-h culture supernatants. Foods were divided into two groups based on patient's clinical history: EoE-Pos (food may trigger symptoms) and EoE-Neg (food may not trigger symptoms).

Results: Histamine levels in 1-h supernatants were below the detection limit. Baseline production of IgE, IL-5, IL-6, IL-8, IL-13 and MCP-1 was significantly higher in 24-h supernatants from EoE biopsy cultures compared with non-EoE. Interestingly, IL-5 and IL-9 levels were higher in the EoE-Pos group compared with baseline production as well as the EoE-Neg and non-EoE groups. Out of the 72 *ex vivo* food antigen challenges (six per patient), 28 induced a marked increase in IL-5 and/or IL-9 production, of which 21 (75%) corresponded with patient's clinical history.

Conclusion: *Ex vivo* stimulation of esophageal biopsies with food antigens may have the potential to guide elimination diets. Our study suggests that food-induced local production of IL-5 and IL-9 may distinguish EoE-Pos from EoE-Neg and non-EoE.

1173 | Effects of local allergen provocation on esophageal motility in adult patients with eosinophilic esophagitis

Haasnoot M. L.[1]; Kleuskens M. T.A.[2]; Terreehorst I.[3]; Akkerdaas J. H.[4]; Van Ree R.[4]; Redegeld F. A.M.[2]; Van Esch E. C.A.M.[2]; Bredenoord A. J.[1]

[1]Department of Gastroenterology and Hepatology, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands; [2]Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands; [3]Department of Othorhinolaryngology, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands; [4]Department of Experimental Immunology, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands

Background: Acutely occurring esophageal symptoms such as narrowing, burning, choking, and pressure sensation appearing within 5 minutes of ingesting specific foods have been described in patients with eosinophilic esophagitis (EoE). The underlying mechanisms for these symptoms are unclear, but food-induced esophageal spasm has been suggested. In order to further explore this phenomenon, we investigated the effects of swallowed allergen provocation on esophageal motility.

Method: Seven EoE patients underwent High Resolution Manometry (HRM) measurements before and after drinking solutions of allergenic foods that induced a visible response after intramucosal injection during endoscopy in a previous study. In total 6 allergenic foods were tested during endoscopy. The last solution (or in case of no response during endoscopy the only solution) consisted of a mixture of the foods that did not induce a response when injected intramucosally. Esophageal motility was classified according to the Chicago Classification version 3. Immediately and 10 minutes after drinking the solution, esophageal motility was measured during five 5-ml water swallows. The contractile vigor was measured by the distal contractile integral (DCI). The integrated relaxation pressure (IRP) a measure of lower esophageal sphincter relaxation and the Distal Latency (DL) as a measure of spasticity were also measured. The proportion of peristaltic, absent and spastic contractions after drinking the solution were investigated. Also, an overall improvement or worsening of the motility was determined.

Results: At baseline, 5 patients had normal motility and 2 patients had ineffective esophageal motility. In Table 1 the changes in DCI after the different solutions are presented for each patient separately. Tomato, wheat, apple, mango and milk induced significant changes in contractile vigor after 10 minutes. No spastic contractions and no significant changes were observed in the IRP (8.8 vs. 7.8, p =0.391) and DL (6.2 vs. 6.4, p =0.603) after 10 minutes. The percentages of peristaltic swallows were 92.9% at baseline, 94.3% immediately after the first mixture and 100.0 % 10 minutes after the first mixture.

Conclusion: Our results suggests that local allergen exposure influences esophageal motility in EoE but not to a degree it can explain the acute food-induced symptoms observed in EoE on its own.

TABLE 1 The contractile vigor before and after swallowed allergen provocation

ID	Motility	DCI	Solution 1	DCI, mean *Direct*	DCI, mean *10 min*	Solution 2	DCI, mean *Direct*	DCI, mean *10 min*	Solution 3	DCI, mean *Direct*	DCI, mean *10 min*	Solution 4	DCI, mean *Direct*	DCI, mean *10 min*
1	Normal	2303.2	Tomato	2146.1	**2731.7**	Peanut	2776.0	2889.2	Mixture*	1984.9	3230.2	-	-	-
2	Normal	1158.8	Mixture*	1014.9	1703.1	-	-	-	-	-	-	-	-	-
3	Ineffective	384.6	Wheat	431.2	**997.9**	Apple	513.7	**1009.5**	Mixture*	191.9	937.3	-	-	-
4	Normal	1022.3	Mixture*	967.9	**2090.3**	-	-	-	-	-	-	-	-	-
5	Normal	3198.7	Beer	3202.9	3753.6	Peanut	3842.7	3479.4	Wheat	3426.5	2996.7	Mixture*	3228.4	**5656.2**
6	Ineffective	392.1	Mango	1062.8	**1315.6**	Milk	**1097.1**	**1974.7**	Mixture*	**1530.7**	**2170.8**	-	-	-
7	Normal	794.6	Apple	922.8	1121.0	Mixture*	1078.5	1164.0	-	-	-	-	-	-

* Mixture consisted of foods that did not induce a visible response after intramucosal injection during endoscopy.

967 | Gastrointestinal eosinophilia and mepolizumab

Delgado González A.; Reaño Martos M.M.; Rodríguez Cabreros M.I.; Martin Voso M.G.; Carabel Lahera M.; Iglesias Cadarso A.
Hospital Universitario Puerta de Hierro, Madrid, Spain

Case Report

Eosinophilic esophagitis is a chronic immune system esophagic disease. It affects to children and young adult. An early clinic and histological diagnosis is needed, because of risk of esophageal stricture.

Treatment includes proton pump inhibitors, empirical or targeted avoidance diet depending on allergy tests to nuts, fish, legumes, egg, milk, or cereals and topical steroids.

In non-responders patients or torpid evolution, anti-Il-5 drugs are being used as a compassionate treatment.

Method:

1) 54-year-old man. Medical records: rhino-conjunctivitis and allergic asthma, eosinophilic colitis, and idiopathic arthritis. He presented abdominal spasmodic pain and pasty bowels.

Asthma was controlled with omalizumab, salmeterol/fluticasone and ipratropium bromide.

Colitis was unsuccessfully treated with infliximab, methotrexate and adalimumab. It responded to oral corticosteroids. Omeprazole, cinitrapide and targeted avoidance diet to milk and gluten were added.

Analitic: Eosinophils 390 u/microL. IgE: 402 Ku/L. ImmunoCAP® and prick test were negative for all 6 food groups.

Normal gastroscopy. Colonoscopy: mild chronic colitis with increased of eosinophils.

Chest CT: suggestive asthma.

Obstructive spirometry: IT 67. PBD positive.

He started treatment with mepolizumab noticing improvement of asthma and reduction of eosinophlic blood count, but no digestive improvement.

2) 53-year-old woman history of eosinophilic esophagitis since 2005 with impaction and dysphagia clinic, allergic asthma and chronic rhinosinusitis.

Treatment: topical fluticasone, formoterol/budesonide, pollen immunotherapy, loratadine and esomeprazole, in addition to the avoidance diet (all 6 food groups).

The patient continues with repetition alimentary impaction and successive endoscopies, melaena after 2 biopsy intakes, so Mepolizumab was added. After 6 months of lack of improvement the treatment was suspended.

Analitic: Eosinophils 490 u/microL. IgE: 75.8 KU/L. ImmunoCAP®: positive to arizonic and olive pollen. ImmunoCAP® and prick-test negative for all 6 food.

Gastroscopy: trachealized mucosa in all esophagus. 100 eosinophils h.m.f

Conclusion: We present 2 clinical cases of gastrointestinal eosinophilia with poor evolution in which mepolizumab has been used as compassionate treatment.

Given the complexity of the cases, we do not extrapolate mepolizumab failure to other patients.

Further studies are needed to obtain more evidence of the use of mepolizumab in this disease.

1326 | Dupilumab efficacy in a patient with eosinophilic gastroenteritis

Spada A.; Scarpa R.; Agostini C.
University of Padua, Treviso, Italy

Case report: we presented a 38 years old man diagnosed with steroid dependent eosinophilic gastroenteritis, chronic rhinosinusitis and eosinophilic non allergic asthma, successfully treated with Dupilumab. Clinical manifestations started in 2016 with abdominal pain and vomit. Endoscopy demonstrated antral gastropathy with pyloric sub-stenosis, duodenopathy with secondary bowel diameter reduction and gastric stagnation and aphthous erosions and oedema of the ileocaecal valve. Histology was significant for gastric lymphocytic infiltration with marked eosinophilia (Eos/HPF > 24) and colonic follicular eosinophilic inflammation. Following the exclusion of other known causes of tissue eosinophilia, patient was treated with metronidazole, proton pump inhibitors and oral steroid with clinical and biohumoral improvement. It was reported peripheral eosinophilia and it was normalized by steroid-therapy. In September 2018 the patient experienced a clinical exacerbation of gastrointestinal symptoms , an entero-MRI showed abundant intra-abdominal liquid

layer with marked wall thickening of the gastric antrum and pylorus region, extending to the duodenum, and moderate circumferential bowel wall thickening. It was treated with prednisone 50 mg once a day, with subsequent slow steroid-tapering. In April 2019 an attempt to steroid withdrawal was done with immediate resumption of blood eosinophilia and gastrointestinal symptoms. Chronic therapy with oral prednisone was then continued until May 2020 (prednisone 7,5 mg once a day) when gastrointestinal symptoms reappeared. Due to disease steroid-dependence, worsening of gastrointestinal symptoms and their impact on the quality of life, Dupilumab was then initiated, at 300 mg once a week, for 9 months, resulting in a brilliant clinical, haematological and histological response. After 4 months from the introduction of Dupilumab the steroid withdrawal was done with The absence of exosinophilic infiltrate on gastric and colic control biopsies on February 2021 is noted.

Conclusions: Dupilumab could be considered a possible targeted therapy for this disease. In our patient it resolved gastrointestinal symptoms, the histologic features of disease and it is a relevant corticosteroid-sparing option.

1323 | Eosinophilic oesophagitis: A unique paediatric case presenting with phagophobia

O'Connor D.; Morris V.; Rodriguez Herrera A.

St. Luke's General Hospital Kilkenny, Kilkenny, Ireland

Eosinophilic oesophagitis (EoE) is a chronic immune mediated condition. The prevalence of EoE is 0.1%, however an increase in the number cases reported is largely due to raised clinical awareness. Though less common in paediatrics, all physicians should consider EoE in a patient with characteristic symptoms as it is a progressive disease with significant impact on growth and development. This case reports a 15 year-old boy with a three-week history of phagophobia with food impaction, reduced oral intake, and significant weight loss resulting from food and liquid refusal for fear of death. Further questioning revealed a 2 year history of progressive difficulty swallowing food and a 2 year absence from school. There was a history of eczema and seasonal allergic rhinitis but no associated food allergies. On examination he was underweight with a BMI of 17, and had an anxious disposition. Initial differential diagnoses included EoE, anxiety disorder, and eating disorder. Preliminary investigations showed elevated total serum IgE of 315kU/L. Upper GI endoscopy was performed and showed linear furrowing of the oesophagus, histological analysis of oesophageal biopsies confirmed EoE with an eosinophilic infiltrate of 20/hpf. The patient had an extensive work-up to determine the aetiology. Skin prick testing was negative for common culprit foods and positive for grass pollen. Initial management required NG feeding due to food refusal, treatment was then commenced with topical steroids and proton pump inhibitor. There was an improvement in symptoms with increased oral intake. Our patient had regular dietitian input and was monitored appropriately for refeeding syndrome. He was reviewed by child psychiatry and commenced on psychotropic medications for anxiety disorder. Inpatient management was required to monitor medication compliance and to ensure adequate weight gain, with an excellent improvement in clinical symptoms and return to normal oral diet. Our case report highlights that EoE can occur at any age, and that early diagnosis and prompt treatment is essential for optimum patient care. There should be a high index of suspicion of EoE based on characteristic symptoms. Our department benefitted from having joint paediatric gastroenterology and allergy care, with swift access to endoscopy. Furthermore, it is important to recognise that psychiatric conditions may coincide with a medical diagnosis, and this relies on careful history taking so as not to delay detection.

999 | Nephrolithiasis in food protein–induced proctocolitis

Islek A.[1]; Guler M. A.[2]

[1]*Çukurova University School of Medicine, Adana, Turkey;* [2]*Atatürk University School of Medicine, Erzurum, Turkey*

Background: Although the relationship between food protein–induced allergic proctocolitis (FPIAP) and nephrolithiasis is unknown, patients with malabsorption have a predisposition to nephrolithiasis. We aimed to investigate the frequency and prognosis of nephrolithiasis in infants with FPIAP.

Method: Data were collected retrospectively from patients under 2 years of age with FPIAP between January 2014 and March 2020. FPIAP was diagnosed with an elimination diet and challenge test. Food elimination was performed with a step-wise approach. Patients who underwent urine examination and renal or abdominal ultrasonography for restlessnes or any other complaints were included in the study. Descriptive characteristics and laboratory results of patients during follow-up were evaluated.

Results: Data were reviewed for 202 patients with the diagnosis of FPIAP between the specified dates. The 51 infants who underwent urine examination and renal ultrasonography included in the study. Overall, 21.5% (11/51) of the patients had nephrolithiasis (Table 1). Random urinary solute excretions were normal in patients with nephrolithiasis on admission. Nephrolithiasis persisted in 2 of 11 patients at the 6th and 12th months of follow-up. Hyperoxaluria was observed in urinalysis of these patients at 6th and 12th months. Patients with nephrolithiasis had longer multiple food elimination diet times than others. The mean body weight Z score was lower for the two patients whose nephrolithiasis persisted at the end of the 12 months than for the patients whose nephrolithiasis was resolved.

Conclusion: Nephrolithiasis is not uncommon in patients with FPIAP, possibly as a result of malabsorption. Infants who undergo long-term food elimination diet may need to be examined in terms of nephrolithiasis.

TABLE 1 Characteristics of patients with nephrolithiasis

	***n* = 11**
Age at diagnosis (months)	
Mean ± SD	6.05 ± 2.46

	n = 11
Median (range)	7.15 (5-24)
Elimination diet time to diagnosis (months)	3.25 ± 1.25 (1.20-4.25)
Gender (M/F)	7/4
Follow-up (months)	
Mean ± SD (range)	16.25 ± 6.50 (11.25-30.25)
Height Z score (Mean ± SD)	-0.42 ± 1.19
Weight Z score (Mean ± SD)	-0.56 ± 1.45
Food restrictions, *N* (%)	
Milk	0 (0.00)
Milk + egg	3 (27.27)
Multiple	6 (54.54)
AA based formula	2 (6.9)
Urine test	
Macroscopic/ Microscopic hematuria	0/3
Urinary solute/creatinine ratio on admission (mg/mg) mean (median)	
Calcium	0.61 ± 0.33 (0.19-0.78)
Oxalate	0.11 ± 0.07 (0.09-0.20)
Uric acid	1.10 ± 0.45 (0.90-1.96)
Citrate	0.92 ± 0.34 (0.61-1.10)

1037 | The involvement of hydroxyproline residues in IgE crosslinking by ara h 2 produced in tobacco leaves

Üzülmez Ö.[1]; Kalic T.[1,2]; Mayr V.[1]; Lengger N.[1]; Tscheppe A.[1,3]; Radauer C.[1]; Hafner C.[3,4]; Hemmer W.[5]; Breiteneder H.[1]
[1]*Medical University of Vienna, Vienna, Austria;* [2]*Karl Landsteiner University of Health Sciences, St. Pölten, Austria;* [3]*University Hospital St. Pölten, St. Pölten, Austria;* [4]*Karl Landsteiner Institute for Dermatological Research, St. Pölten, Austria;* [5]*FAZ - Floridsdorf Allergy Center, Vienna, Austria*

Background: Peanut allergy is a serious immune disorder which develops early in life and is rarely outgrown. It is an IgE-mediated disease responsible for life-threatening symptoms and reduces the quality of life in up to 3% of the Western world. The major peanut allergen Ara h 2, a 2S albumin seed storage protein, harbours post-translational modifications (PTMs) such as four disulfide bridges and several hydroxyprolines. Until now, recombinant Ara h 2 expressions have only been performed in unicellular hosts which are unable to provide sophisticated PTM machinery such as for proline hydroxylation. The quality of diagnostic test results relies on the bioequivalence of recombinant allergens to their natural counterparts.

Method: We expressed Ara h 2 in the leaves of *Nicotiana benthamiana* plants using the plant virus-based transient expression system. Rice apoplast signalling peptide and a C-terminal endoplasmic reticulum (ER) retention tag were investigated for apoplast- or ER-targeted expression, respectively. Plant-made rAra h 2 was analyzed for obtained PTMs using mass spectrometry. We compared the *N. benthamiana*-produced Ara h 2 with the natural protein and with the recombinant expressed in *E. coli* SHuffle T7 Express lysY cells. Immunological characterization of the three proteins was performed by IgE-binding and crosslinking experiments using sera from 20 peanut allergic patients.

Results: Transient expression in *N. benthamiana* leaves yielded 27 mg rAra h 2 per kg fresh biomass. Mass spectrometry results confirmed hydroxylated proline residues at the naturally occurring sites within the immunodominant IgE epitope. We observed different degrees of hydroxylation depending on the subsecullular targeting. We also discovered a novel proline hydroxylation motif in plants.

Plant-made rAra h 2 was detected in immunoblots by IgE from allergic patient's serum as well as by an anti-Ara h 2 monoclonal antibody. Median IgE binding by the natural Ara h 2 was significantly higher than both of the recombinant proteins from *N. benthamiana* and *E. coli*. On the other hand, plant-made rAra h 2 was significantly superior to the one from *E. coli* in IgE crosslinking experiments.

Conclusion: We successfully produced the major peanut allergen Ara h 2 in *N. benthamiana* leaves by employing a plant-virus based transient expression system. The plant-made rAra h 2 performed better in IgE crosslinking assays than the commonly used recombinant from *E. coli*, demonstrating the importance of allergen PTMs for its use in diagnosis.

1100 | Factors associated with lower reaction eliciting dose in children with peanut allergy

Pitkin S.[1]; Lozinsky A. C.[1]; Axelrad C.[1]; Ashley S.[1]; Lloyd M.[1]; Tey D.[2]; Robinson M.[2]; Su E.L.[2]; Orsini F.[1]; Loke P.[1,3]; Tang M.[1,2,3]
[1]*Murdoch Children's Research Institute, Parkville, Australia;* [2]*The Royal Children's Hospital, Department of Allergy and Immunology, Parkville, Australia;* [3]*The University of Melbourne, Melbourne, Australia*

Background: Eliciting dose (ED) under 300mg peanut protein is associated with greater likelihood of accidental reaction to peanut in packaged foods. Currently ED is established by food challenge. Predictors of reaction eliciting dose (ED) may avoid the need for challenge.

Method: As part of the screening process for eligibility to the PPOIT-003 study, children with a peanut allergy completed a double-blind placebo-controlled food challenge (DBPCFC; cumulative 4950mg peanut protein) to confirm their allergic status. Participants were recruited from 3 sites (Adelaide, Melbourne and Perth). Baseline demographics, allergic co-morbidities, peanut sIgE, peanut skin prick test (SPT) were recorded. Associations between ED and other baseline variables were investigated by correlation and multinomial logistic regression analysis.

Results: 235 children completed DBPCFC; 213 reacted to peanut but not placebo and are included in this study (13 did not react, 9

were inconclusive). The median cumulative ED was 320mg (IQR 160mg-1250mg).

There was a significant association between baseline peanut sIgE and ED; a higher baseline peanut sIgE was associated with lower ED (Spearman correlation coefficient: -0.413, p <0.001). Peanut sIgE was the only predictor of ED in the multinomial logistic regression.

There were no significant associations between ED and sex, age, asthma or eczema

Conclusion: Reaction-eliciting dose varied widely in this cohort of peanut allergic children. The majority (74%) reacted to <640mg dose of peanut protein and 71% reacted to >340mg cumulative peanut protein during the DBPCFC. Peanut sIgE was the only variable that predicted a lower eliciting dose in the DBPCFC.

1108 | Is exposure to environmental greenness associated with the risk of food allergy in australian infants?

Peters R. L.[1]; Mavoa S.[2]; Dharmage S. C.[2]; Lowe A.[2]; Wake M.[1]; Ponsonby A.[3]; Tang M. L.K.[1]; Koplin J. J.[1]

[1]Murdoch Children's Research Institute, Parkville, Australia; [2]The University of Melbourne, Parkville, Australia; [3]Florey Institute of Neuroscience and Mental Health, Parkville, Australia

Background: Exposure to environmental greenness in childhood has shown mixed associations with the development of eczema, asthma and allergic rhinitis. The relationship with food allergy is unknown, therefore we investigated the association between exposure to environmental greenness and the development of food allergies in infants.

Method: The HealthNuts study recruited 5276 12-month-old infants in Melbourne, Australia, who underwent skin prick testing to egg or peanut; infants with a detectable wheal underwent food challenges to determine food allergy status. Environmental greenness was estimated using normalised difference vegetation index (NDVI) for five distances around the infant's home address: at the home, 100m, 500m, 800m and 1600m radial distances. Environmental greenness was categorized into 3 quantiles and mixed effects logistic regression models quantified the association between the tertiles of greenness, compared to the lowest tertile, and the risk of food allergy, adjusting for confounding (socioeconomic status (SES), parent's country of birth, season of birth) and accounting for clustering at the neighborhood level.

Results: NDVI data was available for n = 5054. For most distances, medium and high greenness was associated with an increased risk of peanut allergy (e.g. 100m tertile 2 aOR 1.79 95% CI 1.14-2.81, tertile 3 aOR 1.84 95% CI 1.16-2.93). For egg allergy, the effect sizes were smaller (100m tertile 2 aOR 1.47 95% CI 1.13-1.92, tertile 3 aOR 1.39 95% CI 1.04-1.87); Results were similar following additional adjustment for family history of allergy and pet dog ownership. SES modified the association between greenness and peanut allergy, but not egg allergy, with associations apparent in the low SES group but not in the high SES group (p for interaction 0.04) There was no evidence of effect modification by family history of allergy, pet dogs, season of birth or eczema.

Conclusion: Increased exposure to environmental greenness in the first year of life was associated with an increased risk of food allergy. This may be explained by cross-reactivity between some pollen and food allergens and suggests that cutaneous or respiratory exposure to environmental allergens in early life may increase the risk of allergy. Alternatively, these associations could reflect residual confounding or spurious associations, therefore further research is needed to confirm these findings and understand potential mechanisms.

1254 | Patient and caregiver satisfaction with novel en masse oral food challenge performance

Walsh N.[1]; Sanneerappa P. B.[1]; Lewis S.[1]; Alsaleemi A.[1]; Coghlan D.[1,2]; O Carroll C.[1]; Trujillo J.[3]; Fitzsimons J.[1]; Hourihane J. O.[1,4]; Byrne A.[1,2]

[1]Children's Health Ireland, Dublin, Ireland; [2]Trinity College, Dublin, Ireland; [3]Cork University Hospital, Cork, Ireland; [4]Royal College of Surgeons in Ireland, Dublin, Ireland

Background: Oral food challenge (OFC) is the gold standard for the diagnosis of food allergy. OFC are traditionally performed in hospital, as a day ward procedure, with a high medical caregiver to patient ratio. This is likely to enhance communication and patient satisfaction. Despite the high incidence of adverse reactions, families generally report a positive experience . In Sep-Oct 2020 a novel, high throughput, OFC initiative was carried out by a cross-hospital, multidisciplinary Irish paediatric allergy team. Up to 25 OFCs were performed each day at an offsite, COVID-19 stepdown facility. The unique model was designed in response to the impact of the pandemic, on provision of ambulatory allergy services. It was essential to evaluate the patient experience of this unique, alternative OFC model, compounded by COVID related distancing.

Method: An anonymised survey was conducted of randomised cross-section of patients attending. The survey was completed by the primary caregiver of the child attending for the OFC. 178 survey responses were collected from a total of 474 families and included for analysis. The survey was designed to assess patient satisfaction across a number of parameters.

Results: 81% of respondents were highly satisfied with ease of use of a non-hospital facility. 81% reported that the site was "child friendly". Patient experience was scored as "excellent" 82.9% of the time with a further 12.35% reporting it as above average. Communication was effective with 89% of carers reporting good understanding of the results of the OFC. 94.7% stated that their questions were answered by the Allergy Team present.

Conclusion: Our results are remarkable for enhanced patient satisfaction despite a reduced medical caregiver to patient ratio. The patient's overall satisfaction was rated overwhelmingly as "excellent" despite almost 30% of patients experiencing allergic reactions.

The pandemic has forced health services to seek new ways of doing things. This data reassures, that OFC models can be changed without sacrificing patient experience.

1269 | The epithelial barrier damaging effects of professional dishwasher rinse aid on caco-2 gastrointestinal epithelial cells

Ogulur I.[1,2]; Ruckert B.[1]; Ozen A.[2]; Akdis C. A.[1]
[1]*Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland;* [2]*Division of Pediatric Allergy and Immunology, Marmara University School of Medicine, Istanbul, Turkey*

Background: Environmental exposures such as detergents can alter the structure of the epithelial barrier and local microbiome and influence the development of diseases. Given the recent pandemics of food allergy and common use of dishwasher detergents, we investigated the effects of professional dishwasher detergents, including sodium/potassium metasilicate, potassium hydroxide, potassium carbonite and sodium hypochlorite, and rinse aid, including alkylalkoholalkoxylat, citric acid and sodium cumenesulfonate, on cytotoxicity and barrier function of gastrointestinal epithelial cells.

Method: Cytotoxicity was evaluated by fluoremetric lactate-dehydrogenase release. Enterocytic liquid-liquid interfaces were established by culturing Caco-2 cells on permeable supports. Detergent and rinse aid were added to the apical compartment, and then the transepithelial-electrical-resistance (TER) was measured. Paracellular FITC-Dextran-flux measurements were performed by fluorometry. Immunofluorescence staining of occludin, ZO-1 and claudin-1 and quantitative real-time PCR experiments were performed to measure tight-junction (TJ) integrity.

Results: Rinse aid showed dose-dependent cytotoxicity on Caco-2 cells between the concentrations of 1:2500 and1:40000 v/v dilutions. In contrast, there was no toxicity of detergent at the concentrations of up to 1:250 v/v dilution. We did not observe any disruption of the monolayer integrity, as indicated through maintenance of TER with detergent at all concentrations. In contrast, rinse aid induced a dramatical decrease in TER at dilutions of 1:2500, 1:5000 and 1:10000 after 72 h. A disrupted epithelial barrier function was found with increased paracellular-flux in Caco-2 cells exposed to rinse aid at the same dilutions. Irregular and stratified staining of occludin, ZO-1 and claudin-1 were found in Caco-2 cells exposed to rinse aid at concentrations of 1:2500-1:20000. The preliminary results showed that rinse aid downregulated the expressions of claudin-1, claudin-7, ZO-1 and ZO-2 at the concentrations between 1:2500 and 1:20000 dilutions. However, detergent alone did not change the expressions of these proteins.

Conclusion: Our data demonstrated that rinse aid which is commonly used in professional dishwashers shows high cytotoxicity and directly impairs barrier integrity of gut epithelial cells.

1057 | Microarray analysis of tree nut-allergic individuals reveals regional variation in cross-reactivity

Gipson S. A.Y.[1]; Nesbit J. B.[1]; Cheng H.[1]; Teuber S. S.[2]; Dreskin S. C.[3]; Mustafa S.S.[4,5]; Appel M. Y.[6]; Elizur A.[6,7]; Goldberg M. R.[6,7]; Hurlburt B. K.[1]; Maleki S. J.[1]
[1]*United States Dept. of Agriculture-Agricultural Research Service-Southern Regional Research Center (USDA-ARS-SRRC), New Orleans, United States;* [2]*Division of Rheumatology, Allergy and Clinical Immunology, University of California, Davis, Davis, United States;* [3]*Division of Allergy and Clinical Immunology, Departments of Medicine and Immunology, University of Colorado Denver, Aurora, United States;* [4]*Rochester Regional Health, Rochester, United States;* [5]*University of Rochester School of Medicine and Dentistry, Rochester, United States;* [6]*Institute of Allergy, Immunology, and Paediatric Pulmonology, Yitzhak Shamir Medical Centre, Beer Yaakov, Israel;* [7]*Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel*

Background: Allergy to tree nuts such as walnut, pecan, hazelnut, and cashew affects as much as 1.2% of U.S. adults. Due to high sequence homology and evolutionary relatedness among tree nuts, tree nut (TN) allergic individuals often exhibit clinically relevant cross-reactivity with multiple tree nuts. Yet, the specific patterns of immunoglobulin E (IgE) binding which underlies cross-reactivity may exhibit regional variation due to differences in genetics, environment, and dietary preferences. Understanding this regional variation in cross-reactivity will be key in developing improved in vitro allergy diagnostics and therapeutics.

Method: We collected serum from Israeli (IL, n = 45) and American (US, n = 22) patients with known allergy to walnut, pecan, hazelnut, and/or cashew. We measured IgE binding to walnut allergen peptides and previously known epitopes using microarrays with synthetic overlapping 15 mer peptides. Epitope mapping was used to assess regional variation in IgE epitopes and to empirically assess cross-reactivity predicted by Structural Database of Allergenic Proteins (SDAP).

Results: Comparison of epitopes predicted to be cross-reactive among individuals with different TN allergies showed that IL and US patients recognize many of the same epitopes found in allergens Jug r 1, 2, and 4. Yet, we observed regional variation in a series of Jug r 4 IgE epitopes, including a known epitope. SDAP-predicted cross-reactivity and epitope mapping of peptides in this region suggests that this known Jug r 4 epitope may cross react with birch pollen Bet v 1, indicating that Bet v 1 allergy may influence regional variation in IgE epitopes. The identified walnut epitopes are predicted to cross-react with proteins found in different nuts and protein families.

Conclusion: Several unique and shared IgE epitopes were identified in walnut allergens among TN allergic IL and US individuals. The number of peptides recognized in both geographically distant regions indicates that there are cross-reactive peptides which remain consistent despite regional variation. Conversely, the region-specific peptides may reflect unique patterns or prevalence of allergy to TNs or pollen. Appreciating regional variation in IgE epitopes and

cross-reactivity may allow for more accurate characterization of tree nut allergy, which would be valuable for the safe introduction of tree nuts into a patient's diet, improving diagnostics and for more targeted oral immunotherapy.

1061 | Food protein-induced enterocolitis syndrome: 5 years study of a pediatric unit

Dias L. P.; Gomes M.M.; Pais I. P.; Pedrosa C.; Ribeiro A.; Costa C.
Centro Hospitalar Vila Nova Gaia Espinho, Vila Nova Gaia, Portugal

Background: Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated food hypersensitivity that can cause severe acute gastrointestinal and systemic symptoms. It is usually caused by cow's milk protein and, more rarely, by other food proteins.
The purpose of this study was to identify the food triggers and describe clinical features and natural history of acute FPIES.
Method: This is a retrospective observational review from January 1st, 2016 to July 31st, 2020 of the medical records of pediatric patients diagnosed with FPIES according to the AAAAI International Consensus Guidelines for Diagnosis and Management of FPIES (2017).
Results: A total of 14 patients (71.5% boys) fulfilled inclusion criteria. The median age at first FPIES episode was 7 months (min-max 2-31 months), with median age at diagnosis of 8 months (5-36 months), after 1 to 4 episodes (median 3) until diagnosis. The average time to onset of symptoms after the ingestion of the trigger food was 102 minutes (SD: ±0.9 minutes). Clinical symptoms included repetitive and profuse vomiting (100%), pallor (85.7%), lethargy (85.7%) and diarrhea (57.1%). Two patients presented with sepsis-like episodes. The most common food trigger was fish (n = 7), followed by: cow's milk (n = 5), egg (n = 3), rice (n = 3) and potato (n = 1). 64.3% (n = 9) of the patients reacted to only one food trigger, whereas 35.7% (n = 5) reacted to two different kind of triggers. 28.6% (n = 4) of the children had atopic dermatitis and 50.0% (n = 7) had a positive family history of atopy. All patients (100%) had a negative specific IgE to the food trigger. 78.6% (n = 11) were admitted to the emergency room. The majority of the children (64.3%) were diagnosed by clinical criteria, while 35.7% (n = 5) confirmed diagnosis was based on a positive oral food challenge. Tolerance was achieved in 21.4% of the children (n = 3), with an average of 29 months (min-max 15-40 months) after the first FPIES episode.
Conclusion: FPIES diagnosis is difficult and frequently delayed due to the wide spectrum of clinical presentations and to the absence of an available laboratory test. In our series fish was the most common food trigger, followed by cow's milk, the most common trigger in Europe. It may be related to being a coastal country. More epidemiological studies are necessary due to the significant regional variation.

1097 | Long-term outcomes of probiotic and peanut oral immunotherapy (the PPOIT-002 study)

Loke P.[1,2,3,4]; Hsiao K.[1,5,6]; Lozinsky A.[1]; Pitkin S.[1]; Axelrad C.[1]; Ashley S.[1,2]; Lloyd M.[1]; Tey D.[1,2]; Robinson M.[2]; Su E.[1,2]; Orsini F.[1]; Tang M. L.[1,2,3]
[1]Murdoch Children's Research Institute, Parkville, Australia; [2]Royal Children's Hospital, Parkville, Australia; [3]University of Melbourne, Melbourne, Australia; [4]Monash Children's Hospital, Clayton, Australia; [5]Starship Children's Hospital, Auckland, New Zealand; [6]University of Auckland, Auckland, New Zealand

Background: Probiotic and peanut oral immunotherapy (PPOIT) induced long-term sustained unresponsiveness (SU) in a proof-of-concept Phase 2a randomized trial. This open-label study (PPOIT-002) aimed to confirm the tolerability and long-term effects of PPOIT in children with peanut allergy aged 1-12 years.
Method: 20 children aged 1-12 years with double-blind placebo-controlled food challenge (DBPCFC)-confirmed peanut allergy received 18 months of PPOIT. DBPCFC (cumulative 4950mg peanut protein) were performed at end-of-treatment, 8-weeks post-treatment and 3-years post-treatment to assess for desensitisation, SU and long-term SU, respectively. Immunologic measures, peanut skin prick test (SPT) and specific IgE (sIgE), were evaluated at screening, end-of-treatment and 3-years post-treatment. Continuous outcomes for peanut SPT and sIgE were compared between timepoints using paired t-tests and paired Wilcoxon signed rank test, respectively.
Results: Sixteen children (75%) completed study treatment. Intention-to-treat analysis showed desensitisation and 8-week SU rates of 75% (15/20) and 60% (12/20), respectively. 10 of the 12 children who achieved 8-week SU at the end-of-treatment consented to the 3-year long-term 8-week SU challenge, with 6 (60%) maintaining long-term SU. PPOIT was associated with decreased peanut SPT and sIgE levels, with significant reductions persisting at 3-years post-treatment (p =0.0022 and p =0.0012, respectively). 17 of 20 (85%) of children reported treatment-related adverse events (AE) (total 176 events). The majority of AEs (164; 93%) were mild. There were no serious AEs.
Conclusion: This open label study demonstrated that 18 months of PPOIT induced high rates of desensitisation and 8-week SU, with persistence of SU at 3-years post-treatment in the majority of initial responders. PPOIT led to long-lasting reduction in peanut sIgE, suggesting modulation of the underlying allergic response to peanut.

1209 | Monoclonal IgE antibodies reengineered as food allergy therapeutics

Croote D.; Sohail S.; Sanchez Rodriguez R.; Creeks P.; Wong J. J.W.; Boismenu R.
IgGenix, South San Francisco, United States

Background: Circulating B cells producing IgE antibodies are extremely rare, even in allergic individuals. This technical challenge has hindered our understanding of how monoclonal IgE antibodies recognize epitopes on allergens and mediate allergic disease in humans. Furthermore, these allergen-specific IgE antibodies, which often exhibit high levels of somatic hypermutation consistent with high-affinity binding interactions, may serve as an untapped resource for therapeutic and diagnostic development in the field of allergy.

Method: IgGenix leveraged its advanced discovery platform based on single-cell RNA-sequencing to identify high-affinity human monoclonal IgE antibodies specific to a diverse range of food and non-food allergens from large numbers of allergic individuals. Discovered IgE antibodies were reengineered as monoclonal IgG4 antibodies for the development of antibody-based therapeutics capable of blocking the interaction of endogenous IgE with allergen and therefore inhibiting the allergic cascade.

Results: Clonal analysis of paired heavy and light chain monoclonal IgE antibody sequences provided evidence for convergent evolution of Ara h 2-specific antibodies in peanut allergy. Broad screening of IgE antibody specificity revealed monoclonal antibody cross-reactivity that recapitulated clinical co-allergy among tree nut allergic individuals. IgE antibodies reengineered as IgG4 antibodies demonstrated potency in functional proof-of-concept assays involving blood samples derived from allergic individuals.

Conclusion: Single-cell RNA-sequencing is a promising approach for isolating and characterizing rare single B cells that produce IgE antibodies. These IgE antibodies provide novel insights into allergen binding and serve as a promising starting point for the development of therapeutics that avoid the long clinical response times and adverse events consistent with immunotherapy involving prolonged and repeated allergen exposure.

1248 | Accidental allergic reactions on vacation: is food allergy lost in translation?

Crealey M.[1,2]; Byrne A.[1,2,3]

[1]*Children's Health Ireland at Crumlin, Dublin, Ireland;* [2]*Trinity College Dublin, Dublin, Ireland;* [3]*Children's Health Ireland at Tallaght, Dublin, Ireland*

Background: Vacations are an important part of family life. However, they are a high-risk time for severe accidental allergic reactions (AARs) to food, particularly while travelling abroad. AARs are more likely to occur in unfamiliar situations. There is a scarcity of research concerning AARs to food while on vacation, particularly in children. Most research relates to reactions on airplanes. Our aim here is to characterise AARs while on vacation in food allergic children attending an allergy clinic.

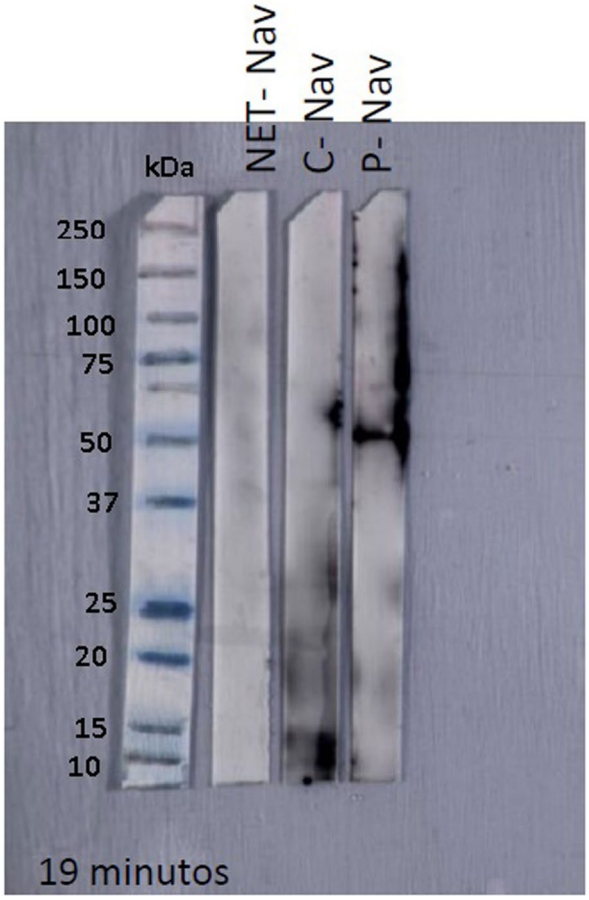
Method: A prospective observational study "ReAACt" (Recording Accidental Allergic Reactions in Children) was established, enrolling children aged 2 to 16 years with confirmed FA between November 2018 and May 2019. Participants were contacted at 3mth intervals for 1yr to prospectively report AARs to food. The coFAR grading system was used to grade allergic reactions as mild, moderate, or severe. The data pertaining to allergic reaction while on vacation is reported here.

Results: The clinical characteristics of the 531 children enrolled into ReAACt are displayed in Table 1. Follow up data was obtained on 498 participants. Overall, 403 (80.9%) participants went on holidays during the study period with 244 (60.5%) going abroad (235 on airplane, 9 on ferry). 307 (76%) stayed in hotels. Overall, 33 (15%) children had AARs giving an annualised AAR rate while on holiday as 8.2% (95% CI 5.7 to 11.3). The reactions were graded as mild (*n* = 14,42.2%), moderate (*n* = 11, 33.3%) and severe (*n* = 8, 24.2%). Adrenaline was administered in 2 of the severe reactions. In nearly half of reactions (*n* = 14, 43%), the implicated allergen was unidentified. When the allergens were known: nut *n* = 6; milk *n* = 5, Egg *n* = 3, Fish *n* = 2. Reactions occurred in restaurants (*n* = 11, 33.3%), hotels (*n* = 8, 24%), shop/ café (*n* = 7,21%), airplane (*n* = 3, 11%) and airport (*n* = 2, 6%). Of note no reactions occurred in self-catering accommodation. In almost half of reactions (*n* = 15, 45.5%), participants had asked about or checked ingredients.

Conclusion: It is reassuring to observe that families with allergic children are taking vacations. However, food allergic reactions, including life threatening ones are occurring in eateries. Results indicate that checking ingredients is not adequate protection, suggesting either high levels of cross contamination, a lack of awareness of food allergy or different labelling regulations abroad. Healthcare professionals should educate allergic families to strategies to minimise risks while on holidays.

Clinical characteristics of 531 children in ReAACt

Gender (*N*) %	
Male	355 (67%)
Female	176 (33%)
Median age at recruitment (years) (lower quartile, upper quartile) (years)	7 (4, 10)
2–4 years (*N*) %	138 (26%)
5–12 years (*N*) %	320 (60%)
13–16 years (*N*) %	73 (14%)
Number of food allergies	
1 food allergy	174 (33%)
≥2 food allergies	357 (67%)
Food allergens *N* (%)	
Milk	79 (15%)
Egg	187 (35%)
Peanut	307 (58%)



Clinical characteristics of 531 children in ReAACt	
Treenut	258 (48%)
Fish	50 (9.5%)
Sesame	54 (10%)
Previous history of anaphylaxis	134 (25%)

1121 | Angioedema due to grilled razor shell ingestion

Caligaris Cataldi H. S.[1]; Guzmán Rodriguez R.[1]; Marchan Martin E.[1]; Sastre B.[2]; Senent Sánchez C. J.[1]; Del Pozo V.[2]

[1]*Hospital Virgen del Valle - Complejo Hospitalario de Toledo, Toledo, Spain;* [2]*Hospital Fundación Jimenez Díaz, Madrid, Spain*

Case description: We present a case of a 45-year-old woman who suffered an episode of facial edema predominantly on the lips 30 minutes after eating grilled razor shell. Immediately she went to the emergency department where methylprednisolone is administered, with total clinical improvement. No pruritus or associated dyspnea. No swallowing difficult or pharyngeal occupation sensation. No other symptoms. After the episode she has not eaten razor shell again. Previously she had tolerated all kinds of shellfish

Methods: Skin prick test (SPT) were carried out with commercial extracts of shellfish (clam, squid, cuttlefish, shrimp, mussel, oyster, lobster, sea crab and prawn), Anisakis simplex and spices. In addition, "Prick-prick" was performed with grilled razor shell, as well as SDS-PAGE and Immunoblotting with grilled razor shell extract, including the control with cooked mussels and oysters extract.

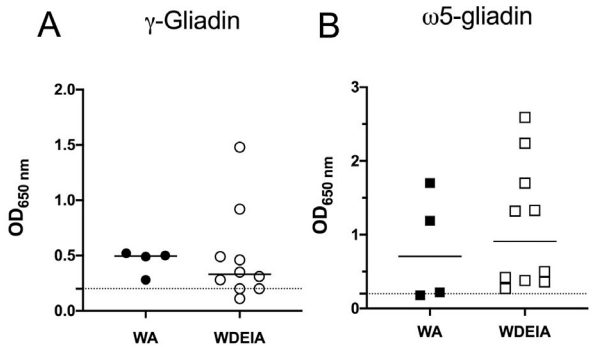
Results: SPT with commercial extracts of shellfish, Anisakis simplex and spices were all negative. "Prick-prick" with grilled razor shell was positive.SDS-PAGE and Immunoblotting revealed a protein band of 50 kDa in the grilled razor shell extract, not identified in the extracts of the other mollusks used as control.

Conclusion: We describe the case of a selective allergy to grill razor shell mediated by IgE. We identified a 50 kDa protein that probably corresponds to an enolase, already described in a series of cases of hypersensitivity to mollusks in a population of northern Spain by Azofra J et al. in 2017. Because it cannot be guaranteed that the protein found corresponds to the one described, it's necessary the performance of proteomics study to identify the nature of this protein band.

968 | Omega-5 and gamma gliadin as important allergens in adult-onset IgE-mediated wheat allergy: results from thai cohort with oral food challenge

Sompornrattanaphan M.[1]; Thongngarm T.[1]; Wongsa C.[1]; Pacharn P.[2]; Reamtong O.[3]; Piboonpocanun S.[4]

[1]*Division of Allergy and Clinical Immunology, Department of Medicine,*



Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok,

Thailand; [2]*Division of Allergy and Clinical Immunology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand;* [3]*Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;* [4]*Institute of Molecular Biosciences, Mahidol University, Nakhonpathom, Thailand*

Background: Various clinical patterns according to routes of sensitization, sensitized allergens are reported in adult-onset IgE-mediated wheat allergy. There still was a paucity of data on IgE-bound wheat allergen profiles in wheat challenge-proven adult-onset wheat allergic cases. Our objective is to identify the major sensitized allergens in Thai adult-onset wheat allergic patients (The first symptom occurred after the age of 18 despite the previous tolerance), primarily focusing on challenge-proven cases.

Method: This cross-sectional pilot study recruited the patients from the Thai Adult-onset IgE-mediated Wheat Allergy Cohort (TAWAC). The serum of patients with challenge-proven was primarily selected for allergen study, including ImmunoCAP and IgE bound gliadins and glutenins profiles. The IgE-bound proteins were identified by Liquid Chromatography-Tandem Mass Spectrophotometry (LC-MS/MS). Direct binding of IgE to recombinant gliadin and glutenin was performed to confirm the results of immunoblot and LC-MS/MS.

Results: Eleven wheat-dependent exercise-induced anaphylaxis (WDEIA) and 4 typical wheat allergy (WA) patients were enrolled. Serum IgE from >50% of bound proteins with a molecular weight ranging from 35-55 kDa in both gliadin and glutenin extracts. Further direct binding of IgE assay demonstrated that γ-gliadin and ω5-gliadin were major allergens of these 2 groups.

Conclusion: Wheat gamma-gliadin and omega-5 gliadin are major wheat allergens among WA and WDEIA Thai adult patients and could be in diagnosis of adult-onset wheat allergic cases.

Fraction	Molecular weight	Molecular mass (kDa)	Protein
Gliadin	L, M	30-45	α/β-gliadin
	L, M	30-45	γ-gliadin, peroxidase
	M, H	45-70	ω-gliadin
Glutenin	L, M	30-45	LMW glutenin, alpha-amylase/subtilisin inhibitor
	H	70-100	HMW glutenin

1034 | Multinational study of sensitization patterns to parvalbumins from ten fish species for next-generation molecular allergy diagnosis

Kalic T.[1,2]; Kuehn A.[3]; Aumayr M.[4]; Bindslev-Jensen C.[5]; Forstenlechner P.[4]; Üzülmez Ö.[2]; Hemmer W.[6]; Leung A.[7]; Leung N.[7]; Bartra J.[8]; Domínguez O.[9]; Pascal M.[10]; Sorensen M.[11]; Wong G.[7]; Hafner C.[1,12]; Breiteneder H.[2]

[1]*Department of Dermatology, University Hospital St. Pölten, Karl Landsteiner University of Health Sciences, St. Pölten, Austria;* [2]*Institute of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria;* [3]*Department of Infection and Immunity, Luxembourg Institute of Health, Esch-Sur-Alzette, Luxembourg;* [4]*MacroArray Diagnostics, Vienna, Austria;* [5]*Department of Dermatology and Allergy Center, Odense Research Center for Anaphylaxis, University of Southern Denmark, Odense, Denmark;* [6]*Floridsdorf Allergy Center, Vienna, Austria;* [7]*Department of Pediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China;* [8]*Allergology Section, Pneumology Department, Hospital Clínic de Barcelona, Barcelona, Spain;* [9]*Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu, Esplugues De Llobregat, Spain;* [10]*Immunology Department, Centre de Diagnostic Biomedic, Hospital Clínic, University of Barcelona, Barcelona, Spain;* [11]*Department of Pediatric and Adolescent Medicine, University Hospital of North Norway, Tromso, Norway;* [12]*Karl Landsteiner Institute of Dermatological Research, Karl Landsteiner Gesellschaft, St. Pölten, Austria*

Background: The one-fits-all approach in fish allergy diagnosis is not adequate due to a large variety of consumed fish species and their allergens. While some patients react to most or all fish, many are sensitized to specific species and tolerate others. Although food challenges are needed for ultimate confirmation of allergy or tolerance, quantification of IgE specific to different fish may be a prerequisite to reduce number of species required for food challenges. We aimed to understand the fish allergic patients' diversity in molecular IgE-signatures to major fish allergen parvalbumin (PV) and extracts from evolutionary distant fish families.

Method: Total and specific serum-IgE to a panel of fish PVs (10), raw (7) and heated fish extracts (6) were quantified for 263 clinically confirmed fish-allergic patients from six countries (Austria, China, Denmark, Luxembourg, Norway, Spain), using the research version of ALEX^2 multiplex assay. Data were analyzed for IgE-signatures of different patients and patient groups using SPSS and R.

Results: Among the beta-parvalbumins, median specific IgE was highest for tuna and mackerel PVs (>10 kUA/L), followed by herring, carp, salmon, swordfish and perch, while it was significantly lower for cod (4.9 kUA/L) and sole PVs (2.55 kUA/L). Median IgE to ray alpha-parvalbumin, considered hypoallergenic, was below the threshold, but was positive for 22% of the patients.

Majority of the patients were sensitized to multiple PVs, but no clustering based on shared responses to groups of PVs or extracts could be observed. Four patients were positive only to salmon PV, of which 3 reported salmon as a causative fish. Of 51 (19%) patients negative to cod PV, 75% were positive to other PVs. As high as 25% of participants were negative to sole PV. Importantly, for 44 patients, a much stronger signal was obtained for raw and/or heated extracts than for PVs from one or more species, showing a need for fish extracts in addition to PVs in diagnostic assays.

Conclusion: Our data demonstrate that many patients may tolerate certain fish species, and will assist in selection of species and allergens for enhanced *in vitro* IgE testing, and for food challenges.

1123 | Clinical application of basophil activation test in fish allergy

Leung A.S.Y.; Leung N.Y.H.; Wai C.Y.Y.; Wong G.W.K.; Leung T.F.
Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR

Background: Oral food challenge (OFC) carries risk to participants and is time-consuming and resource-exhaustive. There is, thus, a need for a reliable and safe biological marker to predict clinical reactivity to a food allergen. We aim to develop a protocol for Basophil Activation Test (BAT) to whole extract of *Ctenopharyngodon idella* (grass carp – GC) and its parvalbumin (PV) Cten i 1 and evaluate the predictive value of BAT on clinical reactivity to GC.
Method: We included physician-diagnosed IgE-mediated fish-allergic participants into our study. All participants underwent a 2-day double blind placebo-controlled food challenge series to grass carp and placebo (pork). BAT was performed on fresh venous blood using the Flow CAST kit. Specific IgE against grass carp was measured by ImmunoCAP.
Results: Thirteen patients underwent double-blind OFCs between Jul 2020 and Jan 2021. Fifty-four percent (7/13) participants failed GC challenges and the median eliciting doses (ED) were 7 (0.09-97.2) and 1.2 (0.02-16.3) grams of fish and fish protein, respectively. The median (range) %CD63$^+$ basophil at 40 ng/ml in the allergic and tolerant group were 75.05 (0-94.3) & 3.9 (0.4-86.8), p = 0.07, respectively for GC extract, and 72.25 (0.5-86.3) & 8.3 (0.6-85.3), p = 0.09, respectively for Cten i 1. Increasing the allergen concentration at 400ng/ml in 3 allergic patients' sera yielded a lower %CD63$^+$ (GC extract: 32.3 [0.3-56.7]; rCten i 1: 34.2 [0-41.3]), but lowering the allergen concentration to 4ng/ml in 5 participants' sera yielded a relatively higher %CD63$^+$ basophil (GC extract: 69.6 [7.7-88.5]; rCten i 1: 84.6 [46.3-92.2]. The diagnostic accuracy of GC allergy is 76.9% with BAT using an allergen concentration at 40 ng/ml and 61.5% with ImmunoCAP.
Conclusion: Higher grass carp allergen concentration appears to inhibit upregulation of the basophil marker CD63, as opposed to the application of BAT in other food allergens. BAT may be a promising biomarker of clinical reactivity to fish, but further study is needed.

1073 | Outcome predictors for oral food challenges in children

Vaughan M.[1]; Daly D.[2]; Tanweer Y. A.[2]; Maris I.[1,2]
[1]*University College Cork, Cork, Ireland;* [2]*Bon Secours Hospital Cork, Cork, Ireland*

Background: Oral Food Challenges (OFCs) are the current gold standard for the diagnosis of food allergies. Considering the risk of a potentially severe allergic event, the ability to predict both challenge outcome and severity of a reaction would greatly improve the overall functionality of OFCs and prioritise those with the highest chance of a negative result.
Method: A retrospective cohort study was performed on children, aged 6 months to 16 years, who underwent OFCs in the Bon Secours Hospital Cork, between January 2019 and December 2019. Variables such as age, gender, allergen, anaphylaxis history, atopy, serum specific IgEs (SpIgE), Skin Prick Test (SPT), and also challenge outcome and reaction severity, were recorded. Reaction severity was graded on a scale of 0-3, based on the number of organ systems involved, with 0 indicating a negative and 3 indicating a severe reaction. Correlations were examined between variables/combination of variables, as possible predictors, and challenge outcome/reaction severity. Sensitivity and specificity were used to examine the diagnostic strength of each variable to challenge outcome (positive/negative). Cramer's V test was used to test association between variables/combination and reaction severity.
Results: A total of 190 OFCs were performed in 134 individuals over a period of one year. 81/190 (43%) of the challenges resulted in a positive clinical reaction of varying severity, 17 (9%) of which were classified as anaphylaxis. SPT ≥6mm in isolation (Cramer's V test 0.472, sensitivity 75.1%, specificity 72.3%) (p <0.001), but also in combination with SpIgE ≥8kU/L (Cramer's V test 0.364, sensitivity 67%, specificity 84.2%) showed a high association to a positive OFC. SpIgE ≥8kU/L (Cramer's V test 0.292), previous anaphylaxis (Cramer's V test 0.223), age (Cramer's V test 0.199) and allergen tested (Cramer's V test 0.195), all showed moderate association to reaction severity. No association was found with gender or presence of atopy.
Conclusion: SPT ≥6mm in isolation showed the highest association to reaction severity and had the highest level of sensitivity in predicting challenge outcome. When in combination with SpIgE ≥8kU/L, it presented a lower strength of association and sensitivity, but a higher specificity in predicting challenge outcome.

1101 | Long-term longitudinal quality of life outcomes following a phase 2a open-label study of probiotic and peanut oral immunotherapy (PPOIT)

Lloyd M.[1,2,3]; Ashley S.[1,3]; Hsiao K.[1,4,5]; Pitkin S.[1]; Dunn Galvin A.[6]; Jayawardana K.[1]; Lozinsky A. C.[1,3]; Loke P.[1,2,3,7]; Tang M. L.[1,2,3]
[1]*Murdoch Children's Research Institute, Melbourne, Australia;* [2]*University of Melbourne, Melbourne, Australia;* [3]*Royal Children's Hospital, Melbourne, Australia;* [4]*Starship Children's Hospital, Auckland, New Zealand;* [5]*University of Auckland, Auckland, New Zealand;* [6]*University College Cork, Cork, Ireland;* [7]*Monash Children's Hospital, Clayton, Australia*

Background: Previously, we have reported that probiotic and peanut oral immunotherapy (PPOIT) improved health-related quality

of life (HRQL), and improvement was specifically linked to acquisition of sustained unresponsiveness (SU). PPOIT-002 is a single arm open-label study which aimed to investigate long-term outcomes at 3-years post-treatment after 18-months of PPOIT treatment.

Method: Participants (aged 1-12 years) with challenge-proven peanut allergy received PPOIT for 18-months. HRQL was evaluated at screening (T0), end-of-treatment (T2), and 12-months (T4) and 3-years (T5) post-treatment, using the Food Allergy Quality of Life Questionnaire – Parent Form (FAQLQ-PF) and Food Allergy Impact Measure (FAIM). FAQLQ-PF total score and sub-scores (emotional impact, food anxiety, and social and dietary limitations) were assessed. Difference in scores between timepoints was evaluated using paired t-tests.

Results: Of 20 enrolled participants, 16 remained in the study at end-of-treatment (T2), and 12 achieved 8-week SU. Twenty participated in outcome assessments at T0, 16 at T2, 14 at T4, and 12 at T5. Both the FAQLQ-PF and FAIM total scores improved significantly in the 12-months following treatment completion (change in score T2 to T4: 0.44, 95% CI 0.17-0.70, p = 0.004; and 0.37, 95% CI 0.10-0.65, p = 0.01; respectively). Improvements in FAQLQ and FAIM scores were maintained at 3-years post-treatment (see Table 1). Improvement was also seen in each of the FAQLQ-PF sub-scores for emotional impact, food anxiety, and social and dietary limitations.

Conclusion: PPOIT treatment for 18 months leads to significant and long-lasting improvement in quality of life and food allergy impact burden, as perceived by caregivers.

TABLE 1 Difference in FAQLQ and FAIM total scores between timepoints

Timepoints of interest	FAQLQ total score (points)*				FAIM total score (points)**			
	Sample size	Mean difference	*p*-value	95% CI	Sample size	Mean difference	*p*-value	95% CI
T0-T2	16	0.32	0.25	(-0.25, 0.90)	14	0.45	0.05	(-0.001, 0.91)
T0-T4	14	0.57	0.08	(-0.08, 1.22)	13	0.73	0.003	(0.30, 1.17)
T0-T5	10	0.65	0.08	(-0.08, 1.38)	12	0.79	0.004	(0.31, 1.27)
T2-T4	14	0.44	0.004	(0.17, 0.70)	13	0.37	0.01	(0.10, 0.65)
T2-T5	10	0.68	0.04	(0.04, 1.32)	12	0.47	0.02	(0.11, 0.84)
T4-T5	10	0.26	0.34	(-0.32, 0.84)	12	-0.08	0.83	(-0.93, 0.76)

*FAQLQ total score is a food allergy specific health related quality of life measure (maximum of 30 questions, each scored 0-6, with 0 representing best quality of life).

**FAIM total score assesses the parent's perception of the chance of an adverse outcome for the child with a food allergy (six questions with a 6-point response scale from 0 (extremely unlikely) to 6 (extremely likely)).

1142 | The relevance of compounding factors and the risk of anaphylaxis in 63 patients allergic to alpha-gal

Martínez-Arcediano A.[1]; Audícana Berasategui M. T.[1]; Longo Areso M. N.[1]; Villarreal Balza De Vallejo M. O.[1]; Velasco Azagra M.[1]; Campandegui Lecuona A.[2]; Marquínez Ruíz De Arbulo M. B.[1]; Ollo Morales P.[1]; Fernandez Ibañez E.[1]

[1]*Allergy Department. Hospital Universitario Araba, Vitoria-Gasteiz, Spain;* [2]*Universidad del Pais Vasco (UPV-EHU), Vitoria-Gasteiz, Spain*

Background: Compounding factors have been frequently described as helpers in food allergic reactions, not only favouring but also intensifying them.

However, in alpha-gal syndrome, cofactors haven been controversial or not clearly identified.

Objective: Analyze the data in 63 alpha-gal allergic patients studied in the last 8 years in Araba University Hospital (HUA;Vitoria-Gasteiz; Basque Country, north of Spain), in order to clarify the envolvement of compounding factors, their relevance, and the risk of anaphylaxis.

Method: We report 10 women and 53 men (range, 9-86 years) including 2 children and 1 teenager, diagnosed of alpha-gal allergy by skin tests to mammalian meat extracts and to cetuximab; specific IgE to mammalian meats, alpha-gal and Activation Basophil Test (BAT) in 26 cases.

The number of patients which presented severe allergic reactions and the implication of possible cofactors involved in severe and non-severe allergic reactions are collected.

Results: In 46 % of the patients (29/63), compounding factors were reported.

Compounding factors were: NSAIDs, exercise, alcohol, emotional stress, intense hot weather, infections, Angiotensin Converting Enzyme (ACE) Inhibitors and Proton Pump Inhibitors (PPIs).

NSAIDs were the most reported (8/29), followed by exercise (7/29); alcohol (6/29); infections (3/29): 1 SARS-CoV-2 virus infection, 1 Varicela virus and 1 bacterial infection. ACE Inhibitors (2/29); PPIs (1/29); intense hot weather (1/29) and emotional stress (1/29).

Severe allergic reactions were presented in 44% (28/63) of total cases.

Cofactors were involved in 12/28 severe patients (43%).
Cofactors were presented in 3/5 anaphylactic shocks (2 alcohol, one of them associated with a bacterial infection, 1 emotional stress) and in 9/23 anaphylaxis (4 exercise, 3 NSAIDs, 1 PPIs, 1 alcohol).
35 cases were non-severe reactions. Cofactors were involved in 29% of non-severe reactions.
In 3/35, various compounding factors were involved (9%).
Case number (no) 1: exercise and NSAID (diclofenac); no 2: exercise and ACE inhibitor; no 3: exercise, NSAID and intense hot weather.
Conclusion: We present 63 allergic alpha gal patients registered in the last 8 years in which,

1. Almost half of the patients, present severe allergic reactions.
2. Compounding factors are presented in 44% of the allergic reactions.
3. In severe cases, compounding factors are involved in 43% of the patients versus in 29% non-severe reactions.

1149 | The α-hairpin scaffold and variable amino acid sequences of ara h 1 and jug r 2 leader sequences collectively determine cross-reactivity between peanut and walnut

Nesbit J.[1]; Foo A.[2]; Gipson S.[1]; Bushel P.[2]; Derose E.[2]; Schein C.[3]; Teuber S.[4]; Hurlburt B.[1]; Maleki S.[1]; Mueller G.[2]
[1]*USDA, New Orleans, United States;* [2]*NIEHS, Research Triangle Park, United States;* [3]*UTMB, Galveston, United States;* [4]*UC-Davis, Davis, United States*

Background: Vicilin seed storage proteins are translated with N-terminal leader sequences (LSs) that are cleaved to yield the mature protein. These LSs were thought to be unstructured and rapidly degraded. However, intact Ara h 1 and Jug r 2 LSs (A1LS and J2LS) have been isolated from seeds, and immunodominant IgE epitopes detected. Here, common sequences containing structured CxxxC-repeat motifs were identified as potential mediators of IgE cross-reactivity despite very low (17%) sequence identity.
Method: Linear IgE epitopes were identified by probing peptide microarrays, generated by printing overlapping 15-mer peptides on glass slides, with sera from peanut, walnut or dual allergic individuals. Peanut A1LS and walnut J2LS fragments (J2.1, J2.2, J2.3, each representing a single CxxxC vicilin LS motif) were identified, cloned, expressed, purified and their structures solved using solution-NMR to locate epitopes on the structure.
Results: All four LSs reveal similar helix-turn-helix motifs held together by disulfide bonds between adjacent CxxxC repeats. IgE from the peanut-allergic individuals bound more frequently to the J2.1 fragment, regardless of walnut allergic status or A1LS binding. Numerous potentially cross-reactive epitopes were identified on structured and unstructured regions of both J2.1 and A1LS suggesting that amino acid composition also plays a role in cross-reactivity.
Conclusion: The shared α-hairpin is a stable peptide scaffold that contributes to conformational cross-reactivity in spite of the low sequence identity, but the amino acid sequence variation modulates the level of IgE reactivity.

1329 | Frequency of detection of IgE antibodies to wheat allergens

Bala A.; Shabanov D.
National Research Center-Institute of Immunology Federal Medical-Biological Agency of Russia, Moscow, Russia

Background: Wheat is used as a daily food intake and is one of the most important food sources in the world. In some countries, wheat is the third most common reaction after allergies to milk and eggs. Wheat allergens can lead to food allergy, wheat-dependent exercise-induced anaphylaxis, respiratory allergy and contact urticaria. The study of sensitization to wheat as a source of the allergen is not very informative, and therefore it is necessary to use a CRD.
Aim: To analyze a frequency of IgE antibodies to wheat allergens in patients (pts) with food sensitization in Russian population.
Method: The presence and level of IgE-aB to by ISAC ImmunoCAP technology (Thermofisher Scientific, Sweeden).
Patients: There were 616 pts aged from 1 to 79 with manifestations of sensitization to various allergens were examined. All sera from these pts was tested to rTri a 19.0101, nTri a aA_TI and rTri a 14.
Results: There were 16 pts positive to wheat allergens. The frequency of detection of IgE antibodies to each of the allergenic proteins did not differ significantly. Sensitization to nTri a aA_TI and rTri a 14 was identified in 8 pts (50.00%). In 37.5% (6/16) pts IgE antibodies to rTri a 19.0101 were identified. The concentrations of IgE-aB to rTri a 19.0101, nTri a aA_TI and rTri a 14 were very different 0,5-1,8, 0,6-15,0 and 1,0-54,0 ISU-E respectively. Most of pts 68.75% (11/16) were sensitized only to one of wheat allergens. Some pts 25.00% (4/16) had IgE-aB to two allergens and it was rTri a 19.0101 and nTri a aA_TI. Only one patient was sensitized to all three allergens that can be identified using ISAC ImmunoCAP.
Conclusion: Sensitization to wheat allergens is not as widespread in Russia as in other countries 2.59% (16/616). At the same time, almost a third of them 31.25% (5/16) have polysensitization to wheat allergens.

995 | Anaphylaxis to pomegranate (punicam granatum)

Fernández Bolívar A. A.[1]; García Menaya J. M.[1]; Dotor Lavado M.[1]; Durán C. C.[2]; Bobadilla González P.[1]
[1]*University Hospital of Badajoz, Badajoz, Spain;* [2]*Don Benito Hospital, Badajoz, Spain*

Case Report
Background: Systemic reactions to exotic fruits are on rise and these include the pomegranate (*Punicam granatum*) which belongs to Lythraceae family native to Iran which consumptions in other regions has increased too. To the date there are very few reports of

IgE-mediated reactions to pomegranate. Pomegranate LTP allergens have been identified as Pun g 1 and other allergens as pommaclein Pun g 7 which sequence is homologous to Pru p 7 (peach peamaclein) and more recently a class III Chitinase allergen has also been identified.
Case report: A 42-year-old woman, with a selective hypersensitivity to celecoxib, developed palmar pruritus, micropapular erythema in arms and scalp and dyspnea within 15 min after ingestion of pomegranate (previously tolerated). In the emergency room she was treated with methylprednisolone and intravenous fluid therapy with rapid improvement of symptoms. Since the reaction, the patient avoids pomegranate and has tolerated other fruits. With a detailed anamnesis, simultaneous use of other food or drugs as well as the presence of possible cofactors were excluded.
Methods and results: Skin prick tests were performed with profilin and LTP commercial extracts with positive result to LTP. A skin prick-prick test with fresh pomegranate was performed with a positive result. Complete blood count, biochemistry, VSG, TSH, basal tryptase and total IgE were performed resulting mild leucocytosis (13,300/mm3), VSG 10 mm/hour and elevated total IgE (203 IU/ml). The rest of the parameters were normal or negative.
Conclusions: We report a case of an immediate IgE-mediated hypersensitivity systemic reaction to pomegranate fruit demonstrated by a positive prick-prick to pomegranate. The patient was advised from rigorous avoidance of pomegranate fruit and was trained in the management of autoinjectable adrenaline. This is an infrequent food allergy, with very few cases published according to bibliographic searches.

1311 | Allergic reaction to manioc (manihot esculenta) and its possible relationship with hypersensitivity to latex

Pitchon A.; Cunha L. A.O.; Goebel G. A.; Cardoso M. F.S.
Hospital das Clinicas da Universidade de Minas Gerais (HC - UFMG), Belo Horizonte, Brazil

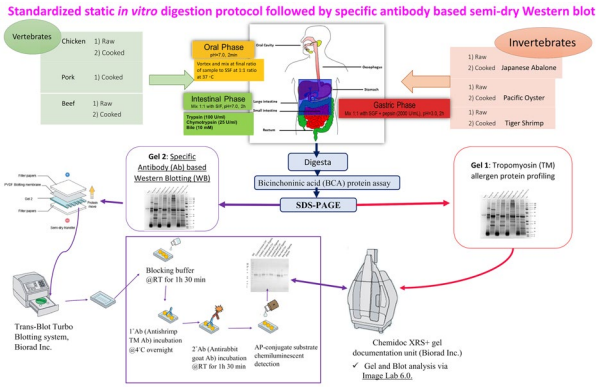
Introduction: Manioc (*Manihot esculenta* or *Manihot utilíssima)* tube is a root usually consumed, boiled or fried, worldwide - mainly in South America, Africa and Asia. At first, it was considered a nonallergic starch, however, since 2003, few cases of allergic reactions after manioc ingestion have been reported in Brazil and in other locations.
Case description: Male patient, 46 years old, military, previous diagnosis of Gout, from Pirapora (MG - Brazil), started three years ago, episodes of itching and generalized skin erythema associated with oropharyngeal pruritus beginning minutes after ingestion of boiled manioc - denies symptoms after eating fried manioc or flour. Improvement of the symptoms after use of antihistamine. Since young adult, reports itchy hands after using latex gloves or contact with balloons. Denies complications during surgical procedures.
He underwent prick to prick tests presenting positive results for raw (8mm x 8 mm), bolied (8 mm x 4 mm) and fried (6mm x 6mm) manioc. The test for manioc flour was negative. IgE specific for látex (K82) was positive (17,8 KU/L).
Discussion: Although uncommon, allergic reactions secondary to manioc intake have become more prevalent in the past two decades. It is postulated that this rise may be related to the growing number of cases of hypersensitivity to latex which precedes symptoms to manioc and the possible cross reaction between its antigens and its involvement in latex-fruit syndrome.
Conclusion: Thus, it is essential for the professionals to be alert to this possible relationship so that diagnoses can be suspected, investigated and confirmed.

1068 | Clinical presentation and diagnosis of cow's milk allergy in children – 10 year retrospective study

Caires A.[1], Brandão Abreu D.[1], Miranda J.[1], Coimbra A.[1], Silva D.[1,2]
[1]*Centro Hospitalar Universitário de São João, Porto, Portugal;* [2]*Basic and Clinical Immunology, Porto, Portugal*

Background: Cow's milk protein allergy (CMPA) has a wide spectrum of clinical presentation and it is frequently associated with egg allergy. This study aimed to assess if age and type of clinical presentation at first reaction were associated with first oral food challenge (OFC) result. Further, we compared children with milk allergy only (CMPA-O) versus those with concomitant CM and EA (CMPA-E).
Method: Medical records of children with suspected milk allergy referred for an oral food challenge (OFC) between 2010 and 2020 were reviewed. Data regarding clinical presentation, atopy and skin prick tests (SPT), total and specific IgE (sIgE) to milk and milk proteins and skin prick-prick tests (SPTT) as well as first OFC outcome were collected.
Results: Of 191 children with milk allergy suspicion, 91 were analyzed, 62 (68%) male, median age of 3.5 years, median age at clinical presentation 5.9 months, 41% were ≤1 year old at first presentation[AC1] , 36% had a systemic reaction at first reaction and median sIgE milk level of 16.7 KU/L.
When categorizing children by age at first presentation, those over ≥2 years old had a higher mean total IgE, sIgE for α-lactalbumin, casein and a higher percentage of positive SPT to α-lactalbumin and casein. Younger children had 21% positive OFC (1 anaphylaxis) versus 49% OFC (4 anaphylaxis) in the older group.
When categorizing by severity of first reaction, a first positive OFC occured in 61% with systemic symptoms versus 27.5% with muco cutaneous symptoms.
Those with CMPA-O had less atopy and atopic dermatitis than CMPA-E and a lower percentage of anaphylaxis at first presentation (9% versus 15% with CMPA-E), median total IgE was 3 times higher in the CMPA-O than in the CMPA-E group.
Conclusion: Older age at first milk allergic reaction and more severe clinical presentation were associated with a higher likelihood of a first positive oral food challenge. These results were associated with a higher IgE sensitization to whole milk, alfa-lactalbumin and casein. The concomitant presence of egg allergy did not influence the first

oral food challenge result although it was associated with atopy and



atopic eczema.

1070 | Comparative digestomics of thermally treated vertebrates and invertebrates tropomyosins in real food matrix

Khulal U.[1,2]; Rajkovic A.[1,2]; Velickovic T. C.[1,2,3,4]

[1]*Ghent University Global Campus, Incheon, South Korea;* [2]*Ghent University, Ghent, Belgium;* [3]*University of Belgrade, Belgrade, Serbia;* [4]*Serbian Academy of Science and Arts, Belgrade, Serbia*

Background: Shellfish tropomyosin (TM) accounts for approximately 90% of all immunoglobulin E food allergies worldwide. Till date, the allergy risk assessment is done via sequence identity against known allergens, *in vitro* IgE serum screening, in vivo skin prick tests and digestibility tests.

Objectives: To compare the digestomics of invertebrates and vertebrates allergen pair in real food matrix under two allergenicity assessment parameters: thermal stability in combination with digestive enzymes resistance.

Method: Thermal treatment of samples (abalone, oyster, shrimp and chicken, pork, beef) to compare TM heat stability followed by standardized static simulated *in vitro* gastrointestinal digestion, SDS-PAGE of digesta (oral phase OP, gastric phase GP, intestinal phase IP) supernatants under reducing and non-reducing conditions, specific antibody based semi dry Western blot (WB) analysis with primary antibody rabbit anti shrimp TM.

Results: Invertebrates TM was, indeed, both heat and pepsin resistant, in agreement with publications. Vertebrates TM was less stable in digestibility assay following thermal treatments. We have observed pepsin resistance just in raw chicken, but not in intestinal digestion phase.

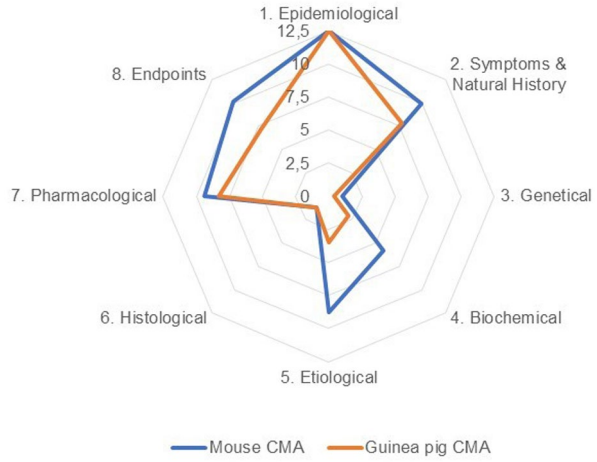
Conclusion: There is a good correlation between combined resistance of TM to digestion following the thermal treatment and allergenicity among vertebrates and invertebrates. Under thermal treatments that mimic human eating habits, invertebrate TMs are resistant to digestion in their real matrix, while vertebrates TMs are not stable and degrade during gastric phase.

1165 | Predictive value for clinical outcome of animal models of pediatric cow's milk allergy – comparison between the dunkin hartley guinea pig model and the C3H/heouJ mouse model

Veening-Griffioen D.H.[1]; Ferreira G.S.[1]; Boon W.P.C.[2]; Schellekens H.[1]; Moors E.H.M.[2]; Van Meer P.J.K.[1,3]

[1]*Utrecht University, Utrecht Institute of Pharmaceutical Sciences, Utrecht, The Netherlands;* [2]*Utrecht University, Copernicus Institute of Sustainable Development, Utrecht, The Netherlands;* [3]*Medicines Evaluation Board, Utrecht, The Netherlands*

Background: Cow's milk allergy (CMA) develops in 3-6% of children



< 1 year of age following the introduction to cow's milk. For children with CMA, cow's milk protein hydrolysates-based formulas are accepted as alternative source of protein if reduced risk to develop allergy is shown (EU Directive 2016/127). For these formulas, non-inferiority (intervention is not worse than standard formula or human milk, the gold standard) or superiority (intervention is better than standard formula or is closer to human milk) must be demonstrated. Animals are useful in demonstrating efficacy of these formula due to their ability to cover the complex multifactorial nature of allergic sensitization to proteins.

Our study aims to evaluate insofar two animal models mimic pediatric IgE-mediated CMA: the Dunkin Hartley guinea pig model and the C3H/HeOuJ mouse model.

Method: A search on Pubmed and Embase was performed to identify all animal models of CMA. Studies with the guinea pig and the mouse model were assessed with the Framework to Identify Models of Disease (FIMD), a question based tool to determine the similarity of the animal model to the human condition across 8 domains: epidemiology, symptoms and natural history, genetic, biochemical, etiological, histological, pharmacological, endpoints. Maximal score per domain is 12.5, graphically represented as radar plot.

Results: 232 (out of 5219) publications reported animal models for CMA: mice 80%, guinea pigs 13%, rats 10%, rabbits 2% and pigs <1%. Of these publication 22 used the guinea pig model and 45 the mouse model. FIMD validation scores were 34 and 59 (out of

100) respectively (Figure 1). Differences were found in the following domains: symptoms and natural history (7.8 vs 9.9), biochemical (2.1 vs 5.8), etiological (3.5 vs 8.8), pharmacological (8.3 vs 9.4) and endpoints (7.2 vs 10.2). Of concern is the poor reporting quality (ARRIVE 2.0) and associated risk of bias (SYRCLE's RoB) of the included studies.

Conclusion: The mouse model is a better predictor for clinical outcomes than the guinea pig model, due to the availability of more studies and parameters measured in the mouse model. We recommend stakeholders to provide a transparent justification of the animal model chosen for the intervention under evaluation in their context of use. Specifically, to align non-inferiority and/or superiority study design between human and animals. Together this will improve the predictive value of the animal data for human outcome.

1309 | Specification of sensitization to soy allergens

Bala A.; Shabanov D.
National Research Center-Institute of Immunology Federal Medical-Biological Agency of Russia, Moscow, Russia

Background: Soy allergens can cause food allergic reactions and occupational inhalation allergies. In Russia a high exposure of birch pollen, which can lead to cross-reactions to soy allergens between Bet v 1 and Gly m 4, however, they are limited to oropharyngeal reactions, in contrast to nGly m 5 and nGly m 6 which can cause acute allergic reactions.

Aim: To analyze a frequency of IgE antibodies to soy allergens in patients (pts) with food sensitization in Russian population.

Method: The presence and level of IgE-aB to by ISAC ImmunoCAP technology (Thermofisher Scientific, Sweeden).

Patients: There were 616 pts aged from 1 to 79 with different severity of food allergy observed. All sera from these pts was tested to nGly m 5, nGly m 6 and rGly m 4.

Results: There were 168 pts positive to soy allergens (27,27%). Most frequently the IgE-aB to rGly m 4 in 157 (93,45%) pts wherein concentrations of IgE-aB were 0,4-84,0 ISU-E. Specific IgE-aB to major components of soy allergens nGly m 6 and nGly m 5 identified in 15,47% (26/168) pts and 8,92% (15/168) respectively. The concentrations of IgE-aB to nGly m 6 and nGly m 5 were similar enough 0,4-24,0 and 0,4-30,7 ISU-E. There are 16 pts that were sensitized to 2 allergen components 9,52% and only 7 pts were sensitized to 3 allergen components (4,16%).

Conclusion: Sensitization to soy allergens available for research in ISAC and it comes to light quite often in the Russian population (27,27%). At the same time, most pts are sensitized only to 1 allergic component of soy 86,30% (145/168) and only 24,40% (41/168) pts sensitized to 2 and 3 allergen components.

1053 | Fish allergy with multiple sensitization: two cases report

Acunzo M.[1]; Pascuzzi M.[1]; Beretta S.[1]; Pendezza E.[2]; Zuccotti G.V.[3]; D'Auria E. C.[1]
[1]*Allergy Unit-Vittore Buzzi Children's Hospital-University of Milan, Milan, Italy;* [2]*Nutrition and Dietetic Service- Vittore Buzzi Children's Hospital-University of Milan, Milan, Italy;* [3]*Department of Pediatrics, Vittore Buzzi Children's Hospital-University of Milan, Milan, Italy*

Background: Fish is one of the most common foods responsible for allergic reactions in children worldwide; most cases are IgE-mediated and are a consequence of ingestion, contact or inhalation of the antigen. It remains poorly investigated the relationship between IgE sensitization to different fish species and clinical cross-reactivity.

Methods: We hereby describe two cases of fish allergy with multiple sensitizations.

Results: B.S. is an 8-year boy with a history of a mild atopic dermatitis. At 6 months he showed, at the second intake of cod, repeated vomiting without other symptoms and urticarious reaction to contact with other types of fish.

C.G. is a 10-year girl with a negative history of atopy and with allergy to inhalants. At the first intake of trout, she showed a trunk urticaria and lip angioedema. Both patients were put on a fish-free diet and they were referred to our Allergy Unit for allergological evaluation. Skin prick test and IgE tests were performed, showing multiple fish sensitization (B.S had salmon 2.68 KU/L, tuna 2.96 KU/L, trout 4.53, plaice 3.47 KU/L and cod 2.96 KU/L ; C.G. had salmon 37.5 KU/L, tuna 4.62 KU/L, trout 40.2 KU, cod, 17.4 KU/L and sole 10 KU/L). Both patients underwent a single-blind placebo-controlled oral food challenge (OFC). During OFC for cod, B.S. presented mild and transient lip pruritus after the first dose (1 g), urticaria at the upper limbs after the third dose (5 g) while he had diffuse urticaria and diarrhea after administration of 20 g (cumulative dose 50 g); the OFC was then stopped. OFC for tuna resulted negative. As far as C.G., both OFC for salmon and sole resulted negative, allowing her to introduce them in her diet.

Conclusions: Our two cases suggest that serum-specific levels are not predictive of in vivo clinical reactivity. Food challenge is required for discrimination between allergy to the different fish species.

Patient	Age of OFC	Seafood	SPT	IgE (KU/L)	OFC
B.S.	8 y	Tuna	N/A	0,96	Negative
	8 y	Cod	N/A	2,96	**Positive**
C.G.	10 y	Salmon	Neg	37,5	Negative
	10 y	Sole	5 mm	10	Negative

993 | Prebiotics supplementation during pregnancy leads to the transmission of microbial and immune factors from mother to child, preventing from food allergy

Brosseau C.[1]; Selle A.[1]; Cherbuy C.[2]; Barbarot S.[3]; Bodinier M.[3]
[1]*INRAE Pays de la Loire, Nantes, France;* [2]*INRAE Micalis, Jouy En Josas, France;* [3]*CHU Nantes, Nantes, France*

Background: Allergies are multifactorial diseases related to the dysfunction of 3 biological actors: the microbiota, the epithelial barriers and the immune system. These alterations lead to a defect in the establishment of immune tolerance. Compelling evidence for the early role of gut microbiota dysbiosis and barrier integrity with allergies is emerging. In this context, pregnancy represents an optimal window of intervention in the regulation of the allergic process through a modulation of the immune and microbial systems. Prebiotics are able to act on the immune system, the microbiota and the intestinal barrier. The aim of this study was to characterize in mice, the effects of prebiotics administered during pregnancy on the mother to child microbial and immune transmission and its protective effect on food allergy occurrence.
Method: Pregnant mice received a standard diet or a diet enriched with prebiotics (GOS/inulin). Stools were collected from mothers before mating, during pregnancy and during lactation and stool from pups at 3 and 6 weeks of age, to determine the fecal microbial composition. Metabolites were also analyzed in the amniotic fluids, and in the stools. B and T lymphocytes were immunophenotyped in the different gestational (decidua, placenta, uterus), maternal (spleen), fetal (intestine, bone marrow) and pups (mesenteric lymph nodes) tissues. Finally, food allergy to wheat was induced in the pups by 2 intraperitoneally sensitization and one oral challenge with gliadins.
Results: We demonstrated that prebiotics supplementation modified the fecal microbiota of pregnant mice toward strains benefic for the health (Firmicutes, Bacteroidetes), and this modification was transferred to the pups and last over time. Interestingly, a significant increase of short chain fatty acids was observed in the stools from mothers supplemented with prebiotics and in their amniotic fluid. Supplementation with prebiotics during gestation increases significantly the frequency of regulatory B and T lymphocytes in the placenta compared to mice on a standard diet. Regulatory B cells were found in the intestine and bone marrow of the fetus. Regulatory B and T subsets were increased in pups from supplemented mothers protecting them against food allergy.
Conclusion: Prebiotic supplementation during pregnancy leads to the transfer of microbial and immune factors from mother to child, allowing the establishment of a tolerogenic environment beneficial for infant health outcomes and preventing from food allergy.

1014 | Activation of murine bone marrow derived dendritic cells by soy protein is dependent on its origin and mouse strain

Zhao X.[1,2]; Knippels L.[1,3]; Chen H.[2]; Garssen J.[1,3]; Hogenkamp A.[1]
[1]*Division of Pharmacology, Department of Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands Antilles*; [2]*State Key Laboratory of Food Science and Technology, Nanchang University, Nanchang, China*; [3]*Department of Immunology, Danone Nutricia Research, Utrecht, Netherlands Antilles*

Background: Soybean (Glycine max) is one of the eight foods that account for the most significant food allergies. At least 34 allergenic proteins involved in IgE binding have been identified in soybean, including subunits of β-conglycinin (7S), and the acidic and basic chains of glycinin (11S).In the current study, we investigated whether exposure to crude soybean protein isolate (SPI), 7S and 11S isolated from soybean obtained from the USA or China would generate different responses in murine bone marrow derived dendritic cells (BMDC).
Method: To assess differences in BMDC activation, cells were exposed to soy proteins and stimulated with LPS. BMDC cell surface marker expression of MHCII, CD40 and CD86 was determined by flow cytometric analysis, and cytokine expression of IL-12p20, IL-4, IL-10, IL-6 was determined by ELISA.
Results: Soy protein from China, especially SPI, increased LPS-induced BMDC expression of CD86 and CD40 compared to LPS-only stimulated cells, but also when compared to cells treated with proteins derived from soybean from the USA. This difference in DC-activation may suggest that there could be differences in allergenicity depending on the source of the soybean.
Moreover, CD86 and CD40 expression was observed to be higher in BMDC derived from female Balb/c mice compared to C3H after exposure to SPI.
Conclusion: In follow-up experiments, we will assess how these in vitro findings correlate to *in vivo* immune outcomes.

1161 | Do allergic co-morbidities influence food challenge outcome?

Sigdel D.; Sheikh F.; Ventilacion L.; Tonge K.
East and North Hertfordshire NHS Trust, Stevenage, United Kingdom

Background: To evaluate whether allergic co-morbidities influence the outcome of oral food challenge (OFC) carried out in children in our day unit who had suspected or previously confirmed food allergy.
Method: This is a retrospective study and data was collected from clinical notes of children who underwent OFC over 12 months period (between January and December 2019). Data was obtained on challenged food, previous exposure of food, skin prick test (SPT) or specific IgE results, allergic co-morbidities and type of reaction if unsuccessful challenge. The data was entered directly into Microsoft excel and analysed.
Results: A total of 76 OFC were performed. Majority of challenges were carried out on nuts (56), followed by egg (15), milk (5) and other foods (2). 47 (62%) challenges were successful whereas 25 (33%) failed and 4 (5%) inconclusive. Success rate was highest in nut challenge (70%), followed by egg (67%) and milk (60%). None of the children had anaphylaxis during the challenge.
Out of 76 children, 36 (47%) had allergic co-morbidities. 15 children has multiple allergic co-morbidities whereas 12 had eczema, 5 had allergic rhinitis and 3 had asthma. Out of 25 children who failed the challenge, just over two third (68%) had allergic co-morbidities. In the successful challenge group, only one third (33%) of children had co-existing allergic conditions. 3 out of 4 children had allergic co-morbidities who had inconclusive challenge.

Conclusion: One third of the children who underwent OFC had failed challenge. We observed higher failure rate during OFC in children with food allergy who also have other allergic co-morbidities. This can be an important factor to consider when planning OFC especially deciding on home or hospital-based challenge.

1085 | Flaxseed allergy due to storage proteins

Moreno Lozano L.[1]; De Aramburu Mera T.[1]; Posadas Miranda T.[1]; López Matas M. Á.[2]; Albéndiz Gutierrez V.J.[3]; Torres Casanova E. A.[4]; Muñoz Daga O. A.[3]; García Rodríguez R. M.[5]

[1]*Vithas Hospital Xanit International. Allergy department., Malaga, Spain;* [2]*R&D Specialist Research & Development Allergy & Immunology Unit LETI Pharma, S.L.U., Madrid, Spain;* [3]*Vithas Hospital Xanit International. Allergy department., Málaga, Spain;* [4]*Hospital General de Ciudad Real. Emergency department., Ciudad Real, Spain;* [5]*Hospital General de Ciudad Real. Allergy department, Ciudad Real, Spain*

Background: Flaxseed allergy is a rare pathology, which has resulted in cases of anaphylaxis due to its ingestion and, less frequently, rhinoconjunctivitis and asthma due to inhaled exposure.

Method: A 51-year-old male showed symptoms consisting of conjunctival hyperemia, eyelid angioedema, nasal pruritus and sneezing. These symptoms were intensified during the cleaning of his 2 goldfinches birds.

He reported oral pruritus with almonds, hazelnuts and sunflower seeds and tolerance to the ingestion of nuts, peanuts, egg, wheat and barley.

Skin prick tests (SPT) and specific IgE are performed with common aeroallergens, nuts, feathers, feed components; ALEX Microarray and Immunoblotting against flaxseed and oat extract.

Results: SPT with environmental aeroallergens and sunflower seed, hazelnut, almond, walnut, peanut, profilin, LTP: positive for sunflower seed: 8x8mm and hazelnut: 4x4mm.

Prick-prick with mixture of feathers, feed components (canary seed, rapeseed, linseed, corticated oats, safflower seed, nigel seed, wheat flour, yeast): positive for linseed: 15x15mm and oats: 6x6mm.

Total IgE: 161 IU/mL; specific IgE: almond 0.88 KU/L, hazelnut 1.38 kU/L, sunflower seed 6.41 KU/L, sesame seed 1.68 kU/L, oat 0.55 kU/L. Negative for Lolium perenne, Phleum pratense, Cora8, peanut, wheat, canary and parakeet feathers.

Microarray ALEX: highlights sensitization to storage proteins.

Immunoblotting to feather, excrement, seed extracts: bands of 10 kDa (2s albumin) and 54 kDa (malate dehydrogenase MDH-1) recognized in the flaxseed extract and 35 and 58 kDa in the oat extract.

Conclusion: We present a patient with respiratory tract symptoms related to his bird exposure and oral allergy syndrome after ingestion of some nuts.

This study evidences IgE-mediated allergy to flaxseed (contained in bird feed). This sensitization may probably occur via the respiratory route, through inhalation of the flax contained in the feed.

Sensitization to globulins is also detected, with an intense band in flax at 10kDA (probably 2S albumin) and another at 54 kDa, (MDH-1). No sensitization to feathers or bird serum products is detected.

Allergy to storage proteins, present in legumes, nuts and other seeds, could justify the oral pruritus symptoms.

It is recommended in patient with regular bird exposure and symptoms, not to consider only the feathers allergy, but also to analysis the products used in the bird diet.

1285 | Allergenic potency of α-gal containing food extracts in patients with α-gal syndrome

Perusko M.[1,2]; Apostolovic D.[1]; Kiewiet G.[1]; Grundstrom J.[1]; Hamsten C.[1]; Starkhammar M.[3]; Van Hage M.[1]

[1]*Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden;* [2]*Innovative Centre Faculty of Chemistry, Belgrade, Serbia;* [3]*Department of Internal Medicine, Södersjukhuset, Stockholm, Sweden*

Background: Patients with the novel food allergy galactose-α-1,3-galactose (α-Gal)-syndrome (AGS) experience delayed severe allergic reactions after ingestion of α-Gal-containing foods due to IgE antibodies against α-Gal. Some patients tolerate larger amounts of α-Gal, while others react to minute quantities. Here we investigated the allergenic potency of several α-Gal-containing foods.

Method: Sera from 10 AGS patients (median IgE level to α-Gal 41 kU_A/L, range 17 – 100 kU_A/L) were included. Aqueous extracts from lean meat (beef, pork, moose), innards (beef liver, pork kidney) meat products (bacon, chorizo, liver pâté, black pudding) and milk were prepared. Protein concentration was determined by BCA assay. Food extracts were assayed in immunoblot using a serum pool (n = 10 AGS patients) and anti-α-Gal antibody. IgE binding was determined by ELISA. The potency of the food extracts was assessed in inhibition ELISA using the serum pool and four individual AGS sera.

Results: Innards demonstrated the highest protein concentration (~95 mg protein/g food). Lean meat and bacon showed moderate (~28 mg protein/g food) and other meat products low concentration (~5 mg protein/g food). Multiple protein bands were recognized by patients' IgE and an anti-α-Gal antibody in all extracts, apart from black pudding and liver pâté which showed only a few positive bands. The strongest IgE bindings was noted to pork kidney extract (median 0.931, measured as OD values), followed by bacon (median 0.383) and chorizo (median 0.273). Among lean meats, IgE binding to moose (median 0.247) and beef (median 0.109) was moderate, but the binding to pork was even lower (median 0.045). IgE binding to black pudding (median 0.027) and milk (median 0.005) was the weakest. With the regards to biological relevance, all food extracts inhibited α-Gal specific IgE binding. Pork kidney was the most potent inhibitor (IC_{50} range 0.05 – 2 μg/mL). The second most potent inhibitor was bacon (IC_{50} range 2 – 29 μg/mL) followed by lean meats, chorizo and beef liver. Among lean meats, beef was the most potent inhibitor (IC_{50} range 4 – 53 μg/mL) and pork the least potent (IC_{50} range 7 – 129

µg/mL). Liver pâté and black pudding were weak, while milk was the weakest inhibitor. Intraindividual differences were noted.

Conclusion: This study demonstrates that pork kidney is the most potent allergenic meat for AGS patients. Interestingly, bacon possess a higher risk compared to lean meats and chorizo. Milk shows the lowest allergenic potency.

997 | Hypersensitivity systemic reaction to date (phoenix dactylifera)

Dotor-Lavado M.[1], García-Menaya J. M.[1], Fernández-Bolivar A. A.[1], Cordobés-Durán C.[2], Bobadilla-González P.[1]

[1]*Allergy Department, Badajoz University Hospital, Badajoz, Spain;* [2]*Allergy Unit, Don Benito Hospital, Badajoz, Spain*

Case Report

Background: The date is the fruit of the date palm (Phoenix dactylifera), which belongs to Aracaceae family and is distributed throughout the Middle East, Mediterranean countries, central Africa, western Asia, Australia, and North America. They are a staple food in the Middle East and are also consumed throughout the world as part of some cereals and sweets. Although dates are not generally recognized as allergens, date pollen can cause severe rhinitis and itchy mouth, and cases of hives, angioedema, and anaphylaxis have occurred after consumption of dates.

Case report: A 38-year-old man with a history of non-allergenic rhinitis and asthma, presented facial erythema, generalized heat, epigastric burning, palpebral and labial angioedema and nasal obstruction 15 minutes after ingesting some dates. He had eaten them with good tolerance beforehand. In the emergency room he was treated with intramuscular methylprednisolone 125 mg and dexchlorpheniramine 5 mg with a rapid improvement of symptoms. With a detailed anamnesis, simultaneous use of other food or drugs as well as the presence of possible cofactors were excluded.

Methods and results: Skin prick tests were performed with common inhalant allergens (mites, pollens, molds, and epithelia), food allergens (egg, milk, cereals, fish, seafood, meat, nuts, fruits, and vegetables), latex, anisakis, profilin and LTP with negative results. A skin prick-prick test with fresh date was performed with a positive result. Total IgE, specific IgE to date and Anisakis and Ascaris, complete blood count, biochemistry, TSH, C3 and C4 and basal tryptase were determined. Total IgE resulted elevated (164 IU/ml) and specific IgE to date was positive (1.91 kU/L). The rest of the parameters were normal or negative.

Conclusions: We report a case of a food IgE-mediated immediate hypersensitivity systemic reaction to date fruit demonstrated by a positive specific IgE and prick-prick to date. This is an infrequent food allergy, with very few cases published according to bibliographic searches, despite the wide worldwide distribution and consumption of this fruit in many countries.

1272 | Allergy to coconut and its relationship with coconut oil and coconut water

Pitchon A.[1]; Pitchon R.[2]

[1]*Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo, Brazil;* [2]*Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte, Brazil*

Introduction: The coconut (Cocos nucifera) is a fruit, not a nut, that belongs to the family of plants Aracaceae (palm trees). Allergy to coconut is uncommon and it is important to evaluate in these cases reaction to oil and coconut water, with the aim of expanding or restricting the exclusion diet.

Case description: Two children with a history of anaphylaxis triggered up to five minutes after eating coconut. The first, a girl of one year and three months old, presented the skin test for coconut with a maximum diameter of 8 mm and negative results for coconut oil and coconut water, histamine 6 mm and control test negative. The dosage or IgE specific for coconut was 4.5 KU/l.

The second case refers to a boy of one year and nine months old, who presented the skin test for coconut with a maximum diameter of 6 mm, negative results for coconut oil and coconut water, histamine 7 mm and control test negative. The dosage specific IgE to coconut was 5.3 KU/l.

Discussion: Coconut allergens were identified as Coc n2 (a 7S globulin) and Coc n4 (a 11S globulin). The interesting point in these cases is that they described the lack of reaction to coconut oil and water, in contrast to the anaphylaxis triggered by eating the fruit. The oral food challenge (OFC) was performed for coconut oil and the two children had good tolerance to their intake. Regarding coconut water, we opted not to perform the OFC due the presence of pieces of fruit in it.

Conclusion: Coconut allergy is uncommon and the presence of a reaction to fruit may not be observed after ingesting coconut oil and water. The OFC performed in an environment prepared to treat anaphylaxis helps to clarify the diagnosis and improve the assertiveness of dietary guidance.

Keywords: Coconut allergy, Coconut oil allergy, Coconut water allergy, Anaphylaxis, Oral challenge test

1331 | Profile of positive specific IgE to food allergens in adult and children tested for food allergy at alrayan laboratory between 2018-2020

Abdelhalim A. T.[1]; Mohammed O. A.[2]; Jadalrab M. O.[1]

[1]*Clinical Immunology Specialty Council, Khartoum, Sudan;* [2]*Faculty of Medicine Omdurman Islamic University. Omdurman, Sudan, Khartoum, Sudan*

Background: Food Allergy is a widespread term for any unpleasant reaction to the ingestion of a food. Serious allergic reaction could follow the food ingestion which is rapid in onset and may cause death that called an Anaphylaxis. Food allergies are broadly categorized

into either immunoglobulin E (IgE)-mediated or non-IgE-mediated processes. IgE related food allergic reactions are rapid in onset, typically beginning within minutes to two hours from the time of ingestion.In children, the most type of food that trigger allergic reactions include egg, cow's milk, peanut, tree nuts, soy, and wheat. Moreover, for adults the most common types of foods are; fish and shellfish in addition to peanut and tree nuts.There is a general perception of poor knowledge about food allergy in Sudan. However, nothing is known about the prevalence and common food allergens in Sudan.

Method: A descriptive cross-sectional study. Conducted in Al-Rayan Laboratory which is located in Khartoum state, The study was conducted in the period from January 2018-December 2020 . The food allergens detection was compared according to gender and age (the cut point of age is 18 years old). The positivity of the result depends on the antibody detection and titter. *p* value of 0.05 or less is considered statistically significant. Data were analysed using SPSS version 26.0

Results: The total study population was 106 food allergy panel. Results of food antigens were collected from Alrayan Laboratory center at Khartoum locality, 67 patients were children (63.2%) and 39 were adults (36. 8%).52 of the participants (49.1%) are females, and the other 54 are males (50. 9%).

The Food panel contains about 20 allergens, participants sensitization are shown in table (1)

The food Allergens degrees of the participants are shown in table (2)

Each food allergens compared with gender and the result shown in table (3).

The effect of participant's Age on food allergy test shown in table (4)

Conclusion: Food allergens detection can be useful to inform decisions such as to avoid food contains such related harmful antigen which would potentially benefit rather than interfere with medicine. The main demographic features that highly affects risk of getting sensitization for certain food substances are, age more than the gender.

The main food allergen that results in higher distribution among our study population are, Nuts, Peanut, and Orang.

The main food allergens that predicts sensitization in female more than male is a nuts .

TABLE 1 Distribution of food allergens among the population (*n* = 106)

Antigen	Frequencyfood allergensamong population
Nut mix2	(71) 67%
Tomato	(60) 56%
Peanut	(53) 50%
Orange	(52) 49.1%
Strawberry	(52) 49.1%
Wheat flour	(47) 44.3%
Carrot	(45) 42.5%
soybean	(43) 40.6%
Onion	(37) 34.9%
Mango	(32) 30.2%
Banana	(30) 28.3%
Egg white	(27) 25.5%
Cow's Milk	(26) 24.5%
Mutton/lamb	(24) 22.6%
Shrimp	(15) 14.2%
Egg Yolk	(11) 10.4%
chocolate	(8) 8.4%
Chicken	(6) 5.7%
Codfish	(6) 5.7%
Baker yeast	(6) 5.7%

TABLE 2 Distribution of specific IgE scorefor different food allergens (*n*=106)

Food Allergens	0	1	2	3	4	5
Egg white	-	1.9%	7.5%	2.8%	9.4%	3.8%
Egg yolk	-	-	4.7%	2.8%	1.9%	0.9%
Cow's milk	-	0.9%	2.8%	8.5%	5.7%	6.6%
chocolate	-	0.9%	2.8%	2.8%	1.9%	-
Wheat flour	-	10.4%	12.3%	17.0%	4.7%	0.9%
soybean	-	14.2%	12.3%	4.7%	7.5%	0.9%
Baker's yeast	-	12.2%	14.2%	4.7%	7.5%	0.9%
Nut mix		3.8%	16.0%	18.9%	16.0%	12.3%
peanut	-	13.2%	9.4%	13.2%	9.4%	3.8%
orange	-	6.6%	17.9%	14.2%	8.5%	8.5%
Strawberry	-	8.5%	16.0%	12.3%	10.4%	1.9%

Food Allergens	0	1	2	3	4	5
Banana	-	9.4%	16.0%	1.9%	0.9%	-
Mango	-	12.3%	13.2%	3.8%	0.9%	-
Tomato	-	8.5%	19.8%	9.4%	4.7%	0.9%
Carrot	-	9.4%	19.8%	8.5%	3.8%	0.9%
Onion	-	4.7%	25.5%	3.8%	0.9%	-
Mutton	-	2.8%	2.8%	5.7%	4.7%	5.7%
shrimp	-	1.9%	0.9%	2.8%	1.9%	5.7%

Table 3 The effect of participant's gender on food allergy test (n = 106)

Food allergens	Female	Male	p value
Egg yolk	(3) 5.8%	(8) 14.8%	0.127
Cow's milk	(12) 23.1%	(14) 25.9%	0.733
chocolate	(4) 7.7%	(5) 9.3%	0.772
Wheat flour	(23) 44.2%	(24) 44.4%	0.987
soybean	(23) 44.2%	(20) 37%	0.451
Baker's yeast	(2) 3.8 %	(0) 0%	0.146
Nut mix	(30) 57.7%	(41) 75.9%	0.046
peanut	(23) 44.2%	(30) 55.6%	0.244
orange	(26) 50%	(26) 48.1%	0.849
Strawberry	(23) 44.2%	(29) 53.7%	0.119
Banana	(15) 28.8%	(15) 27.8 %	0.90
Mango	(15) 28.8%	(17) 31.5%	0.768
Tomato	(22) 42.3%	(24) 44.4%	0.824
Carrot	(24) 46.2%	(21) 38.9%	0.449
Onion	(17) 32.7%	(20) 37.0%	0.639
Mutton	(13) 25%	(11) 20.4%	0.569
codfish	(3) 5,8%	(3) 5.6%	0.118
chicken	(2) 3.8%	(4) 7.4%	0.962
shrimp	(7)13.5%%	(8) 14.8%	0.842

TABLE 4 The effect of participant's Age on food allergy test (n = 106)

Food allergens	Adult	Children	p value
Egg yolk	0%	(11) 16.4%	0.008
Cow's milk	(1)2.6%	(25) 37.3%	0.0001
chocolate	0%	(9) 13.4%	0.017
Wheat flour	(16) 41.0%	(31) 46.3%	0.60
soybean	(15) 38.5%	(28) 41.8%	0.736
Baker's yeast	(1) 2.6%	(1) 1.5%	0.696
Nut mix	(24) 61.5%	(47) 70.1%	0.363
peanut	(18) 46.2%	(35) 52.2%	0.546
orange	(25) 64.1%	(27) 40.3%	0.018
Strawberry	(23) 59.0%	(29) 43.3%	0.119
Banana	(13) 33.3	(17) 25.4%	0.380
Mango	(12) 30.8%	(20) 29.9%	0.921
Tomato	(19) 48.7%	(27) 40.3%	0.399
Carrot	(21) 53.8%	(24) 35.8%	0.07
Onion	(18) 46.2%	(19) 28.4%	0.07
Mutton	(4) 10.3%	(20) 29.9%	0.02
codfish	(4)10.3%	(2) 3%	0.118
chicken	(1) 2.6%	(5)7.5%	0.33
shrimp	(9) 23.1%	(6) 9%	0.44

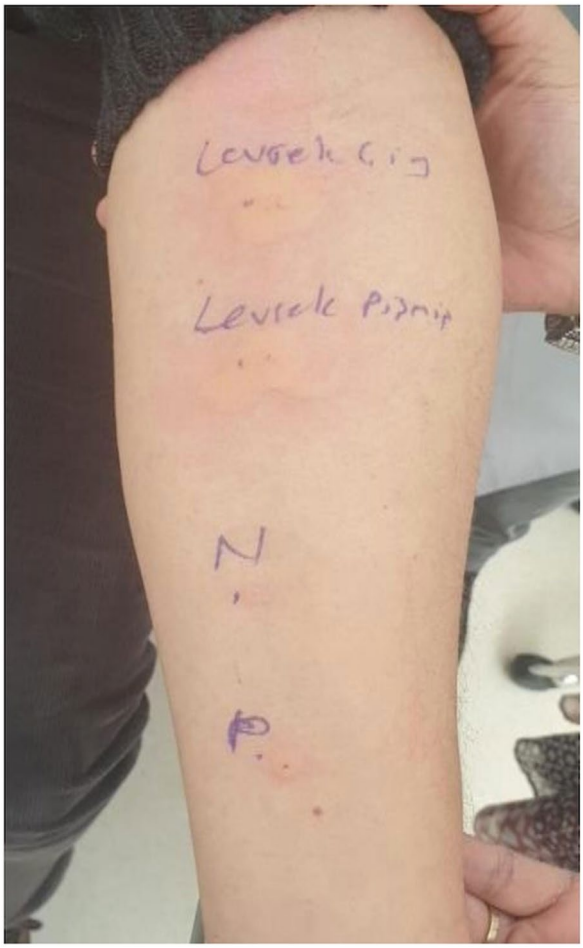
1078 | A rare case of a rare case of anaphylaxis after skin prick test with fish

Atik Ö.; Akyildiz A. B.; Tepetam F. M.

Health Sciences University Süreyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Immunology and Allergy, Istanbul, Turkey

Introduction: The skin prick test is a safe method that is frequently used in the diagnosis of IgE-mediated food, venom, drug and aeroallergen allergies. Although the risk of developing a systemic reaction after a skin prick test is very low, when it occurs it can be life threatening

Case: A 30-year-old male patient was admitted to our outpatient clinic with swelling of the lips after eating fish. In addition, the patient, who works as a waiter, had complaints of rash and swelling in the body after contact with fish products. The patient did not describe any symptoms suggesting a systemic allergic reaction after fish consumption or contact. Since RAST (Radioallergosorbent Test)



is not available to evaluate fish allergy in our hospital, a prick-to-prick test with raw and cooked fish was planned. The patient had history of allergic reaction after consumption of sea bass, so we planned a prick-to-prick test with raw and cooked sea bass. Within 5 minutes following the test, 30-50mm of induration and erythema appeared in the area where both solutions were applied. (Figure.1) In the following two minutes, while the patient complained of numbness in the lips, difficulty in swallowing, and shortness of breath, rash and swelling were observed throughout the body. Physical examination revealed bilateral rhonchi and uvula edema. The present condition was evaluated as anaphylaxis and 0.5 ml of adrenaline was administered intramuscularly.

Discussion: Commercial food allergen extracts or fresh food can be used during the test. Our patient had a history of hyperemic rash after contact with fish only twice. Although there were no risk factors, generalized urticarial rash, respiratory distress and difficulty swallowing developed within 5 minutes following the prick-to-prick test. Sometimes commercial extracts of specific food allergens may not be available in the market and fresh foods may have to be used. Some studies have found that prick-to-prick testing with fresh food is riskier than with commercial nutrient extracts. Despite it is rare, severe allergic reaction or anaphylaxis can be seen with the skin prick test. This case indicates that patients should be observed for an appropriate period of time. It would be better to use commercial allergen extracts. Finally, the physician should be aware of adverse reactions, especially systemic reactions, and should be trained and equipped to treat these reactions.

1193 | Cow's milk allergy in the exclusively breastfed infant - when maternal elimination diet is not enough

Freitas C.; Castro C.; Oliveira G.
Hospital Pedro Hispano - ULSM, Porto, Portugal

Introduction: Cow's milk allergy (CMA) is the most common food allergy in young children, but seldom occurs in exclusively breastfed children. The first line of treatment in these suspicious cases is maternal elimination diet, avoiding food containing cow's milk protein, however, in rare cases this attitude may not be sufficient. We describe two cases of exclusively breastfed children in which an elimination diet was not enough to resolve the allergic symptoms.

Case Report: Case 1: Male infant, exclusively breastfed since birth. At 8 weeks of age he started to have eczema and bloody stools, so the mother was instructed to avoid cow's milk proteins, with no improvement in his condition after 2 weeks. He started an amino acid formula and maintained it for 15 days, with complete resolution of gastrointestinal symptoms and improvement of his dermatitis. After this elimination trial period, he restarted breastfeeding, with maternal avoidance of cow's milk and egg intake, with recurrence of the bloody stools and eczema. We decided to reintroduce the aminoacid formula, and once again there was a complete disappearance of the symptoms.

Case 2: Female infant, exclusively breastfed. At 4 months of age, the baby presented to the emergency department with generalized urticaria rash, associated with mucus feces. Specific IgE and skin prick test to cow's milk, egg and nuts were negative. The mother was instructed to avoid cow's milk, egg and nuts intake, but due to the lack of improvement on the child's condition after two weeks, and the mother's difficulty in maintaining the diet, the baby tried an extensively hydrolyzed formula, without complete disappearance of the urticarial lesions. She was admitted for surveillance and during the first days of hospitalization she maintained the urticaria lesions. It was decided to start an aminoacid formula, with complete disappearance of the lesions after 24h.

Discussion: The currently recommended treatment for an exclusively breastfed infant with a CMA suspicion is maternal elimination diet of cow's milk proteins. However, these two cases show that sometimes this is not enough. The choice of a rigorous maternal elimination diet with the exclusion of several allergens or the introduction of amino acid formula milk should be considered.

1119 | Mouse models of atopic dermatitis and food allergy: does the strain matter?

Svabova T.[1]; Jiraskova-Zakostelska Z.[2]; Thon T.[2]; Schwarzer M.[1]; Srutkova D.[1]

[1]*Laboratory of Gnotobiology, Institute of Microbiology, Academy of Sciences of the Czech Republic, v.v.i., Czech Republic, Nový Hrádek, Czech Republic;* [2]*Laboratory of Cellular and Molecular Immunology Institute of Microbiology ASCR, v.v.i., Prague, Czech Republic*

Background: Atopic dermatitis (AD), one of the most common skin disorders seen in infants and children, has its onset during the first year of life in 20% of children in industrialized countries. Genetic predisposition and environmental factors, such as cutaneous and intestinal microbial dysbiosis, contribute to its development. AD is very often accompanied by the subsequent development of food allergy (FA) due to epicutaneous sensitization (EC) by food allergens. The commonly used mouse experimental model of EC sensitization followed by oral ovalbumin challenge can have different manifestations in different strains. We aimed to assess variation between two common mouse strains: BALB/c and C57BL/6.

Method: Altogether, 11 female C57BL/6 mice and 11 female BALB/c mice were divided into 4 groups. Each mouse had a total of three one-week exposures to ovalbumin (OVA, 2mg/ml) or PBS applied as a patch to tape stripped skin, separated by two-week rest intervals. Then the mice were orally gavaged three times a week for 2 weeks with 50 mg OVA (in 200 µl PBS). One hour after the last gavage, drop in body temperature and occurrence of diarrhea was assessed and after mice scarification samples were collected. The specific OVA antibody responses were measured in sera by ELISA or by rat basophile leukemia cell-based assay. The levels of cytokine (IL-4, IL-5, IL-10, IL-13 and INF-gamma) were measured in OVA stimulated spleen cell supernatants by ELISA after 72 hours of cultivation. Histopathological changes in skin and jejunum were evaluated.

Results: Epicutaneous sensitization and oral challenge of BALB/c mice with ovalbumin led to higher occurrence of diarrhea and anaphylactic hypothermia, common symptoms of FA, and increased levels of OVA-specific IgE in serum compared to C57BL/6 mice. Moreover, we have determined the small histopathological changes only in the skin of OVA sensitized and challenged BALB/c mice compared to PBS controls, accompanied by elevated number of mast cells in their skin.

Conclusion: We observed strain-dependent differences in mouse model of EC sensitization and FA, with more pronounced OVA sensitization and food allergy manifestation in BALB/c mouse strain.

Supported by Czech Health Research Council (NU20-05-00038) and EMBO installation grant (M. Schwarzer).

979 | Clinical features of patients with hereditary angioedema with a mutation in the plasminogen gene

Manto I.[1]; Latysheva E.[1]; Bliznetz E.[2]; Timoshenko D.[3]; Aleshina L.[4]; Bocherova Y.[5]; Gilvanova E.[6,7,8]; Kameneva G.[9]; Platonova M.[10]; Fedorova V.[11]; Polyakov A.[2]; Latysheva T.[1]

[1]*NRC Institute of Immunology FMBA of Russia, Moscow, Russia;* [2]*Federal State Budgetary Institution, Research Centre for Medical Genetics, Moscow, Russia;* [3]*Pirogov Russian National Research Medical University (Pirogov Medical University), Moscow, Russia;* [4]*State Budget Educational Institution of Higher Professional Education "Saratov State Medical University named by Razumovsky" of Minzdrav of Russia, Saratov, Russia;* [5]*SBUZ "TOKB im. V.D. Babenko", Tambov, Russia;* [6]*Bashkir State Medical University, Ufa, Russia;* [7]*Bashkir State University, Ufa, Russia;* [8]*State Medical Institution of the Republic of Bashkortostan City Hospital 2 Sterlitamak, Sterlitamak, Russia;* [9]*?rkhangelsk Regional Clinical Hospital, Arkhangelsk, Russia;* [10]*Laboratory MedLab, Saint Petersburg, Russia;* [11]*Chief freelance specialist of The Ministry of Health of Tula oblast, Tula, Russia*

Background: Recently, a new type of hereditary angioedema (HAE) without C1 inhibitor deficiency have been identified: HAE with a mutation in the plasminogen gene (HAE-PLG). Nowadays, only 146 patients from 33 families with HAE-PLG were reported. There is a truly little experience in diagnosis and follow up of such patients. An observational descriptive retrospective study of Russian patients with HAE-PLG was carried out.

Method: 14 patients from 10 unrelated families with HAE-PLG were enrolled in the study. All enrolled patients had the missense mutation c.988A>G (p.Lys330Glu;K330E) in the *PLG* gene and HAE clinical symptoms. 1 patient (7%) was a man and 13 patients (93%) were women. Patients' mean age was 51.64 ± 13.55 years (range: 29 to 71).

Results: The mean age of clinical onset was 25.07 ± 10.46 years (range: 12 to 45). Facial swelling was the starting symptom for 79% of patients. 100% of participants had a history of at least one episode of facial angioedema (AE), 86% experienced tongue swellings, 79% - laryngeal attacks, 29% - abdominal attacks, 21% - peripheral AE. A relative died from larynx or tongue AE in 40% of families (4/10). 14% patients underwent unnecessary surgery, 7% – tracheostomy. Icatibant was used in 5 patients, 80% of patients (4/5) reported reducing the severity and shortening the duration of 28/29 attacks in total. The non-responder patient had only 1 treated attack with complete resolution within 36 hours without any other treatment. On average, administration of Icatibant shortened the duration of attacks by 71%. C1 inhibitor concentrate wasn't used by any patient. 6/14 patients didn't need long-term prophylaxis due to low frequency of attacks. 8/14 patients need a long-term prophylaxis, but only 4/14 patients received 1-3 g tranexamic acid for 6-24 months. 75% (3/4) of patients reported reducing the frequency of attacks. The mean attack reduction was 73%.

Conclusion: Patients with HAE-PLG are characterized by later onset of clinical symptoms, a higher facial and tongue swellings frequency and a lower abdominal attacks and swellings of extremities frequency than previously described for patients with C1 inhibitor deficiency. Icatibant appeared to be effective in patients with HAE-PLG. Tranexamic acid seems to be effective in most patients. The described clinical features of the HAE-PLG subtype must be taken into consideration in clinical practice in order to ensure timely diagnosis of patients with a potentially life-threatening disease.

1033 | Autoimmunity and inflammation in patients with PID

Kose H.; Cekic S.; Kilic S. S.
Uludag University, Bursa, Turkey

Background: Autoimmunity and inflammation have emerged as the major clinical symptoms affecting patients with PID due to defective immune response and immune dysregulation.
Method: Thirty-one patients with PID associated with autoimmune or autoinflammatory manifestations were included in the study. The data were screened from the medical electronic files of the patients, retrospectively.
Results: The female/male ratio was 15/16, the median age of patients was 18 years (minimum=4, maximum= 59 years) and the median age of PID diagnosis was 6 years (minimum =0.5, maximum 51= years). CVID and DGS were the most common PID subtypes caused by autoimmune disorders in our study (*n* = 10, 32.2 %, *n* = 9. %29), respectively (Table 1). Hashimoto thyroiditis and immune thrombocytopenic purpura were the most common autoimmune diseases in our patients (*n* =11, 35.5%, *n* = 4, 12.9%). Autoimmune and /or autoinflammatory diseases; and autoantibodies were shown in table 2. The most common concomitant disease was chronic lung disease (*n* = 13, 41.9%).
Conclusion: Autoimmunity is generally associated with dysfunction of the adaptive arm of the immune system. Although classical immunodeficiencies are mainly characterized by infectious conditions, autoimmune and autoinflammatory disorders may coexist with PID. Primary immunodeficiency patients should also be evaluated and screened for autoimmune and inflammatory manifestations.

TABLE 1 The distribution of primary immunodeficiencies in our patients

Disease	*n*	%
XLA	2	6.4
C1q deficiency	1	3.2
CID	1	3.2
CVID	10	32.2
DGS	9	29
Good Syndrome	2	6.4
HIES	2	6.4
HIM	1	3.2
MHC Class 2 Deficiency	1	3,2
Ig Subgroup Deficiency	1	3.2
WAS	1	3.2

TABLE 2 Autoimmune and autoinflammatory diseases and autoantibodies of the patients.

	n	%
Autoimmune and autoinflammatory diseases of patients with PID		
Hashimoto thyroiditis	11	35.5
Graves	2	6.4
Vitiligo	1	3.2
Systemic lupus erythematosus	1	3.2
Crohn Disease	2	6.4
Oligoarticular JIA	2	6.4
Behcet's Disease	1	3.2
Psoriasis	1	3.2
Systemic JIA	1	3.2
Morphea	2	6.4
Celiac disease	1	3.2
Sjogren disease	1	3.2
Autoimmune adrenalitis	1	3.2
Immune thrombocytopenic purpura	4	12.9
Autoimmune hemolytic anemia	1	3.2
FMF	1	3.2
Graves disease	2	6.4
Autoantibodies		
Anti- Thyroid Peroxidase Antibody	18	58
Anti- Nuclear Antibody	6	19.3
Direct Coombs	2	6.4
Anti Ro- 52	4	12.9
Anti- Thrombocyte Antibody	1	3.2
Anti-Gliadin Antibody	1	3.2
Anti-Parietal Cell Antibody	1	3.2
Anti -Thyroglobuline Antibody	11	35.4

1301 | Very early onset inflammatory bowel disease (VEO-IBD) genetic profile in a brazilian referral cente

Verzignassi-Fiorotte V.; Sá M.G. V.; Brito De Carvalho C.B.C.; Sobrinho A. S.O.; Oliveira B. R.; Guimarães R. R.L.; Machado L.M. O.; Cândida Rizzo M.C.R.; Aranda C.S.; Solé D.
Federal University of São Paulo - UNIFESP, São Paulo, Brazil

Background: VEO-IBD encompasses a group of diseases affecting children before six years with chronic diarrhea. Monogenic defects found in some of these patients play a special role in the management of VEO-IBD. The aim of this study was to evaluate clinical and genetic characteristics of the patients monitored at our center.
Method: A retrospective review of the electronic medical charts of VEO-IBD patients was carried out following the protocols of the Immunology service of UNIFESP (Federal University of São Paulo), between 2016-2021.
Results: A total of 26 VEO-IBD patients were enrolled, being 15 (57,7%) male. The age of the onset symptoms ranged from one to 60 months (median 7,5 months) and the median of the treatment start-up was 24 months (2 months to 12 years old). Five patients

(19,2%) evolved to surgical approach as ostomies. Half of the patients (*n* = 13) performed genetic tests (exoma), which helped the final diagnosis: IL-10 receptor deficiency in 3 patients (25%); MHC-II deficiency (*RFXANK* mutation) in 2 patients (16,7%); XIAP deficiency (*XLP2* mutation) in 2 patients (16,7%), two (16,7%) SCID patients (*JAK3* mutation/ no variants found); APDS2 (*PIK3R1* mutation) in one patient and finally, TACI deficiency (*TNFRSF13B* mutation) in one patient. Nine (34,6%) children were referenced to Hematopoietic Stem Cell Transplantation (HSCT); two (7,9%) were successfully transplanted, seven (26,9%) are awaiting transplant, and one (3,9%) evolved to death before HSCT.

Conclusion: The VEO-IBD entity is relatively new in the practice of pediatricians and should be regarded as a differential diagnosis of all chronic diarrhea, especially those who do not respond to the withdrawal of trigger foods (as in food allergies) or to immunosuppressive treatments. The technological advances generate a change in the IBD paradigm as provide new lines of treatment and cure for these patients.

1303 | Clinical profile of patients with inborn errors of immunity (IEI) and hematopoietic stem cell transplantation (HSCT)

Said L. S.; Aranda C. S.; Guimarães R. R.L.; Verzignassi-Fiorotte V.; Sá M.G. V.; Medeiros L. C.M.; Machado A. M.; Schmid L. S.; Cândida Rizzo M.C. R.; Solé D.

UNIFESP, São Paulo, Brazil

Background: Inborn Errors of Immunity (IEI) are a heterogeneous group of rare, which involves susceptibility to infections, autoimmunity, inflammation and increased risk of malignancy. Hematopoietic stem cell transplantation (HSCT) has become a successful option in the treatment of some of these diseases in recent decades. The aim of the study was to analyze the clinical profile of patients with IEI referred for HSCT referral center.

Method: Cross-sectional, retrospective study with analysis of electronic medical records of patients seen at a referral center for IEI in Brazil over the past two years.

Results: A total of 16 patients (56% male) were referred for HSCT according to diagnoses: Five Severe combined immunodeficiency's (SCID), Four *Leaky* SCID (two MHC II deficiency), two Wiskott-Aldrich, one IL10 receptor deficiency, two chronic granulomatous diseases, one type 2 lymph proliferative disease (XLP2/XIAP) and one hyper-IGM with refractory neutropenia. The mean age (MA) at diagnosis was 1.7 years and the HSCT referral MA was 5.1 years. Severe malnutrition was found in 75% of patients and 50% had some serious infection (mainly disseminated tuberculosis and cytomegalovirus). Of the 5 children with SCID, 4 evolved with disseminated tuberculosis secondary to BCG vaccination, 1 died before transplantation due to infectious complications, 3 have already been successfully transplanted (SCID transplant MA: 9 months) and one is waiting for that. For the other patients, one died in conditioning and other ten are awaiting yet. Four have fully matched donor and the others present haploidentical donor and are registered in bank to compatible marrow.

Conclusion: In recent years, there has been an increase in the number of patients with IEI with indications for HSCT in our service due to improved availability of biochemistry, flow cytometry molecular diagnosis and neonatal screening. However, we still have a significant delay in the patient's arrival at the referral center, which contributes to the impairment of nutritional status and the development of serious infections that influence the success of the transplant.

1317 | Severe combined immunodeficiency (SCID) due to homozygous rag1 mutation: A case with omenn syndrome and langerhans cell histiocytosis (LHH)

Yilmaz Topal O.[1]; Butun Turk S.[2]; Duksal F.[3]; Karakus E.[4]; Metin A.[5]

[1]*Ankara City Hospital, Division of Pediatric Allergy and Immunology, Ankara, Turkey;* [2]*Ankara City Hospital, Department of Pediatrics, Ankara, Turkey;* [3]*Konya Training and Research Hospital, Division of Pediatric Allergy and Immunology, Konya, Turkey;* [4]*Ankara City Hospital, Department of Pathology, Ankara, Turkey;* [5]*University of Health Sciences, Ankara City Hospital, Division of Pediatric Allergy and Immunology, Ankara, Turkey*

Introduction: Omenn syndrome (OS) is a rare combined immunodeficiency characterized by erythroderma, lymphadenopathy, and autoimmune manifestations. Most cases are due to mutations in the RAG genes. We report a case with coexistence of Omenn Syndrome and LHH.

Case: 11-month-old male patient was born from consanguineous marriage. He was hospitalized with dehydration, malnutrition due to chronic bloody diarrhea; hepatomegaly; generalized lymphadenopathy; furuncles on the back, arms, legs and diaper region; ichthyosis-like dryness and desquamation on the hyperemic background and sepsis at 7 month-old. Hemoglobin 5.7 g/dl, Platelet: 95000, absolute lymphocyte count: 920/mm^3, no atypic cell on peripheral smear, IgG 393, IgM 30, IgA 176 mg/dl (IgA is normal, IgG and IgM borderline low) on the laboratory parameters. TORCH, EBV, Parvovirus PCR had been found negative. In the follow-up CT scan performed because of focal seizure and a right frontoparietal subacute-chronic hematoma was observed. Antibiotic and antifungal treatments were given due to infiltration in the chest radiography, pseudomonas growth in cerebrospinal fluid culture, and candida growth in blood culture. In skin and lymph node biopsies taken due to lytic lesions on skull radiography;histochemically typical CD1A, S100 and Langerin, CD68 and CD163 positive dense histiocytic aggregates and many eosinophils, which disrupted the normal lymph node structure and diffuse spread in the paracortical area, were interpreted in favor of LHH. The patient was diagnosed as T-B-NK + SCID with lymphocyte subset analysis with flow cytometry (CD3+ T cell: 166, CD4 + T cell: 66, CD8 + T cell: 100, NK cell: 635, CD19 + B cell: 46, CD3+HLA DR+: 80%, CD4+CD31+CD45RA+: 13%) .RAG1 NM_000448, c.2327G> A, p.R776Q homozygous mutation was detected by next

generation sequencing. Skin, lymphadenopathy and bone marrow biopsies of the patient were reviewed pathologically in terms of differential diagnosis and the similarity of Letterer-Siwe and Omenn Send in the literature. Short-term chemotherapy followed by bone marrow transplantation was planned for the case in the followed up with oncology department.

Conclusion: The case shows that LHH of unknown etiology may also develop in Omenn syndrome due to RAG1 deficiency for an unknown reason.

1252 | Living with HAE in Australia – the effect of prophylaxis on attack rate

Katelaris C. H.[1,2]; Tognarini D.[3]; Burton P.[4]; Perram F.[4]; Youssef S.[3]; Fenton K.[3]; Button P. B.[5]; Mccloud P. I.[5]

[1]Campbelltown Hospital, Campbelltown, Australia; [2]Western Sydney University, Sydney, Australia; [3]Aesir Health, Melbourne, Australia; [4]Campbelltown Hospital, Sydney, Australia; [5]McCloud Consulting Group, Sydney, Australia

Background: HAE patients in Australia have access to effective on demand therapy. Whilst several prophylactic therapy options are available, the more modern, effective ones are heavily restricted.

In this non-interventional, prospective, observational study in Australian patients with HAE, we sought to understand the various treatment pathways, impacts on individuals, and healthcare resource utilisation.

Method: Patients with HAE -C1INH deficiency types 1&2, 12+ years were recruited via specialist clinics and the patient support group. With informed consent, baseline data regarding HAE and therapy use was obtained. Weekly monitoring was conducted via SMS with two questions: Q1-"What HAE medications have you used this week"? Q2"Have you had an HAE attack this week"? A positive response to Q2 initiated a phone call follow-up to collect detailed information about each attack. All data was entered into a database, coded and analysed.

Results: The study was conducted between July 2019 and November 2020; 50 participants enrolled; 3 withdrew. Average observational time was 9.1 months (4 to 15.9 months). The table summarises the total observational time & attack rates in the various medication categories.

Detailed attack information was obtained in 338 attacks (74%); 58 attacks resulted in 85.5 lost days (work/school), likely to be an underestimate due to work from home rules during COVID-19 restrictions; twenty-three attacks required hospitalisation.

Conclusion: This is the first study of this type for HAE in Australia. It showed that HAE attacks can be frequent, debilitating and resource intensive. Further data analysis may help elucidate the optimal intervention strategy with effective modern prophylaxis therapies that are both patient and healthcare centric.

On Demand only or Prophylaxis Medication	Patients who had time within each category	Total Observed time (Months)	HAE Attacks (total)	Mean No. of HAE Attacks per month	95% CI for Mean
On Demand only*	21	145.3	234	1.89	(1.01, 2.76)
Danazol**	7	56.4	35	0.62	(0.10, 1.15)
Tranexamic Acid	4	32.4	37	1.05	(-0.01, 2.10)
C1INH conc IV #	15	71.0	56	1.31	(0.60, 2.02)
C1INH conc SC#	15	69.8	67	1.17	(0.52, 1.82)
Lanadelumab##	4	22.0	1	0.16	(-0.35, 0.68)
BCX7353^	*1*	4.2	27	6.37	0
TOTAL		401.2 or 33.4 years	457		

*Icatibant or C 1INH conc IV, **Was slowly withdrawn in Aust during the study period, # Only available in Australia for patients having ≥8 attacks/month, ## Compassionate Access only, ^ Trial drug

1082 | Hereditary angioedema and pregnancy, a challenging disease with success. qatar experience

Mudawi D.; Ibrahim T.; Thalappil S.; Al-Nesf M.; Mobayed H.

Hamad Medical Corporation, Doha, Qatar

Background: Hereditary angioedema due to C1 inhibitor deficiency (HAE-C1-INH) pregnant patients require close monitoring as pregnancy may exacerbate HAE attacks due to estrogen level changes. Plasma-derived human C1 inhibitor (pdC1INH) concentrate is the recommended treatment during pregnancy; it is safe and effective; for on-demand therapy, short and long-term prophylaxis.

Case scenario: A 37-years-old Arab female with a positive family history of HAE-C1-INH was diagnosed with HAE-C1-INH type II at 27 and had first symptoms at 16. Investigations revealed low C4 level, high C1NH level, and 25% functional level. Genetic testing confirmed the presence of a heterozygous mutation in the SERPING1 gene. Before HAE diagnosis, she had four successful pregnancies, ended with normal vaginal delivery; however, she suffered from daily swellings and had frequent emergency visits. Her two boys and one girl were diagnosed with HAE based on genetic testing. She was on Ictabinat 3-6 injections weekly, as on-demand therapy. Treatment with Danazol had a modest effect on her symptoms and was associated with amenorrhea and hirsutism. In January 2019, she

got pregnant, and pdC1INH concentrate therapy, 2500 IU intravenously/week, was initiated. During the first and second trimester, she was asymptomatic. Recurrent feet swelling and abdominal pain commenced at 32 weeks gestation; subsequently, the dose of the pdC1-INH concentrate was increased to 2500 IU twice weekly resulted in better symptoms control. Due to the increased frequency of attacks during the last trimester, a prophylactic dose of pdC1IN was administered before delivery. She delivered a baby girl vaginally successfully, without immediate or late angioedema complications.

Discussion: The behaviour of HAE-C1-INH during previous pregnancies does not predict the attacks in later pregnancies. Having a baby with HAE-C1-INH and HAE diagnosis at a young age increases the edematous events during pregnancy. During delivery, the risk of swelling attacks is low, in contrast to the postpartum period. For normal vaginal delivery, short-term prophylaxis is reserved for patients with frequent attacks during the third trimester or those with a previous history of genital oedema precipitated by trauma.

Conclusion: The management of female patients in the childbearing age with HAE is challenging since medications' choices during pregnancy are limited with weak evidence.

1233 | A profile of patients with inborn errors of immunity (IEI) followed in a latin american referral center

Bubach P. H.A.; Ramos B. C.; Vital N. S.; Ferreira C. S.C.; Sá M. G.V.; Medeiros L. C.M.; Gouveia-Pereira M.; Rizzo M. C.; Aranda C. S.; Sole D.

Universidade Federal de São Paulo, São Paulo, Brazil

Background: In the past years, with the advances in molecular biology and better knowledge of the human immune system, the number of diseases described has progressed enormously, with more than 406 pathologies and 430 genes described. Therefore, is particularly important to access patient's profile to improve treatment. The main purpose of this study was to describe the epidemiological profile of patients followed in an Immunology Referral Centre.

Method: We conducted a cross-sectional study in the Clinical Immunology Center of Federal University of São Paulo by analyzing electronic charts from patients followed in the center in 2018. The parameters were age at diagnosis, gender, IEI diagnosis, number of hospital admissions, treatment in course, use of prophylaxis drugs.

Results: A total of 527 patients were enrolled being 55,9% male and the median age of 16,7 years (1 month to 81 years). Sixty-eight percent were pediatric age range. In relation to hospitalizations, 72% (395) had hospital admissions before the diagnosis of IEI with 40% of them admitted in ICU. CVID corresponded to the diagnosis in 48 patients (9%), while 44 (8%) were presented SAD (specific antibody deficiency), 52 (10%) hypogammaglobulinemia, 23 (4%) ataxia telangiectasia; 22 (4%) selective-IgA-deficiency. Besides that, others IEI diagnosis were found in 130 (25%) patients. Some of the patients (161/30%) do not have a confirmed IEI diagnosis. IEI diagnosis was excluded in 47 patients during that year, due to clinical evolution and biochemical tests. Regarding treatment, 168 (31,8%) patients received intravenous immunoglobulin (IVIG) replacement and 155 (29%) had been receiving antimicrobial prophylaxis (amoxicillin in 50%; azithromycin in 43%; sulfamethoxazole+ trimethoprim in 36%). Only 49 patients (9%) had a genetic testing confirming variants related to IEI.

Conclusion: Our service attends mainly pediatric patients, most of them with moderate to severe diseases. Almost one third of the patients receives IVIG replacement regularly and in less than 10% we had performed genetic tests. This is a handicap that most of the services in our country have to face in relation to the access of molecular biology tests.

1310 | Course of Covid-19 in adult patients with primary immunodeficiency who receives intravenous immunoglobulin therapy, case series

Tepetam F. M.; Atik O.; Akyildiz A. B.

Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital, Istanbul, Turkey

Background: Primary immunodeficiency diseases (PID) are rare conditions that occur as a result of defects in one or more components of the immune system, which are clinically characterized by recurrent and/or severe infections, and may be accompanied with autoimmunity. Patients diagnosed with primary immunodeficiency were included in the high risk patient group for COVID-19 by the US Center for Disease Control (CDC). On the other hand, intravenous immunoglobulin (IVIG) therapy, which is used in the treatment of patients with PID, has been used as an immunomodulator in the treatment of COVID-19 patients in reducing hyperinflammation and associated cytokine storm syndrome. In our study, we wanted to present the clinical and laboratory characteristics of patients infected with COVID-19 and the course of the disease while receiving IVIG treatment with the diagnosis of PID.

Method: 11 women 32 patients with an average age of 36.4 from 2 centers included in the study. Patients who were receiving IVIG/subcutaneous IG due to PID have been screened for Covid-19 since March 2019.

Results: It was found that Covid-19 developed in a total of 4 patients, 3 of the cases had common variable immune defficiency (CVID), and last one had Ataxia Telangiectasia. 3 of the cases were

male and 1 female. All 4 patients had comorbid diseases accompanying primary immunodeficiency. Three of 4 patients had lymphopenia. Radiological findings consistent with interstitial pneumonia were observed in the thoracic CT's of all 4 patients, no patients required hospitalization. 3 of 4 patients received favipravir treatment, and 1 patient received hydroxychloroquine. Phenotypic and immunological data of the patients before Covid-19 and clinical laboratory presentation during Covid-19 infection are given in the table below. (Table 1)

Conclusion: Coronavirus disease 2019 (COVID-19) has developed rapidly into a global pandemic. Patients with PID may be at risk of developing severe COVID-19 infection even though they recieve IVIG. On the other hand IVIG probably suppresses inflammatory reactions by a multi factorial mechanisms which leads alleviation of the symptoms caused by cytokine over-synthesis. Although patients have radiological and laboratory findings during Covid-19 infection, they have with milder symptoms.It was observed that Covid-19 infection was not mortal and morbidity was low in our patients with primary immunodeficiency (3 CVID, 1 Ataxia Telangiectasia) who were receiving IVIG and all of them recovered.

		Case 1	Case 2	Case 3	Case 4
Pre-Covid phenotypic and baseline immunologic data	Current age (age at diagnosis)/Sex	39/20/M	55/54/F	32/28/M	35/28/M
	Comorbidities	Seronegative arthritis	Sjogren sydrome	Hepatitis Crohn	Cerebellar Ataxia
	TLC (mm^3)	1300	1460	1190	1300
	T lymphocyte subset %	CD3:74.3 CD4:11.9 CD8:62	CD3:88 CD4:63.2 CD8:24.2	CD3:64 CD4:35 CD8:28	CD3:49 CD4:34 CD8:14
	CD19 %	2.95	7.1	9.4	3.7
	Baseline serum IgG (mg/dL)	177	467	400	2631
Clinical and laboratory charaterizitaion of PID patients with covid 19 infection	Recent serum IgG (mg/dL)	730	578	968	1800
	TLC (mm^3)	600	1660	1190	1340
	Ferritin/D-dimer/CRP	800/888/37	341/0.3/2.1	NA/NA/3.84	22/NA/5.9
	COVID-19 symptoms/ evidence of interstitial pneumonia with Thorax CT	Fever and fatigue/ bilateral (+)	Fever, fatigue, sore throat, malaise, diarrhea nausea/ unilateral (+)	Fever, fatigue cough, dyspnea and malaise/unilateral (+)	Fever/NA
	Treatment specifically for COVID-19	Favipiravir Enoxaparin Teikoplanin	Favipiravir Aspirin	Hydroxychloroquine	Favipiravir
	Other medication (immunosuppressants, antibiotics)	Prednisolone Leflunomide	Hydroxychloroquine	-	Trimetoprimsul-fametoksazol-Flukonazol
	Outcome	Recovery Not hospitalizated	Recovery Not hospitalizated	Recovery Not hospitalizated	Recovery Not hospitalizated

1058 | Kabuki syndrome, atypical for atopic dermatitis

Perea P.; Jaramillo M.D.C.; Reyes N.; Del Río B.
Hospital Infantil de México Federico Gómez, Mexico City, Mexico

Introduction: Kabuki syndrome is a rare genetic disorder attributed to a pathogenic variant either in KMT2D or in KDM6A. Immunologists should be aware that affected patients can have an increased susceptibility to infections and autoimmune disorders. Here we report the case of a boy with Kabuki syndrome and multiple atopic disorders.

Methods and Results: A six-year-old boy with Kabuki syndrome is being followed-up at the Severe Atopic Dermatitis Clinic. On physical examination the patient has the typical dysmorphic features, short stature and developmental delay. At the age of 2 years, he began with atopic dermatitis features, and in his first visit he scored a 29.4 according to the SCORAD index. Initially treated with cyclosporine at a 3.7mg/kg/day dose, but due to a poor response to this medication and nephrotoxicity he was changed to azathioprine at a 2.7mg/kg/day dose. Gastrointestinal symptoms were reported after cow's milk ingestion. Skin prick tests (SPTs) and specific IgE (sIgE) to cow's milk protein were negative. After a one-year restriction diet he now tolerates raw and baked milk products. He also has a severe persistent rhinoconjunctivitis for which SPTs were positive for *Blomia tropicalis* and *Cupressus arizonica*. Up to now he has not developed autoimmune manifestations and has not presented frequent infections. Nevertheless, since July 2020 he has shown a persistent increase on the unconjugated bilirrubin levels along an elevated reticulocyte index. He has never developed anemia, the osmotic fragility test was reported as negative and so was the Coombs test, and

the rest of the hepatic panel is normal. His flow cytometry analysis is within expected parameters, and immunoglobulin levels show an augmented IgE concentration.

Conclusion: It must be remarked that so far atopic diseases have not been reported in the case series of this disease, making this patient the first to be described with such presentation. Immunologists must keep in mind two points: an inherently defective immunity may also render the patient susceptible to allergies, and primary immunodeficiencies have a wide and variable clinical spectrum so this diagnostic suspicion cannot be discarded yet.

1224 | Analysis of immune system tests in children with recurrent infections

Gasiuniene E.; Pilkyte L.

Lithuanian University of Health Sciences, Kaunas, Lithuania

Background: Immune system fully develops at around the age of 7. Because of this number of infections increases when children start attending kindergarten, where they are exposed to many pathogens not recognized by their immune system. We have to suspect PID when there are four or more new ear infections, two or more serious sinus infections within one year; persistent thrush or fungal infections on the skin; recurrent, deep skin or organ abscesses; two or more deep-seated infections including septicemia or other signs of PID.

Aim of the study: This study aimed to evaluate humoral, cellular immunity parameters in children with suspected immunodeficiency (ID), as well as to assess neutrophil phagocytic function, total blood count parameters and ferritin level.

Method: We evaluated 52 children with suspected ID who were consulted by allergologist clinical immunologist in Hospital of Lithuanian University of Health Sciences Kaunas Clinics outpatient department during period 2018-2020. Twenty-five girls and twenty-seven boys were enrolled in the retrospective study. Total blood count, immunogram, IgG, IgM, IgA, IgE, IgG subclasses, nitroblue tetrazolium blood test (NBT) and ferritin level were evaluated.

Results: The study included 52 children. 25 female (48.1%) and 27 male (51.9%) patients. 13 children (25%) had decreased humoral immune parameters – 6 of them were girls, and 7 were boys. Cellular immune parameters showed no significant changes. NBT was tested for 33 children and 20 (60.6%) of them had low levels. 4 girls (8%) had low haemoglobin. Low ferritin levels were founded in 30 children (60%). Immunodeficiency was diagnosed for 9 children (17.3%); they had lower NBT test parameters when compared to children with no PID, 7.63 ± 0.92% vs17.42 ± 2.68%, $p < 0.05$.

Conclusion: Out of 52 patients 9 were diagnosed with immunodeficiency, which most common was phagocytic cells deficiency. No significant difference between male and female immune system parameters were observed. Children with recurrent infections does not necessarily has PID. Similar symptoms also can be caused by low ferritin levels.

1281 | Severe atopic dermatitis (SAD): red flag for primary immunodeficiencies?

Fanti G. C.; De Carvalho C. B.; Lima A. O.d.A.; Said L. S.; Anjos Roque R. M.S.; Moraes M. M.; Aranda C. S.; Guimarães R. R.L.; Harari D.; Camargo L.; Mallozi M.; Solé D.

Federal University of Sao Paulo - UNIFESP, São Paulo, Brazil

Background: Atopic dermatitis (AD) is a multifactorial and chronic disease that comprises difficult treatments. Nevertheless, the robust gain of knowledge in the field of Allergy-Immunology assists in the differential diagnosis of these patients, as well as in primary immunodeficiencies (PID) as Hyper-IgE, Wiskott-Aldrich and SCIDs syndromes. This pilot study aimed to evaluate clinical and laboratory characteristics that can function as red flags for the different PIDs in patients with SAD.

Method: Retrospective analysis of standardized medical records (PID red flags marked) during 2019 to alarm characteristics may be present in both SAD and PID.

Results: 110 medical records of patients followed up at the allergy outpatient clinic were analyzed. SAD was found in 26 (24%) patients. The median age was 8.4 years. In relation the clinical manifestations that may be common in both conditions, coarse faces were present in 38.4% of the group and the early onset of eczema (before 3 months of age) was described in 14% of the patients. Sino-pulmonary infections were present in 10% of patients while viral infections, in 12,5%. Skeletal abnormalities, delayed tooth exchange, joint hyperextensibility was not registered on the charts. All patients had rhinitis and more than 50% had a medical diagnosis of asthma. Related to laboratory, 80% of the patients had more than 1.500 eosinophil/mmm3 and levels higher than the 90th percentile of immunoglobulin E (KU/L). Lymphopenia for age was found in seven (27%) patients. All patients were assessed by the immunology team and have accompanied up together. Two patients had a secondary hypothesis of Hyper-IgE syndromes with mild phenotype.

Conclusion: PID clinical manifestations and laboratory tests should be prioritized in the care of patients with SAD. Standardized medical records should be encouraged so the characteristics common to both groups could be assessed.

1314 | Incidental diagnosis of hereditary angioedema type I in an elderly male after 7 decades free of symptoms

Tsakona C.

Dudley Group of Hospitals NHS Foundation Trust, Dudley, United Kingdom

Hereditary Angioedema (HAE) is a rare, inherited autosomal dominant disease, disabling and life-threatening, caused by C1 Esterase Inhibitor Deficiency and always presenting in childhood or puberty (Types I & II). It leads to excess Bradykinin release because of random activation of the Classical Complement pathway by common

triggers like infection, stress, trauma and hormonal changes. Early diagnosis is essential, as both prophylaxis and symptomatic treatment can prevent fatal laryngeal oedema leading to death from asphyxia. Late presentation in life is extremely rare, We report a case of Type I HAE, diagnosed at the age of 70 years in a non-symptomatic elderly male. We believe it is the second oldest case reported worldwide. In this age the patient was told he has a 49 year old daughter, who had been monitored in our Immunology Outpatient clinic with her teenage grandson, both with Type I HAE. The 70 year old male has never had symptoms to suggest HAE although he had past accidents and operations and a recent tooth extraction without prophylaxis and no swellings.

The low C1 Esterase Inhibitor and low C4, confirmed the diagnosis of Type I HAE, in line with the family history. He now carries emergency self-treatment with a supply of Tranexamic Acid and 1.500 U of C1 Esterase Inhibitor concentrate (to take prior to operations, invasive treatments and in case of injuries and severe abdominal pain or suspected laryngeal obstruction). He was also given to wear a Medic Alert with the relevant inscription.

An extreme case indicating that Physicians should be aware of this rare possibility when making the differential diagnosis of (particularly visceral) angioedema even in the elderly. In 2018 J Berger et al reported the delayed diagnosis of HAE Type II in a 78 year old man who, however, had been symptomatic all his life. Our patient though is the **oldest** incidental diagnosis **worldwide**, as first presentation and diagnosis of HAE beyond puberty are extremely rare and the fact that the patient could manage to reach the 8th decade of life without any symptoms is phenomenal.

1189 | The impact of COVID-19 pandemic on hospital admissions frequency for lrtis and viral infections among pediatric patients

Grochowska M.[1]; Ambrozej D.[2,3]; Feleszko W.[2]
[1]Medical University of Warsaw, Warsaw, Poland
[2]*Department of Pediatric Pneumonology and Allergy, Medical University of Warsaw, Warsaw, Poland*
[3]Doctoral School, Medical University of Warsaw, Warsaw, Poland

Background: It has been over a year since the outbreak of the SARS-Cov-2 pandemic. In response to the rapid escalation of infection cases, many countries from all over the world, including Poland, have introduced measures to limit the transmission of the new coronavirus, from the recommendation of social distancing and wearing masks to strict lockdown. Our aim was to investigate how the SARS-Cov-2 pandemic has changed the morbidity associated with the most common respiratory viruses and the incidence of lower respiratory tract infections in pediatric population.

Method: To achieve the objective of the study, data mining analyzing the electronic health record system of the Children's Hospital of Medical University of Warsaw, one of the two largest pediatric hospitals in the capital of Poland, was conducted. Individual medical records involving LRTI (based on ICD-10 codes) and detection rates for rhinovirus, RSV, influenza, adenovirus, and SARS-CoV-2 infections were collected and compared between March 2020 to February 2021, and four previous seasons (2016-2020).

Results: A total of 5182 medical records of LTRI were obtained, classified into the following categories: a) viral infections (including bronchiolitis), b) influenza and flu-like infections, and c) bacterial infections from the last five years. During 2016-2020 seasons the cumulative, as well as segregated, annual admission rates remained steady (mean 1198, ranging from 1081 to 1294). In contrast, this trend was not reflected during the last 2020/2021 season as the total LRTI admission rate sharply and statistically significantly dropped to 468 ($p < 0.05$). In comparison to the average number of hospitalizations during the 2016-2020 seasons, the reduced hospitalization rates in 2020/2021 in the subgroups of viral infections, bronchiolitis, flu, and bacterial infections accounted for 31% (134/430), 41% (79/193), 65% (76/117), and 27% (179/651) cases, respectively.

Conclusion: The results of our study demonstrate a substantial decrease in the hospitalization frequency from March 2020 to February 2021 compared to four previous years. The research illustrates the lockdown and social distancing are not only reflected in the decline of reported SARS-CoV-2 cases but also in other viral and nonviral respiratory tract infections in children, and shows the effectiveness of restrictions in preventing LRTIs among pediatric patients.

1202 | Approach to vespa velutina nigrithorax venom allergy – real life clinical practice

Miranda J.; Mesquita A.M.; Plácido J.; Coimbra A.
Serviço de Imunoalergologia, Centro Hospitalar Universitário de São João, Porto, Portugal

Background: The first European record of *Vespa velutina nigrithorax* (VVN), also known as Asian hornet, was in 2004. In Portugal, it has been reported since 2011 and it has increasingly become troublesome due to its impact on biodiversity but also as a new health issue. This study aims to characterize the sensitization pattern of patients suffering from VVN venom allergy.

Method: A records review of patients referred to our allergy department between 2017 and 2020 for suspected VVN venom allergy. Clinical and demographic information, results of specific IgE of Hymenoptera venom (HV) and intradermal tests were evaluated.

Results: A total of 6 patients, age ranging from 36 to 75 years, were included.

One of the patients was an amateur beekeeper, 2 were road workers and the remaining 3 didn't have any outdoor hobby or profession.

All identified the culprit hymenoptera as VVN and 3 claimed there was a nest nearby. The episodes occurred outdoors; half were stung more than once (maximum 3 stings/episode). All patients had anaphylaxis and symptom onset was within 30 minutes of the sting. All had respiratory symptoms, half mucocutaneous and/or

cardiovascular and 2 gastrointestinal. They were treated with corticosteroids and antihistamines but only two were given adrenaline.

All patients were previously stung by other hymenoptera species (2 by wasps, 1 by bees and 3 by both) but none reported systemic reactions. Three had, however, local large reactions. None had been previously stung by VVN.

HV allergy diagnostic work up was performed (table I). All patients were sensitized to *Vespula spp*, half also to *Polistes dominula* and half to *Apis mellífera*. *Vespula spp* venom immunotherapy with an ultra-rush protocol was started in 5 patients with tolerance. No patient was re-stung.

Conclusion: All cases in this series presented with anaphylaxis and a history of previous stings by Hymenoptera other than VVN. Only half had high-risk professions/activities. Moreover, there was a sensitization pattern to *Vespula spp* allergens which could be explained by cross-reactivity among different *Vespidae* venoms. As specific diagnostic methods as well as immunotherapy for VVN venom allergy are still under development, *Vespula spp* venom immunotherapy can be a valuable treatment option.

	sIgE											
kU/L	*Apis*	*Vespula*	ID ST µg/mL	*Vespula* 0.1	*Vespula* 1	*Polistes* 0.1	*Polistes* 1	*Apis* 0.1	*Apis* 1	Molecular kU/L	Vesv1	Vesv5	Pold5
P1	0.14	4.16		NEG	NEG	NEG	NEG	NEG	NEG		0.63	1.8	N/P
P2	N/P	14.3		NEG	NEG	POS	POS	N/P	POS		2.48	8.09	6.62
P3	6.17	5.73		D	D	POS	POS	POS	N/P		0.19	3.3	3.2
P4	5.5	15.2		NEG	POS	POS	POS	N/P	N/P		A/R	A/R	A/R
P5	<0.1	4.76		N/P	NEG	N/P	NEG	N/P	NEG		3.08	1.9	0.99
P6	N/P	6.91		NEG	NEG	N/P	NEG	N/P	NEG		A/R	A/R	A/R

P: Patient; sIgE: specific IgE; ID ST: intradermal skin test; NEG: negative; POS: positive; D: dubious; N/P not performed; A/R: awaiting result.

989 | Clinical features of children with mosquito allergy

Yavuz S.T.[1]; Akin O.[2]; Koc O.[2]; Güngör A.[2]; Bolat A.[2]; Gülec M.[3]

[1]*Department of Pediatric Allergy, Children's Hospital, University of Bonn, Bonn, Germany*; [2]*Department of Pediatrics, Gülhane Training and Research Hospital, Ankara, Turkey*; [3]*Department of Allergy and Clinical Immunology, Gülhane Training and Research Hospital, Ankara, Turkey*

Background: Many children encounter unusual or "exaggerated" reactions such as large local, atypical or systemic reactions after mosquito bites. The aim of this study was to document the clinical features of children with mosquito allergy and investigate the possible associations between demographic features and type of reactions in this population.

Method: Children with large local or unusual reactions after mosquito bites who attended to our outpatient pediatric allergy department were enrolled in the study along with control subjects.

Results: A total of 180 children (94 with mosquito allergy and 86 age and sex-matched control subjects) with a median age of 6.8 years (IQR 5.5-9.3) were enrolled. Atopy (35.1% vs. 11.6%, $p < 0.001$) and grass pollen sensitization (28.7% vs. 8.1%, $p < 0.001$) were significantly more frequent in children with mosquito allergy. Skin prick test with mosquito allergen was positive in only 6 children (6,4%). Grass pollen sensitization was most common in children (28.7%) followed by sensitization to house dust mite (9.6%). 30 children (31.9%) had an accompanying atopic disease such as allergic rhinitis, asthma or atopic dermatitis. Bullae were significantly more frequent in children with asthma (41.7% vs.15.9, $p = 0.034$). The median duration of symptoms after onset were significantly longer in patients with ecchymosis, with immediate wheals and in children whose symptoms start in 20 min to 4 hours after mosquito bites.

Conclusion: There is an association between unusual, large local or exaggerated reactions after mosquito bites and allergic diseases in children. The severity of reactions increases with age and particularly in children with atopic background.

1040 | Venom immunotherapy: A real-life experience in a tertiary referral center in turkey

Ediger D.[1]; Erbay M.[1]; seker Ü.[2]; Gunaydin F. E.[1]

[1]*Uludag University Medical Faculty, Section of Immunology and Allergy Diseases, Department of Chest Diseases, Medical Faculty, Bursa, Turkey*; [2]*Section of Immunology and Allergy Diseases, Bursa City Hospital, Department of Dermatology, Bursa, Turkey, Bursa, Turkey*

Background: Venom allergy is an important health problem because of life-threatening reactions and impaired quality of life. The only treatment that can prevent the risk of a subsequent systemic sting reaction is venom immunotherapy. Additionally, there has been limited report about Hymenoptera venom immunotherapy practice from Turkey. In our clinic, which is an important allergy center in Turkey, we aim to share the clinical characteristics of venom immunotherapy patients and to raise awareness by sharing our experience about venom immunotherapy.

Method: Between December 2012 and February 2019, adult patients who underwent venom immunotherapy in Uludag University Faculty of

Medicine, Department of Immunology and Allergic Diseases outpatient clinic were evaluated. The sociodemographic characteristics of the patients, re-stings and reaction type during venom immunotherapy were recorded.

Results: A total of 52 patients (44.2% female, 55.8% men; mean age= 48.4 ± 12.9 years) were included. From a total of 52 patients, 41 (78.8%) received VIT with honey bee, 8 (15.4%) with wasp and 3 (5.8%) with honey bee and wasp. Only 4 (7.7%) patients developed systemic reactions due to venom immunotherapy. During the venom immunotherapy period, 19 (36.5%) patients were re-stung by the culprit bee and none of them had any systemic allergic reactions.

Conclusion: Our data is consistent with previous literature regarding safety and effectiveness of venom immunotherapy.

Table 1. Demographic and clinical characteristics of patients

	Honeybee VIT	Wasp VIT	Honeybee and Wasp VIT	Total
Patients n (%)	41 (78.8)	8 (15.4)	3(5.8)	52 (100)
Age (year) (±std)	49.4 (12.33)	47.7 (15.23)	36.7 (11.85)	48.4 (±12.9)
Gender				
Female-n (%)	18 (43.9)	4 (50)	1 (33.3)	23 (44.2)
Male-n (%)	23 (56.1)	4 (50)	2 (66.7)	29 (55.8)
Allergic rhinitis-n (%)	14 (34.1)	5 (62.5)	2 (66.7)	21 (40.4)
Cardiovascular disease-n (%)	12 (29.3)	2 (25)	0	14 (26.9)
Asthma-n (%)	5 (12.2)	1 (12.5)	1 (33.3)	7 (13.5)
Thyroid disease-n (%)	4 (9.7)	1 (12.5)	0	5 (9.6)
Diabetes Mellitus-n (%)	2 (4.9)	1 (12.5)	0	3 (5.8)
Beekeeping -n (%)	20 (48.8)	1 (12.5)	1 (33.3)	22 (42.3)
Severity of systemic reaction with index bee sting -n (%)				
Grade 1	4 (9.7)	2 (25)	2 (66.7)	8 (15.4)
Grade 2	12 (29.3)	2 (25)	1 (33.3)	15 (28.8)
Grade 3	24 (58.5)	4 (50)	0	28 (53.8)
Grade 4	1 (2.4)	0	0	1 (1.9)
VIT: venom immunotherapy				

Table 2. Characteristics of patients re-stung by the culprit bee during venom immunotherapy

Patient No	Gender/ Age	SAR severity after bee sting	Type of VIT	Reaction to Hymenoptera sting after VIT
1	F/57	Grade 3	Honeybee	none
2	M/50	Grade 3	Honeybee	none
3	M/43	Grade 2	Honeybee	none
4	F/31	Grade 3	Honeybee	none
5	M/50	Grade 2	Honeybee	none
6	M/65	Grade 3	Honeybee	none
7	F/61	Grade 3	Wasp	none
8	M/23	Grade 2	Honeybee +Wasp	none
9	M/64	Grade 3	Honeybee	local
10	M/54	Grade 1	Honeybee	local
11	M/25	Grade 3	Honeybee	none
12	M/54	Grade 3	Honeybee	local
13	M/42	Grade 3	Honeybee	local
14	M/53	Grade 2	Honeybee	local
15	M/68	Grade 3	Honeybee	none
16	M/36	Grade 3	Honeybee	none
17	F/57	Grade 2	Honeybee	local
18	M/44	Grade 1	Honeybee + Wasp	none
19	M/49	Grade 2	Honeybee	None
VIT: venom immunotherapy				

We believe that any effort increasing knowledge of venom allergy is important.

1146 | Mast cell activation syndromes in pediatric population

González-Bravo L.[1]; Matito A.[2]; Jara-Acevedo M.[3]; Henriques A.[2]; Caldas C.[3]; Sánchez-Muñoz L.[2]; Orfao A.[3]; Álvarez-Twose I.[2]
[1]*Allergy Department, Hospital Universitario Fundación Alcorcón, Madrid, Spain;* [2]*Instituto de Estudios de Mastocitosis de Castilla La Mancha (CLMast), Hospital Virgen del Valle. Spanish Network on Mastocytosis (REMA), Toledo, Spain;* [3]*Servicio General de Citometría, Centro de Investigación del Cáncer/IBMCC (USAL/CSIC) and Departamento de Medicina, Universidad de Salamanca. Spanish Network on Mastocytosis (REMA), Salamanca, Spain*

Background: Mast cell activation syndromes (MCAS) and its diagnostic criteria are primarily reported in the adult population. We report 8 pediatric MCAS cases based on these diagnostic criteria.

Method: Three girls and 5 boys with a median (range) age at onset of the disease of 6 (1-12) y.o. All of them fulfilled the diagnostic criteria established for MCAS: 1)Typical clinical signs of severe recurrent acute systemic MC activation –MCA- (e.g. anaphylaxis); 2)Increase in tryptase level (sIT) from individual baseline (sBT) of 20%+2ng/ml within 1–4 hours after onset of the acute crisis; and 3)Response of MCA symptoms to antimediator therapy (ATM).

A complete allergological work-up was performed to evaluate the elicitors identified by patients (different foods/drugs in case #7). The Spanish Network on Mastocytosis (REMA) score was used to predict an underlying clonal mast cell disorder. *KIT* D816V mutation in peripheral blood (PB) cells was assessed by allele-specific oligonucleotide quantitative polymerase chain reaction.

Results: Patients presented a median (range) of 5.5 (1-15) anaphylactic crisis in the absence of skin lesions of mastocytosis. Eight, six, five and four patients had urticaria, gastrointestinal, cardiovascular, and respiratory or angioedema symptoms during anaphylaxis, respectively. Furthermore, patient #6 had 2 syncopal episodes. Elicitors were ruled out but for the involvement of penicillin and ibuprofen in case #7, who tolerated later aspirin and showed negative skin tests for β-lactam antibiotics. Initial ATM consisted on oral disodium cromoglycate, combined with antihistamines in 8 patients, and montelukast in 1 case. Median (range) time of follow-up under ATM was of 20 (4-82) months. Four patients required increasing initial ATM to achieve control of MCA symptoms. PB count and differential, routine biochemistry were normal. Median (range) sBT and sIT were of 5.35 (1.1-13.8) and 9.75 (3.3-29.7) ng/mL, respectively. *KIT* D816V mutation was detected in the only patient who had a REMA score ≥2.

Conclusion: MCAS should be suspected and evaluated in the pediatric population despite normal sBT values. As a non-invasive tool, the REMA score might be routinely used in the pediatric population with MCAS, although further studies are necessary to determine its predictive value for the *KIT* D816V mutation in PB.

1282 | Urticaria unresponsive to treatment? Cutaneous mastocytosis, a case report

Demir N. C.; Tepetam F. M.; Akyildiz A. B.
Süreyyapasa chest diseases and thoracic surgery training and research hospital, allergy and immunology clinic, Istanbul, Turkey

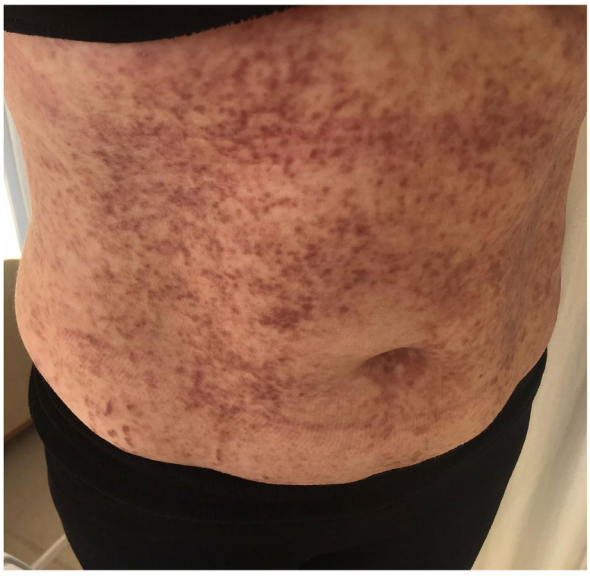
Mastocytosis is a rare disease characterized by the clonal proliferation and accumulation of abnormal mast cells in tissues and organs. According to the criteria revised by the World Health Organization (WHO) in 2008,it is classified as Cutaneous Mastocytosis, Systemic Mastocytosis and Solid Mast Cell Tumors. In cutaneous mastocytosis (CM), the disease is localized in the skin and may present as maculopapular (Urticaria Pigmentosa), diffuse and solitary lesions.

A 48-year-old female patient admitted to the Dermatology outpatient clinic in an external center 1 year ago with complaints of skin rash and itching. Oral antihistamine treatment was administered with a pre-diagnosis of urticaria.

However, she was referred to our clinic due to the persistence of her lesions and severe itching, especially after taking a hot shower. In first evaluations of the patient, there were dark brown, hyperpigmented maculopapular lesions, especially localized on the proximal anterior

surfaces of the upper extremities, also on the anterior aspect of the trunk and abdomen. (Figure.1) On stroking the individual lesions, there was formation of wheal and flare.(Darier's Sign positivity). Since skin lesions are similar to 'Urticaria Pigmentosa', further investigations were planned. In the history of the patient, it was learned that itching increased with heat, stress and spicy foods. It was learned that the lesions were present for 2 years and started on the arms. Serum tryptase level was 4.6 ng/mL (<20 ng/mL). The patient was referred to the Dermatology Hematology clinic for further examination regarding systemic mastocytosis. Skin biopsy was reported as urticaria pigmentosa as a result of histopathological evaluation. KIT mutation scanned in peripheral blood by Hematology was found to be negative. Patient was diagnosed as "Cutaneous Mastocytosis" with current clinical and laboratory findings, and a bone marrow biopsy was planned according to follow-up examinations.

Cutaneous mastocytosis is a serious condition that requires close clinical follow-up due to its frequent persistence in adults and the risk of conversion to systemic mastocytosis. Especially due to initial maculopapular skin lesions and concomitant pruritus, it can be confused with allergic skin lesions.



1170 | Allergic contact dermatitis to rubber additives: Epidemiological clinical profiles and occupational etiologies

Chelly F.[1,2]; Brahem A.[1,2]; Ben Abdelkader M.[1,2]; Chouchene A.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizek N.[1,2]

[1]Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia; [2]University of Sousse, Faculty Of Medicine Ibn El Jazzar, Sousse, Tunisia

Background: Rubber additives are widely used in everyday and professional life. They constitute an important group of contact allergens due to the increased use of protective gloves. Appropriate testing and the identification of allergens is essential for prevention and treatment. The objective of this study is to determine the frequency of allergic contact dermatitis (ACD) to rubber additives and to investigate the clinical, allergologic and etiologic features of this condition

Method: This is a retrospective descriptive study of 225 cases of contact dermatitis to rubber additives that were collected from the Dermato-Allergology Unit of the Department of Occupational Medicine of the hospital Farhat Hached of Sousse (Tunisia). These patients were subjected to percutaneous tests with the European Standard Battery (ESB) during a period of 31 years (1989 to 2020). The data collection was carried out using a synoptic sheet including the epidemiological, socio-professional and clinical characteristics of these patients as well as the data of the results of the patch-tests performed

Results: This is a series of 255 patients with at least one sensitization to one of the rubber additives with a mean age of 39.69 years and with a male predominance (52.5%). The majority belonged to the building industry (17.8%) , followed by the textile sector (15.7%) and the healthcare sector (11.2%). The skin manifestations were dominated by erythemato-veiscular plaques (56.4%) and were mostly located on the hands (76.3%). Itching was the main associated functional sign (92.4%). The onset of these dermatitis was mainly related to the use of rubber gloves (25%). A withdrawal reaction was positive in (56.2%) of cases. The most frequent allergen found was Thiuram-mix (59.2%). A combination of the 4 rubber allergens was found in only 40 cases. The occupational origin of the ACD was estimated to be (39.1%) of the cases. Only 45.4% of the patients were declared as occupational diseases.

Conclusion: Rubber additives are a frequent cause of occupational ACD, especially in construction workers. The main allergens are Vulcanizing accelerators, especially Thiurames-mix. Therefore, new glove manufacturing processes need to be developed to prevent the increased occupational and non-occupational impact of these ACD

1177 | Epidemiological and etiological profile of contact dermatitis in the buildind sector: about 190 cases

Chelly F.[1,2]; Brahem A.[1,2]; Bouhlel M.[1,2]; Chouchene A.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizak N.[1,2]

[1]Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia; [2]Faculty Of Medicine Ibn El Jazzar, Sousse, Tunisia

Background: The building and public works sector (BPW), is a growing sector in Tunisia. However, this sector is known as a major provider of contact dermatitis (CD) by the handling of several irritating and allergenic products and poor working conditions.

Objectives: To determine the epidemiological profile of workers in the construction sector with CD and to identify the main etiological agents involved in this pathology.

Method: This is a descriptive and retrospective study conducted at the Dermato-Allergology Unit of the Department of Occupational Medicine of the hospital Farhat Hached of Sousse (Tunisia) over a period of 29 years. This study was based on information collected from the files of patients working in the BPW sector and presenting clinical manifestations evoking a CD. The patients were patch-tested with the European Standard Battery (ESB). The data collection was based on a pre-established data sheet

Results: 190 cases of workers in the construction sector consulted for a skin lesion suggestive of CD. Patch tests were performed to identify the causative agent. We noted a male predominance (96.3%) with an average age of 41.11 years and an average length of service of 8 years. The most common etiological agent was Chromium (56.4%), followed by Formaldehyde (32.85%), Cobalt (23.15%), Thiuram-mix (14.35%), Nickel Sulfate (7.4%) and Mercapto-benzothiazole (6.65%). The hand was the most frequent location (78.25%). The final diagnosis retained was related to an allergic CD in (92.3%) of cases

Conclusion: Workers in the construction sector are exposed to the risk of developing CD generated by contact with irritant or allergenic chemicals, in particular cement with its main known allergen potassium dichromate. The management of these pathologies involves the coordinated action of occupational physicians and dermatologists, whose main action is individual and collective prevention at the workplace.

1192 | Relationship between overweight, obesity and severity of nasal obstruction in occupational rhinitis

Chelly F.[1,2]; Kacem I.[1,2]; El Maalel O.[1,2]; Sridi C.[1,2]; Maoua M.[1,2]; Brahem A.[1,2]; Chouchene A.[1,2]; Aloui A.[1,2]; Kalboussi H.[1,2]; Chatti S.[1,2]; Mrizak N.[1,2]

[1]*Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia;* [2]*Faculty Of Medicine Ibn El Jazzar, Sousse, Tunisia*

Background: Occupational allergic rhinitis is a common respiratory pathology. The risk factors for its severity are often attributed to working conditions. However, several other factors and pathologies may be involved.

Objectives: To study the relationship between overweight, obesity and the severity of nasal obstruction in occupational rhinitis

Method: This is a descriptive study including patients who consulted the occupational medicine department at the Farhat Hached University Hospital in Sousse for occupational rhinitis between 2011 and 2016. The evaluation of the severity of nasal obstruction was done by the PAREO score and rhinomanometry. The assessment of overweight was done according to WHO recommendations and by calculating the body mass index (BMI).

Results: The population included 163 cases of occupational rhinitis with a mean age of 39 ± 7.5 years with a female predominance 68.1%. The most represented sector of activity was the textile sector (52.8%) with an occupational seniority of 15+/-8.3 years. The average body weight index was 28.2±4.5. Overweight and obesity were reported in 75.5% of cases. Rhinitis was severe in 28.8% of cases. A significant association between PAREO score and obesity was reported (r=0.354, p < 10-3). However, no association was found between excess weight (overweight and obesity) and the severity of nasal obstruction measured by rhinomnometry.

Conclusion: Obesity may have adverse consequences in the aggravation of occupational allergic pathologies, particularly rhinitis. Nevertheless, the results of this study offer new avenues of research on the mechanism of action of overweight on the severity of rhinitis.

1172 | Contact dermatitis in diabetic patients :what are the particularities?

Chelly F.[1,2]; Brahem A.[1,2]; Sridi C.[1,2]; Belhadj Chabbah N.[1,2]; Chouchene A.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizak N.[1,2]

[1]*Department of Occupational Medicine - Teaching Hospital Farhat Hached, Sousse, Tunisia;* [2]*Faculty of Medicine Ibn El Jazzar, Sousse, Tunisia*

Background: Diabetics are particularly prone to exaggerated manifestations of skin allergies due to unfavorable skin conditions and also unknown environmental and occupational factors. The purpose of patch-testing in diabetic patients with allergic contact dermatitis (ACD) is to determine the possible causes of allergies to manage this condition and improve quality of life.

Objectives: To study the epidemiological and clinical profile of diabetic patients with contact dermatitis (CD) and identify the main allergens in this category of patients.

Method: It's a retrospective descriptive study based on 46 diabetic patients with CD collected at the Dermato-Allergology Unit of the Occupational Medicine Department of the Farhat Hached University Hospital of Sousse (Tunisia), from 1989 to 2020. Patients were patch-tested with the European Standard Battery. The data collection was carried out using a synoptic form including the epidemiological, professional and clinical characteristics of these patients as well as the data of the patch-tests results.

Results: Our population had a mean age of 51.8 years. We noted a predominance of males (54.3%). Ten patients had no current occupation or were retired. For the workers (78%), they were mainly employed in the textile (12%) and administrative (12%) sectors. (13%) had a personal history of CD, (9.1%) had a family history of allergy and (19.6%) had other associated allergies. Episodes of fungal infections were noted in (10.9%) of cases. Medication was observed in (30.4%) of cases. The most frequent localization of CD was on the hands (65.2%) and feet (31.8%). The predominant clinical aspect was the erythemato-vesicular form (46.5%) associated in (93.5%) with pruritus. The most frequent diagnosis was ACD (51.2%). The most incriminated allergens were Nickel (20.9%) and chromium (23.3%) followed by cobalt and formaldehyde in (16.3%) of cases

Conclusion: In front of every diabetic patient that present skin reactions characterized by erythema, vesicles and intense pruritus,we must seriously consider the diagnosis of ACD because it can present a quite frustrating condition. It is also possible that these two diseases share common genetic factors, although these are currently unknown. This study could stimulate research on the immunological interaction between ACD and autoimmune disease such as diabetes.

1176 | Contact dermatitis in hairdressers: clinical characteristics and allergens involved

Sridi C.[1,2]; Brahem A.[1,2]; Chelly F.[1,2]; Chouchene A.[1,2]; Aloui A.[1,2]; Kacem I.[1,2]; Maoua M.[1,2]; Kalboussi H.[1,2]; El Maalel O.[1,2]; Chatti S.[1,2]; Mrizak N.[1,2]

[1]Department of Occupational Medicine -Teaching Hospital Farhat Hached, Sousse, Tunisia; [2]Faculty Of Medicine Ibn El Jazzar, Sousse, Tunisia

Background: Hairdressers are in skin contact with numerous irritants and allergens, which explains the high frequency of dermatitis in this group. Occupational dermatitis in this sector has an early onset and a poor prognosis.

Objectives: To determine the clinical aspects of dermatitis observed in hairdressers and to identify the allergens responsible for cases of allergic contact dermatitis (ACD).

Method: This is a retrospective descriptive study of cases of contact dermatitis in hairdressers, collected at the dermato-allergology unit of the Farhat Hached University Hospital of Sousse, over a period of 30 years (from 1989 to 2019). The data collection was carried out using a synoptic form including the socio-professional and medical characteristics of the participants as well as the data of the patch-tests carried out with the allergens of the European Standard Battery

Results: Our population was composed of 30 subjects with an average age of 32.53 years and a predominance of women (76.7%). The average professional seniority was 10.25 ± years. The appearance of the lesions was polymorphous, dominated by erythematous and vesicular lesions in (57.1%) of the cases. The most frequent localization was on the hands (72.4%), particularly on the fingers of the right hand (42.3%). The most frequent diagnosis was ACD (75.9%), followed by irritant contact dermatitis (13.8%). Occupational origin was retained in the majority of cases (57.1%). Ten patients declared their contact dermatitis as an occupational disease. Nickel was the most frequently found allergen (53.3%), as well as conservatives (26.7%).

Conclusion: Occupational dermatitis in hairdressers is frequent. The most common clinical aspects are hand eczema and irritation dermatitis. An early allergological assessment and above all a well-adapted prevention should contribute to reduce their frequency and their gravity.

1246 | Occupational allergy to rice

Basili J. O.V.; Batalha A. P.; Nunes S. A.; Pastana J. C.; Prado A. I.F.; Anagusko C. L.Y.; Santos K. S.; Kalil J.; Yang A. C.

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo, Brazil

Background: Cases of occupational allergy due to food allergens are uncommon but have been described in baker's asthma, where respiratory symptoms usually precede systemic manifestations. We report an atypical food implicated in a case of occupation allergy to rice.

Case report: Male patient, 53 years old, from São Paulo, Brazil. He has been working since 26 years old as a Production Assistant for broken rice, without personal protective equipment. After 16 years working in the same job, he started to have nasal symptoms (runny nose, sneezing, itching and nasal obstruction) in the workstation. Symptoms disappeared at home, weekends and vacations. Due to nasal symptoms in the workplace, he was transferred to a sector with no exposure to rice grains, with remission of the symptoms. Eventually, when he touched his hands on machines that contained rice powder, he immediately had nasal itching, sneezing, diffuse erythema and dyspnoea, requiring antihistamines. Oral contact with raw rice triggers angioedema of the lips, although he tolerates cooked rice. After his 49 years old, he started food allergy reactions by ingestion. He had his first systemic reaction (hives and dyspnoea) immediately after eating granola containing wheat, oat, rice and corn. He has oral symptoms with raw peanuts. After two years, he had another systemic reaction, 90 minutes after eating dessert with boiled corn, characterized by dyspnoea, oppression in the oropharynx and eyelid angioedema, treated at the emergency room. The skin prick test (Table 1) was positive for whole raw rice (13mm), whole raw rice - washed (7mm), boiled whole rice (4mm), broken raw rice (11mm), broken raw rice - washed (8mm), raw corn (11mm), boiled corn (7mm), raw peanuts (7mm). He was advised to maintain regular consumption of cooked rice and avoid exposure to raw rice in meals or at work. Besides that, he is following an elimination diet for corn and peanuts. In addition, he received a written first-aid plan for anaphylaxis.

Conclusion: Rice is a relatively low allergenic food and there are few reports of rice allergies in the West. In this reported case, exposure to the allergen by inhalation may have contributed to sensitization to thermolabile allergens in rice. The possibility of cross-reactivity to corn and peanuts is still under investigation.

TABLE 1 Prick to Prick

Skin prick test (Prick to Prick)	
Negative control	0 × 0 mm
Histamine	9 × 7 mm
Whole raw rice	16 × 10 mm
Whole raw rice - washed	7 × 7 mm

Skin prick test (Prick to Prick)	
Boiled whole rice	4 × 5 mm
Broken raw rice	13 × 8 mm
Broken raw rice - washed	7 × 9 mm
Raw corn	13 × 9 mm
Boiled corn	7 × 7 mm
Raw peanuts	7 × 7 mm
Roasted peanuts	0 × 0 mm

1009 | Nutritional status in infants with severe atopic dermatitis

Borovik T. E.[1,2]; Kozlova E. V.[1]; Zvonkova N. G.[1,2]; Guseva I. M.[1]; Murashkin N. N.[1,2]; Opryatin L. A.[1]; Davydenko S. M.[2]
[1]*National Medical Research Center of Children's Health, Moscow, Russia;* [2]*I.M. Sechenov First Moscow State Medicine University, Moscow, Russia*

Background: Atopic dermatitis (AD) is often associated with food allergies. Elimination diets in infants may negatively affect growth, especially in multi-food allergic. *The aim of the study was* to evaluate nutritional status in infants with severe atopic dermatitis.
Method: In 51 infants (29 boys) with severe AD (SCORAD >40) at the age from 3 to 12 months clinical assessment, anthropometric data (height, weight) and laboratory evaluation (total IgE and sIgE levels to cow's milk, egg and wheat proteins, using the ImmunoCAP assay) were performed on admission to dermatology department. Anthropometric data analysis was accomplished through Z-scores calculation with the support of the WHO Anthro, 2006 software. Undernutrition was defined using WHO classification (Z-scores weight/height, height/age ≤-2.0).
Results: The majority of infants (80.4%) had a family history of allergic disease. Food allergy was detected in 44 infants (88.2%), multiple FA in 42.2% of cases. The average level of total IgE was 684.8 [0.78; 3000] kUA/l (N<15 kUA/l). 16 (31.4%) infants were breastfed, 5 (9.8%) patients had mixed feeding, and more than half of infants (58.8%) were formula-fed. The average values of WAZ, HAZ, and WFH in the majority (60.7%) of patients were within normal values. Undernutrition was detected in 8 (15.6%) infants: acute moderate in 4 (7.8%) and chronic malnutrition (stunting) in 4 (7.8%). All infants with undernutrition had FA, 6 of them had multiple FA with class IV-V sensitization to cow's milk and egg; they were on milk-free elimination diet. Infants with undernutrition had a significantly higher level of total IgE compared to children with adequate nutritional status (2452 kUA/l vs 555 kUA/l, $p = 0.04$). An inverse relationship was found between the body mass index and the level of total IgE (r=-0.4).
Conclusion: Undernutrition has a high prevalence in infants with severe AD. Infants with high levels of total IgE and multiple FA require particular attention in nutritional status assessment and timely organized adequate nutritional intervention.

1147 | Sputum cell count and its association with reflux severity in asthmatic children with gastroesophageal reflux disease

Umanets T.[1], Buratynska A.[1], Lapshyn V.[1], Pustovalova O.[1], Khomenko V.[2], Antipkin Y.[1]
[1]*Institute of Pediatrics, Obstetrics and Gynecology named after academician O. Lukyanova of National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine;* [2]*National Medical University named after O.O. Bogomolets, Kyiv, Ukraine*

Background: Gastroesophageal reflux disease (GERD) and asthma frequently occur together in children. However, there are limited and conflicting data on the difference between the induced sputum in asthmatic children with or without GERD.
The aim our study was to evaluate the features of sputum cell count and its association with reflux severity in asthmatic children with GERD.
Method: Sixty-seven children ages 6-17 years with moderate asthma combined with GERD ($n = 35$), with isolated asthma ($n = 32$) and 30 healthy children ages 6-17 years were observed. All children included in the study were identical in age and gender. Clinical assessment, skin prick testing, spirometry, sputum samples were performed in all patients. Upper gastrointestinal endoscopy was done in the asthmatic group
Results: In children with asthma combined with GERD, induced sputum had a significantly higher number of neutrophils, lymphocytes and macrophages compared to the group of healthy children ($p < 0.005$) and also the difference between these parameters were significant compared to the group of children with isolated asthma. The number of induced sputum epithelial cells in asthma combined with GERD was significantly less than in children with isolated asthma. Reflux severity was positively correlated with sputum cell count (r=0,65, $p < 0.005$) and negatively correlated with FEV1 (r=-0,64, $p < 0.001$).
Conclusion: Airway inflammation in children with asthma combined with GERD seems to be more significant compared to isolated asthma

1237 | Mass food challenges in a vacant COVID-19 stepdown facility: the children's health Ireland food challenge initiative 2020

Alsaleemi A.[1]; Byrne A.[1,2]; Sanneerappa P. B.[1]; Lewis S.[1]; Trujillo J.[3]; Fitzsimons J.[1]; Tariq M.[4]; Gent R.[1]; O Carroll C.[1,2]; Coghlan D.[1,2]; Hourihane J. O.[1,5]
[1]*Children's Health Ireland, Dublin, Ireland;* [2]*Trinity College, Dublin, Ireland;* [3]*Cork University Hospital, Dublin, Ireland;* [4]*Midlands Regional Hospital, Portlaoise, Laois, Ireland;* [5]*Royal College of Surgeons in Ireland, Dublin, Ireland*

Background: Internationally, the COVID-19 pandemic severely curtailed access to hospital facilities for those awaiting elective/semi elective procedures. For allergic children in Ireland, already waiting

up to 4yr for an elective oral food challenge (OFC), the restrictions signified indefinite delay. At the time of the initiative there were approx 900 children on the Chidren's Health Ireland (CHI) waiting list. In July 2020, a project was facilitated by short term (6wk) access to an empty COVID stepdown facility built, in a hotel conference centre, commandeered by the Health Service Executive Ireland (HSE). The aim was to the achieve rapid rollout of an off-site OFC service, delivering high throughput of long waiting patients, while aligning with hospital existing policies and quality standards, international allergy guidelines and national social distancing standards.

Method: The working group engaged key stakeholders to rapidly develop an offsite OFC facility. Consultant Paediatric Allergists, Consultant Paediatricians, trainees and Allergy Clinical Nurse Specialists were seconded from other duties. The facility was already equipped with hospital beds, bedside monitors (BP, Pulse, Oxygen saturation) bedside oxygen. All medication and supplies had to be brought from the base hospital. Daily onsite consultant anaesthetic cover was resourced and a resuscitation room equipped. Standardised food challenge protocols were created. Access to onsite hotel chef facilitated food preparation. A risk register was established.

Results: After 6wks planning, the remote centre became operational on 7/9/20, with the capacity of 27 OFC/day. 474 challenges were commenced, 465 (98%) were completed, 9(2%) were inconclusive. 135(29.03%) OFC were positive, 25(5%) causing anaphylaxis. No child required advanced airway intervention. 8 children were transferred to the base hospital. The CHI allergy waiting list was reduced by almost 60% in only 24 days.

Conclusion: OFCs remain a vital tool in the care of allergic children, with their cost saving and quality of life benefits negatively affected by delay in their delivery. This project has shown it is possible to have huge impacts on a waiting list efficiently, effectively and safely with good planning and staff buy in – even in a pandemic. Adoption of new, flexible and efficient models of service delivery will be important for healthcare delivery in the post-COVID-19 era.

1251 | Prospective observational study of accidental allergic reactions amongst Irish children and adolescents

Crealey M.[1,2]; Byrne A.[1,2,3]

[1]*Children's Health Ireland at Crumlin, Dublin, Ireland;* [2]*Trinity College Dublin, Dublin, Ireland;* [3]*Children's Health Ireland at Tallaght, Dublin, Ireland*

Background: Food allergy (FA) now impacts almost 1 in 20 Irish children. Families attending our service are educated in how to minimise risk and avoid accidental reactions. We sought to establish the incidence of accidental allergic reactions (AAR) in food allergic children attending a tertiary allergy clinic in Ireland.

Method: A prospective observational study "ReAACt" (Recording Accidental Allergic Reactions in Children) was established, enrolling children aged 2 to 16 years with confirmed FA between November 2018 and May 2019. Participants were contacted at 3 monthly intervals for 1yr to prospectively report AARs to food. The coFAR grading system was used to grade allergic reactions as mild, moderate, or severe.

Results: The clinical characteristics of the 531 children enrolled as well as those children with AARs are displayed in Table 1. Of the 498 children with follow up data, 155(31.1%) reported at least one reaction with a mean number of AARs in this group as 1.2 (SD 0.52). There were 220 reactions yielding an annual incidence rate of 0.44 (95% CI, 0.39 to 0.48); 39 (25%) children had ≥2 AARs.

The main allergens implicated were milk (*n* = 25, 11.3%), egg (*n* = 41, 18.6%), peanut (*n* = 16, 7.2%) and treenut (*n* = 27, 12%). In 37% of reactions, the allergen was unidentified.

187 (85%) reactions were caused by allergen ingestion. Half of AARs (*n* = 110, 50%) occurred at home. In 47% of all reactions the parent of the child accidentally administered the allergen containing food.

Reactions were graded as mild (*N* = 152, 69.1%), moderate (*N* = 43, 19.5%) severe (*N* = 25, 11.4%). Of those with severe reactions, only 11(44%) received intramuscular adrenaline. Proportionally, more adolescents had severe reactions (8/73, 10.9%) compared to 2-4yrs (5/138,3.6%) and 5-12yrs (12/320, 3.8%). Among the 25 severe reactions, 8 (32%) were due to accidental administration by parents and 4 (16%) due to cross contamination.

Conclusion: Irish children with FA are frequently exposed to food allergens, however the majority of reactions are mild. The annual incidence of 0.44 (95% CI, 0.39 to 0.48) is much higher than previous reports which is likely due to regular contact with and accurate recall by parents in this prospective study. Nearly half of reactions were caused by unintentional administration by parents. This highlights the difficulty in relying on avoidance to manage FA as well as highlighting the ongoing need for education on avoidance strategies.

TABLE 1 Clinical characteristics of children in ReAACt

	All participants (*N* = 531)	Participants with accidental allergic reactions (*N* = 155)
Gender (*N*) %		
Male	355 (67%)	103 (66.5%)
Female	176 (33%)	52 (33.5%)
Median age at recruitment (years) (lower quartile, upper quartile) (years)	7 (4, 10)	7 (4,10)
2–4 years (*N*) %	138 (26%)	46(29.6%)
5–12 years (*N*) %	320 (60%)	89 (57.4%)
13–16 years (*N*) %	73 (14%)	20 (12.9%)
Number of food allergies		
1 food allergy	174 (33%)	56 (36%)
≥2 food allergies	357 (67%)	99 (64%)
Food allergens *N* (%)		
Milk	79 (15%)	27 (17%)
Egg	187 (35%)	60 (38%)
Peanut	307 (58%)	86 (55%)

	All participants (*N* = 531)	Participants with accidental allergic reactions (*N* = 155)
Treenut	258 (48%)	77 (50%)
Fish	50 (9.5%)	14 (9%)
Sesame	54 (10%)	20 (13%)
Previous history of anaphylaxis	134 (25%)	41 (26%)

[2]Howell WM, et al The HLA system: immunobiology, HLA typing, antibody screening and crossmatching techniques. Journal of clinical pathology. May 2010;63(5):387-390

[3]Hong X, et al. Genome-wide association study identifies peanut allergy-specific loci and evidence of epigenetic mediation in US children. Nature communications. Feb 24 2015;6:6304.

[4]Muraro, A., et al., EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy, 2014. 69(8): pp. 1008-25.

1257 | The role of HLA methylation in the development of food allergy in children

Kostara M.[1]; Chondrou V.[2]; Sgourou A.[2]; Tsabouri S.[3]

[1]Department of Paediatrics, Ioannina University Hospital, Greece, Ioannina, Greece; [2]Laboratory of Biology, School of Science and Technology, Hellenic Open University, Patra, Greece; [3]Department of Paediatrics, Child Health Department, University of Ioannina, School of Medicine, Ioannina, Greece, Ioannina, Greece

Background: The prevalence of food allergy (FA) is increasing during the last decades affecting both children and adults worldwide[1]. Food allergy is a multifactorial disease and is affected by genetic factors and epigenetic regulations as well. DNA methylation seem to pose a leading role in the appearance of FA. The genetic locus of the Human Leucocyte Antigen (HLA), highly polymorphic, is also implicated in the development of FA[2]. In particular, the methylation pattern of specific regions of *HLA-DRB1* and *HLA-DQB1* is associated with a greater risk of FA evolution in children[3]. The aim of this study was to investigate the methylation pattern of specific CG nucleotides located at the HLA-DRB1 gene in food allergic children and healthy subjects.

Method: The study population consisted of 42 children, 28 of them were defined as food allergic and 14 as healthy subjects. Peripheral Blood Mononuclear Cells (PBMCs) were isolated from whole blood samples. Methylation levels of selected CpG dinucleotides across the CpG island of *HLA-BRB1* gene were quantified by Pyrosequencing CpG assay. IgE mediated FA diagnosis based on clinical criteria, skin prick tests (wheal diameter≥3mm) and specific IgEs (>0.35KU/l) (ImmunoCap), according to EAACI guidelines[4]. The diagnosis of food allergy was confirmed for the study sample after open food challenge.

Results: There was a statistically significant difference at the methylation rate of the CG dinucleotides between food allergic children and healthy subjects (p = 0.013). Also,Spearman's point biserial correlation showed parents' smoking and allergy history could affect methylation levels (rs=-0.32, p = 0.042 and rs=0.357, p = 0.022 respectively).

Conclusion: To the best of our knowledge this is one of the very few studies which shows that the methylation rate of the specific *HLA-DRB1* region is associated with the development of FA in children.

[1]Li J et al. Are genetic tests informative in predicting food allergy? Current opinion in allergy and clinical immunology. Jun 2016;16(3):257-264

1275 | What variables can predict the asthma exacerbation during the later six months period: longitudinal analysis from the korean childhood asthma study (KAS) cohort

Suh D.I.[1]; Park J.S.[1]; Kwon J.[2]; Yoo Y.[3]; Lee E.[4]; Shin M.[5]; Kim J.T.[6]; Lim D.H.[7]; Yang H.J.[8]; Song D.J.[9]; Yu J.[10]

[1]Seoul National Univeristy College of Medicine, Seoul, South Korea; [2]Seoul National Univeristy Bundang Hospital, Seongnam, South Korea; [3]Korea University Anam Hospital, Seoul, South Korea; [4]Cheonnam National University Hospital, Gwangju, South Korea; [5]Sooncheonhyang University Bucheon Hospital, Bucheon, South Korea; [6]The Catholic University Uijeongbu St.Mary's Hospital, Uijeongbu, South Korea; [7]Inha University Hospital, Incheon, South Korea; [8]Sooncheonhyang Hospital Seoul Hospital, Seoul, South Korea; [9]Korea University Guro Hospital, Seoul, South Korea; [10]Asan Medical Center, Seoul, South Korea

Background: Assessing future risk of asthma exacerbations is vital in asthma management. Variables that constitute current asthma status can predispose asthma exacerbation for the following periods. This study explores factors that may determine asthma exacerbation in the following six-month period from a childhood asthma cohort.

Method: We have prospectively collected clinical data of asthmatic children aged 5-15 years, enrolled from 19 centers nationwide, at a cohort of Korean childhood Asthma Study (KAS). Laboratory tests and information regarding demographics, asthma control, and environment were archived at an initial visit. Follow-up data was provided every six months. We have paired every consecutive visit as a preceding and following one. The preceding visit's variables were analyzed whether they are associated with an exacerbation during the following six months assessed at the following visit.

Results: A total of 653 subjects made 1746 pairs of visits. Among them 280 (16.5%) asthma exacerbations were observed. Female sex (p = 0.022), history of food allergy (p = 0.030), skin prick test positivity (p = 0.032), parental level of education (p = 0.030), and socioeconomic status (p = 0.024) are associated with the increased risk of exacerbation during a follow-up 6-months period. However, at the final multivariate logistic regression, ICS dosage (p = 0.048) and the asthma exacerbation at the preceding visit (p = 0.018) are significantly associated with the exacerbation during the following 6-months period thereafter.

Conclusion: Variables that constitute the current visit may predispose an asthma exacerbation during the following period. This result

emphasizes the need for regular encounters even though asthmatic children are stable.

1132 | Clinical relevance of cluster analysis in phenotyping allergic rhinitis in the pediatric population of the kuyavian-pomeranian voivodeship

Kowalczyk A.; Krogulska A.

Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum Bydgoszcz, Nicolaus Copernicus University, Torun, Poland, Bydgoszcz, Poland

Background: The clinical picture of allergic rhinitis (AR) varies, due to a different clinical course, sensitization profile to airborne allergens, and severity of the symptoms. Cluster analysis allows to specify AR phenotypes in the study population and use it to individualizing patient management, treatment, and prophylaxis. The aim of the study was evaluation of clinical relevance of cluster analysis in phenotyping AR based on an analysis of selected clinical and environmental factors.

Method: The study sample was 80 children (7-17y.o.) with AR, including 28 children with associated asthma. The effects of AR symptoms on the patients daily functioning, skin prick tests (Allergopharma), allergen-specific IgE for airborne allergens (Biocheck GmbH), total cholesterol, cholesterol HDL, cholesterol LDL, triglyceride levels in the blood (ARCHITECT c System), FeNO concentration (Hypair FeNO Medisoft), nNO concentration (Hypair FeNO Medisoft) and results of metacholine challenge test (Lungtest 1000, Ispa) were analyzed.

Results: Based on cluster analysis 4 clusters of patients with AR were extracted, differing in the incidence and severity of AR symptoms and the coincidence of asthma: cluster 1 (n = 28; 35.00%), cluster 2 (n = 19; 23.75%), cluster 3 (n = 15; 18.75%) and cluster 4 (n = 18; 22.50%). Most of the children from cluster 1 (n = 24; 85.71%) and cluster 2 (n = 15; 78.95%) had persistent ANN, while most of the children from cluster 3 (n = 11; 73.33%) and cluster 4 (n = 14; 77.78%) had intermittent AR. The co-occurrence of asthma was significantly higher in cluster 1 (n = 17; 60.71%) than in another clusters (31.58%; 26.67%; 5.56%) (p = 0.0002). Children in the clusters 3 and 4 reported a lower impact of AR symptoms on daily functioning than in the other two clusters (p = 0.0153). Children in cluster 1 had significantly more often abnormal high total cholesterol level (64.29% vs 31.58%; 33.33%; 38.89%) (p = 0.033) and in cluster 4 significantly more often abnormally high triglyceride levels (66.67% vs 35.00%; 26.32%; 20.00%) (p = 0.009) were observed. Patients in cluster 2 were significantly less likely to have abnormal high LDL levels (15.79%) than children in other clusters (50%; 46.67%; 55.56%) (p = 0.015).

Conclusion: Children with AR from the Kuyavian-Pomeranian voivodeship are a heterogeneous group of patients, differing in the course of AR, the frequency of coexistence of asthma, and occurrence of lipid parameters abnormalities.

1291 | Following advice: factors motivating adherence to infant food introduction guidelines

Odoi A.[1,2]; Soriano V. X.[1,3,4]; Perrett K.P. P.[1,2,5]; Peters R. L.[1,3]; Koplin J. J.[1,2]

[1]*Murdoch Children's Research Institute, Parkville, Australia;* [2]*Department of Paediatrics, Parkville, Australia;* [3]*University of Melbourne, Parkville, Australia;* [4]*Centre for Food and Allergy Research (CFAR), Parkville, Australia;* [5]*Department of Allergy and Immunology, Parkville, Australia;* [6]*Royal Children's Hospital*

Background: In the last 20 years, international infant feeding guidelines have undergone 3 major revisions; from 1990s advice to avoid allergic foods before 12 months (mo), to removal of advice in the 2000's, to current guidelines instituted in 2016 encouraging introduction before 12mos.Throughout changes in these guidelines, limited population-based research has investigated adherence to these directives. The EarlyNuts study, an observational study of 12mo infants, assessed changes in infant food initiation practice following updated Australian guidelines which recommended infants consume allergenic foods before 12mos of age (but after 4mos) for prevention of food allergy in early childhood. At the community level, successful distribution of, and adherence to these guidelines, could impact the effectiveness of this food allergy prevention strategy. We aimed to investigate the content and accuracy of food introduction advice parents received.

Method: Between 2018-19 a population-based sample of 1933, 11-15mo infants (74% response rate) were recruited at community-run immunisation sessions in Melbourne (Australia). Parents completed surveys about foods their child had eaten, and about the source and content of infant food introduction advice they received.

Results: 97.0% of parents reported receiving some form of infant feeding advice (such as solids initiation), however several did not receive specific allergenic food advice for one or more allergic food types such as dairy (10.7%), egg (12.3%), peanut (13.7%) or tree nuts (24.2%). Of those who received peanut advice, 7.2% received incorrect advice to either delay peanut introduction beyond 12mos (6.2%) or introduce too soon (1.0%). Most commonly received peanut advice was: introduce at a specific age (49.6%), within a specific age range (12.2%), when the child is developmentally ready (8.6%), or around 6mos old (7.09%). Parents who did not receive feeding advice about peanut were less likely to initiate peanut before 12mos compared to parents who received peanut advice (76.0% vs. 91.1%). 26.1% of parents self-reported intentionally ignoring some or all infant feeding advice, mainly citing this was due to their child's stage of development (23.2%), personal convictions (10.1%), or allergy and allergic reaction concerns (9.1%)

Conclusion: Specific allergenic-food advice was not available for some parents (10%). Advice access appears to improve food introduction behaviour, so ongoing initiatives are needed to improve public accessibility to guidelines

1280 | Prenatal antibiotics and atopic dermatitis among 18-month old children in Crete, Greece

Stefanaki E.[1]; Kalaitzidou I.[1]; Aristou M.[1]; Lakoumentas J.[1]; Galanakis E.[2]; Xepapadaki P.[3]

[1]*Venizeleion General Hospital of Heraklion, Heraklion, Greece;* [2]*Heraklion University Hospital, Heraklion, Greece;* [3]*National & Kapodistrian University of Athens, Athens, Greece*

Background: The human microbiome is extremely important due to the impact on host immunologic development and potential role in the pathogenesis of allergy-associated diseases and moreover on atopic dermatitis occurrence early in life.

Method: Mothers were interviewed at two different time points: at baseline in the maternity ward and by phone questionnaire when children were 18 months of age. Demographic data (age, weight, sex, smoking status, pet ownership), mode of delivery, yoghurt consumption, anxiety level, antibiotic and other drug use during pregnancy(trimester, route, type), personal and family history of atopy related diseases, diagnosis of atopic dermatitis (AD) and history of infections in the offspring since birth were noted. Statistical analysis included Pearson's Chi-Squared test , Wilcoxon Rank-Sum test and multivariate analysis with logistic regression modeling.

Results: A total of 385 mothers were interviewed at baseline, while 231 mothers (60%) responded at follow up. Participants and drop outs were homogenous in respect to baseline characteristics. Caesarean section was reported in 116 (50.2%) of deliveries. 55/231 (23.8 %) of mothers reported antibiotic use during pregnancy. In 20/48 (41,66%) antibiotic was given in the 3rd semester. 43/236 (18.22%) infants were diagnosed with AD. In multivariate analysis including maternal variables such as age, BMI, caesarean section, smoking, allergies, other children, paracetamol use, antibiotic route, type of yoghurt and anxiety level, the intravenous use of prenatal antibiotics was associated with 7.7 increased risk of AD diagnosis (OR 7.70, 95%CI: 1.23-48.27, p = 0.029). An increased odd for AD was recorded for mothers between 30-40 years of age (OR 4.50, 95%CI:1.08-18.7, p = 0.039). No statistical significant association was recorded between caesarean section and AD (p = 0.70). In multivariate analysis including child variables (food allergy, gender, weight, breastfeeding, wheezing episodes, infections) food allergy was significantly associated with AD diagnosis (OR 8.03, 95%CI 2.30-27.97, p = 0.001) .

Conclusion: Prenatal use of antibiotics was associated with an increased risk of atopic dermatitis only when antibiotics were given by intravenous route and in women between 30-40 years of age. The relative high percentage of caesarean section in our study population was not a risk factor for AD diagnosis. Children with food allergy had an increased risk for AD.

1133 | The relationship between lipid parameters and the course of allergic rhinitis in children

Kowalczyk A.; Krogulska A.

Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum Bydgoszcz, Nicolaus Copernicus University, Torun, Poland, Bydgoszcz, Poland

Background: Allergic rhinitis (AR) is the most common allergic disease in the world, affects 23-30% of the European general population and about 25% of children in Poland. Allergic conditions, including AR, have been shown to increase the risk of cardiovascular diseases. Hypercholesterolemia disturbs the balance between Th1 and Th2-dependent immune responses including of down-regulation the expression of Th1-related cytokines and promotes Th2-related cytokines production, which is characteristic for allergic conditions. The aim of the study was analysis of lipid parameters values and assessment of the relationship between the lipid parameters abnormalities and the clinical course of AR, allergic sensitization profile, FeNO, nNO values, and the occurrence and degree of bronchial hyperreactivity in children with AR.

Method: The study sample comprised 80 children (7-17y.o.) with AR, including 28 children with associated asthma and 40 children without a history of rhinitis symptoms. Total cholesterol, cholesterol HDL, cholesterol LDL and triglyceride levels were evaluated in the blood (ARCHITECT c System). The skin prick tests (Allergopharma), allergen-specific IgE for airborne allergens (Biocheck GmbH), FeNO concentration (Hypair FeNO Medisoft), nNO concentration (Hypair FeNO Medisoft), and results of metacholine challenge test (Lungtest 1000, Ispa) were also analyzed.

Results: There were significant differences in HDL values in children with AR vs the control group. Children with AR had significantly more often normal HDL cholesterol levels than control group (n = 70; 87.5% vs n = 27; 67.50%; p = 0.03). No significant differences were observed between these two groups in the total cholesterol, LDL cholesterol, and triglyceride levels (p>0.05). Abnormally high total cholesterol levels were associated with a higher risk of sensitization to D.pteronyssinus (n = 18; 72%, p = 0.023). Children with normal levels of total cholesterol, and normal triglyceride values were less likely to be sensitized to dog dander (n = 43; 78.18%, p = 0.049) (n = 42; 72.41%, p = 0.042). There were no significant correlations between lipid parameter levels and clinical course of AR, FeNO concentrations, nNO concentrations, and bronchial hyperreactivity in children with AR (p>0.05).

Conclusion: Dyslipidemia in AR children is as common as in the general population. However, it has been shown that lipid abnormalities in children with AR may predispose them for sensitization to perennial allergens.

1206 | Correlation between the spectrum of sensitization and the course of bronchial asthma in children

Tukkaeva N. E.; Stezhkina E. V.; Ogurtsov N. E.; Dmitriev A. V.; Belyh N. A.

Ryazan State Medical University, Ryazan, Russia

Background: 150 million people in Europe have an allergy, 10 million have multiple allergy. A number of cases of the bronchial asthma (BA) are on the rise. Diseases become younger and heavier[White Book, EAACI]. The aim of the study was to assess the relationship between the spectrum of sensitization and the features of the course of bronchial asthma in children.

Method: Outpatient cards including children with BA from 5 to 17 years were researched in a retrospective single-center study. Sensitization spectrum was studied in children with intermittent course (group I, n = 22), mild persistent course (group II, n = 36), moderate persistent course (group III, n = 16) of BA. The diagnosis BA was verified according to GINA 2020. Sensitization spectrum was identify by Skin prick test by the standard method. All statistical analyses were performed using the Statistica 6.0 software package (StatSoft Inc.).

Results: The median of age (Me) in group I-13.5 ± 3, II-13.0 ± 2.8; III-13.3 ± 3.3. The gender structure had no differences in studied groups authentically (boys-69%, girls-31%). The frequency of polysensitized children with BA was 47% in studied cohort. The level of polysensitization is lower in children aged 5-11 years (35%), while in children aged 12-17 years, polysensitization increased to 50%. In group I and II, polysensitization was detected in 41% and 42%, respectively. In group III, the frequency of polysensitization was significantly higher (69%). Home allergens were causally significant (64%) in general cohort, among them Dermatofagoides Farinae prevailed (49%). Pollen, animal and food allergens were reported at 52%, 29% and 12% respectively. After comparing distribution frequency and their variants in children, it was found that the most popular combinations were home + animal (22.2%), pollen + animal (22.2%), home + pollen (22.2%) and home allergens (22.2%) in group I. In group II (46.7%) and III (27.3%) a mix of household dust and pollen allergens prevailed. It is noteworthy that in group III, 18% of patients were sensitized to all groups of allergens.

Conclusion: Thus, the main asthma allergen is Dermatofagoides Farina in studied groups. The polysensitization and frequency of occurrence of all groups of allergens increase with severity of BA. A correlation between age and spectrum of sensitization also was found.

1019 | Drug allergy testing with skin tests and drug provocation tests in children with a reported antibiotic reaction

Kitsos N.; Mavroudi A.; Xynias I.

Aristotle University of Thessaloniki, 3rd Pediatric clinic, Ippokrateio hospital, Thessaloniki, Greece

Background: Allergic reactions to drugs are adverse reactions due to an immune mechanism. The reported drug allergy to antibiotics is likely to be significantly different from the one which is confirmed after the antibiotic challenge test that has been implicated. The aim is to determine the percentage of the reported antibiotic allergy and the percentage of the confirmed antibiotic allergy after oral challenge, in order to find out if their difference is significant.

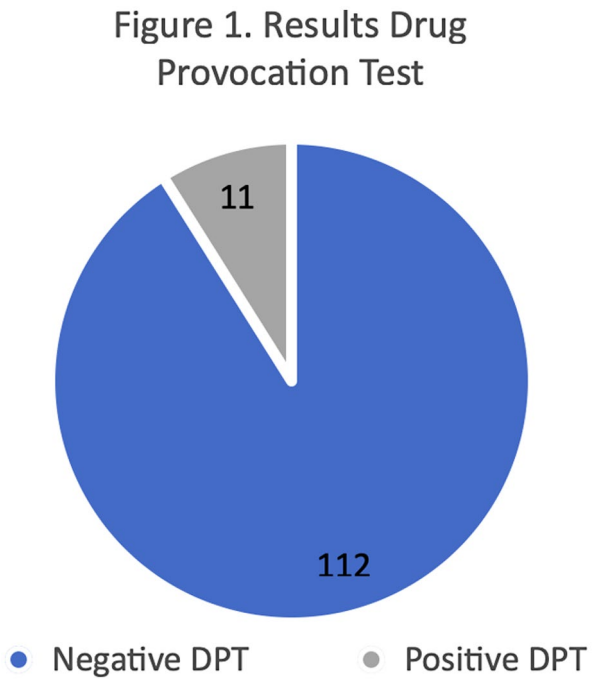
Method: All patients had a detailed history of antibiotic allergy.

The main research method of this study is to perform DPTs in patients with a reported antibiotic allergy. The above named procedure (DPT) is enhanced by the following traditional allergy diagnostic tests: a) Skin prick test (SPT) b) intradermal test (IDT) c)Eosinophil blood count test.

The population of this study is a collection of patients who are examined at the pediatric allergy department of Aristotle University. Exclusion criteria of this study are:Patient's contraindication to perform DPTs, anaphylactic reaction to the culprit antibiotic or severe cutaneous allergic reactions. The age:<1 and >15 years old. We perform eosinophil blood count tests in peripheral blood, SPTs, IDTs and finally DPTs.

Results: A total of 123 patients who had an individual history of mild allergic skin manifestations after receiving antibiotics were evaluated. In 11 of the 123 patients, the outcome of the challenge test (Drug Provocation Test) was positive (Fig.1) The clinical manifestations during the positive challenge test were from the following systems: 1) skin 88% 2) Gastrointestinal 8%, 3) Anaphylaxis 4%. The antibiotics with positive DPTs were the following: 1) Amoxicillin 37%, 2) Amoxicillin/Clavoulanic acid 25%, 3) Clarithromycin 25%, 4) Cefprozil 13%.There was no statistic significance between skin tests (skin prick tests and intradermal test) and the outcome of the drug provocation tests. (p-value >0.05). 3% of the patients had positive skin prick test, while 6% had positive intradermal test.

Conclusion: Antibiotic drug allergy in children confirmed by challenge tests is significantly lower than reported as only 7% of those with a positive individual history are confirmed. The majority of the patients had skin symptoms during DPTs, and a small proportion of patients had a severe systemic anaphylactic reaction.The gold standard for the diagnosis of drug allergy remains the drug provocation test.



1139 | Nut ingestion in infants with early egg and/or peanut allergy. what is the status quo?

Payne J.[1,2]; Mcwilliam V.[1,2]; Koplin J.[2]; Smart J.[1]; Perrett K.[1,2]
[1]*Royal Children's Hospital, Melbourne, Australia*; [2]*Murdoch Children's Research Institute, Melbourne, Australia*

Background: Tree nut (TN) allergies in Australian children are common and increasing. There has been a shift in practice from avoiding allergenic foods to introducing them <12 months to promote immune tolerance. However, there are no guidelines for TN introduction in young children with egg ± peanut who are at higher risk of TN allergy.

Aims: To determine the current practice of allergists at the Royal Children's Hospital (RCH) in Melbourne in young children with egg ± peanut allergy regarding TN introduction and use of screening Skin Prick Test. To determine the impact of clinical phenotype on home introduction of TN and the main barriers to TN introduction.

Method: Medical record review of 97 children aged <12 months diagnosed consecutively with egg ± peanut allergy between 01/12/2017-31/8/2018. Families were followed up by phone after 18-40 months.

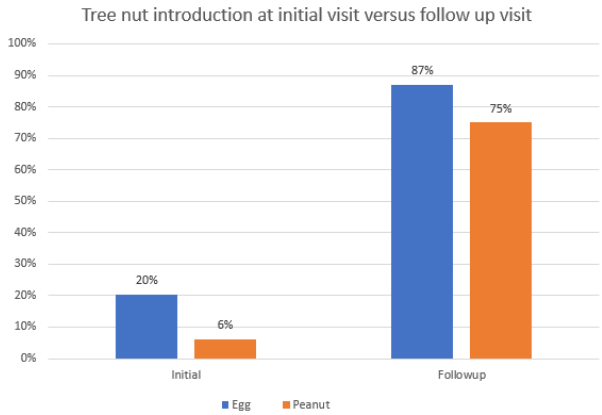
Results: Of the 97 study infants (median age 9m, range 5-11m, 63% male), 72 (74%) had egg allergy, 16 (17%) had peanut allergy and 9 (9%) had egg & peanut allergy. At initial visit only 1 (6%) infant with peanut and 14 (20%) infants with egg allergy had been introduced to at least one TN and 4 of these reported a reaction, none anaphylaxis. 59% of clinicians advised home TN introduction. 14% had screening TN SPT overall however, if peanut reaction, TN SPT screening was done in >30%.

At follow up (median age 35m, range 31-42m), 12 (75%) peanut allergic and 60 (87%) egg allergic infants had introduced ≥1 TN (almond most common). In total 29 (30%) had introduced 1-4 nuts, 37 (38%) 5-8 nuts and 9 (14%) all 9 TN. Patients reporting ongoing reactions to sesame or peanut were the least likely to have introduced TN (<70%). The most common reason for no TN introduction was that families did not eat the TN routinely, followed by concern regarding risk of a reaction. Of the 80 families that had introduced ≥1 TN, only 7 (9%) reported a reaction, none requiring adrenaline.

Conclusion: Around half of RCH clinicians recommend home TN introduction and most do not perform TN screening.

Families of infants with peanut allergy were less likely to introduce TN than those with egg allergy alone.

The main barrier to TN introduction was not routinely eating the TN. The risk of reaction to TN in those with egg ± peanut allergy is low and no anaphylaxis was reported. Larger studies are needed to determine how best to encourage introduction of TN in infants, particularly in those at higher risk of TN allergy.



1140 | Dietary diversity in infancy and the occurrence of sensitization and allergy in toddlers

Kusmierek M.; Gawryjolek J.; Krogulska A.
Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum Bydgoszcz, Nicolaus Copernicus University, Torun, Poland, Bydgoszcz, Poland

Background: The relationship between diet and allergy may be influenced by the degree of dietary diversity in the first year of life. The introduction of different food groups into the diet should be done following accepted guidelines. The study aimed to assess the influence of a diversified diet, changes in the consistency of introduced foods, method of preparation of meals in infancy on the development of sensitization and/or allergy in toddlers.

Method: The study was conducted prospectively in two stages. A survey questionnaire based on validated FFQ sheets was used. Nutrition in the first year of life was evaluated by determining the method of meal preparation, the time of changing the consistency and the variety of the diet (based on the introduced quantities of

food groups from 1-8, in the 3, 4, 6 and 12 months of age). Allergic symptoms and sIgE against 10 food and 10 inhalant allergens (Polycheck; BioCheck) were determined in 86 children. Four groups of patients were selected.

Results: Allergy and sensitization were demonstrated in 35(40.6%) children, sensitization in 46(53.5%), allergy in 55(63.9%) children. The control group consisted of 20(23.3%) healthy children. In children with allergy and/or sensitization fewer product groups were introduced at 6 months vs children without allergy and/or sensitization ($p < 0.003$; $p < 0.001$; $p = 0.008$); similarly at 12 months ($p = 0.001$, $p < 0.001$; $p = 0.001$). Introducing more product groups (5-6 vs 0-4) into the diet at 6 months of age reduced the risk of allergy (aOR = 0.17; 95%CI 0.04-0.71; $p = 0.015$). Similarly, at 12 months (aOR = 0.14; 95%CI 0.03-0.57; $p = 0.006$). Allergic and/or sensitized children were switched to solids later (11 vs 10 months, $p = 0.041$; $p = 0.037$) (12 vs 10 months, $p = 0.013$) vs children without sensitization and/or allergy. Children with allergy and/or sensitization were significantly more often fed ready-made products than self-prepared vs children without allergy and/or sensitization ($p = 0.001$; $p = 0.006$). Frequent use of ready-made products increased the risk of allergy (aOR = 11.5; 95%CI 2.7-49.7; $p = 0.001$).

Conclusion: Earlier introduction of a varied diet (not earlier than at 4 months) reduced the risk of allergy and/or sensitization. Using ready-made products instead of self-prepared ones and delaying the introduction of solid foods increases the risk of allergy and sensitization in toddlers.

1203 | Food proteins in human breast milk and probability of IgE-mediated allergic reaction in a breastfed child: a systematic review

Gamirova A.[1], Berbenyuk A.[1], Levina D.[1], Peshko D.[2], Boyle R. J.[3], Munblit D.[1,3]

[1]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia; [2]Russian Oncological Scientific Center named after N.N.Blokhin, Moscow, Russia; [3]Imperial College London, London, United Kingdom

Background: Food proteins (FP) are excreted into human milk (HM) and it is still unclear if the presence of FP in HM is associated with allergic reactions in children with food allergy (FA). Maternal restrictive diets and switch to infant formula are both very prevalent in clinical practice, however, the evidence behind these approaches is lacking.

Method: We performed a systematic review of all original studies reporting the presence of FP in HM. We then extracted the data regarding proportion of samples with detectable FP level, median and highest protein level if reported. To assess the probability of FP concentrations to cause IgE-mediated allergic reaction we performed calculations based on reported levels of FP and a volume of a large single breast feed and compared the values with known eliciting doses (ED)01 and ED05 of studied allergens, according to the Voluntary Incidental Trace Allergen Labelling (VITAL 3.0). The number of samples with the levels above ED01 and ED05 were calculated across the studies to assess IgE-mediated reaction probability.

Results: 32 manuscripts were included in our systematic review. Cow's milk was the most commonly reported FP in HM with 14 studies assessing beta-lactoglobulin (highest level reported 800 ng/ml) and casein (highest level reported 16 ng/ml); 10 studies looked at the levels of egg proteins - ovalbumin (highest level reported 46 ng/ml) and ovomucoid levels (highest level reported 37 ng/ml); 4 studies assessed levels of peanut proteins – Ara h 1, Ara h 2 and Ara h 6 levels (highest level reported 2602 ng/ml); 2 studies looked at gliadin (highest level reported 1200 ng/ml). Based on calculated levels of FP in a single large breast feed the levels of allergens in HM may trigger an IgE-mediated allergic reaction in less than 1:1000 infants.

Conclusion: Our data suggest that the probability of these being IgE-mediated allergic reactions to food proteins in HM is low. The probability of non-IgE-mediated reactions to food proteins in HM is still unclear due to lack of evidence.

1196 | Generalised cutaneous reaction after intradermal skin tests with beta-lactam

Castro C.; Freitas C.; Carvalho J.; Oliveira G.

Hospital Pedro Hispano, Matosinhos, Portugal

Introduction: Beta-lactam (BL) antibiotics are the most common cause of drug hypersensitivity in paediatric age.

Clinical manifestations range from maculopapular and non-immediate urticarial exanthemas to anaphylaxis and severe cutaneous adverse reactions. Viral and bacterial infections with exanthemas are important differential diagnoses to consider in drug hypersensitivity reactions management.

The diagnostic approach consists of a detailed clinical history, followed by skin and laboratory tests and drug provocation tests. In mild exanthemas resulting from non-immediate reactions, drug provocation tests have been proposed to be safe without prior skin tests.

We report a rare case of a non-immediate systemic reaction to intradermal tests.

Case report: We present a case of a 4-year-old female admitted to our paediatric allergy clinic due to a BL antibiotic allergy suspicion - a disseminated maculopapular exanthema 7 days after the first dose of oral amoxicillin-clavulanate. The child was seen at the emergency department, and symptoms improved after corticosteroids and antihistamines administration. The antibiotic was suspended and she was referred for drug allergy diagnosis.

The investigation was carried out six months after the adverse event, according to the European Academy of Allergy and Clinical Immunology guidelines. Skin prick tests were negative. Intradermal tests were performed and, after 10 hours, indurated wheals larger than 10×10mm with progressive erythema and disseminated maculopapular eruption occurred, related to amoxicillin and amoxicillin-clavulanate. She was

treated with antihistamines and oral corticosteroids and had clinical improvement and complete resolution of the erythema after 72 hours. Drug provocation tests with BL were not performed due to the positive intradermal tests. Five weeks later, a drug provocation test with an alternative BL (cefuroxime) was performed, and no adverse reactions have been reported.

Discussion: Generalised reactions to BL skin tests are rarely reported, and the majority are immediate reactions.

This case illustrates a rare example of a non-immediate generalised reaction to intradermal tests, underlying the importance of a more conservative approach using skin testing prior to the drug provocation tests in cases of moderate to severe non-immediate reactions.

1138 | Time of introduction, degree of processing and frequency of supply of solid foods, and the incidence of sensitization and allergy in toddlers

Kusmierek M.; Gawryjolek J.; Krogulska A.
Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum Bydgoszcz, Nicolaus Copernicus University, Torun, Poland, Bydgoszcz, Poland

Background: Prenatal and infantile period is the time of life when enviromental factors have the greatest influence on the later functioning of the immune system. So far it has not been explained if and which dietary components and in what amounts induce changes in the immune system leading to the development of allergy or tolerance. The aim of the study was to evaluate the relationship between time, type, degree of processing, frequency of solid foods introduction and development of allergy in toddlers.

Method: The study was conducted prospectively in two stages. A survey questionnaire based on validated FFQ sheets was used. Nutrition in the first year of life was evaluated by determining the time, type, degree of processing and frequency of solid foods supply. Allergic symptoms and sIgE against 10 food and 10 inhalant allergens (Polycheck; BioCheck) were determined in 86 children. Four groups of patients were selected.

Results: Allergy and sensitization were demonstrated in 35(40.6%) children, sensitization in 46(53.5%), allergy in 55(63.9%) children. The control group consisted of 20(23.3%) healthy children. Allergenic products, i.e. hen's egg, milk, peanut, wheat, soy, fish, tree nuts, shellfish were most frequently introduced between 7-12 months of age, irrespective of the study group. During this period, egg white was introduced in the allergy group in 47(85.5%) children (p = 0.894), in the allergy and sensitization group in 29(82.9%) (p = 1.00), and in the sensitization group in 38(82.6%) children (p = 0.533). Milk at 7-12 months of age was introduced in 35(64.8%) allergic children (p = 0.64), in 22(64.7%) with allergy and sensitization (p = 0.815), and in 26(57.8%) sensitized children (p = 0.627). Similar results were with other foods. Children without sensitization or allergy (n = 9; 56.2%) were significantly more frequently introduced heat-treated peanuts vs. children with sensitization, without allergy, who more commonly consumed raw peanuts (n = 6; 54.5%; p = 0.028). Children with allergy were significantly more often given fish i.e. 1-3 times/week (n = 43; 79.6%) vs children without allergy, i.e. 1-3 times/month (n = 9; 30%; p = 0.009).

Conclusion: There was no association between the timing and type of solid foods introduced (including allergenic ones) and the development of allergy and sensitization in toddlers. The degree of processing and the frequency of supplementation food can influence the development of allergy and sensitization.

1255 | COVID-19 lockdown: a real-life experiment of pollen avoidance for children affected by pollen allergy

Pecoraro L.[1]; Castagnoli R.[2]; Salemi C.[3]; Fasoli S.[3]; Accorsi P.[3]; Pietrobelli A.[4]; Marseglia G.L.[2]
[1]*Department of Medicine, University of Verona; Paediatric Clinic, ASST Mantua, Verona, Mantova, Italy*; [2]*Department of Pediatrics, Foundation IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy*; [3]*Paediatric Clinic, ASST Mantua, Mantova, Italy*; [4]*Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, University of Verona, Verona, Italy*

Background: It is known that an increase in the risk of asthma exacerbations (AE) requiring emergency department (ED) presentation is demonstrated in children and adolescents exposed to outdoor pollen. On the other hand, COVID-19 lockdown represented a real-life experiment of pollen avoidance for children affected by pollen allergy. This study aims to test if pollen avoidance prevents asthma exacerbations in children affected by pollen allergy in an ED setting.

Method: It is a retrospective study involving all children with a known diagnosis of pollen-allergy asthma who attended our ED for an AE in the town of Mantova and its provincies in the period March 09-May 03 of the years 2018, 2019 and 2020. This period was chosen because it coincided with the Italian COVID-19 lockdown in 2020.

Results: In 2020, 4 (0.7%) children with a known diagnosis of pollen-allergy accessed the ED for an AE. On the other hand, pediatric access for this specific type of illness was a total of 20 (0.5%) and 12 (0.3%) in 2018 and 2019 in the same period. Specifically, the rate of hospitalization was 0 in 2020 versus 3 (15%) and 1 (8.3%) in 2018 and 2019, respectively. Regarding patients' ongoing treatment, 1 (25%) patient was under asthma maintenance therapy in 2020 versus 3 (15%) and 5 (41.6%) in 2018 and 2019, respectively. In addition: the male/female rate was 50% in 2020 versus 55% and 83.3% in 2018 and 2019, respectively. About median age (years), it was 14.7 in 2020 versus 9.5 and 6.8 in 2018 and 2019, respectively (tab. 1).

Conclusion: The inevitable pollen avoidance during COVID-19 lockdown could prevent AE in children affected by pollen allergy. Anyway, further study should be performed to confirm this preliminary experience.

Demographic data and clinical characteristics (Figures in round parentheses represent percentages. Figures represent median values and figures in squared brackets represent 1st and 3rd quartiles)

	2018	2019	2020
Total population, Province of Mantua	411.762	412.292	411.062
Pediatric population, ≤16y, n (% total population)	62.266 (15.1%)	61.125 (14.8%)	60.490 (14.7%)
Pediatric Emergency department visits, n	3781	3502	514
ED visits for seasonal allergic asthma, n (% ED visits)	20 (0.5%)	12 (0.3%)	4 (0.7%)
Demographic data and clinical characteristics of pediatric patients evaluated for seasonal allergic asthma			
Gender: Male, n/N (%)	11/20 (55 %)	10/12 (83.3 %)	2/4 (50 %)
Age (*years*)°	9.5 [6.3 – 10.3]	6.8 [5 - 12]	14.7 [10.8 – 16.6]
Pollen Allergy	20/20 (100 %)	12/12 (100 %)	4/4 (100 %)
Asthma maintenace therapy	3/20 (15 %)	5/12 (41.6 %)	1/4 (25 %)
Hospitalization	3/20 (15 %)	1/12 (8.3 %)	0/4

1256 | Exercise-induced anaphylaxis in pediatric age: not all cases are linked to a specific food

Pecoraro L.[1]; Cecchin V.[2]; Salemi C.[3]; Fasoli S.[3]; Accorsi P.[3]; Pietrobelli A.[2]

[1]*Department of Medicine, University of Verona; Paediatric Clinic, ASST Mantua, Verona, Mantova, Italy;* [2]*Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, University of Verona, Verona, Italy;* [3]*Paediatric Clinic, ASST Mantua, Mantova, Italy*

Introduction: Exercise-induced anaphylaxis (EIA) is a rare but potentially life-threatening disorder characterised by the development of immunoglobulin E (IgE)-mediated hypersensitivity associated with physical activity. The most part of EIA is food-dependent (FDEIA). On the other hand, a minor proportion of cases is represented by non-specific FDEIA (nsFDEIA). Specifically, the intake of any food to which there is no allergic sensitization, it is able to induce anaphylaxis. Temperature, menstrual cycle or use of drugs, particularly aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) can worsen the attacks. Diagnosis is mainly clinical.

Case report: A 15-years-old girl referred to our allergic clinic for 4 episodes of anaphylaxis that occurred during physical activity about 2 hours and 30 minutes after eating. Symptoms have not consistently been associated with a specific food before jogging on these occasions. Specifically, ns-FDEIA occurred respectively after ingestion of macaroon rice, tomato pasta and japanese food. Otherwise, exercise and these types of food were independently tolerated. She did not take drugs such as NSAIDs and neither temperature nor menstrual cycle were associated with those episodes. Aquagenic anaphylaxis was also excluded. Skin-prick tests and sIgE were positive for walnut and peanut. Serum tryptase and other exams involved in differential diagnosis were negative. According to the patient and their parents, an oral food challenge test was not performed for patient safety, her history and the result of allergy tests, which did not reveal a specific food involved in the allergic reaction. The therapy of the patient consisted in avoiding physical exercise 4 hours after and 2 hours before intake of any food. Following these instructions, the patient didn't report allergic reactions later.

Conclusions: The diagnosis of nsFDEIA is based on the patient's history and represents a diagnosis of exclusion. It is necessary that the patient avoids physical exercise 4 hours after and 2 hours before the intake of any food. Moreover, clinicians need to make sure that the patient is able to comply with these limitations. In addition, the patient must be careful in taking NSAIDs or during infectious episodes. Moreover, it is important to instruct the patient and family members to correctly identify early symptoms of anaphylaxis, dealing with them correctly, and prescribe self-injectable adrenaline.

962 | Bronchopulmonary aspergillosis in preschool children, diagnostic difficulties

Selevestru R.[1]; Sciuca S.[1,2]; Tomacinschii C.[1,2]; Rotaru-Cojocari D.[1,2]; Balanetchi L.[1]; Adam C.[1]

[1]*State University of Medicine and Pharmacy "Nicolae Tetemitanu", Chisinau, Moldova;* [2]*Mother and Child Institute, Chisinau, Moldova*

Aim: Diagnostic tests evaluation of the child with allergic bronchopulmonary aspergillosis

Methods: a child of 5 years old was evaluated in the Pneumology Clinic by specific tests for fungi: total IgE assessment by chemiluminescence method (CLIA), quantitative test; Fungi specific IgE by immunoblot method, quantitative test (ALEEX test), and ALATOP Allergy Screen.

Results: The child is admitted with the diagnosis of pneumonia, complicated by bilateral serofibrinous pleurisy, lower bilateral pulmonary fibrosis, respiratory failure - gr. I. moderate, persistent asthma, uncontrolled, exacerbation. His medical history is significant for frequent respiratory infections and bronchoobstructive episodes. Frequently ill child from 3 months with 3-5 pneumonia treated outpatient. Performs periodic rashes without specifying the allergen (in fish, cow's milk, ceftriaxone). On admission SpO2-92%. A series of investigations are being carried out: sweat test nr.1-28,64 mcmol/l; nr. 2-27,64 mcmol/l. In the bacteriological analysis of sputum, sputum culture grew *Pseudomonas aeruginosa* 10^6. Subsequently the child is tested for IgE specific for *Alternaria* alternate (m6 – E - 12,28 kUA/L şi m229 – M(rAlt a 1) – 12,78 kUA/L). Laboratory findings also include a high level of serum IgE (863 UI/ml). Measurement of antibodies IgG-Ab, IgM-Ab and IgA-Ab against *Aspergillus fumigatus* by means of serum/haemagglutination-1/640 (*N* <1/80)

Conclusion: A frequently ill child with rebellious bronchoobstructive syndrome, with hyper IgE and chronic bronchopulmonary manifestations, also needs to be investigated for allergic aspergillosis, in order to provide appropriate therapeutic behavior.

900 | Infant with persistent febrile lymphadenitis following his mother's acute tetraparesis: two parallel stories

Vazouras K.[1,2]; Vangeli D.[1]; Dokou A.[1]; Messaritaki A.[1]; Michos A.[3]; Liatsis E.[2]

[1]*Second Department of Pediatrics, Aghia Sophia Children's Hospital, Athens, Greece;* [2]*Department of Immunology-Histocompatibility, Specialized Center & Referral Center for Primary Immunodeficiencies - Paediatric Immunology, Aghia Sophia Children's Hospital, Athens, Greece;* [3]*First Department of Pediatrics, Division of Infectious Diseases, National and Kapodistrian University of Athens, Athens, Greece*

Background: Acute bacterial lymphadenitis, non-respondent to empiric treatment, may warrant thorough investigation for malignancy, immunity disorder or infection by unusual pathogens.

Case presentation summary: We describe a case of a 6-month old, male infant with acute febrile cervical lymphadenitis. Notably, the onset of his disease was four days after his mother's urgent hospitalization due to acute tetraparesis, following an unexplained spinal cord infarct. The infant received multiple empiric antibiotic regimens, to which he responded poorly. The persistence of fever and lymphadenitis necessitated an extensive work-up for infection, malignancy and immune/autoimmune disease. Further exams revealed the presence of generalized lymphadenitis, probable brain infection and bilateral, chorioretinal lesions. A cervical lymph node biopsy was also performed, showing necrotizing granulomas and lymph nodes' infection by *Staphylococcus aureus* and *Candida parapsilosis*. A rapid pathology review raised the suspicion for either chronic granulomatous disease (CGD) or mycobacterial infection. Mother and infant were subsequently screened for both. Meanwhile, the mother's clinical condition was further complicated by fever without source and pulmonary embolism.

Eventually, the boy was diagnosed with x-linked CGD. He was treated with targeted antimicrobial treatment and corticosteroids, which led to full clinical remission. Remarkably, the infant received totally thirteen different antimicrobial regimens during his course. A definitive diagnosis has not yet been made for the mother's condition, while the CGD's X-link carriage is being considered as a potential contributing factor to her disease.

Learning points

- Complicated, generalized infection may require extensive work-up and multiple antimicrobial regimens. Timely reporting of laboratory results is crucial to optimize treatment.
- Contacts should also carefully be screened for infection or any other remarkable autoimmune family history.
- Expertise and multidisciplinary collaboration is warranted for the treatment of patients with CGD.

1031 | New horizons in the diagnosis and treatment of atopic dermatitis

Sur M. L.[1,2]; Zahariuc T. M.[1,2]; Maák G.[1,3]; Duca E.[4]

[1]*University of Medicine and Pharmacy, Cluj-Napoca, Romania;* [2]*Emergency Clinical Hospital for Children, Cluj-Napoca, Romania;* [3]*Clinical Hospital of Infectious Diseases, Cluj-Napoca, Romania;* [4]*Institute of Gastroenterology Cluj-Napoca – Department of Allergology and Immunology, Cluj-Napoca, Romania*

Background: Atopic dermatitis (AD) has been considered for long an allergic disease. However, studies have shown that the allergic mechanism is proven in less than half of the cases of atopic dermatitis. Clinical evolution, similar to the autoimmune diseases, with periods of exacerbation and remission, has led to the question of whether atopic dermatitis might have an autoimmune component. Studies have shown that a large number of patients with atopic dermatitis have IgE autoantibodies, as well as antinuclear antibodies (ANA). Also proving the autoimmune nature of the disease, treatment schemes in study for AD include different monoclonal antibodies directed against interleukins involved in the pathogenesis of the disease and against IgE.

Method: We included in our study 112 cases of children diagnosed with AD, aged between one month and 18 years old, during a period of 3 years (2017-2019), who were admitted to the Emergency Clinical Hospital for Children Cluj - Napoca. The inclusion criteria were according to EAACI. A control group of 60 children with age and sex characteristics similar to the study group was also selected for the study. We determined biologic parameters, both in the patients with AD and in the control group: specific IgE, total IgE, ANA, IgE autoantibodies, inflammatory markers, blood cell count. The severity of DA was determined using the SCORAD index.

Results: Of the 112 cases, 85 children (79%) had the onset of symptoms before the age of 5 years old. The allergic factor, determined through specific IgE, total IgE and positive skin tests, was proven in 51 cases (46%). The autoimmune component, detected through IgE autoantibodies and ANA, was only investigated in 15 patients. All the 15 patients had positive autoantibodies, but we cannot extrapolate these results for the whole group. In our case study, females predominate: 68 cases (61%), while 44 cases were male (39%). The severity, calculated according to the SCORAD index was: mild – 50 cases (44,6%), medium - 41 cases (36,6%), severe - 21 cases (18,75%).

Conclusion: The allergic component is involved in the pathogenesis of DA in less than 50% of cases.

The autoimmune component is increasingly documented in the pathogenesis of DA.

Current treatments with monoclonal antibodies, which specifically target the interleukin pathways, might have a significant influence on the evolution and intensity of the disease.

1214 | Exposure to cow milk formulas trend in the nursery at King Abdulaziz University Hospital: an atopy risk

Atwah A.[1]; Koshak E.[2]; Alhussaini B.[2]; Alsaedi S.[2]

[1]*Faculty Of Medicine In Rabigh, KAU, Rabigh, Saudi Arabia;* [2]*King Abdulaziz University, Jeddah, Saudi Arabia*

Background: Although all health organizations recommend exclusive breast feeding (EBF), few newborns meet these recommended goals. The early intake of Cow Milk Formulas (CMFs) has been linked to several childhood illness including atopic diseases.

Method: a retrospective, medical records review of feeding practices of neonates born in king Abdulaziz university hospital (KAUH) at Jeddah, Kingdom of Saudi Arabia. Two months from each year (May and December) were selected over the last five years. Approval from the ethical research committee at KAUH was obtained.

Results: 894 different neonates files were reviewed, 487 (54.5 %) were males. Early introduction to CMFs in newborns was in 838 (93.7 %): 797 (89.1 %) received mixed CMFs and breast milk, 41 (4.6 %) received CMFs only, and 56 (6.3 %) received EBF. Surprisingly, the trend of EBF was declining with time from 39 % in May 2016 to 1 % in December 2020.

Conclusion: unfortunately, the prevalence of early exposure to CMFs was very high in nearly all newborns at KAUH nursery, and with an increasing trend. Extensive teaching programs on EBF and allergy prevention for all mothers and nursery health workers is highly recommended.

1207 | Model based meta-analysis of the effect of non-specific immunomodulation with OM-85 for recurrent viral respiratory tract infections and wheezing: a multi-scale mechanistic approach

Arsène S.[1]; Chevalier A.[2]; Couty C.[1]; Faddeenkov I.[1]; Go N.[1]; Granjeon-Noriot S.[1]; Kahoul R.[1]; Kulesza A.[1]; Lehr L.[2]; Pasquali C.[2]

[1]*Novadiscovery, Lyon, France;* [2]*OM Pharma, Meyrin, Switzerland*

Background: Acute viral respiratory tract infections (RTIs) are the main cause for wheezing in preschool children and are associated with a high degree of acute inflammation. Recurrent RTIs lead to exacerbation of the damages and thus increase the risk of developing permanent wheeze and/or asthma due to airway remodeling. Efficient strategies to prevent or reduce frequency of viral RTIs in patients at risk for recurrent infections is currently an unmet need.

In preschool children with recurrent RTIs the bacterial lysate OM-85 (Broncho-Vaxom®) has proven to be efficacious as a prophylactic strategy in the recurrence of RTIs as confirmed previously by a meta-analysis (Yin et al. 10.1016/j.intimp.2017.10.032). Nevertheless, patient recruitment and population heterogeneity are key obstacles to conducting clinical trials that confirm efficacy in the prophylaxis of recurrent wheezing.

Method: We designed a mechanistic model calibrated to OM-85 clinical data. A mechanistic administration and pharmacodynamics response model helps rationalizing the variability and age-dependency of immunomodulation. Epidemiological-immunological viral infection models and an airway size/inflammation submodel translate the RTI into a wheezing context. With this setup we can simulate individual RTIs and wheezing events over time to generate a virtual population with patient level data and assess OM-85 immunomodulation on these phenomena.

Results: With in silico clinical trials with variable virtual patient eligibility criteria, we explored the efficacy of OM-85 as a function of trial design and the target population. In our analysis, we could explain why longer follow up times capture a higher number of prevented RTIs or wheezing episodes (larger mean effect) but suffer from increased inter-patient variability (in particular with wheezing as an endpoint). Patient age and baseline risk modified the mean effect and its variability but their given weight needs to be adjusted for with other non-identified factors explaining inter-trial variability. Our in silico analyses also indicated potential for optimization regarding the dosing-regimen as longer exposure seemed to increase the effect size without affecting the response heterogeneity.

Conclusion: Overall, we have created a modeling and simulation tool that can be used for model-based meta-analysis in a novel way, in particular where data is heterogeneous and individual patient data is hard to access.

1244 | Association between snps of VDR gene, IgE and vitamin D serum levels in obese children of the Colombian Caribbean coast: A case-control study

Egea-Bermejo E.[1]; Fang L.[1]; Pereira-Sanandres N. S.[1]; Moreno-Woo A.[1]; Garavito-Galofre M. D.P.[2]; Del Toro K. Y.[1,2]; Ordoñez J.[2]; Garavito-De Egea G.[1]

[1]*Medicina, División Ciencias de la Salud. Grupo de Inmunología y Biología Molecular. Universidad del Norte, Barranquilla, Colombia;* [2]*Medicina, División Ciencias de la Salud. Grupo de Genética. Universidad del Norte, Barranquilla, Colombia*

Background: Obesity as a public health problem is a disease present in both developed and developing countries. Recent studies have evaluated the relationship between obesity, vitamin D deficiency, and atopy. Although the results are not clear, Single-Nucleotide Polymorphism (SNP) of vitamin-D receptor (*VDR*) gene are associated with the development of this disease. Currently, there are no data on this association in the Colombian school population, nor if this association influences or is associated with total IgE levels in obese children. The aim of this study was to analyze the association between obesity and SNP of *VDR*, and its influence on serum levels of vitamin-D, total IgE, and lipid profile in schoolchildren from the Colombian Caribbean.

Method: Cases (*n*: 119) and controls (*n*: 176) study was carried out with obese children between 5 and 17 years old from the Colombian Caribbean coast. The SNPs *TaqI* [rs731236-A/G], *ApaI* [rs7975232--A/C], *FokI* [rs2228570-A/G] and *BsmI* [rs1544410-C/T] were

genotyped by qPCR. We measured serum markers associated with obesity: vitamin D [1.25 hydroxyvitamin D], Adiponectin, Leptin, total cholesterol, triglyceride, HDL, LDL, VLDL, and total IgE. Values of $p < 0.05$ were considered statistically significant.

Results: High levels of vitamin D and obesity were associated; 48.7% (*n*: 58) of the cases had high levels [>100 ng/mL] compared to 0.6% of the controls ($p < 0.05$). *VDR* SNPs were not directly associated with childhood obesity. There was no evidence of influence on the serum markers studied in the cases. All SNPs were in Hardy-Weinberg equilibrium. No statistically significant differences were found between IgE levels in the groups studied. However, in both groups, IgE was high [> 100 IU/mL].

Conclusion: It could be assumed that, in the sample of obese children studied, the genetic variants *BsmI*, *FokI*, *TaqI*, and *ApaI* of the *VDR* gene did not show an association with obesity or with the serum biomarkers evaluated. However, the high levels of vitamin D found in the cases allow us to infer its relationship with the development of obesity in this Colombian pediatric group.

1064 | Screening for hepatocellular carcinoma (HCC) on people on androgens

Ashoor Z.[1]; Nj S.[2]; Craig T.[3]

[1]*Cairo University School of Medicine, Cairo, Egypt;* [2]*Robert Wood Johnson Medical School, Department of Pediatrics, New Brunswick, Nj, United States;* [3]*Department of Medicine and Pediatrics, Penn State Health Milton S. Hershey Medical Center, Hershey, Pa, United States*

Background: Androgens are effective therapy for prophylaxis of Hereditary Angioedema (HAE). The concern is adverse events to include hepatitis, hepatocellular carcinoma (HCC), hyperlipidemia, weight gain, hematuria and increase hematocrit. Presently guidelines suggest that CBC, chemistry panel, urine and liver function tests should be done every 6 months and liver ultrasound every 12 months. It is our concern that more frequent screening for HCC with ultrasound is necessary for early detection, eligibility for treatment, and improving survival.

Method: We reviewed the literature for doubling time of HCC. We also reviewed the literature on frequency of assessment of the liver in high risk situations for HCC.

Results: Secondary to doubling time of HCC and medical standards for assessment of high risk patients for HCC, it seems the appropriate screening for HCC is every 6 months. Though the ideal situation would be screening every 4.5 months a fair compromise for ease of the health care provider and the patient is 6 months.

Conclusion: Our findings suggest that every 6 months assessment for HCC is more appropriate for patients on androgens especially those who have other risks for HCC and those on high doses of androgens.

1118 | Application of a mechanistic model to assess RTI prophylaxis trial feasibility in the post-COVID era

Arsène S.[1]; Chevalier A.[2]; Couty C.[1]; Faddeenkov I.[1]; Go N.[1]; Granjeon-Noriot S.[1]; Kahoul R.[1]; Kulesza A.[1]; Lehr L.[2]; Pasquali C.[2]; Sireau A.[1]

[1]*Novadiscovery, Lyon, France;* [2]*OM Pharma, Meyrin, Switzerland*

Background: There is a good chance to soon control the COVID-19 pandemic but other respiratory tract infections (RTIs) will continue to impact public health. Viral lower RTIs in children are associated with hospitalization, wheezing and asthma inception, while upper RTIs are less severe but have a higher prevalence. Vaccination against prevalent viruses like RSV and RV are still neither available currently nor in the near future. Non-specific immunomodulation for RTI prophylaxis is an interesting treatment alternative. For example, the oral bacterial lysate Broncho-Vaxom (OM-85) has demonstrated efficacy in prevention of recurrent RTIs, specifically in at-risk pediatric populations. For targeting other populations and RTI-indications, robust efficacy data need to be generated, but clinical trials are strongly impacted by the pandemic. Globally, all trials other than dedicated to COVID-19 are experiencing delays or even halts, e.g. due to patient recruitment issues. At the same time, RTI burden changes - through lockdown or social distancing - with an uncertain trajectory. The feasibility of RTI prophylaxis clinical trials in this context thus remains an open question.

Method: As a step towards feasibility forecasting, we have implemented a dedicated in silico approach. A mechanistic pharmacokinetics/pharmacodynamics and within-host viral infection disease model is interfaced with a population-scale (between-host) SIRS disease burden model - thereby accounting for seasonality and extrinsic factors through time-dependent transmission. On the back of this model and a Virtual Population, we conduct in silico clinical trials with variations in observational periods, eligibility criteria (defining the included at-risk population) and follow-up giving us efficacy metrics and sample size estimates as outputs.

Results: We demonstrate how the SIRS model can be used to reproduce disease burden data under lockdown and social distancing measures with the example of RCGP 2019-2020 data and how we can translate this data into instantaneous control group prevalence and efficacy dependent on this modulation. We also show how and why different containment scenarios vary in their impact of demonstrated efficacy, recruitment needs and difficulty through analyses of the predicted outcome distributions.

Conclusion: We are in the position to forecast probable scenarios of containment strategies with their impact on RTI prophylaxis trials that can serve as to inform go-no/go decisions in clinical development.