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Learning in allergy and immune disease

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Determination of the cytotoxicity of chitin binding mistletoe (*Viscul album L*) fruit lectin (MChbL) on human peripheral blood lymphocytes

Gachechiladze, N; Khurtsidze, E; Gaidamashvili, M
Iv. Javakhishvili Tbilisi State University, Tbilisi, Georgia

Background: The insecticidal activity of plant lectins against a large array of insect species has been well documented. Insecticidal activities were found to be associated mostly with the two main groups of plant lectins: monocot mannose-binding and chitin binding lectin groups. Known as natural defense agents, plant lectins have been implicated as antibiosis factors against insects and considered as promising candidates for biological pesticides. Mistletoe (*Viscum album*) fruit lectin MChbL belongs to chitin-binding lectin group and is considered to expose toxic lesions on human. In vitro, plant lectins effect lymphocyte mitogenesis, aggregate immunoglobulins, induce histamine release from basophiles and mast cells. We have studied MChbL cytotoxicity towards human peripheral blood lymphocytes (PBL) in humans.
Method: Human PBL culture was used to study MChbL cytotoxicity by mitogen stimulated MTT assay. PB from 15 volunteers were examined during this study and control group was compound from 12 healthy donors. The optical densities was measured on spectrophotometer Multiscan MCC at 570 nm wavelength.
Results: Our study showed that any dose of mitogen ConA have stimulated the human PBL (1 μg/mL - OD 0.198, 10 μg/mL - OD 0.467, 100 μg/mL - OD 0.344), whereas MChbL has inhibited the proliferation of PBL MChbL in both concentration (10 μg/mL, 500 μg/mL) decreasing the amount of the cells and their viability. Particularly, this was obvious at higher concentration of MChbL 500 μg/mL applied (OD 0.60).
Conclusion: MChbL expose cytotoxical effects to human peripheral blood lymphocytes (PBL), when administrated at high concentration 500 μg/mL. However, low concentrations of MChbL were less cytotoxic to PBL and exhibit similar results as ConA at the concentration of 1 μg/mL. Most likely, approaches to use MChbL as natural bio-pesticide must be considered at dose-dependent manner and administrated in the nontoxic range.

1247
Specific IgE and IgG and pulmonary fungal disease

De Amici, M[1]; Mariani, F[2]; Corsico, AG[2]; Piloni, D[2]; Paracchini, E[2]; Torre, C[1]; Nigrisoli, S[1]; Campo, I[2]; Marseglia, GL[1]
[1]Foundation IRCCS Policlinico San Matteo, Department of Pediatrics, Pavia, Italy; [2]Foundation IRCCS Policlinico San Matteo, Department of Pneumology, Pavia, Italy

Background: Aspergillus may cause a variety of pulmonary diseases, depending on immune status and the presence of underlying lung disease. Aspergilloma is mainly seen in patients with cavitary lung disease, while allergic bronchopulmonary aspergillosis is described in patients with hypersensitivity to Aspergillus antigens. Definitive diagnosis of fungal disease is often difficult, when culture is negative. The detection of specific IgE may enable clinicians to select the best strategy for managing the disease. Therefore the detection of IgG and IgG4 is considered a marker for exposure in some lung diseases. Aim of this study is to demonstrate the validity of specific IgE and IgG in pulmonary fungal disease diagnosis.
Method: Two hundred and seventeen patients with a possible pulmonary aspegillosis have been evaluated. Serum levels of specific IgE were measured by immunofluorometric assay and expressed in kU/L. Values higher than 0.35 kU/L were considered positive. Serum levels of IgG were measured by immunofluorometric assay and expressed in mgA/L. Values higher than 25 mgA/L indicate a probable sensitization while values in the range 8–25 mgA/L indicate a risk. Aspergillus Fumigatus (AF) was isolated in 36 patients; 10 of them had positive specific IgE to AF. IgG to AF showed that 9 patients were a risk and 23 with a probable sensitization. Aspergillus Niger (AN) was isolated in other 36 patients; 6 of them had positive specific IgE to AN. IgG to AN showed that 10 patients were a risk and 15 with a probable sensitization.
Results: In our preliminary data, IgE specific antibodies level are significantly different between positive and negative coltures of Aspergillus Fumigatus ($p = 0.045$) and Aspergillus Niger ($p = 0.048$). IgG and IgG4 levels show a significant difference between positive and negative coltures of Aspergillus Fumigatus (respectively $p = 0.0062$ and $p = 0.0015$) but not for Aspergillus Niger (respectively $p = 0.059$ and $p = 0.1241$). Moreover specific IgE levels resulted significantly different also comparing A. Fumigatus with A. Niger in positive($p = 0.0001$)and in negative coltures ($p < 0.0001$), with higher values of AF. Also IgG and IgG4 values showed a significant difference between AF and AN in positive (respectively $p = 0.0074$ and $p = 0.0001$) and negative coltures (both $p < 0.0001$), with higher values of AF.
Conclusion: Specific IgE serum levels and IgG serum levels seem to be serologic tests that could potentially predict the pulmonary fungal disease.

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The validity of specific IgG and IgG4 in fungal disease diagnosis

Mariani, F[1]; De Amici, M[2]; Marseglia, GL[2]; Piloni, D[1]; Paracchini, E[1]; Nigrisoli, S[2]; Testa, G[2]; Campo, I[1]; Corsico, AG[1]
[1]Foundation IRCCS Policlinico San Matteo, Department of Pneumology, Pavia, Italy; [2]Foundation IRCCS Policlinico San Matteo, Department of Pediatrics, Pavia, Italy

Background: In allergic disease, specific IgG is used as a marker for exposure in some lung diseases including allergic alveolitis, aspergilloma and aspergillosis. Aspergilloma is mainly seen in patients with cavitary lung disease, while allergic bronchopulmonary aspergillosis is described in patients with hypersensitivity to Aspergillus antigens. Diagnose of fungal disease is often be difficult. Thus a serological method that could help clinicians in diagnose fungal disease is desirable. Our aim was to assess the validity of specific IgG and IgG4 in pulmonary fungal disease diagnosis.
Method: 217 patients with a possible pulmonary aspegillosis were evaluated at the IRCCS San Matteo Hospital in Pavia (Italy) from January 2010 to January 2014. Serum levels of IgG and IgG4 were measured by immunofluorometric assay and

expressed in mgA/L. Values higher than 25 mgA/L indicate a probable sensitization while values in the range 8–25 mgA/L indicate a risk. Aspergillus Fumigatus (AF) was isolated in 36 patients; 9 of them were a risk and 23 with a probable sensitization. Aspergillus Niger (AN) was isolated in other 36 patients; 10 of them were a risk and 15 with a probable sensitization. Serum galactomannan was checked in 25 patients only.

Results: IgG levels show a significant difference between positive and negative coltures of Aspergillus Fumigatus (r p = 0.0062) but not for Aspergillus Niger (p = 0.059). Also IgG4 are significantly different between positive and negative coltures of Aspergillus Fumigatus (p = 0.0015) but not for Aspergillus Niger (p = 0.1241). Moreover IgG and IgG4 values showed a significant difference between AF and AN in positive (respectively p = 0.0074) and negative coltures (p < 0.0001), with higher values of AF. Also IgG4 are significantly different between AF and AN in positive (p = 0.0001) and negative coltures (p < 0.0001), with higher values of AF. Furthermore, in positive culture, specific IgG and IgG4 levels resulted statistically significant also when serum galactomannan was negative (respectively p = 0.0115 and p = 0.0017).

Conclusion: Specific IgG and IgG4 serum levels seem to be serologic tests that could potentially predict the pulmonary fungal disease.

1249
Impact of high serum IgE levels on the risk of atherosclerosis in human

Unal, D[1]; Gelincik, A[1]; Elitok, A[2]; Kocaağa, M[2]; Olgaç, M[1]; Demir, S[1]; Colakoglu, B[1]; Büyüköztürk, S[1]
[1]Division of Immunology and Allergic Diseases, Internal Medicine Department, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey; [2]Department of Cardiology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Background: IgE has a key role in the pathogenesis of allergic responses. Some epidemiological studies showed that IgE levels were higher in subjects with cardiovascular disease, in particular, in those experiencing unstable angina and acute coronary events. But it is as yet unknown, if the increased IgE level is a marker of future coronary incidents and whether it may be regarded as a risk factor of an ischemic heart disease. Our aim was to investigate the relationship between immunoglobulin E levels and some atherosclerotic markers in the patients without known atherosclerotic disease.

Method: Fifty patients (mean age 40.96 ± 10.8 years) with high serum IgE levels who did not have any evidence of atherosclerotic disease and 30 healthy controls (mean age 47 ± 8.27 years) were included in the study. Atherosclerotic disease markers such as adhesion molecules VCAM-1 (vascular cell adhesion molecule-1), ICAM-1 (Intercellular Adhesion Molecule 1), proinflammatory cytokines such as IL6 (interleukin 6), endothelin 1 and systemic inflammatory markers such as high sensitivity C reaktive protein (hsCRP) were determined by ELISA. Endothelial functions of the coronary arteries were determined by coronary flow reserve (CFR) measurements and carotid intima media thickness' using transthoracic Doppler echocardiography.

Results: Total IgE levels were in a wide range in the patient group (min 117-max 4720, median 861 IU/L) while it was in close limits in the control group (min:5.29 -max:100 median 29.7). There were no differences between the patient and control groups in terms of VCAM-1, ICAM-1, endothelin 1, hsCRP and IL6 levels. CFR was significantly lower in the the patient group when compared with the control group [p < 0.001 (95%CI: -0.79 to -0.20%)] while carotid media thickness' were not different between two groups.

Conclusion: Our results showed that CFR which is accepted as an early marker of endothelial dysfunction was significantly lower in the patients with high IgE levels. This finding seems to support the role of IgE in vascular pathology.

1250
Serum endothelin-1 in chronic thromboembolic pulmonary hypertension

Morsolini, M[1]; De Amici, M[2]; Grazioli, V[1]; Marseglia, GL[2]; Pin, M[1]; Torre, C[2]; Nigrisoli, S[2]; Sciortino, A[1]; Testa, G[2]; D'Armini, AM[1]
[1]Foundation IRCCS Policlinico San Matteo, Cardiac Surgery, Pavia, Italy; [2]Foundation IRCCS Policlinico San Matteo, Department of Pediatrics, Pavia, Italy

Background: Endothelin-1 (ET-1) is an endogenous peptide with a role in the pathophysiology of pulmonary arterial hypertension. Elevated ET-1 levels have been largely demonstrated in patients with non-thromboembolic pulmonary hypertension, correlating with the severity of the hemodynamic impairment. We hereby report our findings in patients undergoing pulmonary endarterectomy (PEA), which is the only curative treatment for chronic thromboembolic pulmonary hypertension (CTEPH). Our aims were to study how ET-1 values change after the operation and to build a model to predict ET-1 values.

Method: Three hundred and twenty-seven patients (141 males, 186 females; mean age: 61 years; range age: 18 - 84 years) underwent PEA at IRCCS Policlinico San Matteo of Pavia. Patients were studied preoperatively and during the follow up at three months and one year and according to preoperative presenting symptoms (World Health Organization functional class. Mean pulmonary arterial pressure (mPAP), cardiac output (CO) and pulmonary vascular resistance (PVR) were considered. Plasma ET-1 levels were measured by an enzyme immunoassay technique and expressed as pg/mL. Statistical analysis was performed using the statistical software package Medcalc 9 (Frank Schoonjans, BE). A p-value ≤ 0.05 was considered statistically significant.

Results: ET-1 levels were higher in preoperative distribution and decreased during follow up. ET-1 decreased significantly 3 months after operation (p = 0.0389) but not one year after operation (p = 0.1848). In the overall population, correlations between ET-1 levels and Mpap (r = 0.0766, p = 0.1691), CO (r = 0.0222, p = 0.6901) and PVR (r = 0.00304, p = 0.9565) were not significant. For WHO class II patients, a statistically significant correlation was found between ET-1 levels and mPAP (r = 0.279, p = 0.0375).The correlation between preoperative and postoperative ET-1 levels was statistically significant for both variables after 3 months (r = 0.351, p < 0.0001) and after 1 year (r = 0.187, p = 0.021). We proposed a model to predict ET-1 values before operation, considering, as dependent variables, age, sex, WHO classification and hemodynamic parameters. Results showed that ET-1 could be predict by mPAP (p = 0.015). We also built three inverse models to predict hemodynamic parameters on the basis of the other variables, to test if ET-1 was a good predictor. Results showed that ET-1 was a good predictor only for mPAP (p = 0.279).

1251
The effects of daily dietary intake of fibres on perceived general health immune functioning in young adults

Bury, D[1]; Fernstrand, AM[1]; Garssen, J[1,2]; Verster, JC[1,3]
[1]Division of Pharmacology, Utrecht University, Utrecht, The Netherlands; [2]Nutricia Research, Utrecht, The Netherlands; [3]Center for Human Psychopharmacology, Swinburne University, Melbourne, Australia

Background: Daily intake of dietary fibres provides many health benefits. Generous intake of dietary fibres has been associated with a reduced risk of various diseases and conditions as well as enhanced immune functioning. The purpose of this study was to explore the effects of daily dietary intake of fibres on perceived health state and immune functioning in healthy young adults.

Methods: N = 509 Dutch university students completed a survey collecting data on dietary intake of fibres (food frequency

questionnaire), perceived health status and immune functioning (1-item score ranging from absent (0) to severe (10)). Perceived general health status and immune functioning were associated with daily intake of fibres using nonparametric (Spearman) correlations for the group as a whole, and men and women separately.

Results: Mean (SD) age was 20.8 (2.6) years old, 71.9% of the sample were females. Mean (SD) daily dietary total fibre intake was 15.5 g (6.9). Daily dietary intake of fibres correlated significantly with the general health rating ($r = 0.171$, $p = 0.0001$) and perceived immune functioning ($r = 0.124$, $p = 0.008$). When controlling for total caloric intake, the partial correlation remained significant between general health and fibre intake ($r = 0.151$, $p = 0.002$). The effects were considerably more pronounced in men when compared to women.

Conclusion: A significant association between dietary intake of fibres and perceived general health and immune functioning was found in a cohort of healthy young adults. Future studies should further explore the nature and cause of the observed gender differences.

1252
Severe hypercalcemia secondary to sarcoidosis of the bone

DuBuske, I; Nehme, M; Teufel, K
George Washington University Hospital, Washington, USA

Introduction: Sarcoidosis is a multi-system granulomatous disorder with manifestations most commonly in the lungs. Skeletal involvement is rare, reported in 1–13% of sarcoidosis cases; hypercalcemia can be one of its presenting signs.

Case presentation: A 70-year-old woman presented to the emergency department with general malaise and fatigue. She was found to have severe hypercalcemia 15.9 mg/dL and acute kidney injury Cr 2.15 mg/dL. Further investigation revealed PTH 13 pg/mL, PTHrP < 0.74 pmol/L, ACE level 134 U/L, 25OH-Vitamin D 27.8 ng/mL, and 1,25-Vitamin D 166.6 pg/mL. Mammography and colonoscopy were normal. Chest radiography and CT revealed several small right upper lobe pulmonary nodules and mediastinal and hilar lymphadenopathy. Skeletal survey revealed lucency in the right humerus without any cortical bone thickening or other signs of Paget's disease. SPEP analysis was negative and bone marrow aspirate and core biopsy revealed multiple small non-caseating granulomas. She was diagnosed with hypercalcemia secondary to bony involvement of sarcoidosis. She was treated with high dose prednisone, aggressive fluid hydration, and intramuscular calcitonin. The patient's calcium decreased to 11 mg/dL and her acute kidney injury resolved within 48 hours.

Discussion: Sarcoidosis of the bone is usually found in patients with known pulmonary sarcoid and is rarely a presenting feature of the disease. Radiological findings show lace-like honeycomb cystic and lytic lesions of cortical bone, with cavities of varying sizes and surrounding sclerosis. The differential diagnosis includes metastasis, hyperparathyroidism, Paget's disease, multiple myeloma and lymphoma. Skeletal sarcoidosis usually affects the phalanges in the hands and feet, but has also been described in the nasal bones and vertebrae. To our knowledge, this report describes the first case of lytic humerus lesions and secondary hypercalcemia as the presenting sign of sarcoidosis.

Conclusion: Hypercalcemia can be a life-threatening emergency. Although skeletal sarcoidosis is a rare condition, physicians, especially, in the hospital setting should have a high index of suspicion for sarcoid-induced hypercalcemia. Treatment of hypercalcemia secondary to sarcoidosis consists of a low calcium diet, adequate hydration, and minimizing sunlight exposure and steroids to reduce overproduction of calcitriol in activated macrophages.

1253
Allergic broncho pulmonary aspergillosis associated with eosinophilic gastro enteritis - a case report

Ghiordanescu, IM[1]; Balea, MI[2]; Bumbacea, RS[3]; Bumbacea, D[4]
[1]Life Med Clinic, Allergology, Bucharest, Romania; [2]Colentina Clinical Hospital, Pneumology, Bucharest, Romania; [3]Dermatology and Allergology, Elias Emergency University Hospital, Bucharest, Romania; [4]Pneumology, Elias Emergency University Hospital, Bucharest, Romania

Background: Allergic Broncho Pulmonary Aspergillosis (ABPA) is a rare disease that may be associated with marked peripheral blood eosinophilia, but eosinophilic infiltration of organs other than the lungs is unusual.

Method: We present a case of ABPA associated with Eosinophilic GastroEnteritis (EGE) that raised differential diagnosis issues. A 66 years old female was admitted to our service with breathlessness, wheezing, a history of 2 months of recurrent fever and weight loss. She associated non-bloody diarrhoea and a 9 years history of chronic rhinosinusitis, asthma and persistent hypereosinophilia. Based on paraclinical data we have classified the case as an allergic bronchopulmonary aspergillosis gathering 6 out of 8 major classic criteria: asthma, central bronchiectasis, peripheral blood eosinophilia, increased total serum IgE, serum precipitating antibodies and specific A. fumigatus serum IgE; this case also fulfills recently proposed criteria for ABPA diagnosis. In our case ABPA was associated with biopsy - proven eosinophilic gastroenteritis. Treatment with methylprednisolone resulted in significant clinical improvement.

Results: To our best knowledge, the association of eosinophilic gastroenteritis to ABPA has not been previously described. The presence of marked peripheral blood eosinophilia together with eosinophilic gastrointestinal infiltration raises significant differential diagnosis with hypereosinophilic syndrome (HES) and eosinophilic granulomatosis with polyangiitis (EGPA). The role of Aspergillus (and in general of aeroallergens) in the pathogenesis of eosinophilic gastroenteritis is supported by several lines of evidence. In fact both HES and EGPA are rendered less likely by the immunologic evidence of Aspergillus-related disease (specific IgE and precipitins). Aspergillus-induced Th2 response might be responsible for eosinophilic infiltration of gastrointestinal wall, which might be the case also in our patient. Although swallowed aeroallergens might be the mechanism of EGE, the existence of peripheral blood Aspergillus-specific T-cells and the co-existence of respiratory disease suggest a systemic pathogenesis with involvement of homing receptors in gastrointestinal mucosa.

Conclusion: We describe the first case of allergic bronchopulmonary aspergillosis associated with eosinophilic gastroenteritis, and we hypothesize that Aspergillus-related Th2 response is responsible for both diseases.

1254
Churg-Strauss syndrome (CSS) - progressive, aggressive, disabling disease with multiple organ manifestations: a case report

Petkova, E; Staevska, M; Valerieva, A; Dimitrov, V
Medical University of Sofia, Sofia, Bulgaria

Introduction: CSS is a rare small- and medium-sized vessel vasculitis in an association with asthma and blood eosinophilia. We report a CSS in a male with multiple clinical manifestations-pulmonary, cardiac, dermatologic, renal, neuro-ophthalmologic and peripheral nerve involvement.

Case description: This is a report of a 48-year-old Caucasian man with a medical history of nasal polyposis, sinusitis and nonallergic asthma for 1 year. He was on

budesonide/formoterol and montelukast but reported frequent exacerbations and hospitalizations with gradual worsening after oral steroids (CS) discontinuation. He was admitted with fever, cough, night sweats, malaise, weight loss, worsening of wheezing and shortness of breath. Prior to admission, in addition to increased dyspnea, he reported a palpable purpura and gradual paresthesia in his right extremities. On physical examination, he had tachypnea, prolonged expiration, generalized ronchi and wheezing. SPO_2 upon admission was 86%. The white cell count was 11.3x10^9/L with 33% eosinophils, hsCRP-61.9 mg/l, creatinine 114.6 mkmol/l and he had proteinuria (1.09 g/24 h). He was negative for anti nuclear antibodies, but the test for perinuclear anti neutrophil cytoplasmic antibodies was positive-36.2 U/mL. Echocardiography showed mild to moderate left ventricular hypertrophy and hemodynamically insignificant pericardial effusion. On the 2nd hospital day, the patient reported diplopia, blurred vision and severe pain in his right leg. His neurological status and head MRI scan were without significant pathological signs. High-resolution CT of the chest showed ground-glass opacities, subpleural nodules, without areas of air-space consolidation. During hospitalization, the patient was treated with i.v. CS and was discharged after 10 days in good general health. Continuous oral CS therapy was prescribed. 3 months later he was admitted again with progressive paresthesia and paresis in both arms and legs and we started i.v. pulse cyclophosphamide courses to be followed by prolonged physical rehabilitation.

Discussion: CSS might be easily underdiagnosed because it has no pathognomonic signs. It is of great importance to be familiar with this rare syndrome and to look for blood eosinophilia prior to treatment with systemic CS, especially in patients with late-onset, difficult to treat asthma and sinus abnormalities. Precise diagnosis and monitoring for relapse are of crucial importance for the patients' prognosis.

1255
Early outset of pulmonary involvement in a child case with ulcerative colitis

Senocak, N[1]; Ozmen, S[2]; Bostanci, I[2]
[1]Dr. Sami Ulus Training and Research Hospital of Women's and Children's Health and Diseases, Ankara, Turkey; [2]Pediatric Allergy and Immunology, Dr. Sami Ulus Training and Research Hospital of Women's and Children's Health and Diseases, Ankara, Turkey

Background: Ulcerative colitis (UC), is a disease, which involves mainly the gastrointestinal tract. On the other hand, certain extra-intestinal illnesses can be seen. It is known that the epithelial cells of the respiratory and gastrointestinal tract originated from the primitive foregut. In cases where UC is accompanied by pulmonary illnesses this common embryological origin may play a role in the pathogenesis of the disease. However, information on this topic is scarce. In patients with UC a variety of pulmonary illnesses may be seen. Moreover, allergic sensitization, certain allergic symptoms, and abnormal pulmonary function tests are also common in patients with UC. There is no sufficient data about pulmonary involvement in children with UC.

Method: In this report we present one case involving a child with UC and bronchiectasis whose intestinal and pulmonary symptoms began simultaneously.

Results: A 9.5 year-old girl was referred to our outpatient clinic with suspected asthma. The patient has been complaining of recurrent cough and sputum. In her previous medical history, when she was 4 years old, complaints such as cough, sputum, abdominal pain, bloody stools, and fever had already started. At 5 years of age she was diagnosed with UC and meselazine was started. In our evaluation there were no physical abnormalities. Her skin prick testing and pulmonary function test were normal. Airway hyper reactivity with methacholine challenge test was not detected. Due to refractory cough resistant to asthma treatment, combined with sputum, high resolution computed tomography was taken of chest. Images of light fusiform bronchiectasis in the bilateral central perihiler bronchi, peribronchial wall thickening in the right middle lobe and "signet ring" shadows in the lower lobes were identified. Our patient was diagnosed with bronchiectasis about 5.5 years following the start of respiratory symptoms. Antibiotic treatment was given for two weeks. At follow-up dramatic improvement was seen concerning her cough and sputum. High-dose inhaled corticosteroids with oral methylprednisolone and daily low-dose clarithromycin therapy were given as prophylactics.

Conclusion: When a patient with ulcerative colitis has symptoms of cough and sputum, and after the exclusion of infectious causes and asthma, pulmonary involvement should be considered. Progression of the disease in the lungs may be prevented with early diagnosis and UC treatment.

1256
Lymphangioleiomyomatosis (LAM)

De Vicente Jimenez, T[1]; Jareño, J[2]; Montoro, A[1]; Fonseca, J[1]; Mendoza, A[1]; Mateos, JM[1]; Núñez, MA[1]; de Mateo, B[1]
[1]Hospital Central de la Defensa, Allergology, Madrid, Spain; [2]Hospital Central de la Defensa, IMIDEF, Pneumology, Madrid, Spain

Background: Lymphangioleiomyomatosis is a rare disease resulting from proliferation in the lung, kidney, and axial lymphatics of abnormal smooth muscle-like cells (LAM cells). Cystic destruction of thelung with progressive pulmonary dysfunction and progressive evolution to respiratory failure and the presence of abdominal tumors characterize the disease. LAM typically occurs in premenopausal women, suggesting the involvement of female hormones in disease pathogenesis.

Method: 45-year-old woman from emergency unit with dyspnea in spring. Personal history stand out aschronic migraine treated with Botox and recurrent pneumothorax operated. Prick test, spirometry, ImmunoCAP and thoracic CT are performed. Subsequently, with the results given, she is studied in Pneumology, where bronchoscopy, diffusion test, plethysmography and walk test are performed.

Results: Extrinsic bronchial asthma, rhinoconjunctivitis-confirmed by sensitization to pollen (Olea IgE20.5 kU / l), grasses (Cynodon IgE 7.58 kU / l IgE Cupressus arizonica 10.3 kU / l /), mite-spowder (Dermatophagoides farinae IgE 4.3 kU / l), cat (IgE 39.4 kU / l) and dog (IgE 4.52 kU / l).An intersiticial intraparenchymal pattern was found in high-resolution thoracic CT and cysticlesions were confirmed by transbronchial biopsy. Obstructive ventilatory pattern with decreaseddiffusion. Negative parasites, supplement and other antibodies in normal range.

Extension study (abdominal ultrasound and echocardiogram) resulted normal.

Conclusion: This case demonstrates the usefulness of a comprehensive medical history to focus on thesuspected and final diagnosis. A multidisciplinary approach between Allergology, Pneumology and Radiology is necessary. There is a growing interest in LAM, which has determined the establishment of a registry of patients and has promoted further investigations at clinical and cellular fields.

1257
Pulmonary Langerhans cell histiocytosis - a case report

Moreira, A[1]; Lopes, I[2]; Moreira Silva, J[3]
[1]Centro Hospitalar Vila Nova de Gaia/Espinho, Immunoallergology, Vila Nova Gaia, Portugal; [2]Centro Hospitalar Vila Nova de Gaia/Espinho, EPE, Vila Nova Gaia, Portugal; [3]Centro Hospitalar Vila Nova de Gaia/Espinho, EPE, Immunoallergology, Vila Nova Gaia, Portugal

Background: Pulmonary Langerhans cell histiocytosis (PLCH) is a rare interstitial lung disease which is associated with cigarette smoking. It affects more commonly young adults caucasians, between 20 and 40 years of age, but in women tend to present at an older age.
Method: A 46 year old caucasian non-atopic smoker female (36 pack year) was admitted in our department complaining of daily dry cough and pleuritic chest pain with 10 months of evolution. She denied fever or constitucional symptoms. In previous visits to the emergency department she had been treated with inhaled formoterol+budesonide 160 + 4.5 ug and antibiotics, without relief of symptoms.
Results: The physical examination and laboratory tests (hemogram, hepatic and renal function, immunological study and viral markers) were normal. Plethysmography revealed a mild obstructive ventilatory pattern. On chest X-ray it was visible a reticulonodular pattern of diffuse distribution in the pulmonary parenchyma. High resolution computed tomography (HRCT) showed an increase in the diameter of the pulmonary artery suggestive of pulmonary hypertension associated with multiple cysts and micronodules in the middle to upper lung zones. The bronchoscopy was normal and the bronchoalveolar lavage fluid showed 1% of CD1a cells. Bone scintigraphy showed no changes.
Conclusion: The results support the diagnosis of PLCH. After diagnosis, the patient started to reduce the tobacco intake. Currently she is smoking 5 cigarettes/day and refers symptomatic improvement. The presence of pulmonary hypertension is independently associated with a worse prognosis.

1258
Hand-foot-mouth disease in an adolescent

Anil, H[1]; Harmancı, K[1]; Bulur, I[2]; Koçak, A[3]
[1]Pediatric Allergy and Immunology, Osmangazi University, Eskisehir, Turkey; [2]Dermatology, Osmangazi University, Eskisehir, Turkey; [3]EAACI, Pediatric Allergy and Immunology, Eskisehir, Turkey

Introduction: Hand-Foot-Mouth disease is a viral xanthematous disease primarily caused by Coxsackie virus that mainly affects children under 10 years-old during the spring or summer. It is a rare disease in adults, and rarer still in the immunocompetent. We report the case of a 16 - years old immunocompetent adolescent affected bys Hand Foot Mouth disease.
Case report: A 16-year-old male presented with multiple peripheral vesicles which had begun to appear on the palms of his hands 3 days previously, and which progressed to the interdigital areas, soles, and dorsum of the feet and mounth. Lesions were painfull. His past medical history showed no record of chronic disease and was not taking medications. Before onset of the patient's skin lesions. The patient complained of general weakness and tender, pruritic skin lesions. A physical examination done and a normal temperature, pulse rate, and breathing rate recorded. Conspicuous dark veziculopapüler lesions on hand, feet, vesicles in mouth cavity membrane were observed.. No other abnormality was found during the admission physical examination and laboratuary findings. It has been reported that intravezicüler dermatitis at punch biopsy associated with hand foot mouth disease. The diagnosis of HFM disease was made based on history as well as typical clinical findings, including distribution of skin lesions and punch biopsies results. The patient was treated symptomatically with antihistaminic drugs, and the lesions resolved spontaneously without complications.
Discussion: Our case illustrates the unusual aspects of this variant of HFMD: an adolescent with severe disease and systemic symptoms who presented in the springtime. Generally, HFMD is rare in immunocompetent adults. The patient had debilitating systemic symptoms, and pain of his hands and feet that required hospitalization, whereas most cases of classic HFMD are managed at home. His eruption differed from classic HFMD because his scalp, ears, and mucos membranes were profoundly affected.

1259
Different antihistamines with the same brand name sold in different countries

Wong, HCG[1]
[1]Department of Medicine, University of British Columbia, Vancouver, Canada

Background: Many drugs are sold under different brand names.
Method: Visits were made to pharmacies locally (Vancouver, Canada) and in Europe (London, UK and Copenhagen, Denmark). Antihistamines are found to be readily available.
Results: Antihistamines sold under the same brand name, Benadryl are found in Vancouver, London and Copenhagen.

(1) Benadryl sold in Vancouver contains diphenhydramine 25 mg.

(2) Benadryl sold in London contains cetirizine 10 mg.

(3) Benadryl sold in Copenhagen contains acrivastin 8 mg.

Conclusion: Brand name, Benadryl may contain different antihistamines.

Dosage may range from once daily to four times a day.

Side effects eg. level of drowsiness may be different.

Patients should check for ingredients instead of relying solely on the brand name when purchasing antihistamines.

1261
Peer learning and assessment practice in post-graduate studies and development of allergology and clinical immunology specialists: advantages and challenges

Kobzev, D[1]; Astafieva, N[2]
[1]Leeds Trinity University, Business, Leeds, UK; [2]Allergology and Clinical Immunology, Saratov State Medical University, Saratov, Russian Federation

Background: In our earlier study of peer learning / assessment (PLA) practice in PG studies of allergology and clinical immunology specialists 2 randomized parallel PG groups' performance was compared. The group using PLA demonstrated better performance (post-test mean mark +15%). Students' indicted challenging, but educational nature of PLA, which led to a higher interaction in the group, a better understanding of specialist content and test requirements. This research investigated PLA associated challenges and aimed to identify pedagogic practices, which can help managing these issues.
Method: PLA dynamics was explored in 4 PG courses in 2013–14 (incl. up to 50 health practitioners and health care managers). Semi-structured observations and interviews with participants were conducted for an in-depth investigation of challenges and their mitigation.
Results: This research revealed a better interpretation of key PLA challenges and mitigating pedagogic practices (perceived by students as the most effective): "Reliability" - a concern from more experienced students, which can be addressed through the integration of peer feedback within the initial assessment strategy, followed by detailed instruction, practice and calibration.

"Perceived expertise" (are we really peers?) - a concern of the most and the least experienced participants; lecturer has to create a course climate encouraging peer learning.

"Power relations" - more students preferred to be assessed rather than assess; lecturer has to engage students with marking criteria, quality practice and explain marking criteria and process;

"Time" - a special attention should be paid by a lecturer to a proper integration of PLA tasks into the course by allocating sufficient time for each task and all participants.

Conclusion: PLA can be widely used in PG allergy education, training and specialization as it develops student's communication and critical thinking, allows better understanding of course content and increases their performance; lecturers and instructors has to be aware of possible challenges and may negate them with the help of pedagogic practices described above.

1262
The centres of excellence in allergy care (CoE): improving allergy treatment outcomes

Fox, A[1]; Lack, G[1]; Sastre, J[2]; Demoly, P[3]; Niven, L[4]
[1]Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Fundación Jiménez Díaz Hospital, Madrid, Spain; [3]University of Montpellier, Montpellier, France; [4]PCM Scientific, London, UK

Background: Data to support educational interventions in allergy are limited. The Centres of Excellence in Allergy Care (CoE) programme (funded by an educational grant from Stallergenes) brings novel CME opportunities to healthcare professionals managing patients with allergies. The programme, led by an international committee of experts, addresses real clinical needs through interactive and problem-based practical learning. Since the foundation of CoE in 2013, 191 participants with wide-ranging clinical backgrounds, from 25 countries worldwide have attended 18 courses. For this abstract, data from the 2014 courses were analysed to assess the impact of an educational initiative in allergy practice.

Method: Eight CME-accredited courses were held in the UK, Spain and France in 2014 covering preceptorship, paediatric, drug and food allergy, and inflammatory markers in asthma. Pre- and post-course assessment of participants' knowledge and competence, combined with small group sizes, enabled courses to be tailored to specific educational needs and facilitated outcomes analysis. Participants were invited to complete an online assessment before each course and again 1- and 3-months after. The pre- and post-course results were compared and analysed to assess the learning outcomes and to determine knowledge and competence change. Participant feedback was also evaluated.

Results: The data demonstrate high participant satisfaction and a positive impact on the knowledge and competence of practitioners providing allergy care, as a result of attending the CoE courses. Participants rated the quality of the courses as 4.75 overall, where 1 is 'poor' and 5 is 'excellent', and, on average, all of the individual sessions were rated excellent overall. Preliminary analysis of the 1-month post-course data demonstrate an average 9.7% increase in participants' knowledge and competence, compared with the results of the pre-assessments. Notably, two of the courses resulted in an overall 18.8% increase. The 3-month data are being collected and will demonstrate whether the improvements are sustained over the long term.

Conclusion: Qualitative and quantitative data underpin the educational value of the CoE programme, a CME intervention aimed at generating positive changes in allergy clinical practice. The data demonstrate high participant satisfaction and the beneficial impact of small expert-led courses that combine theory with practice through problem-based interactive learning.

Poster Session Group III - Green TPS 40

Pediatric cutaneous and drug allergy

1263
Filaggrin loss-of-function mutations predispose to atopic dermatitis and allergic sensitisation in Polish children population

Debinska, A; Danielewicz, H; Drabik-Chamerska, A; Kalita, D; Boznanski, A
1st Department and Clinic of Paediatrics, Allergology and Cardiology, Wroclaw Medical University, Wroclaw, Poland

Background: Filaggrin is a key protein involved in a skin barrier function. Loss-of-function mutations in the filaggrin (FLG) gene were identify as a major risk factor for atopic dermatitis. The aim of the study was to investigate the importance of the 4 common FLG null mutations in the susceptibility to atopic dermatitis and its related triats in Polish children population.
Method: The 4 most prevalent FLG mutations were determined in 158 children younger than 2 years of age. All subjects were selected using a detailed questionnaire that included questions on symptoms of atopic dermatitis and blood samples for total and specific IgE measurement were obtained. Atopic dermatitis cases were diagnosed according to the criteria of Hanifin and Rajka and skin examination. Atopic dermatitis severity was assessed by using the SCORing Atopic Dermatitis index (SCORAD). All FLG mutations were genotyped by real-time PCR assays with subsequent melting curve analysis using a SimpleProbe® probes.
Results: The combined genotype of all four mutations (carriage of ≥1 FLG mutation) was significantly associated with atopic dermatitis (p = 0.016). In logistic regression analysis adjusted for potential confounders, the odds ratio (OR) for individuals carrying one of these four null mutations was 5.52 (95% CI; 1.11, 37.12). When the patients with atopic dermatitis were divided into allergic and non-allergic patients groups; a positive and significant association between either the combined FLG genotype or 2282del14 deletion and atopic dermatitis was seen only in allergic group (OR 8,62; 95%CI; 1,64, 60,24 and OR 7,78; 95%CI; 0.83, 181.9 respectively). There was no significant association between FLG mutations and atopic dermatitis severity.
Conclusion: Our study confirm the previous findings that FLG mutations are strongly associated with atopic dermatitis and confer significant risk of allergic sensitization. These results underline the role of the epidermal barrier and filaggrin insufficiency in the pathogenesis of atopic dermatitis.

1265
Gonadotropin releasing hormone analogue drugs hypersensitivity during childhood

Karaatmaca, B[1]; Cavkaytar, O[1]; Alikasifoglu, A[2]; Sekerel, BE[1]; Soyer, O[1]
[1]Pediatric Allergy, Hacettepe University School of Medicine, Ankara, Turkey; [2]Pediatric Endocrinology, Hacettepe University School of Medicine, Ankara, Turkey

Background: GnRH-analogue drugs (GnRH-A) [triptorelin acetate (TA)/leuprolide acetate (LA)] are used in the treatment of central precocious puberty in childhood. Because the prevalence of early puberty increases, widespread use of these drugs take place leading to appearance of hypersensitivity reactions (HR) due to GnRH-A.
Method: The study included patients who admitted to Hacettepe University Department of Pediatric Allergy with history of HR to GnRH-A. Immediate and non-immediate reactions were defined as HR occurrence within one hour and later than one hour after the culprit drug intake, respectively. Epidermal (ED) and intradermal (ID) skin tests and / or provocation tests were done with suspected or alternative GnRH-A as indicated. Diagnostic tests with culprit drug were not performed if the patient had the anaphylactic drug reaction in our hospital and grouped as "physician diagnosed anaphylaxis" (PDA). Tests with alternative drug were perfomed in these group (Table 1).
Results: Seven of 470 patients admitted with suspected drug allergy had a reaction history with GnRH-a (1.4%) [(71% female (n = 5), mean age (min.-max.) 9.7 year (8.6–10.6)]. Three patients (43%) admitted with a history of immediate HR to triptorelin acetate, four patients had a non-immediate HR due to triptorelin acetate (n = 2) and leuprolide acetate (n = 2) (Table 1).
Conclusion: GnRH analogues are important to ensure the physiological growth in precocious puberty. GnRH analogues may cause severe hypersensitivity reactions like anaphylaxis which should be kept in mind during such therapies.

Table 1: Characteristics of patients

Patient No	Drug	Symptom	Skin Test	Provocation	Note
1	LA	Nonimmediate/MP	NA	Negative	DH:Negative
2	TA	Nonimmediate/MP	Negative	NA	Therapy terminated
3	LA	Immediate/Anaphylaxis	Negative	TA: NA LA:Negative	PDA
4	TA	Nonimmediate/Urticaria	Negative	Negative	DH:Negative
5	TA	Immediate/Angioedema	Negative	Negative	DH:Negative
6	TA	Nonimmediate/Angioedema	Negative	NA	Therapy terminated
7	TA	Immediate/Anaphylaxis	LA ID 1/100 Positive	TA: NA LA: NA	PDA

*: Maculopapular rash(MP)
**:Not applicable(NA)
***:Drug Hypersensitivity(DH)

1266
Drug allergy: epidemiology of a cohort of pediatric patient

Caimmi, S[1]; De Amici, M[1]; Caimmi, D[2]; Licari, A[1]; Marseglia, A[1]; Castagnoli, R[1]; Trovamala, V[1]; Torre, C[1]; Nigrisoli, S[1]; Marseglia, GL[1]
[1]Department of Pediatrics, Foundation IRCCS Policlinico San Matteo, Pavia, Italy; [2]Allergy Unit and Cystic fibrosis Center, CHRU de Montpellier, Montpellier, France

Background: We aimed to evaluate the number of real allergic patients among a population of children with a history suggestive of drug allergy.
Method: The study sample included 107 infants (mean age 8.53 years, 1–16 years) evaluated in our Allergy Unit for a history suggestive of drug allergy. In particular, we divided our sample in three groups: 66 patients (mean age 7.7 years, 1–16 years) with history suggestive of allergy to beta-lactams, 26 patients (mean age 9.61 years, 3–16 years) with history suggestive of allergy to NSAIDs, 4 patients (mean age 6 years, 5–8 years) with history suggestive of allergy to Clarithromycin, 3 patients (mean age 11.33 years, 10–14 years) with history suggestive of allergy to local anesthetics, 2 patients (mean age 11 years, 6–16 years) with history suggestive of allergy to Betamethasone, 1 patient with history suggestive of allergy to Infliximab, 1 patients with history suggestive of allergy to Desamethasone, 1 patient with history suggestive of allergy to Clindamicyn, We excluded 3 patients to suspected allergy to general anesthetics. All the other patients have undergone a complete allergy work-up and, in order to confirm or refute the diagnosis of drug allergy, we performed 119 Drug Provocation Tests (DPTs), the diagnostic gold standard.
Results: Considering beta-lactam antibiotics, only 2 patients (3.03%) reacted to DPT, while 64 patients with history suggestive of drug reactions to beta-lactams had a negative DPT. Considering NSAIDs, 7 patients (26.9%) had a positive DPT and were diagnosed as allergic, while 19 patients (73.1%) had a negative DPT and were considered as non-allergic. Considering local anesthetics and Clarithromycin, all the patients did not react to DPT and were diagnosed as non-allergic.
Conclusion: We described data from a real-life pediatric population of patients who were evaluated in our Allergy Unit with a history suggestive of drug allergy. Only a small number of patients reacted to DPT and was diagnosed as allergic. In particular, only 3.03% of patients with suspected allergy to beta-lactams are really allergic. Even if the clinical history is a fundamental step in the diagnostic process, it is not enough to discriminate between drug allergic and non-allergic patients. The Drug Provocation Test remains the gold standard in the diagnosis of drug allergy, also in children.

1267
Cyclosporin A and resistant atopic dermatitis with children

Kudryavtseva, A[1]; Balabolkin, I[2]; Ksenzova, L[2]; Larkova, I[2]
[1]I.M. Sechenov First Moscow State Medical University, Pediatrics Hospital, Moscow, Russian Federation; [2]Scientific Center of Children's Health, Moscow, Russian Federation

Background: Cyclosporin A (CsA) is an agent of choice used to treat severe and resistant atopic dermatitis. There are many world-wide reports on CsA effectiveness and only a few in Russia. This work aims at studying the clinic efficacy and CsA acceptability in children with severe AD.
Method: The CsA therapy was prescribed to 25 children with severe AD (12 boys and 13 girls) aged from 4 to 17 (an average of 10.1 years). Previously all patients got a traditional treatment (topical hormonal agents, tacrolimus ointment 0.03%) which produced no tangible effect. Additionally to the above said therapy a 13-years old patient received prednisolone per os in a dose of 1.3 mg/kg/day. The average SCORAD was 77.8 (from 50 to 92).
Results: The effective dose of the drug was from 2.5 to 4.5 mg/kg/day, the therapy duration varied from 4 to 34 wks (11.4±8.4). The CsA therapy length depended on AD clinic form. In the erythematous-squamous form, short courses were used that lasted from 4 to 12 wks (an average of 4.5 wks), in the erythematous-squamous form with lichenification - from 6 to 30 weeks (an average of 17 wks), in the lichenoid form long courses from 10 to 34 weeks (an average of 21.2 wks) were applied. The CsA treatment was found effective in 24 patients (96%). In the fourth week of CsA therapy the average SCORAD reduced up to 27.7±4.9 (from 16 to 36). With the therapeutic affect obtained, the drug dosage was reduced on case-by-case basis but not early than the third week. In short courses (up to 12 wks) CsA withdrawal was carried out within 1 week; in the prolonged treatment (up to 20 wks) it was done by 25% of the daily dose every week and by 25% every 3 weeks if the course was over 20 weeks. After CsA withdrawal exacerbations did not occur earlier than after 3–4 weeks and it was not so severe as compared to the child's state before the therapy onset. Among the side effects in patients who received the prolonged treatment we noted transient hyposthenuria and isosthenuria (in one case) and paresthesias, headaches (in the other). No patients showed a change of creatinine level in the blood or an increase in arterial pressure. The prednisolone therapy was discontinued in the course of CsA treatment.
Conclusion: Therefore, CsA treatment is effective in severe AD, the treatment efficacy is associated with the clinical form of the disease and does not depend on the child's sex, age and sensibilization severity.

1268
Fever associated with montelukast: a pediatric case

Montoro de Francisco, AM[1]; García Luque, A[2]; Tabakov, A[3]; Fonseca Avendaño, J[3]; De Vicente Jimenez, TM[3]; Mendoza Parra, A[3]; Mateos Galván, JM[4]
[1]Hospital Clínic Central de la Defensa, IMIDEF, Allergy, Madrid, Spain; [2]Hospital Central de la Defensa, IMIDEF, Clinic Pharmacology, Madrid, Spain; [3]Hospital Central de la Defensa, IMIDEF, Madrid, Spain; [4]Hospital Central de la Defensa, IMIDEF, Allergy, Madrid, Spain

Background: Montelukast is a selective antagonist of the cysteinyl leukotriene (Cys-LT1) recetpor, used as an adjunct treatment for asthma and allergic rinitis. Neuropsychiatric disorders, hepatic, cardiovascula, dermatologic, immunologic, gastrointestinal, hematologic, otic, ophtalmic, renal and respiratory effects related to montelukast use have been observed after its commercialization. The incidence of fever induced by montelukast is low (1.5% of adult and adolescent and 2% of pediatric patients) and it is specified in the summary of product characteristics of this drug. This side effect is clinically relevant and might require drug witndrawal.
Method: We present a case of a male 7 years old. Starts montelukast 4mg for asthma control, 12 hours after ingestión he presents fever (38.5°C), after 4 days montelukast therapy is discontinued and fever disappears. Two weeks later the patient received montelukast 4mg, and after 10 hours presents fever, the mother removes the drug and fever disappears.
Results: In order to evaluate the causal relationship between montelukast and fever an oral provocation was performed with positive result. The causal relationship was qualified as defined using a modified Karch-Lasagna algorithm.
Conclusion: Montelukast can cause fever.

Health professionals should pay a special attention to this side effect especially when treating pediatric patients.

1269
Atypical severe form of childhood dress syndrome

Hossny, E[1]; El-Sayed, SS[2]; El-Owaidy, R[2]; Rezk, A[3]
[1]Pediatric Allergy and Immunology, Faculty of Medicine, Ain Shams University, Cairo, Egypt; [2]Pediatric Allergy and Immunology, Faculty of Medicine, Ain Shams University, Cairo, Egypt; [3]Pediatric Intensive Care Unit, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare, potentially life-threatening form of drug allergy inducing skin eruption, hematologic abnormalities, lymphadenopathy, and internal organ involvement. It is characterized by a long latency between drug exposure and disease onset. The most commonly incriminated drugs include: antiepileptic agents, allopurinol, sulfonamides and dapsone.
Case: A 2.5 years old female patient presented to the emergency department with high fever and one day generalized non-itchy erythematous rash over the face and the trunk with progressive facial edema. The condition was preceded by a febrile attack of upper respiratory tract infection with the intake of sultamicillin, diclofenac sodium and cefoperazone 5 days before presentation. The patient was irritable and agitated, with respiratory wheezing, hypotension, tachycardia and tachypnea. Abdominal examination showed marked hepatosplenomegaly with generalized lymphadenopathy. Anaphylaxis was suspected and intramuscular epinephrine was given with nasal oxygen, intravenous hydrocortisone and saline infusion without response. Arterial blood gases showed metabolic acidosis. Inotropes infusion were started and the patient was mechanically ventilated. Patient′s had no previous history of allergy or drug reactions. Laboratory investigations revealed leukocytosis with neutrophilia and shift to the left and prominent eosinophilia (1250 /mm^3) and non-hemolytic anemia and thrombocytopenia. Patient had increased INR (1.5), elevated LDH, CRP titre, ALT, creatinine, BUN and potassium with low serum albumin and sodium. D dimer was 9.8 ug/ml and fibrinogen level was 2.1 g/l. Serum ferritin was 400 mg/dl, fasting serum triglycerides was 210 mg/dl. Lumbar puncture revealed clear CSF (under tension) with cell count 10 cells/HPF (predominantly lymphocytes) and elevated proteins. The patient was diagnosed as a severe form of definite DRESS syndrome according to the RegiSCAR system and was put on pulse methyl prednisolone, intravenous immunoglobulins, packed RBCs and fresh frozen plasma transfusion. On the third day after admission, the facial edema and skin rash started to resolve gradually with exfoliation and gradually improving clinical and laboratory parameters on intravenous dexamethasone over a period of 2 months.
Conclusion: This case represents an atypical aggressive form of Dress syndrome with short latent period after uncommonly incriminated drugs.

1270
Oral desensitization with dasatinib in delayed drug hypersensitivity reaction

Karaatmaca, B[1]; Tavil, B[2]; Sekerel, BE[1]; Soyer, O[1]
[1]Pediatric Allergy, Hacettepe University School of Medicine, Ankara, Turkey; [2]Pediatric Hematology, Hacettepe University School of Medicine, Ankara, Turkey

Background: Protein kinase inhibitors, dasatinib and imatinib are used in the treatment of leukemia which improve survival.
Method: Seven-year-old girl who undergone bone marrow transplantation(BMT) due to acute lymphoblastic leukemia (ALL) was given imatinib as maintenance treatment. On the seventh day of therapy, imanitinib was stopped upon formation of urticarial rash. Alternatively dasatinib was initiated however it was also discontinued because of development of edema of the eyelids and urticarial rash on the seventh day. Epidermal(ED) skin tests performed with imatinib and dasatinib (0.01 mg / ml to 0.1 mg / ml to 1 mg / ml) were negative. Imatinib and dasatinib patch tests (1%, 5%, 10%) were also negative. Oral desensitization with dasatinib was performed in eight steps (20 ng, 200 ng, 2 mcg, 20 mcg, 200 mcg, 2000 mcg, 4000 mcg, 6000 mcg, 8000 mcg, 15 min interval) and no early reaction was observed. The next day daily dose of 20 mg dasatinib was given under supervision, no early and late reactions were observed. She has been taking daily 20 mg dasatinib for the last eight months and did not develop allergic reaction.
Conclusion: Delayed drug hypersensitivity reactions may deprive patients of drug therapy and sometimes no alternative is available. Cases of oral desensitization with imatinib was reported in the literature nonetheless this is the first case of desensitization with dasatinib. Our patient continues to use dasatinib which is an essential drug after BMT. The decision to desensitize a patient must always be made on an individual basis, balancing risks and benefits. The desensitization should be considered also in delayed reactions especially with drugs important for survival.

1271
DRESS syndrome in a pediatric patient

Finelli, E[1]; Paiva, M[1]; Pina-Tincão, D[1]; Garcia, A[2]; Gouveia, C[2]; Prates, S[1]; Leiria Pinto, P[1]
[1]Immunoallergology Department, Dona Estefânia Hospital, Lisbon, Portugal; [2]Infectious Disease Unit, Dona Estefânia Hospital, Lisbon, Portugal

Background: Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is an acute severe hypersensitivity reaction to drugs characterized by cutaneous and systemic involvement. It occurs more often with anticonvulsivants but episodes with beta-lactam and other antibiotics have been described.
Case report: A five-year old, previously healthy, boy, was admitted with diagnosis of mastoiditis complicated by venous sinus thrombosis, with need of surgical drainage. Antibiotic treatment with cephtriaxone and vancomycin was started on day 2 with clinical improvement. Recurrence of fever and a symmetrical maculopapular pruritic rash was observed on day 21, accompanied by eosinophilia (max 1210), and marked elevation of liver enzymes. Withdrawal of the antibiotics was decided two days later. Nevertheless, clinical worsening was observed with persistence of fever and generalized rash, swelling of periorbital area, face and neck, cervical lymphadenopathy and hepatomegaly, oliguria and hypotension. A diagnosis of DRESS syndrome was made based upon European Registry of severe cutaneous adverse reactions (RegiSCAR) criteria. Other causes, including infections by hepatotropic virus were excluded. Both antibiotic were stopped and treatment with ev methylprednisolone (2mg/kg/dose) was initiated. After 72 hours of corticosteroid therapy, he improved symptomatically and haematological and biochemical parameters started to normalize. Epicutaneous tests with maximal non-irritant concentration of ceftriaxone (5% saline) and vancomycin (0.0005% saline) elicited a strong positive reaction to ceftriaxone 48 hours later.
Conclusions: DRESS is a severe and challenging diagnosis that, despite rarely, could be caused by antibiotics, To our knowledge we presented the first pediatric DRESS syndrome associated with ceftriaxone. As DRESS is associated with a type IV hypersensitivity reaction, patch tests could help in finding the culprit drug.

1272
Acute hemorrhagic edema of infancy (AHEI)

Baldaçara, RPC[1,2]; Silva, RC[3]; Miri, C[3]; Pires, BS[3]; Fagundes, FROO[4]; Guedes, VR[5]; Paula, RG[3]; Pacheco, G[3]
[1]Pediatria, Universidade Federal do Tocantins, Palmas, Tocantins, Brazil; [2]Pediatria, Hospital Infantil Público de Palmas, Palmas, Brazil; [3]Pediatria, Universidade Federal do Tocantins, Palmas, Brazil; [4]Dermatologia, Universidade Federal do Tocantins, Palmas, Brazil; [5]Patologia, Universidade Federal do Tocantins, Palmas, Brazil

Background: Acute hemorrhagic edema of infancy (AHEI) is an infrequent acute leukocytoclastic vasculitis that affects infants between 4 months and 2 years of age. The etiology remains unknown, but bacterial or viral infections and drug adverse reactions should be considered.
Method:
Case Report:
Results: A 7-month-old boy, 9500 g, attended at the emergency department with a history of onset of diffuse erythematous plaques in the face, ear, trunk and limbs, then after 4 days of evolution, showed elevated erythematous halo and pale center measuring from one to three centimeters in diameter. Most of them were like target or rosette, some coalescent, accompanied by mild edema of the extremities. There were no signs or symptoms of internal organ involvement. The only clinically relevant antecedent was a history of flu 10 days before the onset of the skin condition, treated with acetaminophen, diclofenac, desloratadine, prednisolone and carbocisteine. In the clinical history was not reported previous allergies, hospitalizations or chronic diseases. He was vaccinated according to the immunization national schedule and had proper growth and development for age. When admitted, he was using methylprednisolone 2mg/kg/day and hydroxyzine. Blood count, clotting screen, urinalysis, CRP, electrolytes, liver and renal function were within normal range for his age and sex. Blood cultures, ANA, anti-SSA-Ro/anti-SSB-La were negative. ASO < 200UI/ml. Dosage of immunoglobulins and complement was normal. Serology for Herpes 1 and 2, Rubella, Hepatitis B/C, Syphilis and Toxoplasmosis were negative. The antiviral antibodies IgG for Cytomegalovirus was reagent (more than 250UA/ml) and non-reactive IgM. Chest X-ray showed normal findings. Biopsy of the skin lesion showed histological findings suggestive of leukocytoclastic vasculitis. Direct immunofluorescence revealed presence focal of immune deposits of IgA, IgM and C3, and minimum deposit of IgG on the capillaries walls. Clinical and histological features of the patient were consistent with acute hemorrhagic edema of infancy. Our patient had complete resolution of cutaneous lesions within two weeks of onset after 10 days of corticosteroids.
Conclusion: AHEI benign disorder should also be considered in the differential diagnosis of drug adverse reactions.

1273
Acute generalized exanthematous pustulosis cases: a report of 5 cases

Ozmen, S[1]; Ertugrul, A[1]; Gurkan, A[2]; Bostanci, I[3]
[1]Pediatric Allergy Immunology, Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Ankara, Turkey; [2]Dermatology, Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Ankara, Turkey; [3]Dr Sami Ulus, Ankara, Turkey

Introduction: Acute generalized exanthematous pustulosis (AGEP) is a rare eruption characterized by acute, extensive formation of sterile nonfollicular pustules on edematous- erythematous skin. It is accompanied by fever, peripheral blood leucocytosis neutrophilia, and sometimes by facial edema, hepatitis and eosinophilia. Most cases of AGEP (90%) is caused by drugs (eg aminopenicillins) and acute infections.
Method: Five pediatric patients presented with AGEP were evaluated retrospectively.
Results: Of the 5 cases four (80%) were male and 1 (20%) was female,None of the patients had a history of adverse reactions to drugs or psoriasis. In the 2 cases, the lesions started on the genital area and one of the cases around the mouth and axilla, and one of the cases on the trunk. All patients complained of itching. 4 patients (92%) had a fever greater than 38 °C, three patients (60%) had facial edema, and four patients (80%) had cervical lymphadenopathy. Patients' skin lesions showed resolution in 5- 15 days. 2 patients had recurren episodes of AGEP.
Conclusion: The diagnosis of AGEP should be considered in cases of acute pustular rashes. Knowledge of the clinical features are necessary to be distinguished from other entities and to avoid unnecessary investigations.

1274
An unusual complication of bedbug bites: bullous reactions in two children

Yavuz, ST[1]; Gungor, A[2]; Kaya, G[2]; Gok, F[2]
[1]Department of Pediatric Allergy, GATA School of Medicine, Ankara, Turkey; [2]Department of Pediatrics, GATA School of Medicine, Ankara, Turkey

Introduction: Bedbug bites may cause a wide spectrum of reactions ranging between mild local skin lesions and fatal anaphylactic reactions. Skin lesions are predominantly macules, urticarial rashes or generalised ertythema with severe pruritus. Herein, we report a rare complication, bullous lesions, due to bedbug bites in two children.

Case 1: A 7-year old boy admitted to our outpatient department suffering from several pruritic, pleomorphic insect-bite like lesions in his arms, legs and body. His medical history revealed that he had stayed in a rural area for 4 nights and similar lesions were also present in his sister. Physical examination revealed two bullous lesions (3.5 × 2 cm. and 2.5 × 2 cm) in his left foot. Laboratory investigations including CBC, erythrocyte sedimentation rate, liver and kidney function tests and serum electrolytes were within normal limits. When the parents carefully examined the bedroom of the patients, bedbugs were noticed on the mattresses. The lesions were attributed to bedbugs and the patient was treated with local steroids recovering uneventfully in two weeks.

Case 2: A 5-year old boy admitted with complaints of several pruritic lesions in his arms, legs and body. His medical history revealed that he had travelled to a rural area and stayed in a wooden cottage for 3 nights. Similar lesions were also present in other family members. Physical examination revealed a bullous lesion (1.5X1.5 cm.) in his left foot. Laboratory investigations for possible etiologic factors were within normal limits. With the help of a thorough investigation in the living room of the house, bedbugs were noticed beneath the wooden furnitures. He was treated with local steroids and recovered uneventfully in two weeks.
Conclusion: Bedbug bites should be considered in the differential diagnosis of bullous reactions in children along with the frequent causes such as drug reactions, burns, mastocytosis, mosquito bites, skin diseases and bacterial infections.

1277
Adverse reaction to Benzathine Benzylpenicillin (BB) due to soy allergy

Barni, S[1]; Mori, F[1]; Sarti, L[1]; Pantano, S[2]; Novembre, E[1]
[1]Allergy Unit, Department of Pediatric, A. Meyer Children's Hospital, Florence, Italy; [2]Cystic Fibrosis Department, San Liberatore Hospital, Teramo, Italy

Background: Soybean (SB) allergy is one of the most common food allergies especially among children. Lecithin, extracted from soybeans, is not only used in the food industry, as antioxidant, but it is widely used in several drugs as emulsifier. Soy lecithin (SL) contains a number of IgE-binding proteins, possibly representing a source of hidden allergens. We reported a case of an 11 years old girl, with a past

medical history of soy allergy, who was referred to the Allergy Unit of Meyer Children's Hospital because of a delayed itching papular rash in the site of injection of BB. The girl was taken on antibiotic prophylaxis with intramuscularly BB every 21 days because of a post traumatic spleen breakage for which she was splenectomized.The girl tolerated three injections of the drug, after the 4th injection she presented the reaction above mentioned.

Method: The skin prick test (SPT), intradermal test (ID) with BB at a concentration of 10.000 UI were performed according to the European Network for Drug Allergy (ENDA) recommendations. SPT and serum specific IgE to SB were also performed. Specific IgE to beta-lactams were additionally measured.An oral provocation test (OPT) with soymilk was carried out over two days with a cumulative dose of 50 ml each day.

Results: SPT and ID with BB were negative, the detection of serum s-IgE to penicilloyl V, penicilloyl G, ampicillin and amoxicillin were negative, SPT with SB was negative and the serum s-IgE to SB was weakly positive (0.21 KU/L). The OPT with soymilk resulted positive: the girl presented diarrhea and abdominal pain 2 hours after 50 ml of soymilk on day 2. Taking into account the following factors:

a)the presence of soy lecithin among the constituents of BB;

b)the positive medical history for soy allergy;

c)the positive OPT with soymilk, a causal-effect link between soy lecithin and the allergic reaction was suspected.

Conclusion: We described a case of delayed reactions to soy acting contained an hidden allergen in the BB pre-filled syringe, misunderstood as a case of drug allergy. In the literature allergic reactions to soy lecithin have been previously reported. The source of lecithin should always be specified among the constituents of drugs and on the labels of food products to avoid a source of hidden allergens and difficulties in the allergy work-up in case of reactions.

1278
Optimisation of the experimental design to study the pharmacokinetics of rupatadine 1 mg/mL oral solution in 2–5 year old children

Santamaria, E[1,2]; Izquierdo, I[2]; Valle, M[1,3]
[1]Cerdanyola del Vallès, Universitat Autònoma de Barcelona, Barcelona, Spain; [2]J. Uriach y Compañía, S.A., Palau Solità i Plegamans, Spain; [3]IIB-Sant Pau. Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background: Due to ethical and physiological considerations it is difficult to study rupatadine's pharmacokinetic (pk) profile in low age children following a classical pk design. Therefore, the study of the pk profile of rupatadine in these children should be focused in obtaining pk data avoiding as much as possible the discomfort of the child and the number of blood drawings. For this reason it was necessary to optimize the dose and the number and timing of blood withdrawals to determine the pk of rupatadine 1 mg/mL oral solution in children 2 to 5 years old.

Method: Data from a previous extensive pharmacokinetic study in eleven 6–11 year old children were used in order to describe the pk of rupatadine employing a population approach, using NONMEM software. Several different compartmental models were tested to describe the disposition of rupatadine. Once the model was found, it was validated by means of a visual predictive check. The model was used to select the best dose to administer in children 2 to 5 years, considering weight as the only factor affecting the pharmacokinetics of rupatadine. Once the best dose was selected, the design of the study in 2–5 year old children was optimised by means of the WINPOPT software taking into account the following constraints: only 40 children would be included in the study and only 4 samples could be collected per children: 3 of them in a single day with the shorter possible sampling window, and the 4th on the last day of the study.

Results: Pharmacokinetic profile of rupatadine in 6–11 year old children was best described using a bicompartimental model with first order absorption and elimination from the central compartment. The clearance of rupatadine was found to increase with age following a linear function, no other covariates showed a possible relationship with the individual bayes estimates of the parametres for rupatadine. The optimization of the study to be performed in children 2 to 5 years old indicated that it was possible to obtain good estimates of the parameters if the study is performed in 40 children and 4 blood samples are obtained from each child. The maximum length of stay of the children at the clinical units would be of 2 hours, and no children would stay at the units later than 10 hours after the dose administration.

Conclusion: The design of a PK study in 2–5 years old children has been optimised in order to obtain the necessary information causing the less possible distress in children.

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Pollen and pollination plus others (HDM, climate...) as risk factors for allergies

1280
Alternaria and *Pleospora* fungal spores in the ambient air of Vinnitsa, Ukraine

Bilous, ES[1]; Rodinkova, VV[2]; Musatova, KV[3]; Motruk, II[4]
[1]Scientific Reasearch Centre, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [2]Pharmacy, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [3]Medical Biology, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [4]Hygiene, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine

Background: In patients who show allergy to molds, up to 70% of those patients demonstrate allergy to *Alternaria*, and *Alternaria* is known to be a risk factor for asthma. *Pleospora* genus is closely related to *Alternaria* while both genera belong to the Pleosparaceae Family and are known to have the same allergenic content.
Method: Spore counts were obtained at Vinnitsa National Pirogov Memorial Medical University (VNMU) in 2009–2011 daily and in 2012–2014 bi-hourly using a Burkard trap at 25 meters height above ground from March 1 to October 31.
Results: *Alternaria* spore is more abundant in the ambient air of Vinnitsa than the *Pleospora*. The highest *Alternaria* concentrations reached up to 500 spores/m^3 seen in the mid of July. *Pleospora* maximum were much lower reaching up to 30 spores/m^3 only in the mid of July as well. However, periods of significant spores count were different for two genera. *Pleospora* were seen through all the season including spring and autumn months with concentration increase in summer while *Alternaria* had prominent active period from July to September.

Higher bi-hourly concentrations of *Alternaria* were recorded at the nighttime and at midday; from 1 AM to 3 PM. *Pleospora* had similar distribution patterns with concentration increase from 3 AM to 1 PM and at 7 PM.
Conclusion: Hay fever symptoms caused by *Alternaria* and *Pleospora* may occur in summer month mostly. However, the active period of *Alternaria* is shorter than *Pleospora*' one starting on May while *Pleospora* is recorded from March. Increased concentrations of both spore types recorded at nighttime till the midday. To increase the hay fever symptoms sensitive individuals are recommended to avoid contact with these spore types at the time noted.

1282
Is the repertoire of allergens produced by HDM influenced by the mite population structure and by the environment?

Vidal-Quist, JC[1]; Ortego, F[1]; Lombardero, M[2]; Castañera, P[1]; Hernández-Crespo, P[1]
[1]Centro de Investigaciones Biológicas, Biología Medioambiental, Madrid, Spain; [2]Departamento de I+D, ALK-Abelló, Madrid, Spain

Background: House dust mites (HDMs) are the most important source of indoor allergy. Research efforts on HDM-derived allergy have been mainly focused on the patient's perspective. We are studying the influence of the environment on the expression of allergen genes in *Dermatophagoides pteronyssinus* with the aim of contributing to the understanding of allergy, as well as to the production of standardized allergenic extracts for clinical use.
Method: The expression of *Der p 1, 2, 3, 4, 5, 7, 10* and *21* genes has been monitored by Reverse Transcription and Real Time quantitative PCR in different mite developmental stages, the two adult sexes, in mites exposed to a change in temperature (16°C or 35°C vs. 24°C) or relative humidity (RH, 44% vs. 76%), and in mites exposed to Diesel Exhaust Particles (DEPs, 12 days, 1 μg/cm^2; 44 days, 10 μg/cm^2), bacterial endotoxins (LPS, 12 days, 0.1 μg/cm^2) and benzyl benzoate (5 days, 3.2 μg/cm^2). The content of major allergens, Der p 1 and Der p 2 has also been estimated by ELISA.
Results: The transcription levels of all genes studied, except *Der p 10*, were higher in nymphs compared to larval or adult stages (from 1.6-fold in *Der p 7* to 2.5-fold in *Der p 3*). The relative amount of Der p 1 and Der p 2 proteins produced by nymphs was also higher. The transcription of *Der p 4* and *Der p 10*, together with the transcription and protein ratios Der p 1 to Der p 2, were higher in males than in females. Exposure of mite cultures to changes in temperature or RH significantly influenced the allergen gene transcription profile. Short-term exposure to DEPs, LPS or benzyl benzoate did not significantly affect the expression of allergens. Exposure of mites to a high concentration of DEPs for 44 days slightly affected the expression of *Der p 3* (1.2-fold) and *Der p 21* (1.4-fold).
Conclusion: Our results demonstrate that allergen expression in the HDM is quantitatively and/or qualitatively influenced by the instar/sex composition of the mite populations as well as by the environment. The analysis performed so far does not show a relevant impact of environmental factors other than temperature or RH. Monitoring allergen gene expression may be a useful tool to assist the optimisation of mite cultures in the production of standardised allergenic extracts for clinical use. Improving our knowledge of the allergen producing sources may help in the prevention, diagnosis and treatment of allergy.

1283
Peak birch pollination shifts nearly 20 days early in Vinnitsa, Ukraine due to temperature increases

Rodinkova, V[1]; Musatova, KV[1]; Motruk, II[1]; Kremenska, LV[1]; DuBuske, LM[2,3]
[1]Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [2]Immunology Research Institute of New England, Gardner, MA, USA; [3]George Washington University, MFA, Washington, DC, USA

Background: Global warming may have a major impact on biota behavior. However, changes in plant pollination recorded in Vinnitsa (Ukraine) were smooth and predictable from 1999 until now. Exception was seen for the birch pollination in 2014 which occurred extremely early and was unusually abundant.
Method: Pollen counts from 1999 to 2000 were obtained by gravimetric sampling. Pollen collection from 2009 to 2014 used volumetric methods employing a Burkard trap placed at a height of 25 meters above the ground on the roof of a Vinnitsa Medical University building. Samples were taken from March 1 until October 31.
Results: Bi-annual pollination mode was established for Betula in Vinnitsa with

every even year having more abundant pollen count than the odd one from 1999. Interestingly, Betula seasonal maximum for the years 2009 through 2012 were recorded on the same day, April 21. Peak pollen of 386 pollen grains per cubic meter in 2013 was noted 3 days earlier on April 18 due to unusually warm weather. Betula peaks for 1999 and 2000 were both seen in the second 10-day period of April. However, seasonal birch peak of 3791 for the year 2014 was recorded on April 2, also date of the first significant seasonal count increase as well. This maximum was observed at the temperature sum accumulated to the 187.6°C from the March 1. The second highest pollen count increase of 2880 pollens per cubic meter of air was recorded on April 8 with a temperature sum of 219.0°C. All seasonal pollen concentration fluctuations correlated well with the daily temperature changes. Birch peak season ended April 20, a day earlier than the usual seasonal birch pollen peak day established before. Seasonal pollen sum of the year 2014 for 22,833 pollen per cubic meter of air, the most abundant of all years of observation.

Conclusions: Seasonal fluctuations of Betula pollen concentrations may help allergy sufferers to predict years and weeks of maximal birch pollen exposure enhancing effective seasonal allergy control in Vinnitsa, Ukraine.

1284
Pollen counts during 2014 in Seville, Spain

López Ruiz, C; Alcaraz Pérez, C; Rubiano Sosa, C; Bellido Linares, V; de Luque Piñana, V; Guardia Martínez, P
Hospital Universitario Virgen Macarena, UGC-IC Alergología, Sevilla, Spain

Background: From a clinical point of view, the most relevant allergenic pollens in Seville are those belonging to the families Poaceae, Oleaceae, Platanaceae and in recent years, the Cupressaceae family is growing in importance. We describe the pollination of these families and other less relevant in the north of Seville.

Method: Daily pollen counts were performed during 2014 using Burkard volumetric collector, model seven-day recording volumetric spore Trap®.

Results: The total pollen count in 2014 was 47,906 grains/m^3. May 2nd was the peak day, with a total of 2,258 grains/m^3.

Poaceae Family. Pollination period: April 30th to June 9th. Total Annual Count: 6,608 grains/m^3. Peak day: May 11th with 1,000 grains/m^3.

Oleaceae Family. Pollination period: April 16th to May 19th. Total Annual Count: 14,842 grains/m^3. Peak day: May 2th with 1,366 grains/m^3.

Platanaceae Family. Pollination period: March 13th to April 13th. Total Annual Count: 5,903 grains/m^3. Peak day: March 17th with 790 grains/m^3.

Cupressaceae Family. Pollination period: February 19th to March 18th. Total Annual Count: 5,024 grains/m^3. Peak Day: February 28th with 322 grains/m^3.

Other pollens non clinically relevant: Fagaceae Family. Pollination period: March 18th to May 18th. Total Annual Count: 10,702 grains/m^3. Peak Day: April 5th with 785 grains/m^3.

Conclusion: The pollination season of the most relevant pollens in our area begins in February and ends in June. The highest pollination period is from April to May, when the maximum values of Poaceae and Oleaceae match, both in May. Other clinically relevant pollens, such as Platanaceae and Cupresaceae, have a maximum pollination in March and February respectively. We stress the importance of pollen counts for a better approach to the etiology, taking into account the clinical history and other diagnostic tools available.

1285
Tree pollen daily distribution patterns in Vinnitsa, Ukraine

Bilous, ES[1]; Rodinkova, VV[2]; Musatova, KV[3]; Motruk, II[4]; Kremenska, LV[2]; Palamarchuk, OO[2]
[1]Scientific Reasearch Centre, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [2]Pharmacy, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [3]Medical Biology, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine; [4]Hygiene, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine

Background: Its known circadian tree pollen peaks occur in early morning, at 5–6 AM However, the actual hourly pollen concentrations in the cities may differ from the physiological patterns due to long-distance transport impact on air pollen distribution. 3-years study data concerning the tree pollen hourly-distribution patters in Vinnitsa presented.

Method: Pollen counts were obtained at Vinnitsa National Pirogov Memorial Medical University (VNMU) in 2012–2014 bihourly using a Burkard trap at 25 meters height above ground from March 1 to October 31.

Results: Study shows circadian pollen maximums recorded in the early morning within 5 and 7 AM for *Populus* and for *Tilia* just in Vinnitsa air. *Tilia* pollen count increase was recorded at 3 PM as well. *Alnus, Corylus* have pollen peaks on midday at 1 PM *Fraxinus* pollen was collected from 9 AM to 3 PM mostly. *Ulmus* pollen also was collected late for the day - at 1 and at 3 PM Highest pollen count levels for *Betula* and *Quercus* were observed at 11 AM and 1 PM The latest concentration increase was noted for *Salix* - from 3 to 9 PM Tree pollen concentrations increase for the midday and for the evening hours may reflect non-local pollen origin in Vinnitsa atmosphere, especially for *Fraxinus, Tilia* and *Salix* pollen. Some *Alnus, Corylus, Betula* and *Quercus* pollen fractions also may be transported to the city atmosphere from surrounding area.

Conclusion: Some tree pollen fractions recorded in Vinnitsa atmosphere may have non-local origin. Application of pollen transport models is required to establish the places of pollen origin. Noted circadian fluctuations of tree pollen concentration may help allergy sufferers to predict the hours of maximal pollen exposure enhancing effective seasonal allergy control in Vinnitsa, Ukraine.

1286
A novel mobile chamber for allergen exposure tests

Sehlinger, T[1]; Bergmann, KC[2]; Zuberbier, T[2]; Goergen, F[1]
[1]Bluestone Technology GmbH, Woerrstadt, Germany; [2]Allergie-Centrum-Charité, Charité-Universitätsmedizin Berlin, Berlin, Germany

Background: Incorporating allergen exposure chamber tests in clinical studies presents a feasible possibility to lower trial costs. Nevertheless, using exposure chambers in multi-center, and possibly multi-national trials requires comparable exposure systems at all trial sites in order to gain the maximum benefit for the trial. Bringing all patients to only one stationary chamber would eliminate the cost benefit and would also raise other issues such as introducing test subjects to different environmental conditions before the test.

Method: A flexible deployable test chamber, able to generate a standardized, controllable and reproducible airborne particle concentration (e.g. pollen), with minimum requirements to the onsite situation and able to be operated in a wide range of outside temperature, should allow data comparability in multinational multi-center trials. Therefore, an inter-connectable container compound was developed, consisting of two standard sized 24" containers, one hosting the test chamber and the technical installations, and the other hosting a control room and a changing room. The test chamber can host up to 9 subjects with temperature and humidity levels being adjustable in a wide range. Each subject can be exposed to an individually adjusta-

ble particle concentration, controlled by dedicated disperse units. These units are loaded with traceable particle blisters, contain a particle counting unit allowing for each particle to be counted before dispersal, and a disperse nozzle which ensures an even particle distribution in a very dedicated and confined area. The test chamber can be operated at an outside temperature ranging from -10°C up to 35 °C.

Results: The system developed showed comprehensive characteristics not only in terms of particle concentration, test environment stability and reproducibility compared to fixed chambers but also whilst operating in various outside conditions, namely temperature and humidity. The system also proved fast and flexible in its deployment with a set up time of less than half a day. Furthermore, the system allowed for an individual exposure while no particles where found within the breathable air of another test subject.

Conclusion: The developed mobile allergen exposure chamber does fulfill the need for using exposure chambers in multi-center trials.

1287
Clinical validation of a mobile environmental allergen exposure chamber

Bergmann, K-C[1]; Sehlinger, T[2]; Bölke, G[3]; Zuberbier, T[1]
[1]Allergy-Center-Charité, Charité Universitätsmedizin, Berlin, Germany; [2]Bluestone Technology GmbH, Woerrstadt, Germany; [3]Allergie-Centrum-Charité, Berlin, Germany

Background: As required by the EMA for pivotal trials involving allergen immunotherapy products, clinical efficacy assessment is currently based on double-blind, placebo-controlled field studies with natural allergen exposure during the allergen season. Problems with the filed studies include the variability of allergen exposure in different trial sites, the uncertainty of time exposure and confounding environmental factors (temperature, humidity etc.).

A novel mobile Environmental exposure chamber (EEC) was designed to operate with stable and reproducible allergen exposure under standardized environmental conditions. To be accepted as an appropriate alternative to natural allergen exposure for clinical trials the clinical validation of the EEC must document a high reliability of provoked symptoms in repeated provocations and the possible impact of seasonal priming on the test results has to be evaluated systematically.

Method: The test chamber with monitored temperature, relative humidity, oxygen and CO2 levels was used for provocations with grass and birch pollen up to 9 adult non-smoking subjects with or without allergic symptoms due to birch and grass pollen during the last two seasons. Each subject was exposed to an individually adjustable pollen concentration, controlled by dedicated disperse units (described in 2). Provocations for a period of time of at least 90 minutes has been done within and outside the birch and grass pollen season to evaluate the impact of seasonal priming. Before, during and at the end of provocation spirometry, peak-flow, exhaled nitrogen oxide (FeNO), peak nasal inspiratory flow, and the classical symptoms on eye, nose and bronchi has been documented. Possible late-reaction has been recorded after 24 hrs.

Results: The repeated provocations with birch and grass pollen in different concentrations provoked reproducible clinical symptoms on all the three organs (and to skin reactions as contact urticaria reactions, too). Generally, the symptoms started to occur after 10 min. and reached a plateau following 30 - 50 min of continuously exposure to pollen.

Conclusion: The influence of possible priming due to an exposure during a preceded season of another pollen species (e.g. birch exposure before grass pollen exposure) in mono- or multisensitized persons has to be clarified in the next step of investigation.

1288
Sensitization pattern to common aeroallergens at Makkah

Tayeb, MM[1,2,3]
[1]King Abdulaziz University, FM - Allergy, Jeddah, Saudi Arabia; [2]Jeddah, Jeddah, Saudi Arabia; [3]King Abdulaziz University, Makkah, Saudi Arabia

Background: To identify sensitization pattern to common aeroallergens in allergic patients.

Method: Lab results of specific IgE (sIgE) to common aeroallergens were sequentially selected from patients with allergic diseases referred to Al-borg laboratory in Makkah city, Saudi Arabia in the period of October 2005 to July 2007.

Results: 199 samples were collected retrospectively. Of these 105 (53%) samples had positive sensitization: 71 female (68%), 34 male (32%), 79 adult (75%), 26 children (25%). There ages range were between 1 month and 75 years. The most common aeroallergens respectively were: American cockroach (periplaneta Americana) 23%, house dust mite (dermatophagoides pteronyssinus) 18%, Cat epithelia (Felis catus) 15%, desert palm pollen (phoenix dactyllifera) 13% and house dust mite (dermatophagoides farina) 11.25%. Negative sensitization were 94 (47%).

Conclusion: The sensitization pattern to common indoor aeroallergens, i.e. dust mites and cat, in allergic patients at Makkah city is compatible with the global picture. Surprisingly, the high sensitization to American cockroach and desert palm pollens needs an additional assessment.

1289
Comparison between house dust mite and Aspergillosis sensitization in patients with high level of TIgE

Shiquan, W; Baoqing, S; Wenting, L; Nili, W
The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

Background: Among the patients with serum total immunoglobulin E (TIgE) higher than 1000 ku/L, who suffered from respiratory diseases, we could found the majority of them were sensitized to house dust mite (HDM) and Aspergillosis. We aimed to find out if there any correlation with TIgE among serum specific immunoglobulin- -E (sIgE) against house dust mite along with Aspergillosis in the patients.

Methods: 64 subjects with high level of TIgE were tested for serum sIgE-derp1 and sIgE-Af by using ImmunoCAP 100.

Result: Of 68.8% (44/64) patients were sensitive to HDM while 40.6% (29/64) were sensitive to aspergillosis. What's more, 37.5% (24/64) patients could be detected sIgE (derp1,Af) while 15/64 (23.4%) patients were found sIgE(derp1, Af)-free. 20/64 (31.3%) patients were merely sensitive to HDM while 5/64 (7.8%) were sensitive to Aspergillosis. Among the patients with TIgE higher than 1000ku/L, those patients sensitive to HDM was significantly more than those sensitive to Aspergillosis (ka=9.00,t= $P < 0.01$). sIgE-Af ($r = 0.410$) was correlated more with TIgE than sIgE-derp1 ($r = 0.228$) was ($P < 0.05$).

Conclusion: Most of the patients with high level of TIgE, complicated with respiratory diseases, were more likely sensitive to HDM rather than Aspergillosis. Compared to sIgE against HDM, sIgE-Af contributed more to the level of TIgE. The detection of sIgE against HDM and Aspergillosis was important for the patients complicated with respiratory and high level of TIgE.

1290
The relationship between environment and the prevalence of allergy rhinitis and asthma in pre-school children in Guangzhou city

Jiaying, L; Huimin, H; Manning, Z; Nili, W; Baoqing, S
State Key Laboratory of Respiratory Disease, Guangzhou City, China

Background: In recent decades, the prevalence of allergic rhinitis in many countries has increased, particularly among children. According to previous study, we know the influential factors included individual characteristics (allergic constitution), genetic factor, and environmental factor and so on. Environmental pollution in china is getting worse, we don't know whether the prevalence of children's allergic rhinitis and asthma related to the environment or not. To investigate the relationship about the environment (passive smoking, long-term exposure to plush or bubble toys, long-term exposure to pets and use carpet at home, etc) and the prevalence of children's allergic rhinitis and asthma could serve as strong evidence for prevention of allergic rhinitis in children.
Method: The questionnaire was designed based on the internationally accepted International Study of Allergic rhinitis and Asthma in Childhood (ISAAC) questionnaire with combination of the epidemiological characteristics of local allergic disorder in Guangzhou city. Kindergartens were selected by a random, cluster-sampling method. There are 15 kindergartens, including 2010 children. Parents of kindergarten children completed the questionnaire after taught by teacher. Relevant investigators confirmed the effectiveness of the questionnaire by phone call. The results were analyzed by SPSS 17.0. Multivariable logistic regression was used to analyze the associations between the environment factors and parent-reported allergic rhinitis and asthma that yielded *P*-values< 0.1 in the univariate analyses.
Results: Of 2010 questionnaires that had been handed out, 1884 were valid. The prevalence of allergic rhinitis in children in this survey was 12.8%. The prevalence of allergic rhinitis and asthma in children was 1.4%. Applied logistic regression analysis of environment factors in children allergic rhinitis, we can found that Home or school near the road; long-term exposure to plush or bubble toys; pet ownership; passive smoking, the risk of children with allergic rhinitis increased ($P < 0.05$). Using cotton pillow or quilt was one of the protection factors.
Conclusion: In Guangzhou city, Home or school near the road; long-term exposure to plush or bubble toys; pet ownership; passive smoking can increase the risk of allergic rhinitis and asthma in children.

1291
The composite assessment of burden of asthma in a sample of outpatients children

Montalbano, L[1,2]; Cilluffo, G[1,3]; Malizia, V[1]; Antona, R[1]; Ferrante, G[4]; La Grutta, S[1]
[1]National Council of Research CNR, Palermo, Italy; [2]Department of Psycology, University of Palermo, Palermo, Italy; [3]Department of Economics, Business and Statistics Science, University of Palermo, Palermo, Italy; [4]Department of Science for Heath Promotion of Mother and Child, University of Palermo, Palermo, Italy

Background: PAQLQ and C-ACT are widely used as standardized tools for the assessment of the quality of life and the control of asthma in children. Pittsburg Sleep Quality of Index (PSQI) is a questionnaire to assess the quality of sleep, while Visual Analogic Scale (VAS) is a scale for the evaluation of general welfare. The aim of this study was to assess differences by severity level of asthma in a sample of outpatients children with Asthma (A).
Method: Spirometry, PAQLQ, C-ACT and PSQI in children visited for suspected respiratory disease at IBIM from September 2011 to October 2014 were collected. Medical history was taken in a standardized way. Spirometry was performed using a portable spirometer (Pony FX, Cosmed, Italy); spirometric values were expressed as percent predicted using GLI-2012equation. Standard methodology was applied for Skin Prick Testing; atopy was defined as at least a positive reaction. Statistical analyses were performed using R (3.1.0).
Results: Of 144 pts, Males 87 (60%), Females 67 (40%) ranged 6 to11 years were included: 76 (53%) with Persistent Asthma (PA), 68 (47%) with Intermittent Asthma (IA). Significant differences ofmean (SD) for PAQLQ total score in PA=5.1(1.01) vsIA=5.44(0.96), $P = 0.04$, for PSQI in PA=2.24(2.47) vsIA=1.53 (1.59), $P = 0.04$, for FEV1% in PA=92.41 (18.77) vs IA=98.89 (14.98), $P = 0.02$, and for FEF25–75% in PA=72.74 (21.86) vs IA=99.42 (32.42), $P < 0.0001$ were found. In PA a greater C-ACT and VAS average score were found in children with Not-Smoke-Exposure-in- Pregnancy (NSEP) than in the exposed ones (SEP), respectively for C-ACT [NSEP=20.74 (3.31) vs SEP=15.83 (7.17), $P = 0.01$] and for VAS [NSEP= 8.1(1.66) *vs* SEP =6.33(2.94), $P = 0.02$]. No difference of C-ACT total score and Atopy index were found in PA *vs* IA. By a logistic regression significant effects for PA were FEF25–75%, indeed if FEF25–75%increases of one unit the risk to be PA decreases of 0.05 ($P < 0.001$), and PSQI, indeed if PSQI increases of one unit the risk to be PA increases of 0.28 ($P = 0.03$).
Conclusion: In persistent asthmatics a greater respiratory function impairment and an higher burden of disease were found. Medical history of early smoke exposure should be also taken into account when a composite (objective and subjective) assessment of asthma is performed in children.

1292
Evaluation of Alt a 1 detection in fungal contaminated oranges by ELISA and PCR

Uriel, N[1]; Teifoori, F[1]; Gabriel, M[1,2]; Postigo, I[1]; Gutiérrez-Rodríguez, A[1]; Suñén, E[1]; Martínez, J[1]
[1]Department of Immunology, Microbiology and Parasitology, Faculty of Pharmacy and Laboratory of Parasitology and Allergy, Lascaray Research Centre, University of the Basque Country, Vitoria-Gasteiz, Spain; [2]Department of Chemistry and CICS-UBI - Health Sciences Research Centre, University of Beira Interior, Covilha, Portugal

Background: Alternaria alternata spores are one of the most frequently identified fungal spore types in the atmosphere. It is recognized that they can spoil a wide variety fruits, including a significant variety belonging to the *Citrus* genus. Since sensitisation to *A. alternata* major allergen, Alt a 1, is considered an important marker for predicting the risk and severity of respiratory symptoms in this work we aimed to evaluate the presence of contamining Alt a 1 in *A. alternata* infected oranges.
Method: Sixty oranges were used for infection with 100 μL of 10^5 *A. alternata* spore suspension. Three oranges were infected with *Penicillium chrysogenum*, and another three oranges without fungal infection were also used as negative controls. Sample material was collected at different incubation times (n = 20) after the fungal inoculation. The material collected from each orange was divided and used for total RNA extraction and protein extraction. The Alt a 1 detection was, then, performed by PCR amplification using Alt a 1 specific primers and Enzyme-linked immunosorbent assay.
Results: The PCR assays revealed the presence of the fragment corresponding to the Alt a 1 gene of 390 bp in 90%, 100% and 100% of the samples from first, second and third week after *A. alternata* infecting, respectively. On the other hand, ELISA quantification was positive for 75%, 85% and 85% of the samples from first, second and third week after *A. alternata* inoculation, respectively. No amplified gene fragments or ELISA positive results were detected in the negative controls.

Conclusion: The experimental model of *A. alternata* spore inoculation in oranges proposed in this work seems to be effective to simulate the fruit contamination and its progression. Although PCR and immunoassay-based techniques had been successfully carried out for detecting Alt a 1 allergen in experimental *A. alternata* infected orange, PCR method was found to be more sensitive than ELISA. Thus, this PCR system may be a valuable tool for the detection of the allergen Alt a 1, as a quality and biosecurity marker in fruits, minimising exposure and reducing incidences of allergic reaction to Alt a 1 from contaminated fruits.

1293
Assessment of house-dust mite allergen-blocking effectiveness of newly developed barrier fabrics for antiallergic covers

Majkowska-Wojciechowska, B[1]; Jarzębska, M[1]; Cieślak, M[2]; Krawczyńska, I[2]; Malinowska, G[2]; Kaleta, A[2]; Kowalski, ML[1]
[1]Department of Immunology, Rheumatology and Allergy, Healthy Ageing Research Centre (HARC), Medical University of Lodz, Lodz, Poland; [2]Textile Research Institute, Lodz, Poland

Background: Mite allergens can easily accumulate in mattresses and on textile surfaces, mainly on linen. Approved strategies for reducing exposure to dust mite allergens include using of covers from certified barrier fabric. Covers may significantly increase the comfort and safety of nighttime sleep and prevent the occurrence of exacerbations of atopic allergies and asthma. The aim of this study was to evaluate the allergen-blocking effectiveness of newly developed barrier fabrics designed for antiallergic covers.
Method: The barrier fabrics made of polyester/cotton woven structure with one-sided polymer coating were manufactured by the Textile Research Institute. Barrier effectiveness of designed fabrics and control cotton woven fabric against dust and house dust mite allergen Der p 1 was tested according to the method previously described. In brief, house dust samples were sucked onto the tested textile material with vacuum cleaner and the allergen was collected on filters. Following a filter extraction, the mite allergen Der p 1 concentration was determined with commercial ELISA method. Barrier effectiveness was defined as the % of permeability of tested woven in relation to control cotton fabric.
Results: Total six fabrics were tested and the one with the best performance in preventing dust and Der p 1 penetration was chosen. This developed textile material (named *Argo Plus)* was characterized by a high barrier effectiveness against Der p 1 allergen (0.15% permeability), but at the same time had sufficient permeability to water vapor. When subjected to 20 washing cycles the *Argo Plus* fabric retained its barrier function.
Conclusion: Using our original method for barrier fabrics testing, we were able to select a textile material with optimal barrier characteristics, which may be used to manufacture mite-impermeable mattress covers.

1294
Patterns of sensitization to Ambrosia species

Perez, I[1]; Pineda, F[1]; Panaitescu, C[2]; Marusciac, L[2]; Tamas, T-P[2]; Ianovici, NI[3]
[1]DIATER Laboratories, Madrid, Spain; [2]Functional Sciences, University of Medicine and Pharmacy Victor Babes Timisoara, Timisoara, Romania; [3]Department of Biology, West University of Timisoara, Timisoara, Romania

Background: The Asteraceae or Compositae family is one of the largest families of flowering plants. Only a few genera are relevant as allergenic sources, the most important being Ambrosia (ragweed) and Artemisia (mugwort). Among ragweed species, *A. artemisiifolia* (short ragweed) and *A. trifida* (giant ragweed) are of special interest due to their highly allergenic potential. In the western part of Romania, *A. artemisiifolia* represents approximately 20% out of the total pollen, and is the most allergenic in this climate zone.

The aim of this study was to evaluate whether there is a concurrent hypersensitivity to multiple Ambrosia species as a result of co-sensitization or cross-reactivity
Method: The study group included 25 patients screened for positive skin prick test to Ambrosia pollen extract (DIATER Laboratories, Madrid, Spain), symptomatic during pollen season (August-October 2014). The patients' sera were tested for specific IgE to Amb a 1, by ImmunoCAP and further specific IgE reactivity to *A. artemisiifolia* vs *A. trifida* pollen extracts, containing allergenic fragments (in range of 10 to 75 kDa), by immunoblotting and ELISA inhibition.
Results: The patients (14 men and 11 women, with mean age of 29.68 ± 5.55 years) presented moderate-severe allergic rhino-conjunctivitis (intermittent in 19 cases, persistent in 6 cases) and 4 patients were additionally diagnosed with mild asthma. Allergic symptoms onset occurred less than 5 years ago in most cases (76%). From the whole group, 9 patients were monosensitized to Ambrosia pollen, and 16 were polysensitized (3 to indoor, 5 to outdoor and 8 to both indoor and outdoor allergens). The degree of sensitivity to Amb a 1 based on specific IgE levels was moderate (class 3–4) in most patients (84%), and mild (class 1–2) or severe (class 5–6) in 8% each. The IgE of patient's sera revealed different patterns of recognition to *A. artemisiifolia* and *A. trifida* allergenic extracts, leading to a greater response for *A. artemisiifolia* vs *A. trifida* (Ag50 = 0.65 and 13.92 mg/mL respectively) by ELISA inhibition.
Conclusion: The clinical data, correlated with the laboratory results, validate that *A. artemisiifolia* is the major allergenic ragweed species in the western part of Romania, and there is no significant cross- or co-sensitization between the two species.

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Clinical aspects of drug allergy

1296
NSAID hypersensitivity during childhood along with different classifications

Cavkaytar, O; Arik Yilmaz, E; Karaatmaca, B; Buyuktiryaki, B; Sackesen, C; Sekerel, BE; Soyer, O[1]
Department of Pediatric Allergy, Hacettepe University Medical Faculty, Ankara, Turkey

Background: Although NSAID hypersensitivity (NSAID-H) was studied broadly in adults, there is still lack of data for phenotypes of NSAID-H in children. Our aim was to define risk factors and different phenotypes of NSAID-H according to clinical features.
Method: Patients with a history of reaction to any of the NSAIDs who had been referred toour department between January 2012-October 2014 were included. After filling a modified ENDA *(European Network for Drug Allergy)* questionnaire, skin tests (with metamizole) and/or oral provocation tests (OPT) were performed initially with the offending drug. Positive OPT was defined as the occurrence of an objective physical finding related with hypersensitivity or a $\geq 15\%$ decrease in FEV_1 during OPT. Additional OPTs were done with aspirin and other NSAIDs in case of a positive initial test to determine the cross-reactivity and to find safe alternative NSAID. Patients with NSAID-H were defined as "Selective Responder" (SR) or "Cross Intolerant" (CI) and further categorized according to either ENDA/GA'LEN classification or an alternative classification scheme by Demoly et al.
Results: 121 patients[(58.7% male), 7.8 years (4.7–10.8)] with 161 suspicious reactions due to NSAIDs were referred. 110 (90%) patients with 148 (92%) reactions were assessed. NSAID-H was diagnosed in 30 (27%) patients with 37 reactions (25%). As a result of multivariate regression analysis, anaphylaxis history with NSAIDs and reaction with only one group of drug increased the personal risk of actual NSAID-H [(OR:3.715,95% CI:1.46–15.24, $P = 0.01$), (OR:2.935,95% CI:1.1–7.85, $P = 0.032$), respectively], and immediate type of HR and respiratory symptoms during the reaction increased the risk of actual NSAID-H related reaction[(OR:3.508,95%CI:1.42–8.7, $P = 0.007$), (OR:3.951,95%CI:1.33–11.77, $P = 0.014$), respectively]. Among patients with NSAID-H, OPTs determined 15SR and14 CIs. They are classified as Single NSAID-Induced Urticaria-Angioedema (SNIUA)(n = 14), Multiple NSAID-Induced Urticaria-Angioedema(n = 4), NSAID-Exacerbated Cutaneous Disease (n = 2) and NSAID-Exacerbated Respiratory Disease (n = 1). Four CIs couldn't be categorized according to either classification system. One SR and 3CIs patients couldn't be categorized according to ENDA.
Conclusion: During childhood, NSAID-H exhibit different characteristics and SNIUA seems to be more frequent. The NSAID-H classifications based on adult data may not fit NSAID-H in pediatric age group.

1297
Characteristics of drug hypersensitivities: a single centre experience

Demirturk, M[1]; Isik, SR[1]; Ersoy, R[1]; Uysal, A[2]
[1]Adult Allergy Department, Yedikule Chest Diseases and Surgery Training and Research Hospital, Istanbul, Turkey; [2]Chest Diseases, Yedikule Chest Diseases and Surgery Training and Research Hospital, Istanbul, Turkey

Background: Drug hypersensitivity is an important health problem appearing in all age groups and gender, and forming an important part of the unpredictable, non-dose related adverse drug reactions. The aim of this study is evaluating the characteristics of drug hypersensitivities and associated risk factors.
Methods: Of 207 patients who were admitted to Adult Allergy Outpatient Clinics of Yedikule Chest Diseases and Surgery Training and Research Hospital between January and December 2013 and were diagnosed as drug hypersensitivities, 140 were included to this study. Questionnaire preapared according to the ENDA guideline was performed to the patients face to face or by phone or using the knowledge in the files of patients, retrospectively. Data was analysed by SPSS 15.
Results: Of 140 patient 106 were female (75.7%). The mean age of the patients was 40.6 ± 12.3 years. The most frequent causes of drug hypersensitivities were antibiotics (53.6%), followed by analgesics (52.9%), local anesthetics (8.6%), proton pump inhibitors (6.4%), cold medicines (5.7%), radiocontrast agents (1.4%) and general anesthetics (0.7%), respectively. Skin manifestations (88.6%) were the most common findings including urticaria (71%) and itching (55.7%), followed by respiratory problems (40%). A patient with oral and cutanos lesions and two patient with bullous lesion were diagnosed as SJS anf fix drug eruption, respectively. Anaphylaxis has been presented by 15.7% of the patients The frequency of sensitization to at least one of the common aero-allergens which was determined by skin prick test was 27.3%. Asthma and allergic rhinitis were most frequent co-morbid disorders. Alternative drugs were determined in 83.6% of the patients. Macrolides and meloxicam were the most common alternative drugs.
Conclusion: The presence of an other allergic disease is an important risk factor for drug hypersensitivities. The characteristic behaviour of an allergy physicians is to determine an alternative drug rather than finding the responsible drug which is searched only by medical history of the patient.

1298
Urticarial vasculitis induced by bupivacaine

Argiz, L; Vega, F; Las Heras, P; Fariñas, M; Jiménez, H; Blanco, C
Hospital Universitario de La Princesa, Allergy, Madrid, Spain

Background: Allergic reactions to local anesthetics belonging to the amide group are scarce, being the delayed hypersensitivity even more uncommon.
Case report: We report 54 years old female patient. In August 2014, a colonic neoplasia was diagnosed and an abdominal surgery was performed. Two days after the surgery, the patient developed a generalized urticaria that was related to the administration of different analgesic drugs (metamizole and desketoprofen). In addition, she also received a continuous epidural analgesia with bupivacaine 0.25% and fentanyl 0.05 mg/mL. The skin reaction disappeared without residual lesions three days after starting treatment with oral antihistamines and topical corticosteroids.

Allergy study: Skin-prick tests and intradermal-tests with bupivacaine, lidocaine and mepivacaine were negative at immediate and delayed readings. A subcutaneous challenge-test with bupivacaine 0.25% was performed showing good immediate tolerance. Twenty-four hours later, she presented a generalized urticaria, improving after treatment with parenteral corticosteroid and antihistamines. But twenty-four hours later, she showed labial angiodema, reactivated urticarial lesions and purple macular lesions of rounded appearance and central hypopigmentation in bilateral inguinal area, suggesting an urticarial vasculitis. Treatment with oral corticosteroids resolved the cutaneous involvement without residual lesions in five days. Subcutaneous challenge-test with lidocaine 1% and mepivacaine 2% showed a good immediate and late tolerance. Oral challenge-tests with metamizole, desketoprofen and fentanyl were negative.

Conclusions: We present a patient with an urticarial vasculitis after administration of bupivacaine. Skin tests with local anesthetics have a low sensitivity, being necessary to carry out challenge-tests for a correct diagnosis. As in the case of immediate allergic reactions, cross-reactivity is not important in delayed allergic hypersensitivity to local anesthetics belonging to the amide group.

1300
Angioedema with acute liver injury induced by angiotensin II receptor antagonists

Nakonechna, A; Dixon, T
[1]Royal Liverpool and Broadgreen University Hospitals NHS Trust, Allergy, Liverpool, UK

Background: Angiotensin II receptor antagonists (AT2 blockers) are antihypertensives developed in part to eliminate cough and angioedema associated with ACE inhibitors. However they may not always be safe alternative medications.

Material and methods: We present three cases of AT2 blockers-induced angioedema along with acute liver injury.

Results: Among three patients 45–64 y.o, with essential hypertension, who had experienced angioedema secondary to ACE inhibitors (Ramipril/Lisinopril) and were switched to the AT2 blocker (Losartan) two presented with angioedema, which involved their head, lips, face and neck and in one patient also tongue. Additionally, in two-three weeks after starting Losartan, all three patients developed anorexia, nausea, jaundice and fatigue. On hospital admission an examination revealed different level of jaundice and fever (37.7 ± 0.4 C). There was moderate elevation in serum bilirubin (9.6–21.2 mg/dL) with significant increase in serum aminotransferase levels (alanine aminotransferase 517–1352 u/L; aspartate aminotransferase 402–815 u/L) and alkaline phosphatase (306–512 u/L). They all had no history of liver disease, jaundice, previous drug hypersensitivity reactions or excessive alcohol use. There were no eosinophilia and negative tests for hepatitis A, B and C. Ultrasound of the liver showed hepatomegaly without evidence of biliary obstruction. Losartan was stopped on admission and beta-adrenoreceptor blocking agents were substituted. A significant improvement was noted after two weeks and three-four months later all patients were free of symptoms and all liver tests were normal, and their angioedema subsided as well.

Conclusion: Clinicians should exercise caution when using AT2 blockers in patients with a history of angioedema: either prior or secondary to ACE inhibitors. Patients with Losartan-induced acute liver injury should probably avoid use of other AT2 agonists, although cross-sensitivity to liver injury among the members of this agent's class has not been shown.

1301
Allergy to an endogenous vitamin - how can this be?

Egner, W; Shrimpton, A; Sargur, R; York, M; Swallow, K
Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

Background: We present the case of a young woman on methotrexate treatment for psoriasis. She was prescribed a 5 mg folate supplement to take weekly and sustained an anaphylactic reaction of grade 3 severity within 15 minutes of administration.

Results: Referred for investigation of her reaction, she was found to be both SPT and IDT positive for two different preparations of folic acid 5 mg tablets. She was not sensitised to the corn starch which was the only other likely excipient.

Conclusion: We present the results of her basophil activation test and a literature review on the extremely rare phenotype of folic acid allergy. We discuss the management issues including cross-reactivity and hypotheses to explain the inconsistency between tolerance of dietary folate and IgE mediated allergy to pharmacological folate.

1302
Phenytoin-induced toxic epidermal necrolysis: a case report

Martins, M; Reis, R; Tomaz, E; Inácio, F
Hospital São Bernardo, Immunoallergology, Setúbal, Portugal

Background: Toxic epidermal necrolysis (TEN) is a serious adverse reaction to drugs and potentially fatal. The most commonly implicated drugs are allopurinol, sulfonamides, aminopenicillins, cephalosporins, quinolones, carbamazepine, phenytoin, phenobarbital and type oxicam nonsteroidal anti-inflammatory drugs.

Case report: We present a case of a 58 years old female patient, submitted to craniotomy for extraction of an expanding cerebral lesion and then medicated in a regular daily basis with phenytoin, methylprednisolone, esomeprazole and acetaminophen. Two weeks later the patient starts a facial edema and a pruritic, maculopapular rash dispersed all over the body. She went to the urgency service (US) and was treated with oral hydroxyzine and topical promethazine. The day after there were no relief so phenythoin and esomeprazole were suspended and the patient began oral methylprednisolone. The next day the patient had generalization and worsening of the skin condition and went back to the US. On examination she was febrile, with generalized maculopapular lesions and blisters on the back. She was admitted with the diagnosis of toxidermia probably due to phenytoin.

In the next days there was an increase of symptoms, with generalized painful and blistering skin eruption, which had a centripetal evolution with coalescing purpuric inflammation. The detachment of the epidermis and mucosa affected around 72% of body surface area. Analytically: C-reactive protein 25, leukopenia (3400), serology, autoimmunity and culture of skin exudate were negative. The patient was isolated and treated with burn care. The therapeutics included prednisolone, hydroxyzine, serum therapy, analgesia and empirical antibiotic therapy with meropenem and vancomycin. The patient was accompanied by a multidisciplinary team, verifying progressive clinical improvement, with regression of lesions and re-epithelialization and was discharged after 1 month of admission. In Immunoallergology evaluation the *lymphocyte transformation* test for phenytoin was positive (SI = 4.9).

Conclusion: TEN is a diagnosis to consider in patients with toxidermia with necrosis and detachment of the epidermis, involving more than 30% of body area. The suspected drugs should be suspended immediately and a multidisciplinary approach

must be considered. In vitro tests are useful for the identification of the drug involved, given the risks of the in vivo tests (skin or challenge tests) in these patients.

1305
Early presenting fixed drug eruption with different quinolones in a patient

Demir, S[1]; Aktas-Cetin, E[2]; Olgac, M[1]; Ertek, B[1]; Unal, D[1]; Kuçuksezer, U[2]; Gelincik, A[1]; Deniz, G[2]; Buyukozturk, S[1]
[1]Division of Immunology and Allergic Diseases, Internal Medicine Department, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey; [2]Department of Immunology, Institute of Experimental Medicine DETAE, Istanbul University, Istanbul, Turkey

Background: Fixed drug eruption (FDE) is an adverse drug reaction characterized by skin lesions which recur in the same sites upon reexposure to the drug, mostly observed within a few hours to days of drug exposure and typically resolve with hyperpigmentation (1). The most frequent cutaneous hypersensitivity reactions to quinolones are urticaria, angioedema and maculopapular eruptions (2). Altough FDRs caused by quinolones are rarely seen, FDR due to ciprofloxacin, norfloxacin, ofloxacin and levofloxacin as well as cross-reactive FDR to ciprofloxacin- levofloxacin and levofloxacin-ofloxacin were reported previously. However FDR caused by moxifloxacin or gemifloxacin was not reported before.
Case: A 55 year-old female patient was reffered to us with a history of hypersensitivity reactions to ciprofloxacin and ofloxacin for allergy tests to find out alternative antibiotics. In her history she described a fixed drug eruption on her lips. We evaluated cross-reactivity with other quinolones in this patient after informed concent was received. Drug patch tests with ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin and gemifloxacin were found negative. Patient did not accept to be tested on the lesion site. Therefore single blind placebo controlled drug provocation tests with levofloxacin, moxifloxacin and gemifloxacin (other than culprit quinolones) were performed. With all the three drugs the same reaction was observed. After the ingestion of these drugs, in 10 minutes edema appeared on the left side of her upper lip. Five or six hours later edema resolved with crusting. Than the lesion left a residuel hyperpigmentation which completely disappeared approximately in a month. We performed leukocyte transformation test with ciprofloxacin by flow cytometry. Drug spesific $CD4^+$T cell response was found positive after stimulation of PBMCs with 5 μg/mL and 10 μg/mL ciprofloxacin.
Conclusion: This report represents an early presentation of a fixed drug eruption with various quinolones. When indicated, alternative quinolones should be cautiously applied to patients taking the cross reactivity into consideration.

1306
Immediate and non-immediate hypersensitivity reaction to single dose moxifloxacin

Demir, S[1]; Olgac, M[1]; Unal, D[1]; Akdeniz, N[2]; Aktas Cetin, E[2]; Ertek, B[1]; Gelincik, A[1]; Colakoglu, B[1]; Deniz, G[2]; Buyukozturk, S[1]
[1]Division of Immunology and Allergic Diseases, Internal Medicine Department, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey; [2]Department of Immunology, Institute of Experimental Medicine DETAE, Istanbul University, Istanbul, Turkey

Background: Both immediate and non-immediate type hypersensitivity reactions to quinolones increased over the past decades. However two types of hypersensitivity reactions to the same quinolone in a single patient have not been reported before.
Case report: Here we present a 47 year-old female patient who referred to our clinic with a history of nonimmediate type hypersensitivity reaction due to a radio contrast agent and an immediate type hypersensitivity reaction to clarithromycin. To find out alternative antibiotics, the skin prick and intradermal tests performed with ciprofloxacin, moxifloxacin, metronidazole and clindamycin were negative. Single blind placebo controlled oral provocation tests with metronidazole and ciprofloxacin were performed separately and angioedema on her lips was observed in an hour in each provocation. On a separate day, a similar provocation test with moxifloxacin was performed. After the second dose of the drug, pruritus and erythema throughout the body in minutes were observed and followed by dizziness. Patient's pulse was weakly palpable and tachycardic and her blood pressure could not be measured. This anaphylactic reaction was treated promptly with epinephrine, fluid replacement, methylprednisole and pheniramine. In two hours she completely recovered. However, on the following day she admitted to the hospital with maculopapular eruptions. The biochemical tests and differential blood counts were normal. Methlyprednisolone 32 mg once daily and oral antihistamine 3x1 for five days were initiated. After the signs and symptoms resolved, the patch test with moxifloxacin was found positive. Basophil activation test (BAT) and leukocyte transformation test (LTT) with moxifloxacin and also stimulated IFN-γ and IL-4 secretion from $CD4^+$ T cells were analyzed by flow cytometry in the patient and in a healthy control. Although BAT was found negative, drug spesific $CD4^+$T cell response was positive with increased numbers of $CD4^+IL\text{-}4^+$ Th2 cells and decreased $CD4^+IFN\text{-}\gamma^+$ Th1cell counts.
Conclusion: To our knowledge this is the first case report of a patient with multiple drug hypersensitivity syndrome who experienced both an immediate and a delayed type reaction after the consumption of a single dose quinolone.

1307
Fixed drug eruption - a case report

Aguiar, R; Lopes, A; Pereira-Barbosa, MA
Hospital de Santa Maria- Centro Hospitalar Lisboa Norte, Immunoallergology Department, Lisbon, Portugal

Background: Beta-lactams antibiotics are often implicated in adverse reactions. However, fixed drug eruption (FDE) caused by beta-lactam is unusual.To demonstrate the importance of an allergological evaluation in a patient with low drug allergy suspicion, with reports of a rare manifestation of allergy to beta-lactams.
Case report: Male, 35 years with a diagnosis of betalactams allergy since 5 years old.In the context of multiple episodes of rhinosinusitis refractory to antibiotic therapy was referred to Immunoallergology out-patient clinic. To evaluate the etiology associated with sinusitis, skin prick tests were carried out with aeroallergens and were all negative. Laboratory evaluation showed no alteration of immunity and specific IgE assays for beta-lactams were also negative.The skin prick and intradermal tests with major (PPL) and minor (MDM) determinants and the native molecules (penicillin, amoxicillin, ampicillin, and cephalosporins) were negative in immediate and delayed reading. Patch tests with the same determinants were also negative.In late March the patient was subjected to provocation with amoxicillin, 24 hours after the onset of the provocation the patient describes the appearance of two oval pruritic erythematous lesions on the anterior face of the left forearm compatible with FDE. In mid-May he underwent provocation test with amoxicillin without complications. In late May, about 6 hours after challenge with penicillin, the patient describes the appearance of 2 lesions with similar characteristics and location. Later, the patient already made provocation with cephradine, cefuroxime and ceftriaxone with tolerance. It has been reported that there is a refractory period in FDE, which may explain the fact that the second provocation test with amoxicillin has not reproduced the characteristic lesions. New

patch tests are scheduled to be carried out at the site of the lesion.

Conclusions: In the literature there are few reports of FDE associated with amoxicillin with cross-reactivity to other beta-lactams. This is the first report of FDE with reactivity to amoxicillin and penicillin.

1311
Acute generalized exanthematous pustulosis induced by phenytoin use

Anil, H[1]; Kiral, E[2]; Harmanci, K[1]; Çarman, KB[3]; Koçak, A[4]
[1]Pediatric Allergy and Immunology, Osmangazi University, Eskisehir, Turkey; [2]Pediatric Intensive Care Unit, Osmangazi University, Eskisehir, Turkey; [3]Pediatric Neurology, Osmangazi University, Eskisehir, Turkey; [4]Pediatric Allergy and Immunology, EAACI, Eskisehir, Turkey

Introduction: Acute generalized exanthematous pustulosis (AGEP) is a severe and rare eruption that develops mostly from factors related to drugs. It is characterized by a fever and a pustular eruption on the erythematous skin with an acute onset and without follicular localization. Etiopathogenesis has not yet been fully explained. We present a case of AGEP associated with phenytoin that developed in a patient followed up in the intensive care unit for uncontrolled seizures. It has been reported that she had a maculopapüler rash occured after receving phenytoin at another service two years ago.

Case report: A 14-year-old female patient was presented with status epilepticus. Phenytoin treatment was started with 5 mg /kg/day and epileptic seizures was controled. On the third day of treatment numerous pustular lesions on erythematous skin of her body and extremities were noticed. Mucous mebranes were intact. Her body temperature was mesured as 39.3°C. The results of routine labooratory investigations revealed that hemoglobin: 10.9 g/dL, hematocrit: 32%, white blood cell count: 9800/mm3 (in peripheral blood smear, 46% neutrophils, 50% lymphocytes, 4% monocytes), thrombocyte: 350.000/mm3, erythrocyte sedimentation rate: 15 mm/h, c-reactive protein (CRP):0.33 mg/dL. Her previous medical history revelaed that she had been admitted to hospital with status epilepticus two years ago and maculopapular rashes were also develeoped after the use of phenytoin. Our patient was diagnosed as AGEP. Phenytoin treatment was stopped, and antihistaminic one was commenced. The patient's rashes subsided within the following 3 days and then diminished with desquamation.

Discussion: We aimed to emphasize that AGEP can rarely be seen in childhood age and the importance of anamnestic reports.The incidence of drug reactions are increasing, and therefore it is important for physicians to be careful about the anamnestic reports. Also different cutaneous reactions might be seen with the same drug.

1312
An interesting case of drug allergy that was diagnosed lately as hereditary angioedema

Bulut, I[1]; Ozseker, F[1]
[1]Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Immunology and Allergy, Istanbul, Turkey

Case: Twenty-eight years old male patient (Y,Ö) applied to our clinic. He mentioned a drug intake 5 years ago and could not remember the name of the drug. He described experiencing swelling in eyelids, lips and face 1 week after taking the drug. He also experienced the same allergic symptoms in the year 2002, when he was administered a local anesthetic by a dentist. In this case, swelling in eyelids, mouth and face occured 12 hours following the local anesthesia. The patient had similar episodes of urticaria and local angioedema in other occasions too. The patient was given safe medications of local anesthetic, antibiotic and analgesic when he applied the clinic the first time. Four months later, the patient applied to our clinic again, describing an episode of swelling in eyelids, face, throat and tongue, also hoarseness, dispnea and difficulty to swallow, all of which occured right after the application of local anesthesia prior to tooth extraction. Upon further questioning, it was revealed that the patient had 3 other attacks of laryngopharyngeal edema prior to this incident.

Method: Although the patient did not have a family history of allergic angioedema, we considered it helpful to assess C4 level as a screening test, since the patient had irregular episodes of local angioedema previously. He was adviced to come back for follow up 15 days later, when the test result would be obtained. The patient di not come back for follow up 15 days later.

The patient applied another time due to larynx edema and this time, the C4 level was found very low. We also assessed C1 esterase level and function, which was also found to be very low.

Result: The patient was diagnosed as hereditary angioedema. The patient was given a certificate for recieving Danazole and C1 esterase extract therapy. He was adviced to come for follow ups regularly.

Conclusion: Unfortunately, many patients with hereditary angioedema remain undiagnosed for many years. They apply to emergency services with frequent episodes of laryngeal edema, which is often treated improperly, and sometimes we may even lose the patient.

1313
Serum sickness-like reaction from cefaclor

Classen, A[1]; Dieks, J-K[2]; Henneke, M[2]; Lippert, U[1]
[1]Department of Dermatology, Venereology and Allergology, University Medical Center, Goettingen, Germany; [2]Department of Pediatrics and Adolescent Medicine, University Medical Center, Goettingen, Germany

Background: A four-year-old child with an urticarial exanthema and swelling of the joints, especially knees and ankles, has been seen on consultation. The temperature was not elevated. He had previously suffered from a streptococcal infection which had been treated with cefaclor for 5 days. Systemic treatment with prednisone resulted in a clinical improvement. An upper respiratory infection, which the patient had incurred three weeks earlier, was also treated with cefaclor. The mother has an allergy to penicillin.

Diagnostics: IgE 4.44KU/L. Amoxicillin, ampicillin, penicillin (G or V) and cefaclor: no specific IgE antibodies were detected. BSG: 6/18 mm/h n. Westergreen. Circulated immune complexes: not detectable. Creatinine 0.31 mg/dL (0.2–0.43).

Conclusion: Serum sickness-like reactions usually cause urticarial exanthema and swelling of the joints. In a few cases fever, lymphadenopathy or proteinuria are reported. Normally there are no circulated immune complexes and no decrease in complement levels. The reaction is non-IgE mediated. Besides cefaclor, other compounds such as ß- lactam-antibiotics can cause a serum sickness-like reaction. Up to now only a few cases have been reported. Hence, the pathomechanism which perhaps involves metabolic hepatic disorders are not yet well described.

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Management of drug allergy

1314

Allergic reaction in a patient with Systemic Mastocytosis treated with Cladribine and with Trimethoprim-sulfamethoxazole (TMP-SMZ)

Ribó, P[1]; de la Hoz, B[1]; Berges, P[1]; Calzada, MP[1]; López, P[1]; Pérez, N[1]; Solano, E[1]; Álvarez-Cuesta, E[1]
[1]Ramon & Cajal University Hospital, Allergology, Madrid, Spain

Background: Systemic Mastocytosis is a serious disease that often has few therapeutic options. In 2013 the European Medicine Agency accepted Cladribine as a treatment for this illness. As cytotoxic it can cause severe infections, therefore it's necessary to associate the prophylaxis with TMP-SMZ. Allergic reactions with TMP-SMZ are more frequent and they have been described in immunosuppressed patients like HIV.
Method: We describe a case report of a patient with systemic mastocytosis starting the treatment with Cladribine and prophylactic TMP-SMZ. An hour and a half after the administration of Cladribine (first dose of the fourth cycle), she suffered from tachycardia, an increase of temperature in the outer ear, some generalized flushing and later, an episode of diarrhoea followed by some vomiting and hacking coughing without wheezing or dyspnoea. The patient referred to a similar episode during the first dose of Cladribine in the third cycle but with minor intensity.

Apart from the cytotoxic, she was taking TMP-SMZ (one every twelve hours during one week). During the two days of the reactions, she had taken the drug 1 hour previous the reaction.

Allergic tests were performed in the Technical Area of Allergy (Prick tests with TMP-SMZ 1:1 and with the special thinner of the drug 1:1; Patch test TMP-SMZ 10% petrolatum and a challenge control with Cladribine).
Results: Skin prick tests and patch tests were negative. She underwent a drug provocation test to full doses of Cladribine without incident or reactions. We did not provoke TMP-SMZ for the baseline risk of the patient and the severe reaction she had. Pentamidine was used to complete the rest of cycles as an alternative for prophylaxis.
Conclusions: Our patient with mastocytosis had an immediate allergic reaction likely related to TMP-SMZ.

In best of our knowledge it is the first reaction to TMP-SMZ used as prophylaxis in patients with mastocytosis immunosuppressant treatment like Cladribine.

Therefore, the full realization of the allergy study is mandatory especially in the use of a drug of absolute and beneficial indication for the course of the disease like Cladribine.

Systemic mastocytosis is a complex disease which patients suffer from severe reactions similar to allergic reactions, including anaphylaxis, by releasing mediators.

1315

Hypersensitivity reaction to filgrastim with tolerance to lenograstim in a patient with severe post-chemotherapy neutropenia

Gutierrez Fernandez, D[1]; Foncubierta Fernandez, A[2]; Moreno Ancillo, A[3]; Cruz Carmona, MJ[4]; Miranda Paez, A[5]; Fernandez Anguita, MJ[6]
[1]Hospital Universitario Puerta del Mar, UGC Neumologia-Alergia, Cadiz, Spain; [2]Distrito Sanitario Bahia de Cadiz-La Janda, UGC Joaquin Pece, San Fernando, Spain; [3]Hospital Nuestra Señora del Prado, Alergologia, Talavera de la Reina, Spain; [4]Hospital Vall d'Hebron, Barcelona, Spain; [5]Hospital Universitario Carlos Haya, Alergologia, Malaga, Spain; [6]Hospital Universitario Puerta del Mar, UGC Farmacia, Cadiz, Spain

Background: Granulocyte-macrophage colony stimulating factor (GM-CSF) is a cytokine produced by T cells, fibroblasts, endothelial cells, and keratinocytes. It is a 23-kd glycoprotein which stimulates the proliferation and differentiation of progenitor cells common to neutrophils, eosinophils and monocytes. The recent availability of recombinant human GM-CSF has allowed its use as a pharmacological agent to promote growth and differentiation of neutrophils and monocytes in various clinical situations, including myelodysplastic syndromes, chemotherapy-induced neutropenia, chronic neutropenia, AIDS, and post-bone marrow transplant. The most common side effects are low fever, thrombophlebitis, bone pain, muscle aches, flushing, headache, nausea, pleural effusion and dyspnoea. Anaphylactic reactions, including angioedema, bronchospasm and rash have occasionally been reported.
Method: Of 57-year patient who developed a generalized urticarial reaction (erythema, edema, pruritus, and wheals) with no signs of dyspnea or of angioedema after administration of the 4th day's dose of filgrastim R. A milder reaction had already appeared after the first administration of the cycle. Treatment with corticosteroids, anti H1 and 2 antihistamines for seven days was required for resolution. The patient had a history of stage IV ovarian neoplasia, adverse reaction to docetaxel and paclitaxel of unidentified origin, NIDDM, and intolerance of NSAIDs. Since the patient requires continued treatment with stimulating factor colonies she was remitted to Allergy Service.
Results: Skin tests with filgrastim (Prick 300 ug/mL and ID): Positive. Skin tests with lenogastrim (Prick and ID): negative. Total IgE: 110 IU/mL. Specific IgE: 2.3 IU/mL to Dpt, 2.2 IU/mL to Df; negative for hamsters and latex. Skin tests with allergens: positive for dust mites, negative for epithelia and latex.
Conclusion: We showed the absence of cross-reactivity between filgrastim and lenogastrim in a case of hypersensitivity reaction to filgrastim and tolerance to lenograstim in a patient who developed clinical symptoms after the second administration. This strategy is a viable alternative in patients with hypersensitivity reaction to filgrastim and who urgently need to continue receiving drugs from this pharmacological group.

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Case of infusion reaction to idursulafase and successful re-administration with desensitization

Gkavogiannakis, N; Aggelides, X; Makris, M
Allergy Unit "D. Kalogeromitros", 2nd Department of Dermatology and Venereology, Medical School, University of Athens, Athens, Greece

Background: Recombinant human idursulfase is effective for the treatment of Hunter syndrome, mucopolysaccharidosis type II. Notwithstanding, hypersensitivity reaction can occur during infusion of idursulfase.

We report an acute non-IgE hypersensitivity infusion reaction and subsequently successful rapid desensitization to idursulfase.
Case report: A 34 years old male, suffering from Hunter syndrome referred from Neu-

rology Department to our clinic on July 2014 due to an infusion reaction to idursulfase. During the 6th infusion session, the patient developed face flushing, generalized erythema and dyspnea, 90 minutes after onset infusion. One week later (7th session), despite pretreatment with antihistamine and corticosteroids the patient developed from the first 2 minutes the same reaction as above. The infusion was stopped immediately and the reaction was successfully treated with H1 antihistamine iv and methylprednisolone iv. Ten weeks later allergy testing was carried out with prick (2 mg/mL) and intradermal tests (0.02, 0.2 and 2 mg/mL), but all were negative. Likewise, in vitro evaluation (ELISA, Shire, USA) for specific IgE antibodies was negative; in contrary IgG antibodies against idursulfase were detected. Due to the necessity of the drug for the patient and the acute type of the reaction, though there was no evidence of type I hypersensitivity, we decided to perform a rapid desensitization protocol (Table) consisting from 9 steps reaching the therapeutic dose of idursulfase(24 mg), which was well tolerated.

[Proposed 156 min Desensitization Protocol]

Step	Duration (min)	Infusion rate (ml/hr)	Dose (mL/mg)	Cumulative Dose
1	15	4	1/0.24	1 mL/0.24 mg
2	15	8	2/0.48	3 mL/0.72 mg
3	15	12	3/0.72	6 mL/1.44 mg
4	15	18	4.5/1.08	10.5 mL/2.52 mg
5	15	24	6/1.44	16.5 mL/3.96 mg
6	15	36	9/2.16	25.5 mL/6.12 mg
7	15	48	12/2.88	37.5 mL/9 mg
8	15	60	15/3.6	52.5 mL/12.6 mg
9	36	80	47.5/11.4	100 mL/24 mg

Conclusion: This is the first, to our knowledge, report of a successful desensitization procedure to idursulfase. The patient receives the vital treatment with no adverse events until now. Besides our case points out that desensitization might be also effective in other than IgE mediated reactions.

1317
Rapid desensitization protocol with etarnecept in a patient presenting an adverse reaction to the drug

Moreno Ancillo, A[1]; Gutierrez Fernandez, D[2]; Foncubierta Fernandez, A[3]; Cruz Carmona, MJ[4]; Medina Varo, F[5]; Fernandez Anguita, MJ[6]
[1]Alergologia, Hospital Nuestra Señora del Prado, Talavera de la Reina, Spain; [2]UGC Neumologia-Alergia, Hospital Universitario Puerta del Mar, Cadiz, Spain; [3]Distrito Sanitario Bahia de Cadiz-La Janda, UGC Joaquin Pece, San Fernando, Spain; [4]Hospital Vall d'Hebron, Barcelona, Spain; [5]Hospital Universitario Puerta del Mar, UGC Aparato Locomotor, Cadiz, Spain; [6]Hospital Universitario Puerta del Mar, UGC Farmacia, Cadiz, Spain

Background: Etanercept acts as a competitive inhibitor of the binding of TNF-a and TNF-β to their cell surface receptors. Is used in rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis. Local reactions have been observed in 37% of patients with psoriasis treated with this drug and various types of skin reactions have been reported: lichenoid eruption, urticaria, and leukocytoclastic vasculitis. In the long term, etanercept induces antinuclear antibodies in 18.3% of patients. It is administered weekly at a dose of 50 mg/mL. We report a case of non-IgE-mediated adverse reaction to etanercept and its subsequent desensitization.
Method: Thirty-seven year-old patient diagnosed with seronegative psoriatic arthropathy five years previously. Two hours after the administration of the second dose of etanercept, she presented skin pruritus at the injection site and widespread urticarial reaction without angioedema, which persisted for four days and resolved after treatment with antihistamines and corticosteroids. In view of the failure of previous treatment with methotrexate and hydroxychloroquine, and the partial improvement observed with prednisone 30 mg, the patient consulted our department to assess the possibility of desensitization, given her good response during administration. Intraepidermal and intradermal tests and desensitization tests were performed.
Results: Skin tests with pneumoallergens: positive for house dust mites. Skin tests with latex, epithelia (hamsters), trometamol and mannitol: negative. Skin tests with etanercept (prick, 25 mg/mL) and ID (5 mg/mL): negative. Total IgE: 56.3 IU/mL, specific IgE: 5.70 IU/mL to Dpt and 3.10 IU/mL to Df. Desensitization was performed with premedication one hour earlier, in eight steps, via subcutaneous route. For the last six months, the patient has tolerated administration of 50 mg/week of etanercept without any reactions of note.
Conclusion: This new eight-step desensitization protocol proved safe and effective. It appears to be a valid alternative for patients who have had adverse reactions to etanercept, since it allows them to continue with the drug in order to control their underlying disease.

1318
Hypersensitivity to tocilizumab. Desensitization failed

Araujo, CG[1]; Gaig, P[1]; Dalmau, G[1]; Poveda, MJ[2]; Pascal, M[3]; López-Matas, MÁ[4]; Prat, L[1]; Gázquez, V[1]; Journet, S[5]; Carnés, J[4]
[1]Hospital Universitario Joan XXIII, Alergología, Tarragona, Spain; [2]Hospital Universitario Joan XXIII, Reumatología, Tarragona, Spain; [3]Hospital Clinic de Barcelona, Inmunología, Barcelona, Spain; [4]Laboratorios Leti, Madrid, Spain; [5]Hospital Universitario Joan XXIII, Farmacia, Tarragona, Spain

Background: Tocilizumab is a recombinant humanized monoclonal antibody IgG1 anti-interleukin-6 receptor indicated for the treatment of rheumatoid arthritis.
Method: Patient aged 52 with the diagnosis of severe rheumatoid arthritis treated with methotrexate, prednisone (50 mg/day), calcium carbonate, cholecalciferol, teriparatide, folinic acid and omeprazole. History of allergic reaction starts in 2012 after the application of the second dose of tocilizumab, consisting of urticaria and edema of upper respiratory tract. Allergy tests (prick-test and positive basophil activation test) confirmed the immediate hypersensitivity to tocilizumab. Two years later due to poor progression of disease and lack of response to treatments, as requested by his rheumatologist and with the agreement of the patient, tocilizumab desensitization program started.
Results: On March 13, 2014 first tocilizumab desensitization was done with premedication (montelukast, ebastine, AAS, ranitidine and diazepam) at the recovery room, during six hours, reaching a total dose of 480 mg, in 12 steps.

Same desensitization was performed one month later but after administration of 100 mg IV of tocilizumab the patient presented one not itchy rash on pelvic, abdominal and axillary areas. Infusion with tocilizumab was then suspended and treatment with dexclorfeniramina IV was initiated. One hour later the patient reported feeling unsteady, with abdominal pain and vomiting. The subject presented a decrease in blood pressure, maintaining appropriate oxygen saturation. Intramuscular epinephrine, hydrocortisone IV, ranitidine, methylprednisolone, ondansetron, and paracetamol were administered, making the situation under control. Two hours later the patient remained 18 hours at the rocevery room without presenting any

more problems. The tryptase value in reaction was 21.6 ug/L (baseline:5.1 ug/L).
Conclusion: We present the first documented case of hypersensitivity reaction to tocilizumab. Desensitization with premedication and the used regimen was unsuccessful in the second administration.

1319
A case with omalizumab hypersensitivity reaction

Köycü Buhari, G; Öner Erkekol, F
Immunology and Allergy Department, Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

Background: Omalizumab is a well known therapy for patients with uncontrolled moderate to severe allergic asthma with inhaled corticosteroids and long acting beta agonists. However hypersensitivity reactions that lead its discontinuation have been reported.
Case: Of 47 year old female with previously known lansoprazol anaphylaxis was consulted to our clinic because of uncontrolled severe asthma. Skin prick tests were positive for house dust mites and aspergillus. She was evaluated as severe uncontrolled allergic asthma and omalizumab therapy was started as 150 mg every 4 weeks. The first 4 doses were given without any problem. Thirty minutes after the 5th dose she had urticaria on her face and back. We decided to apply the 6th dose with desensitization procedure. Since prick test with 125 mg/mL and intradermal tests with 1.25 and 12.5 mg/mL concentrations were negative, procedure was started with 1.25 mg/mL dose. A 10-step desensitization procedure was applied. During procedure no reaction was observed but eight hours after desensitization she had erythema on her face and back and had pruritus on whole body and considered as desensitization failure. Omalizumab therapy was terminated.
Conclusion: The mechanism for omalizumab hypersensitivity is not well known. Patients using omalizumab should be closely monitored after administration of the drug in terms of systemic allergic reaction. Successful desensitization protocols are needed.

1320
Cross reactivities between low molecular weight heparins

Köycü Buhari, G; Öner Erkekol, F
Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Immunology and Allergy Department, Ankara, Turkey

Background: Although rare both immediate and non-immediate type of hypersensitivity reactions (HSRs) to low molecular weight heparins (LMWH) can be seen. Cross reactivity between these drugs are described. Two cases of HSRs with LMWH and skin test results of these patients will be presented

First case: 31 years-old female consulted to our clinic because of anaphylactic reactions with enoxaparin. Although she had an anaphylactic reaction with the first dose of enoxaparin her physician insisted on giving the second dose. After application of the second dose on the next day second anaphylactic reaction occured. In our clinic skin tests (prick test with undiluted solution and intradermal tests with 1/100 and 1/10 dilutions) were performed with enoxaparin, bemiparin, nadroparin, tinzaparin and unfractioned heparin (UFH). ID tests with enoxaparin and bemiparin were positive in 1/10 dilution and with nadroparin in 1/100 dilution. No positivities were seen with tinzaparin and UFH. We performed iv drug challenge with UFH. Since it was negative we recommended the use of UFH for the management of patient, challenge with tinzaparin was not applied.

Second case: 43 years-old female was treated for pulmonary embolism for 3 months. Since INR levels were ineffective, bemiparin was started by her physicians. On the 10^{th} day of bemiparin therapy she was consulted to our clinic because of erythemateous and itchy plaques on the injection site lasting for 3 days. Skin tests (prick and patch tests with undiluted solution, intradermal early and late readings with 1/100 and 1/10 solutions) were performed with enoxaparin, bemiparin, nadroparin, tinzaparin and UFH. Prick tests and intradermal early readings were negative. Intradermal tests were positive with 1/10 dilution of enoxaparin and bemiparin on 72^{nd} and 96^{th} hours. Although patch test results were positive with only enoxaparine, bemiparin and UFH on 72^{nd} hours, positivity with all drugs were detected on 96^{th} hour. On the 24^{th} hour of the tests her physicians applied enoxaparin injection without our recommendation depending on the negativity of tests at that time. An erythemateous local reaction at that injection site was also detected on 96^{th} hour of the tests.
Conclusion: In case of both immediate and non-immediate hypersensitivity reactions to LMWH, cross reactivity between these drugs must be considered.

1322
A successful desensitization protocol with aromatase inhibitor letrozole

Conte, M; Martelli, P; Villalta, DR
A. O. 'S. Maria degli Angeli', Laboratory Medicine, Pordenone, Italy

Background: Aromatase inhibitors (AIs) Letrozole, Anastrozole and Examestane have become a standard care as adjuvant treatment for hormone receptor positive breast cancer, either alone or in combination with chemotherapy and biologics in both the early and the metastatic setting. AIs block the aromatization of testosterone to estradiol and androstenedione to estrone reducing circulating estrogens from 1 to 10% of pre-treatment levels. Moreover, they showed to be superior to Tamoxifen in reducing the risk of relapse.
Case report: In August 2014 a 43-years-old woman with metastatic breast cancer, was admitted to the the Allergology unit of Pordenone Hospital for the suspect of an immediate adverse drug reaction. She underwent radical mastectomy in 2005 and in January 2014 she started adjuvant therapy with Letrozole 2.5 mg/daily for bone metastases. In May, 10 minutes after every daily intake, she referred oral itching lasting 30 minutes and on May 28^{th}, she referred dysphonia, dispnoea, dysphagia and swelling of her tongue, requiring treatment in emergency unit with i.v. steroids. Two days later, after Letrozole intake she experienced the same symptoms with severe dispnoea, swelling of her tongue and hypotension and she was treated again in emergency unit with i.m. epinephrine; Letrozole therapy was immediately stopped. Two weeks later she underwent an oral drug administration with Examestane in Hospital setting referring an immediate anaphylaxis reaction (Muller Grade III) requiring a new i.m. epinephrine treatment. Suspecting an immediate immunologic hypersensitivity reaction to AIs, we performed a skin prick test with indiluted drug Letrozole with negative result (histamine positive control +++). Nevertheless, we attempted an experimental desensitization protocol, starting from 0.1 ml of a 1/1000 solution of Letrozole 2.5 mg, updosing drug every 15 minutes to reach in 180 minutes the final dose of 2.75 mg. Two ours after the last drug administration the patient did not report any adverse reaction and the day after we administered the whole dose 2.5 mg of Letrozole safely.
Conclusion: In a patient with suspected immediate severe hypersensitivity reactions to Letrozole, a successful experimental desensitization protocol with Letrozole was attemped, allowing the patient to continue the therapy.

1323
Importance of allergy assessment before treatment with cetuximab

Lefèvre, S[1,2,3]; Kanny, G[1,2]
[1]EA 7299, Université de Lorraine, Laboratoire d'Hydrologie et Climatologie Médicales, Faculté de Médecine, Vandœuvre-les-Nancy, France; [2]Médecine Interne, Immunologie Clinique et Allergologie - CHU de Nancy, Vandœuvre-les-Nancy, France; [3]Hopitaux Civils de Colmar, UF Allergologie, Colmar, France

Introduction: Cetuximab is a chimeric monoclonal IgG1 antibody directed against the epidermal growth factor receptor, indicated for the treatment of colic or head and neck metastatic cancers. Specific IgE directed against an oligosaccharide epitope, galactose-alpha 1,3 galactose (α-gal) has been associated with delayed-onset anaphylaxis after ingestion of mammalian meat and immediate-onset anaphylaxis during first exposure to intravenous cetuximab. Studies have suggested that tick bites could be the cause of IgE-sensitization to α-gal. We report 3 patients who presented anaphylaxis to cetuximab.
Materials and methods: Patients, respectively 57, 67 and 85 y.o., presented anaphylaxis with severe hypotension that occurred between 10 and 15 minutes after the beginning of infusion during the first exposure to intravenous cetuximab. They have no history of allergy. All patients reported tick bites history. Skin-prick-tests (SPTs) to mammalian meat, cetuximab at 5000 μg/mL (Erbitux®; Merck Serono, Geneva, Switzerland) and intradermal tests (IDTs) at the concentrations of 5, 50, and 500 μg/mL were performed. Dosage of specific IgE to α-gal were assayed, as previously described (1).
Results: SPT to cetuximab is negative for the 3 patients. IDTs were positive at 5 μg/ml for one patient and 50 μg/mL for the 2 others. SPTs to mammalian meat were positive for two patients (raw kidneys of pork, veal, beef, raw meat of lamb and rabbit for one patient, raw pork, raw and cooked kidneys of pork and beef for the second) and negative for the third. Anti α-gal IgE were positive for the three patients (respectively 2.19, 0.84 and 1.13 kU/L).
Conclusion: Hypersensitivity reactions to cetuximab can occur during the first exposure to intravenous drug. This fact justifies the need of allergologic check-up to search sensitization to alpha-Gal before initiation of the treatment. The presence of seric anti α-gal IgE could be pertinent for the diagnosis and prediction of the risk for severe reactions to cetuximab.
Reference: 1. Jacquenet S, Moneret-Vautrin D-A, Bihain BE. Mammalian meat-induced anaphylaxis: clinical relevance of anti-galactose-alpha-1,3-galactose IgE confirmed by means of skin tests to cetuximab. J Allergy Clin Immunol. 2009;124:603–5.

1324
Effective desensitization to tocilizumab in hypersensitivity reaction to the drug, type not immediate

Cortellini, G; Santucci, A; Lippolis, D; Mascella, F; Ballardini, G
Rimini Hospital, Internal Medicine, Rimini, Italy

Background: In last years biological therapy has completely changed Rheumatoid arthritis treatment. Many employed drugs are Tumor Necrosis Factor inhibitors. Tocilizumab is an Interleukin 6 receptor inhibitor and is the drug of choice for patients not responders to methotrexate and Tumor Necrosis Factor inhibitors. Biologicals drugs can elicit both IgE mediated immediate reaction and not immediate reactions. In recent years diagnosis was standardized for etanercept and adalimumab by identification of non irritant concentration (NIC) for skin tests. We find also experiences for rapid desensitization for etanercept and adalimumab,but only case reports exist for desensitization in non immediate reactions, and no case for tocilizumab.
Method: Clinical case report: Female Patient, affected from Rheumatoid Arthritis,non responder to methotrexate. The patient develop an non-immediate urticaria reaction after infliximab. The patient has developed also underarm and gluteus dermatitis after tocilizumab therapy. The patient undergoes skin test at NIC reported in the literature and confirmed with control in 4 healthy subjects. Skin test has became positive after 6 h from injection of tocilizumab 20 mg/mL and has confirmed diagnosis of non immediate hypersensitivity.
Results: Patient has accepted desensitization procedure,in weekly schedule:8.8 mg cumulative dose in 1°step, 28 mg in 2° step, 80 mg in 3° step, 160 mg in 4° step, 240 mg in 5° step (cumulative dose:516 mg). After a month the patient have intake 520 cumulative mg in double daily administration, and then in single dose every month, before with premedication; after without premedication.
Conclusion: Biological therapy may be fundamental in Rheumatoid arthritis treatment. Drug allergy, also with non-immediate reactions can appen. This is the first case report of desensititization to tocilizumab for non immediate reaction.

1325
Successful desensitization protocol for enzymatic replacement in Pompe disease

Jimenez, EN[1]; Fuentes, JM[1]; González, RH[1]; Carbajal, L[2]; Zuñiga, G[1]; Orozco-Martinez, S[3]; Mendoza, DA[1]
[1]Instituto Nacional de Pediatria, Allergy, Mexico, Mexico; [2]Instituto Nacional de Pediatria, Internal Medicine, Mexico, Mexico; [3]Instituto Nacional de Pediatria, Head of Allergy Department, Mexico, Mexico

Background: Pompe disease also referred as acid maltase deficiency (AMD) or glycogen storage disease type II (GSDII) is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid-α-glycosidase (GAA) rare progressive and fatal. The steady accumulation of glycogen substrate in target tissues leads to progressive debilitation, organ failure and/or death; resulting in a spectrum of disease severity. Severity varies by age of onset, organ involvement including degree and severity of muscular involvement and rate of progression. Due to the presence of weakness and hypotonia, it has also been classified as a neuromuscular disease of metabolic myopathy.
Method: We present a case of 1 year and 8 months female; she initiate at 4 months of age presenting with hypotonia, mitral insufficiency grade I, left ventricular hypertrophy and diastolic dysfunction being diagnose with Pompe disease, treated with enzymatic replacement (α-glycosidase) 30 mg/kg every 2 weeks since 13 months old presenting allergic reactions characterized by urticaria after treatment.

At the age of 20 month developed an Anaphylactic reaction (urticaria and angioedema). Given the essential and irreplaceable therapy; the Allergy department confirm hypersensitivity type 1 (positive specific IgE) reaction; whereby desensitization protocol (Castells M) was performed on 3 occasions, premedicated with methylprednisolone 1 mg/kg/dose and chloropyramine chloride 20 mg. The desensitization procedure consists in 14 steps with 3 different solutions: solution 1 (0.0012 mg/mL), solution 2 (0.032 mg/mL) and solution 3 (0.8 mg/mL); in every procedure at step 12 develop urticaria in face and inguinal region, management with infusion suspension and intravenous antihistamines when the symptomatology disappeared the procedure was continued and finalized without any other allergic reactions.
Results: Since reaction is observed during desensitization procedures is expected shorten administration of the enzyme to achieve tolerance and minimize risks.
Conclusion: This procedure is safe and efficient for treat systemic allergic reactions to the enzymatic replacement therapy.

1326
Adrenaline infusion pump helps control breakthrough reactions during rituximab desensitisation

Gonzalez Medina, M; Cardona Dahl, V; Gomez Duque, M; Moreno Perez, N; Delavalle, B; Labrador Horrillo, M
Hospital vall d'Hebron, Barcelona, Spain

Background: Desensitisation procedures are not devoid of adverse reactions which may be difficult to control.
Method: We describe the case of a patient on periodical rituximab desensitisation who required intensive therapy to control breakthrough reactions.

We report the case of a 44-year-old woman with a history of flaccid tetraparesis of indeterminate origin (probably autoimmune), having responded poorly to a number of therapies and with several admissions to intensive care unit. She commenced biologic therapy in 2010, receiving 5 cycles of rituximab with clinical improvement. A year later a new cycle was administered but she soon developed adverse reactions during infusions, consisting of bronchospasm, cough and upper respiratory tightness with stridor and desaturation. Given the early clinical improvement, confirmed by EMG, and the failed response to standard treatments, after informed consent was obtained, therapy with rituximab (1000 mg) was restarted using a 14 step desensitization protocol with premedication. The subsequent rituximab desensitisation procedures were carried out in the intensive care unit, but despite the use of high doses of premedication (antihistamines, corticosteroids, montelukast, ASA) and prolonged infusion protocols, she still experienced severe breakthrough reactions requiring multiple adrenaline doses. Therefore, we assessed the use of a continuous adrenaline pump infusion (20 μg/mL at between 10–20 mL/h), which could be adjusted to the clinical response (maximal increase of 20% over basal heart rate).
Results: This therapy allowed optimising the desensitisation procedures, avoiding severe reactions and speeding the infusion of rituximab to the maximal flow-rate recommended by the manufacturer (3.5 hours). She has now completed 4 more cycles without relevant reactions.
Conclusion: Therefore, we believe that a continuous adrenaline pump infusion maybe a good therapeutic tool to improve the tolerance in difficult desensitisation procedures.

1327
Desensitization with pyrazinamide in a patient with multidrug-resistant tuberculosis

Sanchez de la Vega Reynoso, P; Ramirez Jimenez, F; Garcia Cruz, MD; Camacho Ordoñez, N; Ruiz Morales, RD[1]; Perez Estrella, Z; Pavon, R-GF; Teran, LM
National Institute of Respiratory Diseases 'Ismael Cosio Villegas', Immunogenetics and Allergy, Mexico, Federal District, Mexico

Background: Tuberculosis is prevalent worldwide and fatal if proper treatment is not instituted on time. Pyrazinamide (PZA) is one of the most effective antituberculosis drug that is used for multidrug-resistant tuberculosis (MDR-TB). PZA can induce hypersensitivity reactions; however, true hypersensitivity reactions are rare. We report a case of a 22 year old female with pulmonary MDR-TB who developed urticarial rash secondary to administration of PZA.
Method: The patient presented rash in face, neck, arms and chest 30 minutes (min) after the administration of PZA. Other antituberculosis drugs were administered at intervals of 24 hours without reactions. We first proceeded to skin prick test and it was negative, so intradermal test was performed in a 1:100 dilution. A positive reaction occurred after 15 min with a 9 mm wheal, 25 mm erythema (positive control with histamine wheal=6 mm, erythema=22 mm and negative control with saline solution wheal=2 mm, erythema=2 mm). Due to the need of rapid re-institution of therapy, a desensitization protocol was established. It consisted in a 3 day procedure of ascending dose of PZA until therapeutic dose was achieved (1600 mg of PZA daily). The patient was premedicated each day with oral and intravenous (IV) antihistamine, oral antileukotriene and IV anti-H2. The first day we made a solution of 800 mg of PZA in 200 ml of grape juice. Protocol:

Day 1: 0 min, Dose (D): 6.25 mg, Cumulative Dose (CD): 6.25 mg, milliliters (ml) 1.6; 30 min, D: 12.5 mg, CD: 18.75 mg, ml: 3.2; 60 min, D: 25 mg, CD: 43.75 mg, ml: 6.4; 90 min, D: 50 mg, CD: 93.75 mg, ml: 12.8; 150 min, D: 75 mg, CD: 168.75 mg, ml: 18.75; 210 min, D: 125 mg, CD: 239.75 mg, ml: 31.25; 270 min, D: 250 mg, CD: 543.75 mg, ml: 62.5.

Day 2: 0 min, D: 400 mg (1 tablet of PZA= 400 mg), CD: 400 mg; 30 min, D: 1200 mg, CD: 1600 mg.

Day 3: 0 min, D: 800 mg, 60 min: D: 800 mg.

Results: Day 1:no reactions. Day 2:rash on face and neck 45 min after 1200 mg of PZA (CD:1600 mg). She responded to IV steroid and antihistamine. Day 3:uneventful. She continued with 800 mg bid of PZA without symptoms in the next days.
Conclusion: We successfully desensitized a patient with IgE-mediated hypersensitivity to PZA proved by intradermal test. Only 1 case was published of anaphylaxis to PZA where we took the protocol and modify it according to the dose required for the patient. Allergy to antituberculosis drugs occurs in countries where tuberculosis is a problem that we treat every day.

1328
Successful desensitization in a case of lenalidomide-induced drug eruption

Asaf, JM[1]; Homey, B[1]; Meller, S[1]; Klossowski, N[2]
[1]Department of Dermatology, Medical Faculty, University Hospital Düsseldorf, Heinrich-Heine-University, Düsseldorf, Germany; [2]Department of Dermatology, University Hospital düsseldorf, Düsseldorf, Germany

Multiple myeloma is a cancer of plasma cells which can be treated with chemotherapy and stem-cell transplantation. Immunmodulatory agents like lenalidomide (an analogue of thalidomide) are novel agents in the therapy of multiple myeloma, myelodysplastic syndrome and mantle cell lymphoma.

Lenalidomide is generally well tolerated, but cutaneous adverse effects were observed in up to 72 percent of treated patients. These rashes, that represent a serious threat to patients′ therapy adherence, may present as morbilliform, urticarial, eczematous, and acneiform eruptions. Moreover, severe cases such as erythema multiforme (EEM), Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN) have been reported.

Here, we present the case of a 74-year-old male patient with generalized pruritic maculae and papules and partly urticarial exanthema following the administration of lenalidomide 15 mg for the treatment of IgG kappa light chain multiple myeloma. The exanthema started one day after the second cycle of lenalidomide 15 mg. Topical glucosteroids were administrated until the complete remission of the rash after 6 weeks. *In vitro* tests including lymphocyte and basophil activation tests failed to detect drug-specific T cells or specific IgE, respectively. Furthermore, epicutaneous testing of lenalidomide showed no pathological reaction.

The patient was initially treated with chemotherapy, which leads to a Guillain-Barré syndrome. Because of the limited alternative treatment options, we performed a desensitization beginning in a dose of 2.5 mg lenalidomide. In the following seven weeks we carefully increased the dose of the lenalidomide up to 10 mg,

which was well tolerated without any symptoms. Finally the patient was able to reach and be maintained on the recommended dose.

Our findings support that desensitization with lenalidomide is a safe and effective avenue to continue the first line therapy without further drug-associated cutaneous adverse events.

1330
Are third generation cephalosporins safe alternatives in patients with penicillin allergy?

Amaral, L; Carolino, F; Castro, ED; Cernadas, JR
Serviço de Imunoalergologia, Centro Hospitalar São João, Porto, Portugal

Background: Most studies indicate that cross reactivity between penicillins and some second, and all third and fourth-generation cephalosporins is negligible. A caveat is that negative predictive values of cephalosporins skin testing have not been fully established and severe reactions can still occur among a few cross-reacting patients.
Aim: Evaluate the results of oral drug challenges (ODC) with a third generation cephalosporin in patients with documented history of penicillin allergy and with negative intradermal test (IDT) to cephalosporins.
Method: We performed a medical record review of the patients referred to our drug allergy unit with history of allergic reaction to one penicillin, with positive ODC or positive results in the skin tests for one or more penicillin reagents (penicilloyl-polylysine (PPL), minor determinant mixture (MDM) and benzylpenicillin), one semisynthetic penicillins (amoxicillin) and negative IDT concentration (10 mg/mL) to ceftriaxone. All patients underwent ODC with cefixime.
Results: Inclusion criteria were met in 17 patients, aged 2 to 54 (24.35 ± 18.1 years-old), 12 (70.6%) females. Nine patients (52.9%) had a previous positive ODC with amoxicillin/clavulanate. Eight patients (47.1%) had positive skin test with a penicillin reagent (2 PPL, 1 MDM, 1 benzylpenicillin and 4 amoxicillin). Fourteen patients underwent cefixime ODC without any reaction. Three patients presented a positive ODC with cefixime: one with immediate anaphylactic reaction after full dose was achieved; one with a late anaphylactic reaction, 72 h after the ODC, which required observation at the emergency department and one with immediate generalized urticaria. Of these, all had previous severe systemic reactions to amoxicillin/clavulanate.
Conclusion: Drug provocation performed by trained Allergists remains the best way to exclude or confirm the diagnosis of drug hypersensitivity and to find a safe alternative for future use. The generalized approach that third and fourth generation cephalosporins can be safely prescribed to patients with confirmed allergy to penicillin should be reviewed. Although our findings were obtained from a small sample of 17 patients, we report that 3 (17.6%) had severe reactions on ODC with cefixime. Based on this study, for now, the authors advise to perform skin tests followed by ODC to third or fourth generation cephalosporins, before its prescription.

1331
Successful desensitization with adalimumab in a patient with hidradenitis suppurativa

Foncubierta Fernandez, A[1]; Gutierrez Fernandez, D[2]; Cruz Carmona, MJ[3]; Moreno Ancillo, A[4]; Anguita Carazo, JL[5]; Fernandez Anguita, MJ[6]
[1]Distrito Sanitario Bahia de Cadiz-La Janda, UGC Joaquin Pece, San Fernando, Spain; [2]Hospital Universitario Puerta del Mar, UGC Neumologia-Alergia, Cadiz, Spain; [3]Hospital Vall d'Hebron, Barcelona, Spain; [4]Hospital Nuestra Señora del Prado, Alergologia, Talavera de la Reina, Spain; [5]Complejo Hospitalario de Jaen, Alergologia, Jaen, Spain; [6]Hospital Universitario Puerta del Mar, UGC Farmacia, Cadiz, Spain

Background: Hidradenitis suppurativa (HS) is a chronic inflammatory disease that usually manifests in skin areas with a high density of apocrine. Its prevalence in the general population is 1% and the female/male proportion is 3:1. The aetiology is unknown, though a primary defect of the hair follicle has been implicated. Predisposing factors include immune system dysregulation and other controversial triggers such as obesity, smoking, clothing, etc. The diagnosis is clinical and the possible complications are important. The management of this condition includes local measures such as hygiene and antibiotics and systemic measures such as corticosteroids and antibiotics though they are ineffective in most cases. Recent studies have used biological drugs (anti-TNF), after observing similarities with immune system-based disease. The last option is surgery.
Method: Of 42-year-old woman who had presented suppurative lesions in groin and to a lesser extent in armpits for the last four years, worsening significantly in the last six months. She was diagnosed with HS Hurley grade II. Treatment with Augmentine® and minocycline achieved improvement but the patient relapsed after discontinuation. Evaluation for general surgery ruled out surgery due to the possibility of keloids. Treatment with adalimumab 40 mg every two weeks with a good response to the first dose, and the appearance with the second dose of a generalized urticarial reaction four days after administration which required treatment with corticosteroids and antihistamines for several days until resolution. Un allergy study was performed and desensitization was proposed after the patient presented clinical and analytical relapse.
Results: Biochemistry: ESR and CRP, high

1. 1 Skin tests with adalimumab (prick and ID): negative
2. 2 Skin tests with polysorbate 80 and mannitol: negative
3. 3 Skin tests with pneumoallergens and latex: negative
4. 4 Total IgE 80 IU/ml and specific IgE: negative
5. 5 Eight-step desensitization protocol for adalimumab, following Gutiérrez Fernández et al.: successful. Currently receiving adalimumab 40 mg every 2 weeks, without reactions of note.

Conclusion: We report a case of adverse reaction following administration of adalimumab in a patient with HS Hurley grade II. The desensitization process itself allowed continuation of treatment, with partial remission of the disease and tolerance of the drug.

1332
Successful desensitization protocol in a patient with moderate carboplatin hypersensitivity and ovarian cancer

De Vicente Jimenez, T; Montoro, A; de Mateo, B; Burgos, A; Fonseca, J
Hospital Central de la Defensa, Allergology and Clinical Immunology, Madrid, Spain

Aim: The goal of the current study was to evaluate the tolerance and effectiveness of carboplatin challenge using a 6- hour desensitizing carboplatin infusion regimen in a patient with clinically documented moderate carboplatin hypersensitivity.
Background: Carboplatin is one of the most useful and well tolerated cytotoxic drugs for gynecologic malignancies. Hypersensitivity to carboplatin is not rare among these patients receiving recurrent treatments with this drug.
Methods: A 75-year-old woman with advanced ovarian cancer (Stage 4) and salicylate hypersensitivity already known, presented a moderate- hypersensitivity reaction to carboplatin during the sixth course of Taxotere and Carboplatin. Cutaneous tests confirmed hypersensitivity. Premedication was administered before the desentization procedure. It consisted in a 12- step protocol based on 3 different dilu-

tions of the drugs that were used during 5 h 52'.

(TABLE including: Infusion rate (ml/h), Concentration (mg/ml), Time (min), Administered dose (mg), Cumulative dose (mg), Volume and Cumulative volume (ml)

Results: Desensitization was successful, and the patient subsequently tolerated four additional courses of chemotherapy, with no further signs or symptoms of hypersensitivity. She only developed a mild urticarial rash in the last step.

Conclussion: We report a successful desensitization protocol for a patient with a proven allergic reaction to Carboplatin. The protocol was safe and convenient, and offers an effective therapeutic strategy to patients with platinum- sensitive ovarian cancer who require this drug to continue to benefit from therapy. However, rapid desensitization protocols are not risk-free. The case of cancer patients is particularly challenging, as chemotherapy is often the only way their disease can be controlled.

Poster Session Group III - Green TPS 44

Can we treat asthma better? (II)

1333
Asthma exacerbations after omalizumab treatment discontinuation

Budny, W; Skiepko, R; Lukaszyk, M; Zietkowski, Z; Bodzenta-Lukaszyk, A
Medical University of Bialystok, Department of Allergology and Internal Medicine, Bialystok, Poland

Background: The anti-IgE has an important place in the treatment of patients with severe allergic asthma. In 2013, Poland introduced severe asthma treatment program with omalizumab refunded by the National Health Fund. Five of the patients were treated for several years before the program started. They did not receive continuation the therapy after its launch due to formal restrictions. The aim of the study was to assess asthma parameters in patients that discontinued the five-year therapy with omalizumab.
Method: The study included: clinical evaluation, monitoring of pulmonary function tests, FENO, hospitalization, inhaled (ICS) and systemic corticosteroids dosing, exacerbations and use of rescue medication after cessation of treatment with omalizumab.
Results: In the whole group was observed a deterioration of spirometry parameters, an increase in consumption of rescue medication, some patients required a higher dose ICS or introducing systemic steroids and additional visits in outpatient clinic/GP. In two cases FENO values increased.
Conclusion: Due to significant possibility of asthma control worsening after discontinuation of treatment with omalizumab it is advisable to carefully monitor asthma control parameters.

1334
Might speckle tracking echocardiography be more useful for early assessment of changes in left ventricular function in children with bronchial asthma?

IŞık, S[1]; Demircan, T[2]; Kızılca, Ö[2]; Çağlayan-Sözmen, Ş[1]; Unal, N[2]; Anal, Ö[1]; Kır, M[2]; Karaman, Ö[1]; Uzuner, N[1]
[1]Pediatric Allergy and Immunology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey; [2]Pediatric Cardiology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey

Background: The aim of the present study was to evaluate the role of conventional, color tissue doppler and speckle tracking echocardiography (STE) in assessment of ventricular function in pediatric patients with bronchial asthma (BA).
Material and methods: Fifty-seven children with bronchial asthma (BA) and 41 age- and sex-matched healthy subjects were studied. BA patients were divided into four groups: Intermittent BA (n = 20), mild (n = 19), moderate (n = 17) and severe persistent BA (n = 1). All subjects were examined by conventional, tissue doppler and speckle tracking echocardiography.
Results: In conventional echocardiography, the right ventricular systolic pressure and interventricular septum thickness were found to be significantly higher in the asthmatic children compared to control. In STE, left ventricular functions were found to be significantly higher in the persistent asthmatic children compared to intermittent group. However, left ventricular functions were normal in conventional and color tissue doppler echocardiography in both persistent and intermittent asthmatic group.
Conclusion: The increase in the left ventricular function of persistent asthmatic children in STE was thought to be secondary to ventricular interaction due to increase in right ventricular pressure. STE can be suggested as a better method than conventional and tissue doppler echocardiography for assessment of change of left ventricular function in asthmatic children.

1336
Poorly controlled allergic asthma: real-life experience

Ricciardi, L[1]; Arena, EM[2]; Genovese, C[1]; D'Angelo, AG[1]; Gambino, M[1]; Liotta, M[1]; Saitta, S[3]; Casciaro, M[4]
[1]Allergy and Clinical Immunology Unit University of Messina, Clinical and Experimental Medicine, Messina, Italy; [2]Allergy Unitt, Locri (RC), Italy; [3]Clinical and Experimental Medicine Department, Messina, Italy; [4]Allergy and Clinical Immunology Unit University of Messina, Clinical and Experimental Allergy, Messina, Italy

Background: Despite the currently available treatments for allergic asthma, many patients remain symptomatic and experience exacerbations; Omalizumab, an anti-IgE monoclonal antibody, is a treatment option. We report our experience on 18 patients (8 m-10 f; mean age 47.7) with uncontrolled allergic asthma.
Method: Patients were evaluated at T0,T1, T2 and T3 (6 months, 1.2 years after starting Omalizumab) regarding anti-asthmatic drug consumption, FEV1 and asthma control test (ACT) results.

Total and specific IgE were measured at T0. Patient's weight was also recorded in order to calculate the dose of Omalizumab.
Results: Three patients abandoned the study at T2 due to significant improvement.

All patients took anti-asthmatic treatments at T0, 16/18 at T1 and T2 and 13/15 at T3; there was no statistical difference in drug consumption ($P = 0.112$).

There was a statistical reduction in systemic corticosteroids consumption (T0: 18/18 patients; T1: 2/18; T2: 2/18; T3: 0/15; $P < 0.0001$), the reduction was statistically significant between T0 and T1 ($P < 0.0001$) while there was no statistical difference between the other times.

There was a reduction, although not statistically significant, in inhaled corticosteroids (T0: 18/18; T1: 15/18; T2: 15/18; T3: 13/15; $P = 0.112$) as in inhaled long-acting β2 agonists (T0: 18/18; T1: 14/18; T2: 14/18; T3: 12/15; $P = 0.112$) and anti-leukotrienes (T0: 13/18; T1: 6/18; T2: 6/18; T3: 7/15; $P = 0.096$).

The ACT improved in times (T0: 8.5; T1: 21; T2: 21; T3: 21; $P < 0.0001$), in particular the improvement was statistically significant between T0 and T1 ($P = 0.0002$). FEV1 improved in times (T0: 74 L; T1: 83.5 L; T2: 87.5; T3: 80 L; $P = 0.038$), in particular the improvement was statistically significant between T0 and T1 ($P = 0.031$) while other FEV1 variations were not statistically significant. A statistical significant reduction of exacerbations was recorded between T0 and T2 ($p < 0.005$).

It is interesting to note that our population consisted of never smokers, former smokers and 1 low cigarette smoker and in all cases an improvement with omalizumab treatment was obtained. Allergic rhinitis was also present in some patients as well, in two of them, nasal polyposis and also these comorbidities improved during omalizumab treatment.
Conclusions: Therefore in our population, followed in a real-life setting, Omalizumab proved to be able to improve asthma control and reduce exacerbation risk as well as the burden of asthma and its comorbidities.

1337
Clinical effectiveness of montelukast (Singlon ®) in the control of mild persistent asthma in children aged 6–14 years

Zharnasek, U
Belorussian Medical Academy of Post-Graduate Education, Minsk, Belarus

Background: Research aim - to generalize the experience of montelukast (Singlon®) application for children with mild persistent bronchial asthma.
Method: 30 children 6–14 years old (16 boys, 14 girls) with mild persistent partly controlled asthma were observed. They have not been getting any anti-inflammatory medicines during previous 3 months. Average duration of disease - from 0.8 to 10.7 year (Me – 3.0, LQ:UQ – 3.9:5.0). All patients have been taking Singlon® 5 mg one time per day during 3 months. The dynamic of level of control of asthma and dynamic of indexes of spirometry were estimated monthly according to the recommendations of ICONPA, 2012. In the beginning and in the end of course of therapy the general and biochemical blood tests were carried out. The monitoring of Singlon® tolerance was been conducted.
Results: Found that treatment with montelukast (Singlon®) in the form of chewable tablets 5 mg in children aged 6–14 years with mild persistent asthma after 3 months of therapy effectively reduces the risk of daytime symptoms from 80% to 7%, nighttime symptoms - from 43% to 7%; means to reduce the need for emergency assistance from 67% to 13% and also reduces the likelihood of acute asthma with 77% to 10%. Effectiveness of montelukast (Singlon®) in the form of chewable tablets 5 mg in achieving complete clinical control in children aged 6–14 years with partially controlled mild asthma was 83%, and the overall effectiveness in children with controlled and partly controlled asthma, is to achieve and clinical monitoring retention - 87%.

Shown that treatment with montelukast within three months to stabilize and maintain respiratory function characterizing airway (FEV_1, PEF, $MEF_{25,\ 50,75}$) at baseline. Patients aged 6–14 years with mild persistent asthma, inappropriate criteria controlled by the end of 3 months of therapy Singlon® recorded a significant increase in the indicator MVL .
Conclusion: The treatment with montelukast (Singlon®) in the form of chewable tablets 5 mg in children aged 6–14 years with mild persistent asthma after 3 months are effectively.

1338
Better quality of life for the ill of bronchial asthma treated whit ciclesonide

Yakovliev, PH[1]; Vulcheva, T[2]; Takovska, N[3]; Komsiiska, D[4]
[1]Medical College, Tracian University, Stara Zagora, Bulgaria; [2]Medical University of Sofia, Sofia, Bulgaria; [3]Consulting Room of Allergology, Blagoevgrad, Bulgaria; [4]Department of Psychiatry and Medical Psychology, Tracian University of Stara Zagora, Srara Zagora, Bulgaria

Background: There was explored the connection between the treatment with ciclesonide and the quality of life to 72 patients ill of moderate bronchial asthma,.
Method: The study is multi centred; open and comparative. We are investigated 72 patients ill whit moderate bronchial asthma, treated with ciclesonide of 160 μg two times daily. 51 of the patients are women and 21 men of age 18 to 75 years old. During study it is used the most spread in the clinical Allergology questionnaire of QL that is compiled of 32 questions for the bronchial asthma and show problems connected with the respiratory syndromes. The patients filled in the questionnaire two times - in the beginning of the study, before using ciclesonide of 160 μg two times daily, and on the 30th day after using the medicine in the given dosage. The questions are separated into two groups:Group one: Indication of the five most important activities from which the patients were restricted. Group two: Indication of the subjective suffering and discomfort of the explored patients.
Results: All patients completed the study and contributed to its implementation. Patients with atopic asthma had more subjective complaints. Non atopic patients live has changed much more than the atopic at baseline prior to administration of ciclesonide. Their improvement in quality of life, at 30 days of treatment is significant ($P < 0.001$) compared with atopic - ($P < 0.01$). In reporting the results of group A significantly ($P < 0.01$) improved activities such as maintenance of the house, fast, sleep and climb of professional duties. In reporting the results of group B was also significantly improved ($P < 0.005$) in the manifestations of asthma as a result of exposure to house dust, and smoke at the end of the study when lowered significantly ($P < 0.005$) manifestations of asthma as a result of exposure to strong odor and perfume. Analysis of the results showed that women quality of life is improved by significantly ($P < 0.005$), than males ($P < 0.01$) at the end of therapy. The mean change in FEV1 at the end of the study was significant ($P < 0.001$) higher (0, 54 l/min) from baseline.
Conclusion: 1. Bronchial asthma as a chronic inflammatory disease of the airways and powerful psychosocial stressor requires precise care.

2. Patients with bronchial asthma in the most active age ha social networking and professional appearance between 35–40 years showed the greatest improvement in their quality of life.

1339
Cytokine changes in patients of asthma undergoing Ayurvedic intervention

Joshi, K[1]; Nesari, T[2]; Dedge, A[2]; Dhumal, V[2]; Shengule, S[3]; Gadgil, M[3]; Salvi, S[4]; Valiathan, MVS[5]
[1]Sinhgad College of Engineering, Department of Biotechnology, Pune, India; [2]Tilak Ayurved Mahavidyalaya, Pune, India; [3]Sinhgad College of Engineering, Pune, India; [4]Chest Research Foundation, Pune, India; [5]Manipal University, Pune, India

Background: Emerging evidence published in reputed scientific journals have demonstrated the scientific basis of Ayurvedic treatment for diseases[i], [ii]. The present study was undertaken to explore the effect of Ayurvedic treatment widely used in the management of bronchial asthma in India.
Methods: Patients with mild to moderate asthma (n = 76) were enrolled for the treatment. The treatment protocol was approved by the Institutional Ethics Committee of the hospital and registered at CTRI (CTRI/2014/12/005322). Lung functions and cytokines were measured before and at the end of 24 weeks treatment in patients and healthy controls.
Results: Significant improvement in PEFR ($P < 0.0001$), FEV1 (% predicted) ($P < 0.001$) and FVC (% predicted) (< 0.05) were observed after the treatment. Imbalance of immune homeostasis is responsible for pathological changes in Asthma and Cytokines play an important role in orchestrating the inflammatory response. We observed significant modulation of Th1 and Th2 cytokines and reduction in IgE concentrations ($P = 0.035$).
Conclusions: Ayurvedic treatment improved asthma outcomes by mechanisms related to airway inflammation through cytokine modulations.
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1340
Efficacy of ciclesonide in the treatment patients with asthma exacerbation

Zietkowski, Z[1]; Lukaszyk, M[1]; Skiepko, R[1]; Budny, W[2]; Skiepko, U[2]; Klimek, M[2]; Bodzenta-Lukaszyk, A[1]
[1]Department of Allergology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland; [2]Medical University of Bialystok, University Hospital in Bialystok, Bialystok, Poland

Background: Progressing deterioration of lung function, dyspnoea, cough, wheezing and chest tightness are the main features of emerging asthma exacerbations. The first step in prevention of severe asthma exacerbations is to intensify the anti-inflammatory treatment with high doses of inhaled corticosteroids (ICS). The aim of the study was to assess the efficacy of ciclesonide in patients who have been losing asthma control despite being treated with medium doses of inhaled corticosteroids and LABA as the second controller.
Method: The study was conducted in a group of 63 asthmatic patients who have been losing asthma control. Subjects entering the study received following anti-inflammatory interventions: high doses of ciclesonide (1280mcg) or 640mcg of ciclesonide added to current dose of ICS or doubled dose of current ICS.
Results: Treatment options containing ciclesonide have shown statistically and clinically important advantages (improvement of Asthma Control Test Score, reduction of rescue medications consumption, reduction in day and night symptoms score, improvement in spirometry parameters, decrease of exhaled nitric oxide, and no necessity of oral corticosteroids treatment) in comparison to patients, in whom medium doses of previously used inhaled corticosteroid were doubled.
Conclusion: Treating with high doses of ciclesonide characterise with quick and potent anti-inflammatory effect as well as prompt clinical improvement along with proper safety profile in patients suffering from asthma exacerbation.

1341
Long-term follow-up outcomes of clinical remission and pulmonary function following early anti-inflammatory therapy for asthma in children under 2 years old

Ikeda, M[1,2]; Tsuchimoto, K[2]; Sekimoto, K[2]; Uehara, H[2]; Fujiwara, K[2]; Mera, M[2]; Kimura, N[2]; Kodera, A[2]; Sakamoto, T[2]; Takasugi, M[2]; Kitada, K[2]; Nojima, I[2]; Takahashi, N[2]; Sugai, K[2]; Araki, T[2]; Kikkawa, T[3]; Fujii, Y[1]; Yashiro, M[3]; Tsukahara, H[3]
[1]Department of Pediatric Acute Medicine, Dentistry and Pharmaceutical Sciences, Okayama University Graduate School of Medicine, Okayama, Japan; [2]Department of Pediatrics, National Hospital Organization Fukuyama Medical Center, Fukuyama, Japan; [3]Department of Pediatrics, Dentistry and Pharmaceutical Sciences, Okayama University Graduate School of Medicine, Okayama, Japan

Background: The ultimate goal of childhood asthma treatment is for the disease to enter remission, allowing children to outgrow it. After pediatric guidelines for the management of asthma were devised and anti-inflammatory treatment became widespread, quality of life improved in many asthmatic children. However, the long-term outcomes of early anti-inflammatory treatment for asthma in young children remain unclear.
Method: We evaluated 63 children <2 years old who were diagnosed with asthma with recurrent wheezing between October 1998 and September 2000 and who had allergenic sensitization and family history of asthma. Early anti-inflammatory treatment with inhaled corticosteroid/leukotriene receptor antagonist/disodium cromoglycate was initiated to induce active remission before 2 years of age in accordance with the Japanese Pediatric Guidelines for The Treatment and Management of Asthma 2000–2005. In 2011 and 2013, subjects were evaluated by forced oscillometry (FO), eNO, spirometry, and assessment of clinical symptoms. Airway hyperresponsiveness (AHR) was measured by continuous methacholine challenge.
Results: The long-term remission (≥5 years without treatment) rate 13 years after initiating early anti-inflammatory therapy was 77.6% (intermittent asthma, 100%; mild persistent asthma, 70.8%; moderate persistent asthma, 78.6%; severe persistent asthma, 75.0%). Long-term remission rates improved compared with past asthmatic convalescence surveys (mild asthma, 50.0–69.2%; severe asthma, 5.0–30.8%). Improvement of eNO level was observed from 55.0 ± 48.1 ppb in 2011 to 31.1 ± 21.8 ppb in 2013. Complications involving allergic rhinitis (AR) were seen in 78.6% of subjects, and eNO level and asthma recurrence were significantly higher in AR(+) subjects. In 2013, %V50, %V25, and %FEV1 were $80.7 \pm 16.2\%$, $79.3 \pm 26.6\%$, and $92.5 \pm 9.9\%$, respectively, and were normal in 78% of subjects. AHR was 4.01 ± 6.46 U and 37% of subjects had only mild or no AHR. Total (R5) and proximal (R20) airway resistance by FO were 0.316 ± 0.074 and 0.264 ± 0.046 kPa/L/s respectively, and none exceeded ±2SD.
Conclusion: Early anti-inflammatory therapy and maintenance of long-term total control of asthma not only may prevent progression of disease severity and improve quality of life, but also may allow normal development of pulmonary function and outgrowth of asthma in young children.

1342
Influence of obesity and overweight in lung function in adult asthmatic patients

de Barayazarra, S[1,2]; Bainotti, N[1,2]; Corelli, S[1,2]; Cornaglia, S[1,2]; Recuero, N[1,2]; Winchel, R[1,2]; Zanacchi, A[1,2]; Sosa, S[1,2]; Teijeiro, A[2,3]; Baena-Cagnani, CE[2,3]
[1]San Roque Hospital, Department of Allergy and Immunology, Cordoba, Argentina; [2]Catholic University of Cordoba, CIMER, Cordoba, Argentina; [3]Pediatric Hospital of Cordoba, Respiratory and Allergy Center, Cordoba, Argentina

Background: The association between obesity and asthma has not been fully clarified, but it is known that obesity precedes asthma prevalence increases both as its severity and can alter the efficacy of drugs commonly used for treatment.. When you gain weight, adipose tissue expands and thus the mass of tissue that must be mobilized, which decrease pulmonary ventilation. The relationship between obesity and impaired FEV1 is not fully proven, in case this function can decrease and in others not changed.
Method: A sample of 50 patients aged 16–64 years who attended the Allergy and Immunology, Hospital San Roque was taken. The Asthmatic patients were selected according to symptoms and spirometry (normal> or equal to 80%) FEV1 and FEV1 / FVC ratio (normal> or equal to 75% value). He classified them in intermittent asthma, mild, moderate and severe persistent asthma according to GINA. They were divided according to BMI (Body Mass Index) in overweight between 25 and 29 and greater than or equal to 30. Processing of statistical data through Ep Iinfo 7.1. Taking as statistically significant value of P
Results: Of the patients 70% were female and 30% male, were divided into 26% intermittent asthma, mild persistent asthma 20%, 50% moderate persistent asthma and severe persistent asthma 4%.Considering the functional tests FEV1 was within normal limits in 76% of patients of whom 22% were overweight and obese patients 54%. And 24% of all patients had FEV1

altered, of which 16% were obese and 8% were overweight. These results showed no statistically significant P values ($P = 0.5$). and we found no association between obesity and bronchial hyper-reactivity (BHR), ($P = 0.5$)Moreover considering the FEV1 / FVC was normal in 88% of patients (24% overweight and 64% obese) and revealed an obstructive pattern in 12%, of which 6% were obese and 6% were overweight patients. Also showing a value of OR 95 CI: 0.6 to 23 ($P = 0.08$).

Conclusion: We found no significant changes in pulmonary function tests spirometric especially in FEV1, or when we associate HRB with obesity but if we could observe that in our group had a significant but with a range 95% partnership FEV1 / FVC in patients obese asthmatics, similar to what the study found Ciprandi al. Which suggests that BMI should be considered routine inthe bronchial obstruction in asthmatic patients.

1343
Aspirin-exacerbated respiratory disease and pulmonary lymphangioleiomyomatosis: a case report

Márquez Hernández, D; Bastidas Parlanti, JA; Mederos, E; Herraez, L; Mielgo Ballesteros, R; Fernández Rodríguez, C
Hospital Universitario 12 de Octubre, Allergy, Madrid, Spain

Background: Pulmonary Lymphangioleiomiomatosis is a rare lung disease, that afflicts young women of childbearing age. It is often misdiagnosed as asthma or chronic obstructive pulmonary disease because of significant airflow limitation. Otherwise, patients with aspirin-exacerbated respiratory disease (AERD) frequently have severe persistent asthma. We report a patient who suffers both diseases.

Method: A 48-year old female non-smoker was diagnosed with AERD at 14-year-old. Until 2012, asthma symptoms and pulmonary function were well controlled by short agonist beta 2 and low dose of inhaled corticosteroids. Nevertheless, she had 3 nasal polypectomies. Several chest radiographs were performed without abnormal results. Three years ago, she started a progressive impairment of her asthma symptoms despite high dose of inhaled corticosteroids, LABA, antileucotrienes and inhaled anticholinergic and systemic corticosteroids bursts. A new assessment was carried out including: pulmonary function tests (spirometry, lung volumes and diffusing capacity for carbon monoxide), complete blood cell count, erythrocyte sedimentation rate, biochemistry, liver function tests, antinuclear antibodies, factor rheumatoid, serum alpha-1-antitrypsin, arterial blood gases and high resolution computed tomography of the chest (HRCT).

Results: Spirometry and Post-Bronchodilator spirometry (PBS) showed a mixed pattern: FVC: 2,17 (67.3%) FEV1: 1,48 (53.6%) FEV1/FVC (68.47%), with significant PBS,TLC 6,41 (125%), RV 3,81 (219%), RV/TLC 170%. DLCO 6,45 (76%), DLCO/AV 1,33 (80%). Complete blood cell count, erythrocyte sedimentation rate, biochemistry and liver function tests were normal. Antinuclear antibodies and factor rheumatoid were negative. Serum alpha-1-antitrypsin level was normal. Arterial blood gases: pH: 7,57, pCO2 26 mmHg, pO2 73 mmHg and HCO3 23,8 mEq/L. HRCT showed multiple thin-walled cysts lesions diffusely distributed throughout both pulmonary fields, pulmonary lymphangioleiomyomatosis (LAM) was suggested as possible diagnosis.

Conclusion: In asthmatic patients who develop a clinical and functional impairment is necessary to rule out other lung diseases.

1343-A
Case report: therapeutic efficacy of omalizumab in a problematic severe asthmatic child with Kartagener's syndrome

Yasunobu, T[1]; Mitsuo, N[2]
[1]Sapporo Tokushukai Hospital, Pediatrics and Allergy, Sapporo, Japan; [2]Sapporo Tokushukai Hospital, Pediatrics, Sapporo, Japan

Introduction: Kartagener's syndrome (KS) is a rare hereditary disorder fundamentally based on the ciliary dysfunction. The clinical triad of KS is situs inversus, chronic sinusitis, bronchiectasis, that lead to recurrent exudative otitis media and recurrent pulmonary infections. We report a female case of 12-year-old Kartagener's syndrome with problematic severe asthma whose symptom management were difficult for which omalizumab was effective.

Case report: The case is a 12-year-old girl who had been diagnosed with KS. She had recurrent episodes of exudative otitis media needing ear-tubes and chronic sinusitis with severe discharges, and with medical histories of asthma, atopic dermatitis, allergic rhinitis, pollinosis, pollen-food allergy syndrome. She had experienced several times of hospitalization from infancy, because of her asthma exacerbations which were induced easily by seasons, respiratory infections and exercises and sometimes progressed to severe asthma exacerbations. We initially treated her with high-dose inhaled corticosteroids in combination with a long-acting bronchodilator (salmeterol/fluticasone 25/250 μg twice-daily and ciclesonide 160 μg once-daily), montelukast for asthma control, and oral antihistamine with nasal corticosteroids for allergic rhinitis. Despite these treatments her symptoms and severity levels did not improve. We added omalizumab to her therapy, which successfully reduced her allergic related symptoms, asthma exacerbations, extra visits, hospitalizations, inhaled corticosteroids doses, systemic corticosteroid use, nasal congestion, obstruction, discharge and pollinosis. While we found clinically apparent decrease of ear discharges after 5times injection of omalizumab, clinical effectiveness for atopic dermatitis and pollen-food allergy syndrome was not observed.

Discussions: The management of KS patients who have poorly controlled allergic diseases is difficult. Add-on omalizumab therapy for our case revealed a significant clinical effectiveness for asthma control and allergic related symptoms, in addition to her severe ear discharge. Our findings strongly suggest the beneficial effects of add-on omalizumab therapy for problematic severe asthma cases in children who have congenital diseases, which must help improve their quality of life.

1344
Gamma globulin replacement - a potential new treatment in uncontrolled asthma associated with humoral immunodeficiency?

Tiotiu, A[1]; Martinet, Y[1,2]
[1]CHU Nancy, Nancy, France; [2]Université de Lorraine, Nancy, France

The association asthma- humoral immunodeficiency is rare in adults. We report five cases of patients with humoral immunodeficiency and persistent uncontrolled asthma related to recurrent sino-pulmonary infections with improved asthma control following the introduction of gamma globulin supplementation. For all patients asthma was confirmed by a compatible clinical history and functional respiratory tests according to GINA guidelines, and bronchiectasis diagnosis was excluded by chest CT scan. Two men (28 and 60-years-old) with pollens allergies, chronic rhinosinusitis, Ig G deficiency (7.8 g/L and 7.6 g/L) had uncontrolled asthma despite optimal therapy due to recurrent sino-pulmonary infections. Both underwent surgery for nasal polyposis, but relapsed with acute sinusitis and severe asthma exacerbations requiring systemic corticosteroids and antibiotics. Gamma globulin replacement improved asthma control with reducing exacerbations number (ACQ 7 score from

0.8 to 0.4 for patient 1, and from 1 to 0.2 for patient 2). For a 55-years-old woman with non-allergic corticosteroid-dependent asthma (20 mg / day prednisone) and Ig G deficiency (5.72 g/L), the gamma globulin replacement improved asthma control and allowed systemic corticosteroid therapy withdrawal (ACQ 7 score from 4 to 1.7). For a 47-years-old woman with Ig G 2 subclass deficiency (1.9 g/L) and asthma, gamma globulin infusions improved asthma control and lung function (ACQ 7 score from 3 to 1.1). Gamma globulin treatment in a 75-year-old woman with corticosteroid-dependent asthma (40 mg / day prednisone) and Ig M and Ig G deficiencies (0.28 g/L and 5.36 g/L) with recurrent respiratory, skin and urinary infections, improved asthma control, with a reduction of systemic corticosteroids daily dose to 30 mg prednisone, and of hospitalizations for asthma exacerbations (ACQ 7 score from 3.5 to 2). In view of these observations we suggest that gamma globulin treatment in selected cases of asthma with humoral immunodeficiency could improve asthma control.

1345
The critical asthmatic patient: a case report

Martins, M[1]; Gonçalves, I[2]; Inácio, F[1]; Ribeiro, R[2]
[1]Hospital São Bernardo, Immunoallergology, Setúbal, Portugal; [2]Hospital São Bernardo, Intensive Care, Setúbal, Portugal

Background: Patients with critical asthma have sudden deterioration of vital signs, peakflow <25% of their better value and refractory response to therapy. They are also prone to complications and have an important use of hospital resources. The mortality rate for critically ill asthmatics that need intubation is between 10 to 25%, mainly from cardiopulmonary arrest and anoxia.

Case report: We present a case of a 56 years old male patient with a previous history of bronchial asthma and ischemic heart disease. He was presented to the emergency service with sudden malaise and dyspnea, that rapidly progressed to clouding, cyanosis and subsequent cardiac arrest with a heart rhythm in asystole. It was applied advanced resuscitation care, with a total of 10 cycles of Advanced Life Support. The patient was admitted in Intensive Care Unit (ICU) in need of invasive mechanical ventilation, sedoanalgesia and curarization. The physical examination showed a severe bronchospasm and a marked decrease in breath sounds. The laboratory evaluation showed leukocytosis of 12200, C-reactive protein of 1.89. The Simplified Acute Physiology Score was of 53.

The patient remained curarized for 72 h and sedated for 10 days. The therapeuthics realized included bronchodilators, systemic corticosteroids, aminophylline, magnesium sulfate, montelukast, and antihistamine. It was also administired five days of empirical antibiotic therapy with ceftriaxone and azithromycin for a presumably community-acquired pneumonia, later being changed to Piperacillin/Tazobactam after isolation of Pseudomonas aeruginosa in tracheal aspirate sample. The research of respiratory viruses was negative. During the hospitalization in the ICU the patient presented a Score Glasgow between 6–9. The cranial Computed Tomography and Electroencephalography performed showed alterations that suggested diffuse brain atrophy. At the time of discharge from the ICU the patient was no longer sedated, on spontaneous ventilation with tracheostomy. He presented flaccid tetraparesis, with only spontaneous eye opening and not following orders.

Conclusion: The status asthmaticus is a medical emergency, that can progress rapidly to near fatal asthma or even fatal asthma, given the associated risk of sudden cardiopulmonary arrest and cerebral anoxia. Timely evaluation and treatment is fundamental to avoid morbidity and mortality in critical asthmatic patients.

1347
Development of cold dry air bronchial provocation test for the evaluation of airway hyper-reactivity

Jang, TY[1]; Kim, YH[1]; Lim, DH[2]; Kim, JH[2]
[1]Department of Otorhinolaryngology, Inha University College of Medicine, Incheon, Korea; [2]Department of Pediatrics, Inha University College of Medicine, Incheon, Korea

Background: Methacholine challenge test is still one of the most popular method to evaluate airway hyper-reactivity (AHR). However, there is some risk for sudden bronchospasm and respiratory difficulty. Therefore, practitioners need alternative provocative study protocol which is safe and highly reproducible. We tried to develop cold dry air (CDA) bronchial provocation test and prove its usefulness in evaluating AHR.

Method: we used air for medical use in the hospital. We cooled air temperature below 0 centigrade by passing it through the refrigerator. After passing through mist separator and various filters, we could get air of relative humidity below 10% and free of any micro-organisms. The resultant CDA was delivered to patients′ mouth using pediatric continuous positive airway pressure (CPAP) mask. We determined the total amount of air as 21 times of FEV1 (Forced Expiratory Volume in 1 second). Before CDA provocation, patients answered questionnaire about the symptoms of asthma and subjective feeling of AHR. They also answered Visual Analogue Scale (VAS) questionnaire for asthma and rhinitis symptoms. We performed spirometry and gained baseline values for FEV1 and FVC (Forced Vital Capacity). Five, 10 and 15 minutes after CDA provocation, we repeated VAS questionnaire and routine spirometry and evaluated their change before and after the provocation.

Results: In a representative case of 8-year-old boy with history of chronic rhinitis, total symptom score was aggravated by 2 VAS score after the test. Repeating routine spirometry, we could find that there was significant decrease of FEV1 (1.22–0.7 L/s) and FVC (2.81–2.34 L).

Conclusion: CDA bronchial provocation test could be a useful adjunct tool for the diagnosis and evaluation of AHR.

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Immunology mechanisms

1348

Fold Stability is a key factor for immunogenicity and allergenicity of the major birch pollen allergen Bet v 1.0101

Machado, YJ[1]; Mayr, M[1]; Thalhamer, T[1]; Steiner, M[1]; Freier, R[1]; Brandstetter, H[1]; Briza, P[1]; Isakovic, A[1]; Grutsch, S[2]; Ahammer, L[2]; Tollinger, M[2]; Johnson, CM[3]; Lackner, P[1]; Scheiblhofer, S[1]; Thalhamer, J[1]; Weiss, R[1]

[1]Department of Molecular Biology, University of Salzburg, Salzburg, Austria; [2]Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innsbruck, Austria; [3]MRC Laboratory of Molecular Biology, Cambridge, UK

Background: Among all the environmental proteins, only a relatively small group has the potential to induce allergies. Molecular features like protease activity, interaction with Toll-Like receptors and glycosylation patterns have been linked to allergenicity. However, additional molecular features are likely to influence the allergenicity of a given protein. Here, we used the major birch pollen allergen Bet v 1.0101 as a model allergen to study the impact of fold stability on immunogenicity and allergenicity of proteins.

Method: Stabilized Bet v 1 structures were calculated *in silico* using knowledge-based potentials to estimate structural changes of the protein structures upon iterative mutations. Four mutants (M1 to M4) with a predicted increase in fold stability were selected. Thermal stability was monitored by Differential Scanning Calorimetry. Molecular flexibility was assessed by NMR. Antigen processing and presentation kinetics was studied for these mutants in human monocyte derived dendritic cells. Immunogenicity was studied *in vivo* using BALB/c mice. Antibody titers, basophil activation and cytokine patterns were determined.

Results: Crystal structures of the four hyperstable mutants of Bet v 1 revealed similar folding compared to the wild type protein. Remarkably, the first mutation was enough to increase the melting point of Bet v 1 from 58°C to 84 °C while the other mutations had no further effect on thermal stability. Yet the molecular flexibility of the protein was reduced stepwise from M1 to M4. The mutants were more resistant to proteolysis *in vitro* by endolysosomal proteases. However, they were more efficiently processed and presented by human antigen presenting cells. Furthermore, mice immunized with the highly stable M4 in the absence of any adjuvant showed typical Th2 immune response with elevated titers of IgG1 antibodies, high basophil activation and secretion of IL-4. The same Th2 pattern was obtained for all the mutants but the magnitude of the immune response was decreasing from M4 to M1. The wild type Bet v 1 was not immunogenic in this adjuvant-free setup.

Conclusion: Our novel approach of protein stabilization based on *in silico* calculations allowed to generate hyperstable Bet v 1 mutants while preserving the original Bet v 1 fold. We showed that changes in fold stability impact the processing and presentation of an immunodominant peptide and identified fold stability as a key factor for Bet v 1 immunogenicity and allergenicity.

1349

Regulator of Calcineurin 1 (RCAN1) is a potential regulator of sensitivity to anaphylaxis in humans

Esteban, V[1]; Jensen, BM[1]; Mendez-Barbero, N[2]; Larsen, LF[1]; Redondo, JM[2]; Klitfod, L[3]; Garvey, LH[4]; Poulsen, LK[1]

[1]Laboratory for Medical Allergology, Gentofte Hospital, Copenhagen University Hospital, Hellerup, Denmark; [2]Department of Vascular Biology and Inflammation, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; [3]Department of Vascular Surgery, Gentofte Hospital, Copenhagen University Hospital, Hellerup, Denmark; [4]Department of Anaesthesiology, Gentofte Hospital, Copenhagen University Hospital, Hellerup, Denmark

Background: Anaphylaxis is the most aggressive manifestation of allergic disorders well characterized in terms of clinical features. Most of the organs are affected, but vascular system including endothelial cells (EC) and smooth muscle cells (SMC) is ultimately involved in clinical symptoms of anaphylaxis. Capillary permeability, peripheral vascular resistance (vasodilation/vasoconstriction) and drop in blood pressure are key contributing to anaphylactic reactions. Underlying signaling in these episodes is still poorly understood in humans. Moreover, since Regulator of Calcineurin 1 (RCAN1) has been incriminated in FcεRI-mediated signaling and vascular remodeling in mice; we study its role in human vascular anaphylaxis-related processes.

Method: Our current study mainly includes the use of human saphenous vein HSV-EC and HSV-SMC (from patients undergoing surgery). Histamine (as the main mediator released by effector cells) is used as stimuli. Functional permeability transwell texts and *in vitro* molecular assays using lentiviral constructs to exogenously over-express RCAN1 are also applied.

Results: Histamine induces HSV-EC dilation in a similar way than epinephrine does. Accordingly, the phosphorylation status of MLC (MLC-P) diminish in response to histamine and assays reproducing *in vitro* vascular permeability show HSV-EC relaxation at very short-time. Moreover, intracellular RCAN1 over-expression presents a similar behavior, reducing MLC-P and significantly blocking vascular permeability process in HSV-EC. Otherwise, histamine but not epinephrine stimulation modulates mRNA and protein RCAN1 expression in HSV-EC and HSV-SMC. RCAN1 over-expressed HSV-EC and HSV-SMC present differences in expression pattern for important signaling pathways involved in vascular permeability and reactivity, such as MLC-K, Rho-K, eNOS and COX-2.

Conclusion: Both the endothelial barrier and SMC layer play important roles regulating non-immunological processes which happen in allergic-exacerbated and anaphylactic reactions. Particularly, we here demonstrate histamine-permeability and -contractility impact on HSV-EC. Moreover, histamine modulates key signaling molecule, as RCAN1 with a high involvement in barrier integrity and human vascular anaphylaxis-related processes. It is tempting to speculate that the vasculature may be conditioned to make some patients hyperreactive to mediators, but also to search for a pharmacological normalization to prevent anaphylaxis.

1350
Gauging signal-1 strength: does signal one strength influence the phenotype of human allergen-specific T lymphocytes?

Candia, MR[1]; Tauber, P[1]; Neunkirchner, A[1]; Trapin, D[1]; Rosskopf, S[1]; Steinberger, P[1]; Campana, R[2]; Valenta, R[2]; Pickl, W[1]
[1]Center for Pathophysiology, Infectiology and Immunology, Institute of Immunology, Medical University of Vienna, Vienna, Austria; [2]Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria

Background: TCR signal strength is a major relaying mechanism to control T cell differentiation and function. In the thymus, low affinity interactions with self-peptides generate weak TCR signals allowing T cells to undergo positive selection, while strong interactions and consequently strong TCR signals cause their deletion. Moreover, the notion that low level tonic signaling is essential for T cell survival in the periphery speaks for the exquisite capability of T cells to read-out TCR signal strength. Subsequently, a second phase of T cell activation caused by the encounter with cognate antigens in the periphery promotes induction of effector T helper cell subsets with very distinct cytokine patterns, i.e. Th1, Th2, Th17 and Treg. Since allergic sensitization but also late phase allergic reactions have been linked to altered $CD4^+$ T cell function, we sought to investigate the contribution of TCR signal strength to the differentiation of allergen-specific $CD4^+$ Th cells.
Method: We here used a recently developed Art v 1 TCR/HLA-DRB1*0101 double transgenic system to define possible altered peptide ligands (APL) of the major allergen of mugwort pollen, Art v $1_{25–36}$. Furthermore, variation of the amount of antigenic peptides as well as targeted pharmacological inhibition of T cell signaling pathways was used to alter signal strength. For the quick and facile determination of the binding-characteristics of APL a robust, flow cytometry-based assay for peptide binding to cell surface expressed HLA molecules was established.
Results: So far, two APL with differential T cell activating capabilities as determined by proliferation and cytokine secretion assays have been characterized. One of them, APL1, giving rise to enhanced proliferation and increased IL-4, IL-10 and IL-17 production, while the other, APL2, acting as an antagonist that prevents both T cell proliferation and cytokine production. Moreover, some drugs could be identified, which resulted in *in vitro* differential cytokine production in allergen-specific T cells. Additionally, variation of the amount of antigenic peptide resulted in a clear-cut Th2 polarization when low amounts of peptides were used, whereas high concentrations of peptide skewed the t cells towards a Th1-like phenotype.
Conclusion: In summary, altering TCR signal strength might represent a useful way to shape allergen-specific T cellular immune responses.

1351
Ligand binding influences the physicochemical properties of the major birch pollen allergen Bet v 1

Aglas, L[1]; Asam, C[1]; Gilles, S[2]; Traidl-Hoffmann, C[2]; Ferreira, F[1]; Wallner, M[1]
[1]Molecular Biology, University of Salzburg, Salzburg, Austria; [2]Institute of Environmental Medicine, UNIKA-T, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

Background: Over 95% of birch pollen allergic patients are sensitized to Bet v 1, the major birch pollen allergen, rendering it the main cause of spring pollinosis in the temperate climate zone of the northern hemisphere. The structure of Bet v 1 is characterized by an intrinsic cavity traversing the protein, which was shown to act as a binding site for a variety of hydrophobic ligands. However, influences of ligand binding on the physico-chemical as well as immunological properties of Bet v 1 remained elusive.
Objective: In the present study, we investigated the effects of ligand binding on the intrinsic properties of recombinant Bet v 1.0101 (called Bet v 1 in the following). Therefore, six different ligands including molecules with immune-modulatory properties were selected.
Method: Interactions of Bet v 1 with ligands were investigated by extrinsic fluorescence studies using an ANS (8-anilinonaphthalene-1-sulfonic acid) displacement assay. Analyses of secondary structure elements as well as thermal stability of Bet v 1 in the presence or absence of ligand molecules were performed by circular dichroism spectroscopy. Furthermore, both ligand-bound and naked Bet v 1 was treated with a cocktail of endo-/lysosomal proteases to determine proteolytic stability in a time-dependent manner.
Results: ANS displacement assays revealed binding to Bet v 1 of all six ligand molecules used in the study. CD spectroscopy revealed that ligand-binding did not induce alterations in the protein secondary structure. However, bound ligands altered the thermal as well as proteolytic stability of the allergen. Of note, ligands with low molecular weight (< 3 kDa) had an overall stabilizing effect on the protein, whereas high molecular weight ligands (> 3 kDa) decreased the stability of Bet v 1.
Conclusion: Recently, a natural ligand of Bet v 1 has been identified in the extract of birch pollen. Our data indicates that the binding of various ligands influences the intrinsic stability of Bet v 1 in one way or the other. Thus, ligand binding might have a direct impact on the process of allergic sensitization.

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1352
Generation of new cassette vectors for the targeted presentation of human-relevant allergens in humanized mouse models

Kratzer, B; Neunkirchner, A; Pickl, WF
Center for Pathophysiology, Infectiology and Immunology, Institute of Immunology, Medical University of Vienna, Vienna, Austria

Background: IgE-mediated immune reactions (allergies) affect more than 25% of individuals in our population. The manifestations of allergies include besides allergic rhinitis, conjunctivitis and dermatitis also severe organ-specific forms such as asthma, food allergy and life-threatening anaphylaxis. During sensitization and late phase of allergic disease, the presentation of allergen-derived peptides on MHC class II molecules to T cells is essential. However, experimental animals able to present the immunodominant peptides of human-relevant aeroallergens are scarce, making mechanistic studies investigating the consequences of allergen-exposure, their organ-specific manifestations and cure difficult. In order to solve these shortcomings, we here created a pair of novel cassette vectors for tissue-specific expression of human MHC class II HLA-DR molecules in mice.
Method: The human variable, membrane-distal domains of HLA-DRA*01:01 and HLA-DRB1*07:01 were therefore chimerized to the corresponding constant, membrane-proximal domains of murine H-2 IE alpha and beta, respectively. These chimeric molecules ensure binding and presentation of human-relevant allergenic peptides with the human variable, membrane distal domains, whereas the constant, membrane-proximal domains remain murine, leaving the interplay with murine CD4 coreceptor molecules unaltered. In our novel pair of cassette vectors, the human HLA-DR sequences, comprising exon 2 of HLA-DRA*01:01 and HLA-DRB1*07:01 were flanked by unique Not I and Cla I restriction enzyme sites to enable rapid, directed exchange with other allelic

sequences. HLA-DRA and -DRB1 variable sequences were flanked by 5 kb and 6 kb or 10 kb and 6.5 kb of murine H-2 IE 5'- and 3'-genomic sequences, respectively. Thus, transgenes are under the control of the natural H-2 IE promoter/enhancer elements.

Results: Functional evaluation of the plasmids revealed clear-cut, MHC class II transactivator-dependent expression of transgenes in HEK-293T cells as detected by flow cytomety and as confirmed by functional assays with allergen-specific T cell receptor transgenic $CD4^+$ T lymphocytes restricted to HLA-DRB1*07:01.

Conclusion: The novel HLA-DR::IE cassette vectors will allow the quick and facile creation of a collection of HLA transgenic mice, which contribute to better understanding of immune-mediated diseases, such as allergies, and to evaluate novel immunotherapeutic concepts.

1353
Human IgE is efficiently produced in biologically active form in lepidopteran cells

Plum, M[1]; Seismann, H[2]; Wolf, S[1]; Bantleon, F[1]; Dam, S[1]; Lorentzen, A[3]; Miehe, M[1]; Jabs, F[1]; Rafei-Shamsabadi, D[4]; Jakob, T[4]; Spillner, E[1]
[1]Aarhus University, Aarhus, Denmark; [2]Euroimmun AG, Lübeck, Germany; [3]University of Southern Denmark, Odense, Denmark; [4]University Medical Center Freiburg, Freiburg, Germany

Background: The potential of specific and high affinity IgE in reacting against minute amounts of allergens and to provoke severe anaphylactic reactions renders IgE a mechanistically outstanding isotype. Despite large progress in antibody technologies however the recombinant access to IgE still is scarce, a consequence of the demands of the immunoglobulin and the capacity of the expression systems used.

Method: In order to overcome limitations of mammalian expression systems we established the recombinant production of IgE in insect cells. The IgE was purified via affinity chromatography and characterised by ELISA, immunoblotting and SPR. RBL assays were used to prove biological function and the glycosylation was assessed by mass spectrometry.

Results: Recombinant human IgE (rIgE) was efficiently assembled and secreted by Sf9 insect cells into culture supernatant in yields of >30 mg/L. Purification via affinity chromatography from serum free insect cell medium using different means provided large amounts of rIgE. The rIgE exhibited a highly specific interaction with its antigen, a therapeutic anti-IgE and its high affinity receptor FcεRI. Lectins and glycoproteomic analysis revealed the presence of a prototypic *N*-glycosylation of the epsilon heavy chain. Mediator release assays demonstrated the biological activity of the IgE in activating effector cells in response to trace amounts of antigen.

Conclusion: In summary the expression in lepidopteran cells provide molecular access to IgE of retained characteristics and biological activity. Our data also contribute to the understanding and potential use of this important antibody isotype.

1354
Mitochondrial ROS activate NLRP3 inflammasome through PI3K-HIF-VEGF pathway in LPS-induced lung inflammation

Kim, SR[1]; Lee, YC[1]; Kim, HJ[1]; Kim, SH[2]
[1]Chonbuk National University Medical School, Jeonju, Korea; [2]LG Life Sciences Ltd., Seoul, Korea

Background: Oxidative stress caused by reactive oxygen species (ROS) and reactive nitrogen species (RNS) has been implicated in various pulmonary pathological conditions. The mitochondria respiratory chain is considered as an important site of ROS production within most cells. The NLRP3 inflammasome is an intracellular complex that regulates release of pro-inflammatory cytokines such as IL-1b, in response to exogenous pathogen-associated molecular patterns and endogenous danger signals. Although some studies have demonstrated that mitochondrial ROS is one of endogenous PAMPs activating NLRP3 inflammasome, to date, there is little information on which molecular mechanisms contribute to the assembly of NLRP3 inflammasome induced by mitochondrial ROS, especially in lung.

Method: In this study, we used LPS-instilled mice to define the molecular mechanisms implicated in mitochondrial ROS-induced NLRP3 inflammasome activation in LPS-induced lung inflammation, specifically in the relationship with PI3K-HIF-VEGF axis activation.

Results: The administration of mitochondrial ROS inhibitors, Nerox-5 or -7 decreased the LPS-induced mitochondrial ROS generation, the levels of NLRP3 expression and IL-1b in lungs, the numbers of inflammatory cells in BAL fluids, the histologic changes in lung tissues, and the increase in the levels of inflammatory cytokines in LPS-inhaled mice. In addition, the increases in phosphorylation of Akt, activation of HIF-1a and HIF-2a, and expression of VEGF in lung tissues from LPS-instilled mice were significantly inhibited with the administration of NecroX compounds. Our results also revealed that LPS-induced increases of nuclear translocation of NF-κB, infiltration of DCs, and TLR4 expression in the lung were significantly reduced by inhibition of NecroX compounds. TLR4 inhibition using TAK-242 decreased mitochondrial ROS and the phosphorylation of Akt and p85 expression in lung tissues and attenuates the LPS-inflammation. Interestingly, blockade of VEGF resulted in the substantial suppression of the activation of NLRP3 inflammation.

Conclusion: These findings suggest that mitochondrial ROS activates NLRP3 inflammasome, a crucial player in the pathogenesis of LPS-induced lung inflammation, at least in part through PI3K-HIF-VEGF axis.

1355
The interaction between mitochondrial ROS and SIRT1 contributes to the pathogenesis of LPS-induced lung inflammation

Lee, YC[1]; Kim, SR[1]; Kim, HJ[1]; Kim, SH[2]
[1]Chonbuk National University Medical School, Jeonju, Korea; [2]LG Life Sciences Ltd., Seoul, Korea

Background: Mitochondria are now considered as one major target for many therapeutic approaches. Oxidative stress has been a particular fulcrum of interest since mitochondrial oxidative damage has been recognized as being involved in many diseases and in the aging process itself. Also, disrupted mitochondrial metabolism may be one of the critical elements leading to cancer, diabetes, age-associated and neurodegenerative disorders. In addition, the link between sirtuin activity and mitochondrial biology has recently emerged as an important field. Moreover, sirtuins can be classified by their subcellular localization as well as tissue specificity; for instance, SIRT1 and SIRT2 show both cytoplasmic and nuclear localization, SIRT6 and SIRT7 are only located in the nucleus and nucleoli, and SIRT3, SIRT4 and SIRT5 are mitochondrial proteins, although their localization and functions are very different depending on the tissues/organ. Studies have demonstrated that sirtuins show anti-aging, anti-inflammatory, anti-tumor effects and so on, however, SIRT1 has also been reported to play an important role in the pathogenesis of various inflammatory disorders including bronchial asthma. To date, there are little experimental data on the relationship between SIRT1 and mitochondrial ROS in respiratory disorders.

Method: To define the role of the interplay between mitochondria ROS and SIRT1, we performed experiments using the lung tissues and cells from LPS-instilled mice.

Results: In this study, we have found that the SIRT1 expression and activity was sig-

nificantly increased in LPS-induced lung inflammation with showing the increased generation of total cellular ROS and mitochondrial ROS, the increased plasma exudation, the increased numbers of airway inflammatory cells in BAL fluids, the histologic changes in lung tissues, the increased nuclear translocation of NF-κB, and the increase in the levels of inflammatory cytokines. These findings were attenuated by the administration of mitochondrial ROS inhibitor, NecroX-5 or -7. Moreover, the administration of the SIRT1 inhibitor, sirtinol significantly reduced the LPS-induced lung inflammation, pathologic damage, and plasma exudation.

Conclusion: These findings suggest that the interaction between mitochondrial ROS and SIRT1 contributes to the pathogenesis of LPS-induced lung inflammation cooperatively, providing a new target for the therapeutic approach to various lung inflammatory disorders including infectious disease.

1356
Apical exposure to dietary non-digestible oligosaccharides and bacterial CpG DNA suppresses Th2 type chemokine release by activated intestinal epithelial cells

Overbeek, SA[1]; Boks, M[2]; de Jager, W[3]; Garssen, J[1,4]; Willemsen, L[1]
[1]Universiteit Utrecht, Utrecht, the Netherlands; [2]VUMC, Amsterdam, the Netherlands; [3]UMC Utrecht, Utrecht, the Netherlands; [4]Nutricia Research, Utrecht, the Netherlands

Background: Dietary short chain galacto- and long chain fructo-oligosaccharides (scGOS/lcFOS) and TLR9 ligand CpG DNA affect intestinal epithelial cell (IEC) function. Epithelial derived IL-1a is known to contribute to allergic sensitization in the lung. To study the effect of IL-1a on Th2 polarizing chemokine release by IEC and the modulatory effect of scGOS/lcFOS and CpG DNA in presence or absence of monocyte derived dendritic cells (moDC).

Method: HT-29 cells (IEC) cultured in transwells were pre-incubated basolaterally with IL-1a ± IFNg/TNFa and apically with scGOS/lcFOS ± CpG DNA for 6 hours, washed and basolaterally exposed to immature moDC or medium while apically exposed to scGOS/lcFOS ± CpG for 24–48 hours. Th2 driving IL-25, CCL2, CCL22 and regulatory galectin-9 and TGFb were measured in basolateral supernatants. After 48 h of co-culture, moDC were added to allogenic naïve T-cells for 6 days (MLR) and cytokines were measured.

Results: Combined IFNg/TNFa activation induced the release of CCL2 and CCL22 by IEC, which was further enhanced by IL-1a. IFNg/TNFa ± IL-1a activation also increased galectin-9 and TGFb (24 h). Exposure to scGOS/lcFOS ± CpG DNA reduced CCL2 and CCL22, while galectin-9 and TGFb remained high. In the 48 h supernatants of IEC/moDC co-cultures, scGOS/lcFOS enhanced galectin-9 in presence or absence of CpG DNA. scGOS/lcFOS plus CpG DNA reduced IL-25 in co-cultures pre-exposed to IFNg/TNFa/IL-1a while increasing IFNg concentrations in the MLR.

Conclusion: IL-1a enhances Th2 polarizing chemokine release by IFNg/TNFa activated IEC. Combined exposure to dietary scGOS/lcFOS plus CpG DNA suppresses this response skewing away from the allergic phenotype.

1357
The 2D:4D digit ratio and susceptibility to immune-related disease

Fernstrand, AM[1]; Bury, D[1]; Lensvelt, LMH[1]; Ribbert, LLA[1]; de With, AC[1]; Goede, LXY[1]; Garssen, J[1,2]; Verster, JC[1,3]
[1]Division of Pharmacology, Utrecht University, Utrecht, Netherlands; [2]Nutricia Research, Utrecht, Netherlands; [3]Center for Human Psychopharmacology, Swinburne University, Melbourne, Australia

Background: Amniotic fluid sample analysis revealed a significant relationship between prenatal testosterone - produced by the fetus - and adult disease susceptibility. The 2D:4D digit ratio is a biological correlate for prenatal testosterone exposure. The purpose of this study was to determine if the 2D:4D digit ratio is related to susceptibility to atopic diseases.

Methods: A survey was held among N = 557 Dutch students. In addition to demographics, overall perceived health and immune status was scored on a scale ranging from 0 (very poor) to 10 (excellent). Further, past year's presence, severity and duration of common cold, fever, allergic rhinitis, eczema, and asthma were recorded. For both hands, digit length of the second (2D, index finger) an fourth (4D, ring finger) finger were measured using digital vernier calipers recording to 0.01 mm. The 2D:4D digit ratio was correlated to atopic disease scores, overall and for female and male participants separate. In addition, subjects with a hawk-type (2D:4D < 1) and dove-type personality (2D:4D > 1) were compared.

Results: Data from N = 509 subjects was used in the statistical analyses, N = 143 (28.1% of them were men. The right 2D:4D digit ratio correlated significantly with the general health rating ($r = -0.096$, $P = 0.032$). The left 2D:4D digit ratio correlated significantly with the number of common cold days ($r = -0.108$, $P = 0.019$). Subjects with a left 2D:4D < 1 reported more common cold days ($P = 0.052$). For men, the left 2D:4D digit ratio correlated significantly with perceived immune status ($r = 0.191$, $P = 0.023$), and the right 2D:4D digit ratio with the number of fever days ($r = -0.387$, $P = 0.009$). Men with a right 2D:4D >1 reported having significantly more periods of fever ($P = 0.029$). Allergic rhinitis ($P = 0.08$) and eczema ($P = 0.06$) were also more commonly experienced. In women, the right 2D:4D digit ratio also correlated significantly with general health ($r = -0.115$, $P = 0.029$). Women with a left 2D:4D < 1 reported significantly more severe common cold scores.

Discussion: The data suggest that a 2D:4D > 1 is associated with increased presence, duration, and severity of fever and atopic diseases such as allergic rhinitis and eczema. A 2D:4D < 1 was associated with reduced perceived immune status and increased presence, duration and severity of common cold. Research in diagnosed patient populations should confirm our findings.

1358
Changes in the immunological properties induced by glycofullerenes and nanohorns

Palomares Jerez, MF[1]; Fernandez, TD[1]; Muñoz, A[2]; Illescas, B[2]; Martín, N[2]; Rodriguez, MJ[1]; Galindo, L[1]; Rojo, J[3]; Torres, MJ[1]; Mayorga, C[1]
[1]Laboratorio de Investigación, UGC de Alergología, Hospital Regional Universitario de Málaga-IBIMA, Malaga, Spain; [2]Departamento de Química Orgánica, Facultad de Química, Universidad Complutense de Madrid, Madrid, Spain; [3]Instituto de Investigaciones Químicas [IIQ], CSIC-Universidad de Sevilla, Glycosystems Laboratory, Sevilla, Spain

Background: The glycofullerenes and nanohorns are very promising structures as they provide a spherical presentation of carbohydrates. These tools have been recently described and used to interact with proteins and macromolecules that are highly specific for carbohydrates. Currently, there are works which describe that these glycoconjugates are able to inhibit a DC-SIGN-dependent cell infection by pseudotyped viral particles. The physicochemical properties of these structures are essential in the modulation of immune responses and for instance in the field of immunotherapy. In this study, we analysed changes in the dendritic cell (DC) maturation and T cel proliferation after the stimulation with glycofullerenes and nanohorns, that include different number and type of carbohydrates.

Method: The glycofullerenes and nanohorns are soluble structures based on hexaadducts of C60 with different number of

carbohydrates constituted with 12, 36 and 120 mannoses, fucose or galactose. For the assays we used two concentrations, 5 and 50 μM.

The immunological responses in the presence of these new structures were analysed by studying maturation changes in monocyte-derived-DC (moDC) and lymphocyte proliferation (by culturing with moDC as antigen presenting cells) by flow cytometry.

Results: Our results indicate that the glycoconjugates, independently of the carbohydrate in the structure, did not show any cytotoxicity. The degree of DC maturation was analyzed by determining the expression of the specific cell surface markers: CD83, CD86, CD80 and HLA-DR. Only nanohorns induced a significant increase in DC maturation ($P < 0.05$). Toxicity on T and NK cells was tested and no effect on the cell viability was found. We investigated changes in the proliferative response of T lymphocytes (CD3, CD4, CD8 and CD56). There was a low T cell proliferation for glycofullerenes but an increased proliferation of cytotoxic T cells (CD8) and NK cells (CD56) after incubation with nanohorns.

All these data indicate that the nature of the structure, independently of the type and the number of the carbohydrates, cause changes in the immunological response.

Conclusion: These compounds could be a platform for vaccine displays, with the ability to enhance the delivery of antigen/allergen to antigen presenting cells inducing a Th1 response that could be beneficial for immunosuppression therapy.

1359
Hypertonic seawater solutions exhibit anti-inflammatory actions and improve nasal cell function in epithelial cell cultures isolated from an allergic human donor

Alevizopoulos, K
Gerolymatos International SA, Kryoneri, Athens, Greece

Background: Hypertonic saline sprays are frequently used as adjunct agents providing symptomatic relief and/or reducing the need for prescribed medication in allergic rhinitis patients. Despite reported mechanisms of action including induction of osmotic gradients or mechanical removal of mucus in nasal epithelia, direct and conclusive evidence linking hypertonic saline solutions to inflammation reduction and improvement of nasal function are still lacking.

Method: Airway epithelial cells isolated from an allergic human donor were cultured as 3-dimensional, fully differentiated cultures in the presence of HCPt (ammonium hexachloroplatinate IV), a well-known respiratory allergen capable of inducing potent inflammatory responses in cells. To assess potential benefits of a hypertonic seawater solution comprising 2.3% NaCl (HSS), its effects on the secretion of HCPt-induced inflammatory mediators IL-8 and IL-6 were measured by ELISA over a time-course of 3 days. Cilia Beating Frequencies (CBF) of the nasal epithelia were also determined by digital high-speed video imaging at day 3 post HCPt challenge. Finally, effects of HSS on the mucociliary clearance of allergic cells were analyzed by measuring the speed of clearance of micro-beads added to the apical surface of cells by video imaging.

Results: HCPt induced a potent inflammatory response as measured by strong IL-8 secretion in the supernatant of allergic epithelial cells (25-fold increase in Day 3). HSS (2.3% NaCl) was capable of blocking the HCPt-induced increase of IL-8. Similar effects were observed for IL-6 although the action of HSS was less profound in comparison to IL-8. Furthermore, treatment with HSS resulted in increased CBF of the nasal epithelia at day 3 post HCPt challenge. Directly proving the beneficial effects of the solution, measurements in naïve allergic epithelia not treated with HCPt showed increased mucociliary clearance speed in response to seawater treatment. Of note, similar anti-inflammatory effects on IL-8 and IL-6 and increased CBF were observed in epithelia from normal human donors treated with bacterial lipopolysaccharide in the presence of HSS.

Conclusion: Hypertonic seawater solutions comprising 2.3% NaCl have direct anti-inflammatory effects and improve nasal cell function in physiological cultures of epithelial cells isolated from an allergic donor. These results may help explain the beneficial effects observed with hypertonic solutions in allergic patients.

1360
BAFF (B-cell activating factor) expression in IgG4-related disease

Pizzimenti, S; Viglino, F; Boita, M; Heffler, E; Novero, D[1]; Bucca, C; Rolla, G
Department of Medical Sciences, University of Torino, Torino, Italy

Background: The IgG4-related disease is a systemic syndrome, which may involve virtually any organ or system. The most characteristic clinical-pathological presentation complaints are autoimmune pancreatitis type 1, the symmetrical swelling of the lacrimal, parotid and submandibular glands, the inflammatory pseudotumor, retro peritoneal fibrosis and involvement of lymph nodes. Lymphocytes and plasma cells tissue infiltrate, with a ratio IgG4 + / IgG+ cells > 40% and a peculiar tissue fibrosis, named storiform, are the pathologic characteristics of the disease. The purpose of the study was to evaluate the expression of B-lymphocyte stimulating factors BAFF (B-cell activating factor) and APRIL (a proliferation induced ligand), as well BAFF-Receptor, by immunohistochemistry of bioptic specimens of a case-series of patients with proved diagnosis.

Methods: Nine patients (age range 34–78 yrs) with mean IgG4 serum concentration 548 mg / dl (range 124–1520), 6 with sclerosing pancreatitis, 5 with lymphadenopathy, 4 with sialadenitis, 3 with inflammatory orbital pseudotumor, 2 with dacryoadenitis and 1 with prostate hypertrophy had been enrolled. Bioptic tissue samples have been evaluated by immunohistochemistry with anti-BAFF, anti-BAFF-R, anti-APRIL antibodies and semi-quantitative analysis was performed and Immuno Reactivity Score was used (IRS=% of positive cellsxstaining intensity).

Results: APRIL and BAFF were expressed at same level (IRS mean 52.5 ± 24 and 67.5 ± 55, respectively) in tissues biopsies. APRIL and BAFF were localized outside the germinal center, with a cytoplasmic staining. BAFF R (IRS mean 170.6 ± 109) was positive in the lymphocytes agglomerates and inside the germinal centers. Moreover, IgG4 correlates with BAFF R IRS ($r = 0.56$), and do not correlate with APRIL and BAFF immune staining.

Conclusion: Our data reinforce the hypothesis of the major role played by B lymphocyte activation in this disease and suggest a possible therapeutical approach by monoclonal antibodies specific for B-lymphocytes activating factors.

1362
Serum mannose binding level and gene polymorphism in Down syndrome

Kilic, SS[1]; Budak, F[2]
[1]Pediatric Immunology, Uludag University Medical Faculty, Bursa, Turkey; [2]Immunology, Uludag University Medical Faculty, Bursa, Turkey

Background: Mannose binding lectin (MBL) is a multimeric lectin that initiates lectin pathway of complement activation. The gene encoding MBL, *MBL2*, contains several common polymorphisms that influence transcription and assembly of the molecule into multimers. Children with Down syndrome (DS) have an increased rate of infection and it has been proposed that this is secondary to derangements of

the immune system. We conducted a study to examine the rate of MBL deficiency and status of MBL polymorphism in children with DS. The possible influence of MBL deficiency on the development of recurrent infections was assessed.

Method: Eighty-five patients with DS and 40 healthy control were included in this study. MBL concentration was measured using enzyme linked immunosorbent assay (ELISA). Point mutations of the MBL gene were detected by polymerase chain reaction (PCR) restriction fragment length polymorphism.

Results: MBL level of DS patients was lower than the control group ($P < 0.05$). Frequencies of genotype AB and BB were also significantly higher in the study group ($P < 0.001$) compared with the control group. Significant correlation was found among low serum MBL levels, presence of homozygous BB allele, and the infection frequency.

Conclusion: We documented that many children with Down syndrome do have abnormalities of serum levels of MBL and MBL gene allels. MBL deficiency may be a risk factor for recurrent infections for DS.

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Molecular methods and their epidemiological applications in allergology

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Changes in allergen distribution's depending on geographical ares: an ISAC investigation

Caimmi, S; De Amici, M; Marseglia, A; Licari, A; Trovamala, V; Desmet, N; Testa, G; Marseglia, GL
Foundation IRCCS Policlinico San Matteo, Department of Pediatrics, Pavia, Italy

Background: Because of the increase of allergic disease in the last years, we investigate what are the allergens that carry more sensitization and carry out a study on patients referred to the immuno-allergology laboratory of IRCCS Policlinico San Matteo of Pavia. The study was extended to the entire region of Lombardy, dividing into three bands (north, center, south).
Method: Of 318 patients were enrolled in this study. ImmunoCap ISAC methodology is used for the analysis of specific IgE, that allows to recognize false positives due to multiple cross-reactivity, allowing to divide positivity with less symptoms from other more dangerous. The patients are dividing in three groups: those who live in Lombardy (257/318, 81.5%), those from other region (54/318, 16.95%) and those who is not tabulate their region (7/318, 2%). Patients were assigned at the area of belonging (north, center, south). This division was made for Lombardy and for rest of Italy. For all the 112 molecules tested with ISAC we calculated the number of patients who have shown sensitization and their relative IgE value that is divides in 4 groups (group 1: value < 0.3, group 2: 0.3 < value < 0.9, group 3: 0.9 < value< 14.9, group 4: value >15).
Results: Divided depending the protein group the 112 molecules and their relative recombinant is calculated for Lombardy dividing in north center and south the number of sensitized patients for each one molecule, calculating also the percentage and making a sort about the ten molecules more sensitizing. Once we find the number of sensitized for each molecule we designs three bar charts (one for each Lombardy area) that represent all recombinant group by ranges of IgE values. In the graphs we can see that in the third graph there is the more concentration of sensitized patient. Patients were assigned a value of 1 to 3 depending on the area of belonging (1 = north, 2 = center, 3 = south). This division was made for Lombardy and for rest of Italy; the values which are not tabulated the region of origin are excluded from the analysis. For all the 112 molecules tested with ISAC we calculated the number of patients who have shown sensitization and their relative IgE value that is divides in 4 groups (group 1: value < 0.3, group 2: 0.3 < value < 0.9, group 3: 0.9 < value< 14.9,
group 4: value >15).
Conclusion: Our results show that the most sensitized area is the south of Lombardy and the most sensitizing molecules are grasses, dust mite tree pollens and nuts.

1365
Cross sectional study for identification of culprit allergens according to the age of Korean atopic dermatitis patients

Kim, JH; Lee, JH; Jeong, KY; Park, KH; Park, HJ
Yonsei University College of Medicine, Institute of Allergy, Seoul, Korea

Background: Atopic dermatitis (AD) usually occur in childhood and some may be remitted but others persist to adulthood. Culprit allergens may be changed as the disease progress. In this study, we tried to distinguish important culprit allergens according to age in AD patients.
Methods: Total 110 AD patients' sera were tested to detect allergen specific immunoglobulin E (sIgE) for each 11 allergens - milk, egg white, peanut, shrimp, wheat, *Dermatophagoides farinae* (DF), *Candida albicans* (CA), *Trichophyton rubrum* (TR), *Pityrosporum ovale*(PO), Staphylococcal enterotoxin B (SBE), recombinant Hom s 1. Mean age of the enrolled patients was 12.2 years olds (range: 1~47).
Results: Sensitization rates of allergens were varied from 17.3% (for TR) to 52.7% (for DF). Milk and egg white sIgEs were more detected in young aged patients and their sensitization rates decreased according to age increment. Conversely, sensitization rates of shrimp, DF, SBE, CA, TR, PO and SBE increased according to age increment. There were no differences in peanut and wheat sensitization rates. Interestingly, rHom s 1 sIgE was detected more frequently in younger patients (36.5% in age 1–5 vs. 12.1% in age ≥ 18).
Conclusions: There was distinct difference of sensitization pattern. Milk and egg white are more important allergens in young aged patients. On the contrary, microbial and house dust mite allergens were more important in adult patients. Autoantigen can also be important cause at early stage of AD.

1367
Prevalence of skin prick and IgE positive subjects in the Greater Toronto Area (GTA), Canada

Sadoway, T[1]; Nelson, V[2]; Pathmanapan, S[1]; Patel, P[1]; Salapatek, AM[1]; Couroux, P[1]
[1]Inflamax Research, Mississauga, Canada; [2]Inflamax Research, Research and Development, Mississauga, Canada

Background: Many human populations are very homogenous and it has been suggested that this results in a low diversity of the allergies present. We analyzed a multicultural, ethnically-diverse population in the GTA for allergic potential. This area is characterized as being a moist, mid-latitude climate with cold winters (Köppen climate classification Dfa). The GTA is known to have a robust pollen season including high seasonal peaks of ragweed and oak.
Method: More than 1700 subjects with self-reported allergies consented to screen for a study over a 6 month period. History, Physical and skin prick test (SPT) panel to 13 allergens and allergen specific IgE (8 allergens) was done. SPT wheal size 3 mm larger than the negative control, or an IgE class 2 or higher (0.70KU/L) was considered positive. These data were analyzed with regression and statistical methods with respect to the prevalence of allergy.
Results: Although all subjects indicated a history of allergy, a small percentage (0.3%) did not test positive on SPT for any allergen. However, only 10.3% were monoallergic. Seasonal allergies were the most common, with 67.5% of subjects allergic to ragweed and 63.1% allergic to a grass mix

SPT. Only 47.7% of subjects were positive to Birch even though the birch peak is higher than the other seasonal allergens. The most common perennial allergen was cat (54.4%), which is much higher than German literature would suggest. Additionally, house dust mite prevalence (40.0%) was higher than similar populations in Russia and China. Despite the moist climate in this region, fungal allergies were very low (1.4%). When the positive SPTs were parsed with the positive IgE, there were wide discrepancies between allergens. For example, although half the population showed a cat SPT response, only half of those people (48.2%) had a corresponding IgE positive result. Conversely, of the 63% of individuals with a grass allergy, 80.8% showed a positive IgE. In low prevalence allergies, such as dog (3%) and Alternaria (1.4%), only 4% and 2% respectively demonstrated a positive IgE response.

Conclusion: The prevalence of skin test or specific IgE to many seasonal and perennial allergens is very high in the GTA, likely related to the prevalence of high allergens levels in the North East.. This confirms that the GTA is an excellent area to recruit subjects with specific allergies for clinical trials.

1368
Radiolabeling and *in vitro* evaluation of a recombinant canine anti-cancer IgG

Fazekas, J[1,2]; Rami-Mark, C[1,3,4]; Singer, J[1,3]; Willmann, M[5]; Andreae, F[6]; Wadsak, W[3,4]; Mitterhauser, M[3]; Jensen-Jarolim, E[1,2]
[1]Institute of Pathophysiology and Allergy Research, Medical University Vienna, Vienna, Austria; [2]Messerli Research Institute of the University of Veterinary Medicine, Medical University and University Vienna, Vienna, Austria; [3]Division of Nuclear Medicine, Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria; [4]Institute of Inorganic Chemistry, University of Vienna, Vienna, Austria; [5]Department for Companion Animals and Horses, University of Veterinary Medicine Vienna, Vienna, Austria; [6]piChem R&D, Graz, Austria

Background: Pathophysiologic processes in dogs (*Canis lupus familiaris*) show remarkable similarities to humans. Especially tumor biology and immunity are comparable in both species, suggesting the dog patient as a translational model for human clinical oncology. We thus generated in a previous study Can225IgG, a recombinant, caninized version of the monoclonal anti-EGFR antibody Cetuximab being clinically applied in human colorectal and head and neck cancer patients. In this study we aimed to establish radiolabeling of Can225IgG for diagnostic and theranostic approaches in dog cancer patients.

Method: Can225IgG was functionalized with diethylene triamine pentaacetic acid (DTPA) and radiolabeled with ^{99m}Tc. Stability of ^{99m}Tc@DTPA-Can225IgG was tested in canine serum and PBS. Binding properties of ^{99m}Tc@DTPA-Can225IgG to EGFR were determined using Western blot and in vitro autoradiography of canine mammary carcinoma sections.

Results: Stability testing of ^{99m}Tc@DTPA-Can225IgG revealed that after 1 h incubation in dog serum 60.5% ±1.8%, and that after 4 h 30.2% ±2,3% of the antibody had still remained intact. The radiolabeled Can225IgG recognized human and canine EGFR in Western blot, but not control antigens BSA or HER-2. In vitro autoradiography revealed binding of ^{99m}Tc@DTPA-Can225IgG to EGFR expressing regions in canine cancer tissues.

Conclusion: This study describes radiolabeling of the caninized antibody Can225IgG with ^{99m}Technetium. The suitable stability and high specificity of the radiolabeled molecule makes it an optimal candidate for the first proof-of-concept application in canine cancer patients.

1369
Analysis of short and longer term variability of nasal vs. breath condensate inflammation markers in healthy individuals

Koppen, G[1]; Janssens, H[1,2]; De Prins, S[3]; Geysen, J[1]
[1]Environmental Risk and Health, Flemish Institute of Technological Research VITO, Mol, Belgium; [2]Intensive Care Unit, University Antwerp, Antwerp, Belgium; [3]Division of Pediatric Hematology/Oncology/BMT, University of Arizona, Tuson, USA

Background: The measurement of inflammation markers in nasal mucus and exhaled breath condensate (EBC), can provide valuable information about a.o. respiratory disorders. In the current study, inflammation markers in nasal mucus and EBC were measured and the variability between sampling moments was examined.

Method: The study population consisted of healthy men ($N = 3$) and women ($N = 3$) (20–50 years). On six time points of one day, and on five different days in a 20 days period, nasal mucus and EBC were sampled. Nasal mucus was collected (during 2 min) via a polyurethane sponge in both nostrils. EBC was collected by breathing in a controlled way through a RTubeTM collection devise (Respiratory Research, USA). The inflammation markers IFN-γ, IL-1β, IL-8, IL-10, IL-13 and TNF-α were analyzed with the Meso Scale Discovery technology based on ELISA. The intra-individual variability of the measurements was examined by using repeated measures ANOVA, and calculating the intraclass correlation coefficient (ICC).

Results: All inflammation markers were well detectable in nasal mucus and this was in contrast to the measurements in EBC, in which only IL-8 and IL-13 could be detected in the majority of the samples. EBC collected for 2 min with the applied breathing technique gave a repeatable almost constant volume (300–500 μL). The collected volume of nasal mucus was more variable (10–150 μL). The intra-individual repeatability of IL-8 in EBC on one day was good (ICC of 0.49). The other inflammation markers were more variable, possibly due to technical variability of the measurement in the lower range of the ELISA method. The intra-individual repeatability of inflammation markers in nasal mucus were both good for the different sampling moments during one day (ICC between 0.50 and 0.94) and for the five different days in a 20 days period (ICC between 0.39 and 0.75).

Conclusion: The current study indicates - given the measurability and repeatability of the inflammation markers determined in nasal mucus - that collection of nasal mucus, more than EBC, is potentially more useful for assessing inflammation in the respiratory system.

1370
Availability of an independent two level quality control for in vitro extract-base and molecular-based allergy diagnostics

Villalta, D; Da Re, M; Conte, M; Martelli, P
Allergy and Clinical Immunology, Pordenone, Italy

Background: Molecular-based allergy (MA) diagnostics is increasingly entering routine care, allowing a higher accuracy in allergy diagnosis and prognosis. It is a useful approach to identify patients and triggering allergens for specific immunotherapy and to assess the risk of severe reactions in food allergy. However until now no specific quality control (QC) materials for MA were available. Aim of the study was to evaluate the availability of a commercial independent control, designed for monitor the precision of specific IgE (sIgE) detection to different crude allergen extracts, as QC for both extract-base assays and MA diagnostics.

Method: We tested with ImmunoCAP 250 (Termofisher, Uppsala, Sweden) the sIgE to the main allergenic molecules contained in the inhalant and food allergens sources (Dermatophagoides pteronissinus, cat dander, horse dander, dog dander, Cynodon dactylon, Phleum pretense, birch, mugwort, Aspergillus fumigatus, Alternaria tenuis, egg white, cow milk, peanut) declared to react with the Lyphochek Allergen sIgE Control (Bio-Rad Laboratories, USA). Lyphochek Allergen sIgE multi-analytes (15 allergens) control utilizes

human source material and it offers two distinct control levels (negative and positive).

Results: The levels of sIgE to the allergenic molecules (mean of five determinations) expressed as kUA/L were: Der p 1, 5.9; Der p 2, 5.48; Der p 10, 1.23; Pen a 1, 0.58; Fel d 1, 8.08; Equ c 1, 6.66; Can f 1, 5.05; Can f 2, 4.93; Can f 3, 19.2; Can f 5, 3.79; Cyn d 1, 7.0; Phl p 1, 6.34; Phl p 2, 0.79; Phl p 4, 5.99; Phl p 5, 2.13; Phl 11, 0.15; Bet v 1, 2.64; Bet v 2, 0.23, Bet v 4, 5.51, Bet v 6, 0.10; Art v 1, 0.25; Art v 3, 1.03; Asp f 1, 0.95; Asp f 2, 0.21; Asp f 3, 2.05; Asp f 4, 0.11; Asp f 6, 0.96; Alt a 1, 7.08; Gal d 1, 0.24; Gal d 2, 1.06; Gal d 3 0.44; Bos d 5, 0.89; Bos d 8, 6.55; Ara h 1, 0.50; Ara h 2, 0.53, Ara h 3, 0.21; Ara h 9, 1,31. The sIgE levels resulted negative (<0.1 kUA/L) for all the molecules tested in the negative Lyphochek control.

Conclusion: Lyphochek can improve lab efficiency offering in a single vial 15 allergens for testings and may be used both for the QC of sIgE to the crude extracts and to the allergenic molecules. It represents an important toll for the QC of MA diagnostics and to satisfy the regulatory requirements. Finally, with a three-year shelf life it enables a long term QC monitoring and results may be compared with peer labs worldwide by means of Unity interlab program.

1371
The importance of external valuation of quality for laboratories

De Amici, M; Trovamala, V; Torre, C; Nigrisoli, S; Desmet, N; Testa, G; Ferraro, I; Marseglia, GL
Department of Pediatrics, Foundation IRCCS Policlinico San Matteo, Pavia, Italy

Background: Quality is an important means to understand the efficiency of sanitary system when we compare patients.External valuation programs(V.E.Q) certificate the quality of laboratory. Our aim is to monitore the diagnostic activity in allergological field, comparing it with the other laboratories data of Lombardy region.

Method: For Lombardy region the V.E.Q protocol forecasts as analytes the total IgE, and specific IgE for some inhalants, food, professionals and insects poison. The samples of control are sent every twenty days in controlled temperature box in lyophilized form. Specific IgE test was performed with a fluoroimmunoenzymatic assay. Values are expressed in KUa/l, with a cut-off of 0,35. In the case of food allergy it is possible that specific IgE are not revealed because of industrial preparation, of cook and of digestion that are not present in the food at its natural status. A negative answer could be present also in ipersensitive subjects when the sample is taken too early or too late from the last allergic reaction. We could avoid the problem of false negative repeating the test two weeks after the reaction.

Results: Every year, from 2011 to 2013, the z-score percentage of intra-laboratory data are valued and grouped by quality. The great part of valuation is in acceptable interval with 94,97% of data and only the 5,53% of data is in defective interval. The acceptable interval could be subdivided into three groups: excellence, full satisfaction, acceptable. For our Laboratory the percentages are respectively 47,26%, 27,12% and 20,29%. The same method is used for inter-laboratory data obtained from different laboratories divided in different groups. The great part of valuation is in acceptable interval with 97,30% of date and only the 2,70% of date is in defective interval. The acceptable interval could be subdivided in three group: excellence, full satisfaction, acceptable. For our Laboratory the percentages are respectively 51,69%, 27,70% and 19,91%. The same good results is obtained for total IgE but with more data in defective interval for intra-laboratory and for inter-laboratory.

Conclusion: Our results are part of excellence and full satisfaction group according to other laboratories which belong to V.E.Q program. These projects are important to obtain more accurate data and to reveal possible valuation mistakes; it forecasts preventive working to improve services and maintain them constant in time.

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The usefulness of laboratory data in the clinical context

De Amici, M; Caimmi, S; Licari, A; Marseglia, A; Trovamala, V; Montalbano, C; Ruffinazzi, G; Nigrisoli, S; Marseglia, GL
Department of Pediatrics, Foundation IRCCS Policlinico San Matteo, Pavia, Italy

Background: Understanding how many times sensitizations conduce to a real allergy, could be useful for clinicians to give the correct diagnosis and therapy. Our aim is to verify the importance of laboratory data in the clinical context and to define a cut-off for total and specific IgE to distinguish between allergic and non-allergic patients.

Method: Sixty-nine patients (39 males, 30 females; mean age= 8,97 years; age range: 1–17 years) were enrolled in this study. Serum levels of total IgE were measured by a fluorescence immunoassay, while specific IgE levels were measured by immunofluorometric assay. Both tests were expressed in kU/L. A p-value ≤ 0.05 was considered statistically significant.

Results: A statistically significance ($P < 0{,}0001$) was observed between sensitized and real allergic patients. Only 2 sensitized patients (2,89%) did not develop allergy while 7 allergic patients (10,14%) did not show previous sensitizations to food recombinant allergens but they were allergic to inhalants.This result shows that laboratory data provide, in the most of cases, the correct indication to allergy development.We defined numeric scores (from 0 to 10) to describe the diagnostic and therapeutic appropriateness.In our data these scores were high (range: 4–10) and, in particular, the median values (IQR: 25th-75th percentiles) for diagnosis and therapy were, respectively, 8(7–9) and 7(5–9).Therefore, a strong relationship between scores was obtained ($P < 0{,}0001$): when the diagnosis was appropriate, the therapy was adequate too. A multiple regression analysis has been performed to predict the presence of allergy. We obtained a significant model ($P < 0.0001$) in which the result of total IgE ($P = 0.0013$) and the presence or absence of sensitization ($P < 0.0001$) resulted predictors. A Receiver Operating Curve analysis has been performed for total IgE, according to the presence or the absence of allergy and showed the best cut off at 72,1 kU/L (area under the curve = 0.869; sensitivity = 87.23; specificity = 81.82, $P = 0.0001$). Another ROC analysis has been performed for specific IgE which showed the best cut-off at 2.7 kU/L (area under the curve = 0.866; sensitivity = 80.85; specificity = 100, p = 0.0001).

Conclusion: A correct diagnosis of allergy is important to prevent any reactions and laboratory data about sensitizations could give the right indication for allergy development. Also defining numeric scores could be useful in order to increase the appropriation.

1373
Accreditation of allergen-specific IgE determination under the EN ISO 15189 standard: a French strategy

Lambert, C[1]; Sarrat, A[2]; Bienvenu, F[3]; Brabant, S[4]; Nicaise Roland, P[5]; Alyanakian, M-A[6]; Apoil, P-A[7]; Capron, C[8]; Couderc, R[9]; Evrard, B[10]; Jaby, D[11]; Hémont, C[12]; Lainé, C[13]; Lelong, M[14]; Mariotte, D[15]; Martinet, J[16]; Rénier, G[17]; Sainte-Laudy, J[18]; Tabary, T[19]; Treiner, E[20]; Uring-Lambert, B[21]; Vigneron, C[22]; Vivinus, M[23]; Withuhn, F[24]; Vitte, J[25,26]; AllergoBioNet
[1]CHU de Saint-Etienne, Immunology Laboratory, Saint-Triest en Jarez, France; [2]CHU de Bordeaux, Immunology Laboratory, Bordeaux, France; [3]CHU de Lyon, Immunology Laboratory, Lyon, France; [4]CHRU de Lille, Immunology Laboratory, Lille, France; [5]APHP Hôpital Bichat, Immunology Laboratory, Paris, France; [6]APHP Hôpital Necker - Enfants Malades, Immunology Laboratory, Paris, France; [7]CHU de Toulouse, Hôpital

de Rangueil, Immunology Laboratory, Toulouse, France; [8]APHP Hôpital Ambroise Paré, Immunology Laboratory, Boulogne BIllancourt, France; [9]AP-HP - Hôpital d'Enfants Armand Trousseau, Biochemistry and Immunology Laboratory, Paris, France; [10]CHU de Clermont-Ferrand, Immunology Laboratory, Clermont-Ferrand, France; [11]CH de Saint-Denis, Biochemistry and Immunology Laboratory, Saint-Denis, France; [12]CHU de Nantes, Immunology Laboratory, Nantes, France; [13]CHU de Rennes, Immunology Laboratory, Rennes, France; [14]CH Le Mans, Biochemistry Laboratory, Le Mans, France; [15]CHU de Caen, Immunology Laboratory, Caen, France; [16]CHU de Rouen, Immunology Laboratory, Rouen, France; [17]CHU d'Angers, Immunology Laboratory, Angers, France; [18]CHU de Limoges, Immunology Laboratory, Limoges, France; [19]CHU de Reims, Immunology Laboratory, Reims, France; [20]CHU d'Amiens, Immunology Laboratory, Amiens, France; [21]CHU de Strasbourg, Immunology Laboratory, Strasbourg, France; [22]CHU de Tours, Immunology Laboratory, Tours, France; [23]CHU de Nice, Immunology Laboratory, Nice, France; [24]CHU de Poitiers, Immunology Laboratory, Poitiers, France; [25]Assistance Publique Hôpitaux de Marseille, Immunology Laboratory, Marseille, France; [26]Aix-Marseille University, Marseille Medical School, Marseille, France

Background: Allergen-specific serum immunoglobulin E detection and quantification have become an important step in allergy diagnosis and follow-up. In line with the current trend of laboratory test accreditation to international standards, we set out to design and assess an accreditation procedure for allergen-specific serum IgE.
Method: Method validation according to the accreditation procedure under the EN-ISO 15189 standard was carried out for allergen-specific immunoglobulin E determination using the fluoroimmunoenzymatic method ImmunoCAP® (Thermo Fisher Scientific, Phadia). Data were produced by 25 hospital laboratories in France. A total of 29 allergen specificities including mixes, extracts, and molecular allergens were assayed. Allergen-specific serum immunoglobulin E concentrations ranged from 0.1 kU_A/L to 100 kU_A/L.
Results: Repeatability, reproducibility, and accuracy results fulfilled method validation criteria for automated laboratory tests and proved similar irrespective of the allergen specificity, allergen-specific serum immunoglobulin E concentration, or individual laboratory.
Conclusion: Allergen-specific serum immunoglobulin E determination with the fluoroimmunoenzymatic method ImmunoCAP® is a highly repeatable, reproducible, and accurate method irrespective of the allergen specificity, the concentration of specific IgE and the laboratory performing the determination.

The FEIA method may therefore be considered as a single analyte assay in view of the EN ISO 15189 accreditation procedure.

1374
Use of filter disks or sinus packs for single and repeated measurement of total and house dust mite specific IgE in nasal secretions

Berings, M[1]; De Ruyck, N[1]; Holtappels, G[1]; Bachert, C[1,2]; Gevaert, P[1]
[1]Ghent University, Upper Airway Research Laboratory, Ghent, Belgium; [2]Karolinska Institutet, Division of ENT Diseases, Clintec, Sweden

Background: There is evidence for local production of IgE in the nasal mucosa of patients with allergic rhinitis (AR). Collection of nasal secretions (NS) by validated methods for measurement of local IgE is of great interest. We aimed to compare two methods for collection of NS - sinus packs (SP) and filter disks (FD) - and to evaluate the suitability of using a fixed dilution instead of a fixed volume when processing.
Method: In a first experiment, NS were collected by means of FD and SP in 15 HDM AR patients and 15 controls. During processing, saline solution was added in order to mobilize the NS. For each sample the volume to be added was calculated in order to obtain a fixed dilution. In a second experiment, NS from 2 HDM AR patients were collected by means of FD and SP on 4 consecutive days. This experiment was performed once with fixed volume and once with fixed dilution. At last, repeated collection of NS was performed by means of FD and SP in 5 HDM AR patients on several time points before and during HDM SCIT. Ig levels were measured with the UniCap system.
Results: In the first experiment, levels of total IgE and HDM sIgE were significantly higher in HDM AR patients compared to controls. With the FD, total IgE and HDM sIgE were below the detection limit (BDL) in 2 and resp. 6 out of 15 AR patients. With the SP, total IgE and HDM sIgE were BDL in 3 and resp. 4 out of 15 AR patients. When comparing FD and SP in the same patients on 4 consecutive days, more variation in IgE levels was seen with the FD. When comparing a fixed volume to a fixed dilution, the latter is more time consuming and prone to error. The fixed dilution brings along a risk of excessive dilution when larger volumes are added, and insufficient mobilization of NS when smaller volumes are added. In the third experiment, an increase in HDM sIgG and sIgG4 was observed in serum of 4 resp. 3 out of 5 patients during HDM SCIT. In 3 resp. 2 out of 5 patients, an increase in HDM sIgG and sIgG4 was also observed in their NS collected by means of SP.
Conclusion: Overall, SP seem to be superior to FD in many aspects. However, SP cause stimulation of the nasal mucosa, making them not suitable for serial measurements on the same day. Fixed dilution raised several difficulties and was not superior to a fixed volume. Using the SP with addition of a fixed volume of saline seems to be the most reproducible method to measure total and allergen specific IgE, IgG, and IgG4 in clinical trials.

1375
Biological standardization of *Ambrosia elatior* allergen extract to determine the biological activity in HEP units

Riffelmann, F[1]; Sager, A[2]; Nieto, E[3]; Erbiti, L[3]
[1]Fachkrankenhaus Kloster Grafschaft, Schmallenberg, Germany; [2]LETI Pharma GmbH, Witten, Germany; [3]Laboratorios LETI, S.L., Madrid, Spain

Background: In the past years ragweed (Ambrosia elatior) became of interest in Germany since an increasing distribution of this type-1 allergy causing plant was observed in Europe. Therefore we investigated the concentration of a native *Ambrosia elatior* extract inducing the same wheal size as provoked by 10 mg/mL Histamine dihydrochloride.
Methods: Titrated Skin Prick test biological study. Five concentrations of *Ambrosia elatior* allergen extract- at 15, 10, 1.0, 0.1 and 0.01 mg/mL - together with a positive and negative control, were tested in every patient in duplicate on the volar surface of the forearm. The tests were performed at the study site and all patients remained in the medical rooms under observation at least 30 min after the application of the Titrated Skin Prick test. The primary variable was the wheal size area (mm^2) on the skin at the site of the puncture during the immediate phase.
Results: A total of 30 patients (mean age 30 years) were enrolled. A total number of 30 patients received the study medication (ITT population). Nine were excluded from the PP population ($n = 21$) since they did not meet Nordic Guideline criteria. The wheal data of the 21 patients included were analysed to determine the primary variable in the PP population and ITT population, which coincided with the Safety population. 23.86 mg of *Ambrosia elatior* allergen extract elicit a wheal size equivalent to that of histamine 10 mg/mL.
Conclusions: The biological activity of the *Ambrosia elatior* allergen extract is equivalent to 10 HEP = 23.86 mg. The administration of the study medication by Skin Prick testing was well tolerated and safe.

1376
A comprehensive analysis of natural and recombinant allergens from banana prawn (*Fenneropenaeus merguiensis*) using proteomics, for improved allergy diagnostics

Waltenspiel, B[1,2]; Kamath, SD[1,2,3]; Koeberl, M[1,2]; Saptarshi, SR[1,2]; Rolland, JM[4]; O'Hehir, RE[4]; Lopata, AL[1,2,3]
[1]James Cook University, Centre for Biodiscovery and Molecular Development of Therapeutics, Townsville, Australia; [2]James Cook University, Molecular Immunology Group, Townsville, Australia; [3]Australian Institute of Tropical Health and Medicine, Townsville, Australia; [4]Department of Allergy, Immunology and Respiratory Medicine, The Alfred Hospital & Monash University, Melbourne, Australia

Background: Shellfish allergy, and in particular prawn allergy, is amongst the leading causes of IgE-mediated food hypersensitivity. Current *in vitro* diagnostic platforms account for only a few species of prawns which are derived from the northern hemisphere, and often not consumed in the tropical regions of the world. This study aims to identify and characterize the major allergens from a commonly eaten prawn species, the banana prawn (*Fenneropenaeus merguiensis*) using a comprehensive allergenomic approach for improved allergy diagnostics in the tropics.
Method: Crude allergen extracts were prepared from banana prawns for IgE binding analysis. The prawn allergens were identified using in-gel tryptic digestion and mass spectrometric analysis. Using specific primers, gene sequences of the identified allergens were elucidated using RNA extraction and cDNA sequencing. Recombinant prawn allergens were expressed in *E.coli* and purified using affinity chromatography and characterized for their secondary structure using circular dichroism. Serum samples from fifteen patients with confirmed clinical reactivity to prawns were used to analyze the serum IgE antibody binding using immunoblotting to the natural and recombinant prawn allergens.
Results: Five putative banana prawn allergens were identified by mass spectrometric analysis. Furthermore, these prawn allergens; arginine kinase, myosin light chain, triose-phosphate isomerase, tropomyosin and sarcoplasmic Ca2 + binding protein were successfully sequenced and published in Genbank. IgE antibody binding was demonstrated to purified recombinant prawn allergens, ranging from 6% to 80% patient reactivity.
Conclusion: Current *in vitro* diagnostics for prawn allergy quantifies IgE antibodies against crude extracts of non-relevant species, which may lead to low sensitivity and specificity. In this study, a comprehensive allergen analysis was conducted for banana prawns, which are commonly consumed in the Asia-Pacific region. Further investigations involving larger patient cohort to investigate the prevalence among allergic adults and children are necessary for the development of improved diagnostics for prawn allergy.

1377
In-silico bioinformatics approach for the identification and characterization of allergens from the Pacific oyster (*Crassostrea gigas*)

Nugraha, R[1,2]; Zenger, K[3]; Kamath, SD[1,2]; Lopata, AL[1,2]
[1]Centre for Biodiscovery and Molecular Development of Therapeutics, James Cook University, Townsville, Australia; [2]Molecular Immunology Group, James Cook University, Townsville, Australia; [3]College of Marine & Environmental Sciences, James Cook University, Townsville, Australia

Background: Utilizing crude protein extracts is currently inadequate to reveal most mollusk IgE antibody binding allergens. Currently, only three proteins - tropomyosin, arginine kinase, and paramyosin - have been fully identified and characterizes as mollusk allergens. Bioinformatics analysis could provide a powerful and versatile tool for the in-depth molecular characterization of biological species. Bioinformatics approaches have recently been used to identify putative allergens in rice, chickpea and Johnson grass pollen. Therefore this study was aimed to identify putative and cross-reactive allergens using *in-silico* analysis of the transcriptome from the Pacific oyster (*Crassostrea gigas*).
Method: Several allergen sequences related to shellfish allergy including from Black tiger prawn, lobster and abalone were documented from different databases. TBLASTN analysis was performed on these sequences against the genomic database of Pacific oyster to retrieve putative and cross-reactive allergen sequence. The retrieved sequences were used to generate phylogenetic trees using the Neighbor joining method in Mega6 software, after association using the MUSCLE multiple alignment program. Following this, structure model of the proteins were built using Chimera 1.9 program.
Results: Based on amino acid sequence similarity, cross-reactive allergens and several putative allergen genes were identified after *in silico* analysis of the genomic data of Pacific oyster. Some of the putative oyster allergens demonstrated the potential to cross-react to crustacean allergens, based on conserved domains and similar structural features. This method also revealed the presence of various isoforms of the oyster allergens. The phylogenetic trees of the allergens demonstrate that the Pacific oyster clusters with the corresponding allergens from other mollusk and is grouped separately from crustaceans.
Conclusion: Bioinformatics approaches reveal several putative and cross reactive allergens that have not been fully elucidated using immuno-chemical IgE-based methods. These findings are of importance for the development of specific allergy diagnostics for molluscs and other allergens. *In-silico* approaches, in combination with recombinant allergen generation, will be an eminent method for the comprehensive assessment of allergenicity and opens an additional path for efficient allergy diagnostics.

1378
Identification of the major allergens of hymenoptera venom through mass spectroscopic techniques and sequence matching

Hutchings, JW; Mwange, JD; Starchenka, S; Hewings, SJ; Skinner, MA
Allergy Therapeutics Plc, Worthing, UK

Background: The stings by insects of the order Hymenoptera can cause systemic, sometimes life threatening, allergic reactions. Hymenoptera stings are some of the most common triggers of anaphylaxis with the predisposition to systemic anaphylactic sting reactions occurring in 0.6–7.5% of the populous of European countries. A large proportion of the allergenicity of these venoms is caused by several major allergens; a series of proteins with the majority of molecular weights between 10–50 kDa. A single major allergen can form up to 15% of the dry weight of the venom and many have enzymatic effects that further increase the potential allergenicity of the venom. At AT we have identified these major allergens for both aqueous extractions of *Vespula spp*. and *Apis mellifera* venoms.
Method: Aqueous extractions of *Vespula spp*. and *Apis mellifera* venoms were prepared before separation via SDS-PAGE, trypsin digestion and mass spectrometry. The resulting peptide fragments were then searched against well-established protein databases using the MASCOT search engine in order to confirm the presence of hymenoptera major allergens.
Results: All of the samples returned good matches to proteins within the database, with >20% sequence coverage and high peptide and protein scores according to the MASCOT search tool. For both *Vespula spp*. and *Apis mellifera* venoms group 1, 2 and 5 allergens were identified.
Conclusion: The presence of the most crucial major allergens to Hymenoptera venom sensitisation have been identified through mass spectrometric analysis and protein matching against well-established protein databases. This enhanced charac-

terisation through identification of major relevant allergens in venom preparations provides a consistent measure of batch-to-batch quality when manufacturing allergen products.

1379
Breastfeeding is effective in crying infants during skin prick testing

Bostanci, I; Corut, N; Senel, G; Ozmen, S
Department of Pediatric Immunology and Allergy, Dr Sami Ulus, Ankara, Turkey

Background: Skin prick testing (SPT) is often applied in the diagnosis of varying allergic diseases. There have been no studies into whether or not breastfeeding may be effective in reducing pain.
Methods: In prospective, cross-sectional study, patients were randomly divided into two separate groups. The first group of infants (32) was breastfed, the second group (32) wasn't breastfed prior to SPT.
Results: There was no difference between the two groups age, gender and other socio-demographic characteristics ($P > 0.05$). The percentage of crying among non-breastfed infants prior to testing was greater than among those who were breastfed ($P = 0.002$). During SPT, the pain scale values were significantly lower among the breastfed infants and this was independent of any histamine response or skin prick test positivity ($P = 0.00$).
Conclusion: It would appear that any sensitivity to pain felt by infants during SPT may be reduced if the tests are performed soon after breastfeeding.

1378-A
Study of the changes of lipid composition of red blood cell membranes in patients with atopy

Djambekova, G[1]; Ismailova, E[2]
[1]Specialized Therapy Centre, Allergology and Immunology, Tashkent, Uzbekistan; [2]Tashkent Pediatric Medical University, Medical, Tashkent, Uzbekistan

Background: Atopic Dermatitis (AtD) is a disease associated with food allergy, asthma, allergic rhinitis. Oftentimes, when respiratory allergy (RA) is developed, the diagnosis is formulated as dermo-respiratory syndrome (DRS), which leads to belated diagnostics of bronchial asthma. The objective: researching the lipid composition of red cell membranes in patients with skin and respiratory manifestations of allergy.
Method: Thirty-two patients with immunologically confirmed atopy (total and specific Ig E, RIDA AlergyScreen test) aged 15–20 have been examined; the control group was comprised of 14 healthy individuals.
Results: In cases of AtD activity significant defects in lipid composition of red cell membranes have been identified. Reduction of the major phospholipid fractions (phosphatidylcholine and phosphatidylethanolamine) as well as increase of their toxic lisoforms have been marked which indicates increase of phospholipase activity. Imbalance of phospholipid fractions is associated with reduced expression of b2 adrenoreceptors, which maintains permanently high cutaneous sensibility, causes vegetative disorders of the skin and organism as a whole. In patients with active RA symptoms, the changes in the lipid composition of the membranes were identical, which confirms patogenetic unity of the process. Complex therapy including vitamins and antioxidants did not lead to normalization of the lipid matrix. Significant improvements in indicators were achieved by the use of essential phospholipids (polyenylphosphatidilcholine 1800 mg per day).
Conclusion: Research of red cell membranes can be recommended for early diagnostics of atopy, prognostication of relapses and severe forms of the disease. Further research of the membrane protection possibilities of essential phospholipids for atopic diseases is promising.

1380
Gene expression profile assessement using RT-PCR in patients with mastocytosis

Górska, A[1]; Niedoszytko, M[1]; Chełmińska, M[1]; Skrzypski, M[2]; Maciejewska, A[3]; Pawłowski, R[3]; Słomiński, J[4]; Jassem, E[1]
[1]Department of Allergology, Medical University of Gdansk, Gdańsk, Poland; [2]Department of Oncology and Radiotherapy, Medical University of Gdansk, Gdańsk, Poland; [3]Department of Forensic Medicine, Medical University of Gdansk, Gdańsk, Poland; [4]Department of Pneumonology, Medical University of Gdansk, Gdańsk, Poland

Background: Mastocytosis is a group of disorders characterized by an abnormal proliferation and accumulation of atypical mast cells in different organs including bone marrow, skin, liver, spleen, lymph nodes and gastrointestinal tract. Symptoms resulting from the activation and release of mediators from the mast cells are frequent among patients with mastocytosis. The most severe - anaphylactic reactions occur in 30% of all patients with mastocytosis and in 50% of patients with systemic mastocytosis.
Objective: The aims of this study were to find differences in gene expression in peripheral blood cells of patients with mastocytosis compared to healthy controls and to analyze any differences in gene expression in peripheral blood cells between patients with insect venom allergy (IVA) compared to patients without anaphylaxis in history.
Method: The study group included 57 adult patients with mastocytosis who were qualified to assess gene expression analysis using RT-PCR (TaqMan® Array Micro Fluidic Cards, Applied Biosystems). The control group included 19 healthy persons.
Results: Significant differences in gene expression were found for B3GAT1 ($P = 0.006$) and ITGB1 ($P = 0.02$) in mastocytosis patients compared to controls. Furthermore significant differences were found in gene expression for B3GAT1 ($P = 0.003$) and ITGB1 ($P = 0.02$) in patients with IVA compared to patients without anaphylaxis in the medical history.
Conclusions: We found differences in gene expression in peripheral blood cells of patients with mastocytosis compared to healthy controls. Furthermore these differences were also found in patients with a history of IVA compared to those without anaphylaxis. We assume that gene expression assessment may be useful in clinical practice to predict the presence of mastocytosis and the risk of anaphylaxis on insect venom in patients with mastocytosis.

1381
The analysis of the whole genom expression profiles in peripheral and bone marrow blood of mastocytosis patients

Niedoszytko, M[1]; Gorska, A[1]; Jassem, E[1]; van der Vlies, P[2]; Gruchała-Niedoszytko, M[3]; Oude Elberink, H[4]
[1]Medical University of Gdansk, Allergology, Gdańsk, Poland; [2]University Medical Center Groningen, Genetics, Groningen, the Netherlands; [3]Medical University of Gdansk, Clinical Nutrition, Gdańsk, Poland; [4]University Medical Center Groningen, Allergology, Groningen, the Netherlands

Background: Mastocytosis is a myeloproliferative disorder with a high risk of anaphylaxis. The routine diagnosis includes bone marrow analysis and serum tryptase analysis. A clinical tool using gene expression in the peripheral blood could be a usefull method in patients with unclear diagnosis. Our previous study shown clear differences in gene expression in the peripheral blood of mastocytosis patients, however we did not know if the results from the peripheral blood may be related to the bone marrow gene expression differences. The aim of the study was to validate the the gene expression profile in the Polish patients with mastocytosis. Additionally we wanted to compare the results of the bone marrow and peripheral blood gene expression.
Method: The group of 13 adult patients with mastocytosis and 49 controls were

qualified to compare gene expressions between peripheral blood and bone marrow aspirate RNA samples. The bone marrow and peripheral blood was analysed in mastocytosis patients. The peripheral blood was studied in the control group. Whole genome gene expression analysis was performed on RNA samples isolated from all blood cells in whole blood using the Illumina Human HT-12_V3_expression arrays. Data analysis was performed using GeneSpring.

Results: Significant results were found both in the comparison of the peripheral blood of the control and mastocytosis group and the bone marrow with peripheral blood. The analysis of the peripheral blood replicated the significant difference in the gene expression, additionally significant differences among the bone marrow and the peripheral blood were found in 7689 of the analysed transcripts (Benjamin Hochberg test). A fold change difference > 2 in gene expression was found in 943 of the 32379 analysed transcripts, among them 361 were overexpressed and 582 underexpressed. However the results from the expression of the crucial genes from the peripheral blood may related to the bone marrow results.

Conclusion: We found significant differences in whole genome expression in peripheral blood cells compared to bone marrow aspirate. We assume that gene expression assessment might be a useful tool to predict the presence of mastocytosis in the future.

Poster Session Group III - Green TPS 47: Epidemiology and treatment of rhinitis and conjunctivitis:

1382
Comparison of self-reported allergic rhinoconjunctivitis, rhinitis symptoms and nasal polyps between Finland, Sweden, and Estonia

Pallasaho, P[1]; Kainu, A[2]; Sovijärvi, A[3,4]; Lundbäck, B[5]
[1]Finnish Institute of Occupational Health, Helsinki, Finland; [2]HUCH, Heart and Lung Center, Vantaa, Finland; [3]HUCH, Medical Imaging Center, Helsinki, Finland; [4]Helsinki University, Helsinki, Finland; [5]Krefting Research Centre, Gothenburg, Sweden

Background: We aimed to compare different types of self-reported nasal symptoms comparing data from a population based epidemiological study, the FinEsS study, performed in Finland, Sweden, and Estonia

Method: Adult subjects representing the general population in each country underwent a structured interview on respiratory symptoms and diseases, smoking habits, allergic conditions among other items by a physician involved in the study. Number of interviewed subjects was 1338 in Helsinki, 1953 in Sweden, and 1430 in Estonia.

Allergic rhinoconjunctivitis was defined as an affirmative answer to the question:" Do you have or have you ever had hay fever or allergic rhinitis or allergic conjunctivitis?"

Rhinitis symptoms were assessed by questioning "Are you often bothered by a blocked nose or a runny nose?", and nasal polyps by asking "Do you have or have you had nasal polyps?"

Results: Self-reported allergic rhinoconjunctivitis was reported by 36.3% in Finland, 29.5% in Sweden, and 24.1% in Estonia ($P < 0.001$). Respectively, rhinitis symptoms were reported by 36.6% in Finland, 28.2% in Sweden, and 38.3% in Estonia ($P < 0.001$). Smoking habits were not associated with the occurrence of rhinitis symptoms. Nasal polyps were declared by 4.9% in Helsinki, 13.0% in Sweden, and 6.8% in Estonia ($P < 0.001$). Allergic rhinoconjunctivitis was more common among women, 33.4%, than men, 25.7% ($P < 0.001$). No gender difference was found for rhinitis symptoms, but nasal polyps were more common among men, 10.3%, than women, 7.5% ($P = 0.001$).

Conclusions: Self-reported allergic rhinoconjunctivitis was most common in Finland, whereas rhinitis symptoms were most often reported in Estonia, and nasal polyps in Sweden. Nasal symptoms were common in each of the countries and would probably deserve more attention in diagnostics and treatment.

1383
Exhaled nitric oxide in adolescence in relation to rhinitis symptoms 15 years later

Malinovschi, A[1]; Janson, C[1]; Kalm-Stephens, P[2]; Nordvall, L[2]; Alving, K[2]
[1]Medical Sciences, Uppsala University, Uppsala, Sweden; [2]Women's and Children's Health, Uppsala University, Uppsala, Sweden

Background: We have previously reported that high exhaled nitric oxide (FeNO) levels in adolescence predicted new-onset rhinitis within a timeframe of 4 years (Malinovschi *et al*. Clinical and Experimental Allergy 2012; 42:433–40). However, the relationship between FeNO in adolescence and rhinitis in adulthood is not known.

Method: FeNO at 100 mL/s was measured during 1998–1999 in 959 adolescents aged 13–14 years, and the subjects responded to a questionnaire on rhinitis symptoms. A total of 413 subjects (56.4% women) responded to the same questionnaire in 2014 (15 years later). Current rhinitis was defined as having rhinitis symptoms during the 12 months prior to administration of the questionnaire, in the absence of a cold. The prevalence of rhinitis was 25.4% at baseline and 48.6% at follow-up.

Results: A total of 120 of 308 subjects had incident rhinitis, and these subjects had similar baseline FeNO (GM (95% CI) as subjects without rhinitis at both timepoints (n = 188): 4.3 (3.6, 5.1) *vs* 4.2 (3.6, 4.8) ppb, $P = 0.77$. Further, no significant difference in baseline FeNO was found between subjects with persistent rhinitis (n = 80) *vs* those with remission of rhinitis (n = 25): 5.9 (4.5, 7.6) vs 4.8 (3.4, 6.8) ppb, $P = 0.43$. However, subjects with persistent rhinitis ($P = 0.02$), but not subjects with remission of rhinitis ($P = 0.49$), had higher FeNO levels compared with subjects without rhinitis at both timepoints.

Conclusion: Higher exhaled nitric oxide levels in adolescence were not related to incident rhinitis within 15 years. This is in contrast to our previous findings on incidence of rhinitis over a four-year period, and may relate to different inflammatory mechanisms behind new-onset rhinitis in adolescence and adulthood. The clinical importance of higher values of baseline FeNO in subjects with persistent rhinitis *vs* subjects without rhinitis at both timepoints remains to be established.

1385
Frequency, intensity and impact of ocular symptoms in allergic rhinitis: FIRE study

Maigret, P[1]; Fontaine, JF[2]; Elias Billon, I[1]; Allaert, F[3]
[1]Menarini, Medical Management, Rungis, France; [2]Cabinet d'Allergologie, Reims, France; [3]Department of Biostatistics, Chair for Medical Evaluation, Dijon, France

Backgroud: The purpose of the study was to describe the frequency, intensity and impact of ocular symptoms in allergic rhinitis and identify the existence of a specific profile of patients with major ocular symptoms.

Methods: Cross-sectional observational study conducted in daily practice. Ocular involvement was assessed by the TSSS score (Total Score Subjective Syndrome) and the score TOSS (Total Ocular Sign Score) and quality of life by Mini RQLQ. The identification of the profiles was performed by logistic regression analysis and cluster analysis.

Results: 2719 patients aged 38.0 ± 14.0 among whom 53.1% of women were analysed. 22.4% had mild intermittent rhinitis, 15.0% moderate to severe intermittent rhinitis, 13.3% mild persistent rhinitis and 49.2% moderate to severe persistent rhinitis. Their PAREO score was 1.9 ± 0.6. Their Toss score was 41.5 ± 22.8 in 100,

their TSS score was 6.4 ± 3.3 in 15 and 25.9% of them had a value > 8 corresponding to a major symptomatology. Cluster analysis identified among all patients the existence of a homogeneous group of patients characterized by a more significant ocular involvement (TSSS: 8,5 ± vs 4,6 ± 2,7 $P < 0.0001$; TOSS: 60,3 ± 16.0 vs 25,8 ± 14.1 $P < 0.0001$) whose rhinitis was more frequently persistent with a moderate to severe intensity (61.4% vs 39.0% $P < 0.0001$), and with a greater impairment of the quality of life (3.5 ± 1.0 vs 2.5 ± 1.0 $P < 0.0001$). The logistic regression analysis confirmed these data showing also that pollen but also fungal spore allergens are more frequently identified. In these patients the practitioners more frequently associated intranasal corticosteroids

(73.9% vs 67.6% $P < 0.001$) and cromones (76.0% vs 52.6% $P < 0.0001$) with oral H1 antihistamines,

Conclusion: The association of rhinitis and ocular symptoms could be a frequent and specific entity requiring a specific treatment combining oral H1 antihistamines and cromones.

1386
Severe allergic rhinitis is associated with the use of emergency care

Salo, T[1]; Kauppi, P[1]; Peura, S[2]; Salimäki, J[2]; Maasilta, P[3]

[1]Helsinki University Central Hospital, Respiratory Diseases and Allergology, Helsinki, Finland; [2]Association of Finnish Pharmacies, Helsinki, Finland; [3]Helsinki University Central Hospital, Meilahti Triangle Hospital, Helsinki, Finland

Background: As a part of The Finnish Allergy Programme 2008–18 the survey of allergy symptoms, use of medication and health care services was carried out.

Method: This was a questionnaire study to those seeking for allergy or asthma medication in pharmacies all across Finland during one week in September 2010. The respondents were 1114 patients with self-reported physician diagnosed allergic diseases with a mean age of 47 years (SD 18.5 years, 5–75 years). In this study, we examined symptom severity (Rhinasthma questionnaire and self-reported severity with the numeric rating scale, NRS, from 0 to 10) and use of health care services in allergic rhinitis patients.

Results: Of 277 patients with a mean age of 45 years (SD 17.7) had self-reported physician diagnosed severe allergic rhinitis. 79.4% of these were women. In the last 12 months, 8.3% of the patients with severe allergic rhinitis had emergency care because of allergies compared to 4.2% of the controls and all patients ($P = 0.023$). Only 3.0% of the patients with severe allergic rhinitis had received specific immunotherapy in the past 12 months, but 31.9% had used per oral steroids as short courses and 2.5% regularly. In the total study population, activity restriction domain (correlation 0.38, $P < 0.001$) and nasal symptoms (correlation 0.44, $P < 0.001$) of Rhinasthma questions correlated best with NRS score.

Conclusion: Severe allergic rhinitis is associated with use of emergency care and even regular use of per oral steroids. Specific immunotherapy and new treatment options should be used more often to treat severe allergic rhinitis patients.

1387
Prevalence of allergic rhinitis in 3 to 6-year-old children in Chiba city (urban area), Japan

Yamaide, F[1]; Inoue, Y[1]; Okamoto, Y[2]; Shimojo, N[1]

[1]Department of Pediatrics, Graduate School of Medicine, Chiba University, Chiba, Japan; [2]Department of Otorhinolaryngology and Head and Neck Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

Background: The sequential development of allergic diseases (beginning with food allergy and atopic dermatitis followed by asthma and allergic rhinitis (AR)) during early childhood is often referred to as the allergy march. Recently, the number of school-age children with AR has shown to increase in Japan. But early onset of AR is poorly described, and it remains unknown about the prevalence of AR in young children.

Objective: We aim to evaluate the prevalence, clinical characteristics, and treatment of AR in a population of 3 to 6-year-old children in Chiba city (urban area), Japan.

Method: A total of 13,963 children aged 3 to 6 years in all 84 kindergartens of Chiba city, Japan were surveyed. Prevalence of symptoms of AR was assessed using a modified version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.

Results: A total of 9822 (70.3%) questionnaires were returned for evaluation (sex: Male 50.5%, Female 49.5%; age 3y = 2.3%, 4y = 31.7%, 5y = 35.1%, 6y = 30.9%). The prevalence of lifetime, current and physician-diagnosed AR were 54.1%, 50.7% and 37.3%, respectively. The prevalence of AR was higher in males than that in females (cf. physician-diagnosed AR; 40.6% vs. 33.6%, $P < 0.05$) and increased with age (cf. physician-diagnosed AR; 3y = 18.5%, 4y = 28.3%, 5y = 37.3%, 6y = 46.7%).

[Prevalence of allergic rhinitis]

	3y (%) (M:F)	4y (%) (M:F)	5y (%) (M:F)	6y (%) (M:F)
Lifetime AR	48.0 (52.7:41.8)	50.0 (53.5:46.5)	54.0 (56.6:51.2)	59.1 (63.3:55.0)
Current AR	44.5 (47.3:40.6)	47.3 (50.7:43.9)	50.5 (53.3:47.6)	55.1 (59.4:50.9)
Physician-diagnosed AR	18.5 (19.2:17.4)	28.3 (31.0:25.1)	37.3 (39.9:34.2)	46.7 (51.7:41.2)

Many children showed AR symptoms during September and April, especially in February and March (cedar pollen allergy season). About 70% of children with AR visited clinic or hospital, but more than half of them were dissatisfied with their treatment.

Conclusion: The prevalence of AR symptoms was high and starting early in life.

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Antihistamines and driving ability: evidence from 30 years Dutch on-road driving research

Verster, JC[1,2]; van de Loo, AJAE[1]; Garssen, J[1,3]

[1]Division of Pharmacology, Utrecht University, Utrecht, the Netherlands; [2]Center for Human Psychopharmacology, Swinburne University, Melbourne, Australia; [3]Nutricia Research, Utrecht, Netherlands

Background: Since all antihistamines are capable of crossing the blood-brain barrier, they may also cause sedation which may impair daily activities such as driving a car. The purpose of this review was to examine the effects of antihistamines on driving ability.

Method: A literature search revealed 18 double-blind placebo-controlled clinical trials that applied the on-road highway driving test. In this test, subjects are instructed to drive 100-km on a public highway with a steady lateral position and a constant speed (95 km/h). Primary outcome measure is the Standard Deviation of Lateral Position (SDLP, cm), i.e. the weaving of the car.

Results: The literature search yielded 18 clinical trials. At therapeutic doses, a single dose of diphenhydramine, emedastine and hydroxizine impaired driving comparable or greater than the effects of BAC 0.08%. Clemastine, triprolidine, mizolastine, acrivastine, dexchlorpheniramine CR and mequitazine impaired driving performance to the same extent as BAC 0.05%. For mizolastine significant impairment was only seen after higher than therapeutic doses. Results for cetirizine were mixed, illustrating the drug has the potential to impair driving performance, especially in sensitive subjects. Terfenadine, loratadine,

levocetirizine, desloratadine, ebastine, bilastine fexofenadine and rupatadine showed no driving impairment in the standard driving test after acute administration of their recommended dose. Several studies examined subchronic effects of antihistamines on driving performance. After 4 days of daily treatment significant driving impairment was found for emedastine (2 and 4 mg bid), diphenhydramine (50 mg), clemastine (2 mg bid), triprolidine (5 mg bid), after 5 days of ebastine (30 mg), and after 8 days of hydroxyzine (50 mg). Mixed results were found for cetirizine (10 mg), terfenadine (120 mg) and loratadine (20 mg). No significant differences from placebo were observed after 4 days of subchronic treatment with triprolidine (10 mg), levocetirizine (5 mg), fexofenadine (up to 120 mg), and after 8 days of daily treatment with dexchlorpheniramine (6 mg), bilastine (20 and 40 mg), and mequitazine (10 mg).

Conclusion: First- and second-generation antihistamines may significantly impair driving performance. The newer antihistamines such as levocetirizine and fexofenadine that cross to blood brain barrier to a much lesser degree do not show clinically relevant sedation or driving impairment.

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Epidemiology of vernal keratoconjunctivitis in a Spanish pediatric population

Villalón García, ÁL[1]; Alarcón Tomás, M[2]; Vásquez Bautista, AA[1]; Rodriguez Cabreros, M[1]; Martín Carribero, R[2]; Rodriguez Mosquera, M[1]
[1]Hospital Universitario Puerta de Hierro de Majadahonda, Allergy, Madrid, Spain; [2]Hospital Universitario Puerta de Hierro de Majadahonda, Pediatric Ophthalmology, Madrid, Spain

Background: Vernal keratoconjunctivitis (VKC) is a relative rare, chronic allergy inflammatory disease of the ocular surface. Affecting mainly children, it is an IgE and T cells-mediated disease without a totally identified pathogenic mechanism. Several therapeutic measures are required to control the signs and symptoms of the disease.

Method: A retrospective, observational study was conducted with children diagnosed with VKC in the last two years at Majadahonda (Madrid) University Hospital "Puerta de Hierro". The aim of the study is to present the epidemiology of VKC in our population. For that purpose, data such as age, sex, race, atopic familiar history, asthma, rhinitis or dermatitis personal history and treatment with cyclosporine A (CsA) or inmunotherapy were analyzed.

Results: Data of 30 patients were recorded: 4 female (13%) and 26 male (27) with mean age of 10 (range 4–18). 29 of them (97%) were Caucasian and 19 (63%) had atopic familiar history. Atopic dermatitis was observed in 10 patients (33%), asthma and rhinitis in 15 (50%) of them. Allergic tests were performed in 27 (90%) patients, of whom 13 had seasonal allergy (pollen) and 6 (32%) perennial allergy (house dust mite, fungus and animal epithelium). Of those 19 patients showing positive allergic tests, 10 (53%) were treated with specific immunotherapy; and 29 (97%) with CsA 1%, either seasonally or continuously, depending on the severity of the disease, so as to avoid chronic steroids secondary effects. Good response and control was obtained in 27 (93%) of the latter group of patients.

Conclusion: Among the population under study, it is more frequent in male, Caucasian race and patients with allergic positive tests to allergens, such as pollen. No statistical differences were found between allergic and non-allergic patients when comparing personal and familiar history, while allergic patients with VKC were found to more frequently suffer from atopic dermatitis, although with no statistical significance in the study due to the small size of the sample under analysis.

Understanding and treating VKC has been a challenge for ophthalmologists and allergists since the pathogenesis is unclear. Topical CsA has proved to be effective in improving signs and symptoms without significant side effects by the group of patients under study. Currently, the beneficial effect of immunotherapy for treating VKC is under study.

1391
Staphylococcus aureus enterotoxin B induces airway epithelial barrier dysfunction *in vitro*

Steelant, B[1]; Lan, F[2]; Zhang, N[2]; Seys, S[1]; Kortekaas Krohn, I[1]; Ceuppens, JL[1]; Bachert, C[2]; Akdis, C[3]; Hellings, PW[1]
[1]KU Leuven, Clinical Immunology, Leuven, Belgium, [2]U Gent, Upper Airway Research Laboratory, Ghent, Belgium, [3]University of Zurich Hospital, Swiss Institute of Allergy and Asthma Research, Davos, Switzerland

Background: Epithelial barrier dysfunction is involved in the pathophysiology of allergy. Staphylococcus aureus enterotoxin B (SEB) has recently been shown to have immunomodulatory effects in the upper airways of patients with chronic rhinosinusitis. Whether SEB directly affects epithelial barrier integrity is unknown.

Method: A bronchial epithelial cell line (Calu-3) was grown in air-liquid interface (ALI) on transwell inserts. The effect of 4 h incubation with SEB (100, 10 and 1 μg/ml) on epithelial barrier function was evaluated by measuring transepithelial resistance (TER) and permeability of FITC-dextran 4 kDa (FD4). Claudin-1, claudin-4, occludin and zonula occludens-1 expression was determined by RT-qPCR and Western Blot.

Results: Calu-3 cells exposed to 100, 10 and 1 μg/ml SEB showed a dose dependent decrease in TER (-7%, -18%, -27% respectively, $p < 0.05$) in parallel with an increased FD4 passage (+38%, +22%, +44% respectively, $p < 0.05$), suggesting a disrupted epithelial barrier function. Claudin-4 (431 vs. 557, $p < 0.01$), occludin (262 vs. 300, $p < 0.05$), and ZO-1 (23 vs. 28, $p < 0.05$) mRNA expression was significantly decreased after 100 μg/ml SEB stimulation. Western blots showed lower protein levels for claudin-1 (4.1 vs.7.8 fold changes, $p < 0.01$) and phosphorylated-occludin (3.7 vs. 5.5 fold changes, $p < 0.05$). In line, occludin protein levels were higher after 100 μg/ml SEB stimulation, resulting in a higher internalization of occludin after SEB stimulation.

Conclusion: SEB disrupts the epithelial barrier intergrity in Calu-3 cells with higher disassembly of occludin, which is accompanied by changes in TJ expression. These data may help to explain the effects of SEB on mucosal airway homeostasis.

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Local exercise-induced inflammatory response in upper airways is attenuated in professional athletes

Kurowski, M[1]; Jurczyk, J[2]; Olszewska-Ziąber, A[1]; Jarzębska, M[1]; Krysztofiak, H[2]; Kowalski, ML[1]
[1]Department of Immunology, Rheumatology and Allergy, Medical University of Lodz, Healthy Ageing Reasearch Centre, Lodz, Poland; [2]COMS National Centre for Sports Medicine, Warsaw, Poland

Background: Intensive exercise provokes changes in the innate immune response, which may modulate systemic inflammation. The aim of this work was to assess changes in selected innate immunity proteins in serum, nasal lavage fluid (NLF) and exhaled breath condensate (EBC) after exercise challenge.

Method: Study group consisted of 15 competitive athletes (5 speed skaters and 10 swimmers) aged 15–25. Control groups comprised 10 mild-to-moderate asthmatics aged 19–39 (asthma controls, AC) and 7 healthy, non-smoking subjects aged 21–27 (healthy controls, HC). Control subjects were not performing sports regularly. Athletes were assessed in two time-points: in-training (period 1) and out-of-training (period 2) depending on individual training schedule. Levels of heat shock protein (HSP) A1, IL-1RA, TNF-α, IL-10 in serum, NLF and EBC were assessed by

ELISA. Exercise load was assessed with IPAQ questionnaire. Treadmill exercise challenge was conducted according to the ATS guidelines.

Results: Exercise challenge was positive in 2 athletes (13%), 6 AC (60%) and none of HC subjects. Exercise-associated median relative changes in IL-1RA NLF levels in athletes in both assessment periods (period 1: 3.84% increase; period 2: 36.5% decrease) were significantly different ($p < 0.03$ and $p < 0.01$, respectively) from those in AC (60.1% increase) but not in HC (28.5% increase) subjects. In athletes, despite notable IL-1RA NLF level decrease in period 2 the difference with period 1 was not significant. No differences between athletes and controls were observed with regard to IL-1RA in EBC and serum; TNF in NLF and EBC; HSPA1 in serum, NLF and EBC; and IL-10 in EBC. TNF-α was undetectable in serum and IL-10 in serum and in EBC. In athletes during in-training period the changes in TNF level in NLF (but not in EBC) negatively correlated with total exercise load over 7 days ($R = -0.65$, $p = 0.03$) and 28 days ($R = -0.62$, $p = 0.04$) before exercise challenge.

Conclusions: Selected aspects of exercise-associated inflammatory response in upper airways may be attenuated through regular intensive exercise.

1394
Immune reactivity in allergic rhinosinusitis in association with its pathogenetic form

Smirnova, SV; Kolenchukova, OA; Lapteva, AM; Tereshchenko, SY
Scientific Research Institute of Medical Problems of the North, Krasnoyarsk, Russian Federation

Background: Complex interactions of innate and adaptive immune cells, as well as structural cells and their cytokines, play crucial roles in regulating allergic airway inflammation. We aimed to determine the characteristics of immune response in rhinosinusitis of allergic and pseudo allergic genesis.

Method: We examined allergy rhinosinusitis (ARC) patients, (n = 156) and practically healthy subjects (n = 87) in the ages from 21 to 50 years. In the structure of ARS pathology we defined: true ARS (atopy - TARS, n = 98) and pseudo allergic polypous rhinosinusitis (PARS) (n = 58). We used the methods of specific allergological diagnostics. Phenotypic content of blood lymphocytes was evaluated by flow cytometry. We defined A, M, G, immune globulins, secretion A and E, as well as IgG typing, and also the concentration of cytokines in blood serum and nasal secretion by immune enzyme analysis. Concentration of circulating immune complexes (CIC) was determined by turbidimetric method. Statistical processing of the results was carried out by software Statistica 7.0.

Results: In atopy we marked the increase of quantity (both absolute and in per cent) of $CD3^+$-lymphocytes, IgA, IgE and CIC concentration in blood serum and sIgA in nasal lavage, the lowering of the level of $CD19^+$, $HLA\text{-}DR^+$-cells, and also phagocytic index regarding polypous rhinosinusitis group. In polypous rhinosinusitis we found high concentration of Ig-G1 and Ig-G4 as compared to atopy. In atopy the concentration of IL-4, IL-6 and IL-10 in blood serum and in nasal lavage was higher as compared to polyposis. In polypous rhinosinusitis group there was increased content of IFN-γ and IL-2 in blood serum and nasal lavage as compared to atopy.

Conclusion: So, there is immune disbalance of T-cellular type under the increased activity of humoral link of immunity and also the concentration of cytokins, which indicate the deviation of immune response towards Th2-lymphocyte side under TARS. This phenomenon is reported after studying immunological indices and cytokine concentration in ARS associated with pathogenic form. We also found PARS characteristics like increased B-lymphocytes, T-Lymphocyte late activation markers in regard to atopy and the concentration of cytokins, which activate Th1-lymphocytes.

1395
A nasally applied cellulose powder in seasonal allergic rhinitis (SAR) in adults with grass pollen allergy. Supplementary analyses of reduction of severity and duration of symptoms

Åberg, N[1]; Emberlin, J[2]
[1]Department of Pediatrics, University of Gothenburg, Askim, Sweden; [2]Allergy UK, Kent, UK

Background: A nasally applied cellulose powder forms a gel layer with a barrier protection on the nasal mucosa. The product is used increasingly in many countries as a remedy for allergic rhinitis. In 2009 a 4 week double blind, randomized, placebo controlled study in birch pollen allergic children in Sweden showed a significant reduction of nasal symptoms; the highest efficacy seen on days with moderate to low pollen counts. The present study in grass pollen allergic adults used the same design and a significant efficacy has previously been reported from the study. The present findings are based on further analyses of the data regarding the relative reduction of severity and duration of symptoms and have not been reported before.

Method: In May 2013, in two cities in the eastern part of Ukraine, a double blind, placebo controlled randomised study was conducted over a 4 week period in the grass pollen season in 108 grass pollen allergic subjects, 18–40 years of age.

Results: All means of reported severity scores from upper and lower airways were approximately 50% lower in the actively treated group (each separately and altogether $p < 0.001$). The group differences increased with time during the study period resulting in a significantly earlier complete freedom from nasal symptoms in the active group (Kaplan-Meier log rank $p < 0.001$). No clinically or statistically significant adverse effects were reported.

Conclusion: The product provided a highly significant protection against all SAR symptoms from both upper and lower airways during the grass pollen season in an adult population. An increasing effect with duration of treatment induced a complete freedom from nasal symptoms in a notable percentage of subjects in the active group. Considering the magnitude and scope of efficacy as well as the absence of adverse effects we recommend that the product be considered as an early choice in the treatment of allergic rhinitis. The complete lack of side effects from this product is a particularly important aspect for many SAR patients including children, pregnant and breast feeding women, those operating machinery and the elderly.

1396
Validation interobserver of clinical score in nasal challenge with lysine-aspirin (L-asa) for diagnosis of aspirin exacerbated respiratory disease (AERD)

Ramirez-Jimenez, F; Pavón-Romero, GF; García-Cruz, ML; Sanchez de la Vega-Reynoso, P; Camacho-Ordoñez, N; Ruiz-Morales, RD; Pérez-Estrella, Z; Terán, LM
INER, Immunogenetics & Allergy, Mexico City, Mexico

Background: AERD is an illness characterized by nasal polyps, chronic eosinophilic sinusitis, asthma and aspirin hypersensitivity (AH); there is not *in vitro* tests for identification of AERD. The diagnosis of AH is obtained by history and established through provocation test. Nasal challenge is less sensitive than oral, although is safest. Nasal provocation tests required a special equipment to measure the nasal flow by anterior rhinomanometry, is considered an objective method for established the AH, all the protocols that used this method include a subjective clinical score (CS) but it had not been validated. Our

objective was to validate the clinical score in nasal challenge.
Methods: Nasal challenge was made to asthma patients with or without polyps. We diluted 160 mg of L-asa in 3.2 ml of NaCl0.9% (12.5 mg/250 μl). At baseline CS and total nasal flow (TNF) obtained with Jaeger rhynomanometer were recorded. L-asa 12.5 mg were instilled into each nostril, CS and TNF were measured over the following 30 minutes, if the patient didn't develop a positive reaction, we proceed to repeat this procedure until 4 times (maximum accumulated dose 100 mg L-asa); If exist 40% decrease of TNF and/or an increase of 8 points on the CS compared with baseline values we considered positive criteria and the challenge was stopped. The CS was constituted by 10 items (nasal obstruccion, sneezing, rhinorrea, facial color, pruritus, hyperemia conjunctival, size/color of right and left inferior turbinates) with a score of 0–3 in each one, it was evaluated by two different blind allergists. We used Wilcoxon and concordance test.
Results: 40 patients were enrolled, 20 had history of AH in the last 12 months and 20 had history of intake aspirin without any reaction in the same time. 19/20 challenges in patients with AH had positive criteria; the 20 challenges in asthma patients without history of HA were negative. We obtained $\kappa = 1$ between the two allergist; the concordance with the challenge positive criteria was 95% (only two patients with a decrease of 40% of TNF didn't have increase of ≥ 8 points in CS). The mean of decreased of TNF was 47% ($p = 0.001$), and mean of the increase of CS a in the positive challenges was 11.75 points ($p = 0.001$). In negative challenges we found an increase mean TNF of 28.37% but had not significance ($p = 0.940$).
Conclusion: The increase of the ≥8 points in CS is a good method for establish AH and could be option in centers that not have specific devices.

1397
Increased Th1 cells infiltration in nasal polyps from patients with refractory chronic rhinosinusitis and asthma

Yoshikawa, M; Sakaguchi, Y; Takahata, Y; Inoue, N; Sawai, R; Okubo, H; Yamaguchi, S; Moriwaki, H
Department of Otorhinolaryngology, Toho University School of Medicine, Tokyo, Japan

Background: Bronchial asthma is recurrently associated with chronic rhinosinusitis (CRS) and influence endoscopic sinus surgery (ESS) outcomes. Common mucosal eosinophilia is frequently associated with more severe disease and with recurrence of nasal polyps (NPs) after ESS. Furthermore, CRS patients with aspirin-intolerant asthma (AIA) often have particularly severe asthma that is associated with rhinorrhea and recurrent NPs. These findings suggest that concomitant asthma may contribute to the pathophysiology of CRS. On the other hand, T-cell immunity has been suggested to play an important pathogenic role in many chronic inflammatory diseases including CRS. In order to determine whether T helper (Th) 1 or Th2 cells were increased in NP tissues, we detected T-bet or GATA-3 and CD3 by double immunofluorescence staining.
Method: A specimen of NP mucosa was obtained during surgery from patients who had been referred to our hospital for ESS. Specimens of NP and mucosal tissues were obtained from 3 groups of CRS patients:
1) patients without asthma (CRS group),
2) patients with aspirin-tolerant asthma (ATA group), and
3) patients with AIA (AIA group).

Biopsy specimens from these CRS patients were subjected to immunohistochemistry for detection of T-bet and GATA-3 expression in CD3 + T cells by double labeling.
Results: CD3 + cells were restricted to the perivascular and subepithelial regions of nasal biopsy specimens. Representative double-stained images of T-bet+CD3 + cells (Th1 cells) and GATA-3 + CD3 + cells (Th2 cells) in nasal biopsy specimens are shown. CD3 + cells were detected in all specimens, but the number of CD3 + cells was significantly higher in the ATA and AIA groups than in the control and CRS groups. In addition, the number of T-bet+CD3 + cells and GATA-3 + CD3 + cells was significantly higher in the AIA group than in the control or CRS groups. In the ATA group, the number of T-bet+CD3 + cells and GATA-3 + CD3 + cells was slightly higher than in the control group or the CRS group, but there were no significant differences.
Conclusion: In addition to Th2 cells, there was more abundant infiltration of Th1 cells into tissues from the AIA and ATA groups. Both Th1 and Th2 cells were significantly increased in NP tissues from the AIA group compared with the control, CRS, and ATA groups. These findings suggest that concomitant asthma is a major reason why CRS may become refractory to treatment.

1398
Self-reported improvement of chronic rhinosinusitis symptoms in patients on omalizumab therapy for asthma

Sussman, G[1,2]; Saperia, C[2]; Lasso, A[3]; Raffaghello, J[2]; Mcauley, P[2]; Santucci, S[4]; Yang, W[4,5]; Kilty, SJ[3,6]
[1]University of Toronto Faculty of Medicine, Toronto, Canada; [2]Gordon Sussman Clinical Research, Toronto, Canada; [3]The Ottawa Hopsital, Department of Otolaryngology - Head and Neck Surgery, Ottawa, Canada; [4]Ottawa Allergy Research Corporation, Ottawa, Canada; [5]University of Ottawa, Ottawa, Canada; [6]Ottawa Hospital Research Institute, Ottawa, Canada

Background: The purpose of this study was to evaluate the effect of omalizumab on self-reported improvement of chronic rhinosinusitis (CRS) symptoms in patients receiving omalizumab as part of their asthma treatment.
Method: A chart review and survey were performed at two private asthma and allergy clinics in Ottawa and Toronto, Ontario, Canada.

Patients identified for investigation were receiving omalizumab as part of their asthma treatment, and were also diagnosed with chronic rhinosinusitis with polyps (CRSwNP) or chronic rhinosinusitis without polyps (CRSsNP). Data on demographics, omalizumab therapy and medical history were obtained from the patients' medical charts. Patients were invited to complete a survey about their CRS symptoms. Patients graded the level of improvement of their olfaction, rhinorrhea, facial pain, nasal obstruction and overall improvement in CRS symptoms since the start of omalizumab therapy on a 10 cm Visual Analogue Scale (VAS) (0 = no improvement, 10 = complete improvement). The mean self-reported improvement for each symptom was compared between CRSwNP and CRSsNP patients using a t-test.
Results: Thirty-four charts were available for review, 18 patients were male, 16 female. 23 (76.5%) patients had CRSwNP and 8(23.5%) had CRSsNP. All patients were receiving concurrent treatment for their CRS. 25 patients answered the survey. Patients with CRSwNP reported 42.9% improvement in olfaction, 77.5% in facial pain, 68% in nasal obstruction, 59.1% in rhinorrhea and 57.3% overall improvement of CRS symptoms since the start of omalizumab treatment. Patients with CRSsNP reported 53.5% improvement in olfaction, 78% in facial pain, 72% in nasal obstruction, 70.3% in rhinorrhea and an overall improvement of 76.7%. There was no significant difference between the improvement reported by patients with CRSwNP and those with CRSsNP for any of the symptoms or overall improvement.
Conclusion: Omalizumab treatment was beneficial for over 75 percent of patients

with chronic rhinosinusitis, with or without nasal polyps. Omalizumab may be a useful treatment for this patient population, for which there are few efficacious, cost-effective, long-term therapeutic modalities.

1399
The significance of allergen specific Ig E in the diagnosis of allergic rhinitis

Chung, SK
Sungkyunkwan University School of Medicine, Samsung Medical Center, Otorhinolaryngology H&N Surgery, Seoul, Korea

Background: Usually rhinitis is classified simply allergic and non-allergic rhinitis according to the allergic reaction to airborne allergens. Ig E-mediated inflammation is confirmed with positive skin test or presence of specific IgE and the positive result from the one of the two tests is usually enough for the diagnosis. However, the presence of specific IgE or positive skin reaction is a necessary condition not a sufficient condition for the allergic rhinitis. Therefore the false positive clinical allergic rhinitis may be increased. We are interested in the diagnostic power of the allergen specific Ig E. Recently, during Korean National Health and Nutrition Examination Survey 2010, presence of rhinitis and the specific Ig E for major airborne allergens were checked in the population. Purpose of this study is to evaluate the significant level of allergen specific Ig E in the diagnosis of allergic rhinitis.
Method: The data were obtained from the 2010 Korean National HANES, which was a cross-sectional survey of non-institutionalized population all around the country. Presence of rhinitis was defined as have you experience the rhinitis symptoms or have you diagnosed as have allergic rhinitis from doctor. Serum specific IgE was checked for dermatophagoides farinae, cockroach and dog. Data was obtained from 1,922 adult (older than 18). The statistical parameters for the diagnostic test such as sensitivity, specificity, positive predictive value and positive likelihood ratio were calculated according to the level of the specific Ig E.
Results: The prevalence of rhinitis was 16.5%. The specific Ig E higher than 0.34 kU/L was found in 44.3%. The the positive rate was 54.8% in the rhinitis group and 40.7% in group without rhinitis. When the diagnosis of allergic rhinitis was decided with the each level of the specific IgE, sensitivity was 100% in all levels. Positive predictive predictive value and positive likelihood ration were were 37.3% and 3.00 for one +, 39.5% and 4.07 for two +, 49.3%, 9.89 for three +, 63.8% and 35.92 for four +, 77.4% and 133.86 for five +.
Conclusion: Capacity of the specific IgE to classify the rhinitis was not high when the level of 0.35 kU/L was adopted. The level of specific IgE equal or higher than 3.50 kU/L seems to be more clinically significant especially for selection of allergen specific treatment.

1401
Does the duration of participation to orieentering effects the frequency of allergic rhinitis in adolescent orienteers in West Mediterranean Region: a prospective, blinded, clinical study

Selcuk, O[1]; Eraslan, A[2]; Filiz, S[3]; Renda, L[1]; Selcuk, N[4]; Eyigor, H[1]; Osma, U[1]; Yılmaz, MD[1]
[1]Otolaryngology, Antalya Research and Teaching Hospital, Antalya, Turkey; [2]Sports Medicine, Antalya Research and Teaching Hospital, Antalya, Turkey; [3]Pediatric Allergy and Immunology, Antalya Research and Teaching Hospital, Antalya, Turkey; [4]Pulmonology and Allergy, Antalya Research and Teaching Hospital, Antalya, Turkey

Background: Allergic rhinitis (AR) is a symptomatic disorder of the nose which affects quality of life, sleep, school, work and sport success with the symptoms of sneezing, nasal obstruction and mucous discharge. AR is the most common allergic airway disease in childhood with the prevalence of 1.4–24.5% in different studies. In recent years there are many epidemiological studies reported that the incidence of asthma and rhinitis in athletes are higher comparing with the general population. AR rate have been reported in athletes as 15–29%. Orienteering is a olympic outdoor sport in which the partipicant have to proceed from the start to finish by visiting a number of control points with the help of map and compass. Orieentering in Antalya mostly takes places in wooded areas with an polen exposure that may cause AR. We aimed to determine the prevalence of AR in orienteers, compare with basketball players and tto find he effect of the sport duration on the AR.
Method: There were 33 licensed orienteers and 27 licensed basketball players included in to study. Modified ISAAC 2 questionnaire, epidermal prick test and clinical assessments were used for allergic rhinitis identification criteria. All athletes diagnostic nasal endoscopic and nasopharyngoscopic examinations were made by same otolaryngologist. Inferior turbinates, presence of secretions, nasal passages and mucous membranes were evaluated. Nasopharyngeal examination is done and the presence of adenoid tissue were evaluated. Pulmonary function tests, serum eosinophil numbers, percentage and total IgE levels were assessed.

The skin tests were performed by the same nurse in a standardized manner and evaluated by the same pediatric allergy and immunology specialist.
Results: There were 21 males and 12 females in orieenter group and 14 males and 13 females in the basketball group. The ages were between 10–18 and 10–16 with a mean age of 14.1 ± 2.3 and 13.4 ± 1.6 respectively. As a result of AR investigation and ENT examination 14 orienteers (42.4%) and 7 basketball players (25.9%) were diagnosed as AR. Presence of AR was higher in orieenters but this was not statistically significant (0.144). When we compare orieenters with AR and without AR we found that duration of exercise in years was higher in AR group as 2.9 ± 1.4 to 2.1 ± 1.3. This was statistically significant ($P = 0.046$).
Conclusion: With the longer duration of participation to orieentering, the frequency of AR increased.

Poster Session Group III - Green TPS 48

Allergens and allergenicity

1402

Production and characterization of recombinant mature Amb a 11, a new major allergen of short ragweed (*Ambrosia artemisiifolia*) pollen with a cysteine protease activity

Groeme, R[1]; Jaekel, J[1]; Le Mignon, M[1]; Jain, K[1]; Nony, E[1]; Baron-Bodo, V[1]; Briozzo, P[2]; Bordas-Le Floch, V[1]; Mascarell, L[1]; Moingeon, P[1]
[1]Stallergenes SA, Antony, France; [2]UMR 1318, IJPB, INRA, Versailles, France

Background: Short ragweed (*Ambrosia artemisiifolia*) causes severe pollinosis in central Europe and Northern America. We recently identified Amb a 11 as a novel major ragweed allergen, exhibiting a cysteine protease activity. Herein, we report on the production and characterization of recombinant mature Amb a 11.
Methods: The recombinant pro-Amb a 11 zymogen was refolded *in vitro* from *E. coli* inclusion bodies and matured at pH 5. The structural characterization of recombinant mature Amb a 11 was performed by mass spectrometry and circular dichroism. The cysteine protease activity was assessed by enzymatic fluorescent assay and IgE reactivity by immunoblotting with sera from ragweed allergic patients.
Results: Using wild type and mutated forms of the molecule, we demonstrate that the Amb a 11 zymogen can be refolded *in vitro* and further processed into a mature form at acidic pH by an autocatalytic mechanism. Mass spectrometry analyses confirmed the removal of both N- and C-terminal propeptides during this process. Circular dichroism spectra documented a folding pattern comparable for recombinant mature and natural Amb a 11. Moreover, mature rAmb a 11 exhibits a strong cysteine protease activity. Like natural Amb a 11, the recombinant molecule reacts with seric IgEs from 60% of ragweed pollen-allergic patients. No IgE cross-reactivity is observed between Amb a 11 and the homologous cysteine protease Der p 1 allergen of *Dermatophagoides pteronyssinus*.
Conclusion: We successfully produced in *E. coli* a recombinant mature Amb a 11 which exhibits cysteine protease activity as well as IgE reactivity in a majority of allergic patients. These results confirm that Amb a 11 is an important component for the diagnosis and immunotherapy of ragweed pollen allergy.

1403

The effect of thermal processing on the structural and immunological behavior of Art v 3

Wildner, S[1]; Stock, L[1]; Mari, A[2]; Stutz, H[1,3]; Gadermaier, G[1,3]
[1]Christian Doppler Laboratory for Innovative Tools for Biosimilar Characterization, University of Salzburg, Salzburg, Austria; [2]Associated Centers for Molecular Allergology, Rome, Italy; [3]University of Salzburg, Department of Molecular Biology, Salzburg, Austria

Background: Pollen grains of *Artemisia vulgaris* (mugwort) are a frequent cause of allergic reactions in late summer and autumn. Art v 3 is an allergen of mugwort which belongs to the non-specific lipid transfer protein (LTP) family. It represents a stable allergen and previous studies have shown that Art v 3 behaves differently at various pH conditions after heating. This study aims to investigate structural changes and immunochemical properties of recombinant Art v 3 in response to thermal treatment.
Method: Recombinant Art v 3.0201 was expressed in the *E. coli* strain Rosetta-gami B pLysS and purified using cation exchange chromatography. Solutions of Art v 3 buffered to acidic (pH 3.4) and neutral (pH 7.3) pH were incubated up to 120 min at 95°C. Physico-chemical properties of the non-heated and heated allergen were analyzed in circular dichroism spectroscopy, dynamic light scattering, SEC, Fourier transform infrared spectroscopy and capillary zone electrophoresis hyphenated to a time-of-flight mass spectrometer. Using sera from Italian mugwort pollen allergic patients (n = 8) the IgE-binding activity of recombinant Art v 3 was investigated in ELISA.
Results: Recombinant Art v 3 was produced as a non-tagged protein with a yield of 3.4 mg per liter of expression culture. Circular dichroism showed high thermal stability at acidic pH while the alpha helical fold was lost upon heating for 15 min at pH 7.3. Conformational changes were investigated by capillary zone electrophoresis hyphenated to a time-of-flight mass spectrometer indicating a decay of disulfide bonds by beta elimination and formation of lanthionine(s). Native Art v 3 is monomeric with a hydrodynamic radius of 1.8 nm. Relaxation of the compact shape is observed upon heat treatment at neutral pH which is not attributed to protein aggregation as determined by SEC. Notably, IgE reactivity to Art v 3 was abrogated upon heating at pH 7.3 but remained largely unaffected at pH 3.4 suggesting involvement of conformational epitopes.
Conclusion: Within this study we were able to obtain soluble and folded recombinant Art v 3 from *E. coli*. Susceptibility of Art v 3 to thermal treatment is highly dependent on pH conditions. These findings will have direct implications on studies enrolling pollen and food derived LTPs.

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1405

Description of a new cockroach allergen revealed with serum patients from Iran

Teifoori, F[1,2]; Postigo, I[1]; Gutierrez-Rodriguez, A[1]; Suñén, E[1]; Martínez, J[1]
[1]Laboratory of Parasitology and Allergy, Center for Research Lascaray and Department of Immunology, Microbiology and Parasitology, Faculty of Pharmacy, University of the Basque Country, Vitoria-Gasteiz, Spain; [2]Department of Mycology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background: Increased asthma and allergy is associated with cockroach infestation houses in Iran. Molecular diagnosis is currently the most accurate method to define the cause of IgE-mediated allergy; however a more complete panel of individualized allergens is needed to avoid diagnosis limitations. With this in mind, the objective of this work was to identify new allergens from cockroach that are able to cause allergic asthma in exposed individuals.
Method: Fifty atopic patients from Iran suffering asthma and sensitized to cockroach allergens were studied (Loghman Hakim Hospital and Pasteur Institute of Tehran, Iran from 2011 to 2012). Cockroach extract specific IgE were analyzed by

the ImmunoCAP system. SDS-PAGE IgE-immunoblotting associated with MALDI-TOF-MS and MALDI-TOFMS/ MS were performed to study the cockroach IgE-binding proteins.
Results: The prevalence of sensitization to *Blatella germanica* in the Iranian atopic sample was 35%. Four IgE-binding components of 75, 53, 42 and 36 kDa, reactive in 63.6%, 86.4%, 72.7% and 54.5% of cockroach-sensitized patients, respectively, were revealed. Only 2 out of the 4 IgE binding components were identity by mass spectrometry (53 and 42 kDa) as an alpha-amylase and an arginine-kinase, respectively. The arginine kinase identified here corresponds to the Bla t 9 cockroach allergen existing in official allergen databases (www.allergome.org, www.allergen.org). In turn, the alpha-amylase IgE-binding protein has not been previously described as a cockroach allergen. Allergen databases show other alpha-amylase homologues in *Blomia tropicalis* (Blo t 4), *Dermatophagoides pteronyssinus* (Der p 4) and *Euroglyphus maynei* (Eur m 4). The lack of IgE reactivity against *Dermatophagoides* allergens found in the sample (prevalence ≤ 10%) suggests that there is little cross-reactivity between cockroach alpha-amylase and homologue proteins from mites.
Conclusion: A novel major allergen from *Blattella germanica* cockroach (alpha amylase, 53 kDa) that could sensitize a relevant percentage (86.4%) of a cockroach sensitized population was identified.

1406
Implementation of a 3D-coculture model for the evaluation of sensitizing effects of chemicals

Chary, A[1,2]; Serchi, T[1]; Gutleb, AC[1]; Blömeke, B[2]
[1]Luxembourg Institute of Science and Technology LIST, Esch/Alzette, Luxembourg; [2]University of Trier, Trier, Germany

Background: Chemical respiratory sensitization resulting from exposure to synthetic compounds has increased over the last decades leading to occupational health issues. Currently, no validated *in vitro* model to assess the respiratory sensitization potential of chemicals is available.
Aim: A model composed by alveolar type-II cell line (A549), endothelial cells (EA.hy926), mast cells (HMC-1) and macrophage like cells (differentiated THP-1) has been developed by us to mimic the alveolar surface. Cells were grown under air-liquid interface conditions, allowing a more realistic exposure. The system, originally developed to study alveolar toxicity, needs adaptations to be used to study sensitization relevant processes. The *in vivo* role of Dendritic Cells (DCs) in the sensitization process is crucial, since they are deputed to antigen recognition and capture. For their central role in the immune response process, DCs must be included in the model design. The possibility of migration for the DCs has to be ensured to have a functional model.
Method: Alamar Blue assay was used to assess the viability of cells grown on microporous membranes of different pore sizes (1, 3, 5 and 8 μm) and the surface tension was evaluated using dimethyl phthalate octanol droplet. In a modified version of the original model, the undifferentiated monocyte cell line THP-1, used as a model for DCs, is placed in the system. Their migration capacity over the different pore sizes inserts was investigated using Monocyte Chemoattractant Protein-1.
Results: Cell viability and surface tension were not affected by membranes' use in different pore sizes. No migration of the THP-1 cells was observed with 1 μm pore size insert, while size-dependant increase mobility was calculated in the other inserts.
Conclusion: We expect that this modified version of the alveolar model could represent a relevant tool to study respiratory sensitization. Further optimization and development steps will be necessary before the proposed model can be used to predict the respiratory sensitizing potential of inhaled chemicals.

1407
Identification and characterization of polcalcin from *Salsola kali*

Peñalver, M; Pedreño, Y; Sola, JP; Cerezo, A; Orts, L
Probelte Pharma S.A., Murcia, Spain

Background: Polcalcins are calcium-binding proteins identified as cross reacting pollen panallergens that have been detected in trees, grasses and weeds. Polcalcins are considered, together with profilins, markers of multiple pollen sensitization. *Salsola kali* is a member of the *Chenopodiaceae* family and allergy to pollen of this plant is common in coastal areas of Europe, Mediterranean area and North America. We have identified the polcalcin from *Salsola kali* pollen and we have characterized the recombinant protein expressed in *Pichia pastoris*.
Methods: The complete cDNA coding for polcalcin from *Salsola kali* was amplified by PCR and deduced sequence of protein was aligned with sequences of polcalcin from other relevant allergenic species. The cDNA of polcalcin was cloned in a vector of *Pichia pastoris* for expression of recombinant protein. The recombinant polcalcin from *Salsola kali* was produced and secreted to the extracellular media of *Pichia pastoris* culture and then was purified by two steps of ultrafiltration and finally by size exclusion chromatography using FPLC. The purified recombinant polcacin from *Salsola kali* was characterized to IgE response by immunoblotting using a pool of sera from patients sensitized to *Salsola kali* pollen and by indirect ELISA using individual serum of twenty patients with a positive SPT to *Salsola kali*.
Results: The cDNA of polcalcin from *Salsola kali* was 261 bp in size and encoded a protein containing 86 amino acids with a theoretical molecular weight of 9524.58 Da and pI of 4.38. The deduced sequence of polcalcin shares a sequence identity of 91%, 83% and 76% with Che a 3, Ole e 3 and Phl p 7 respectively. The recombinant polcalcin expressed in *Pichia pastoris* was purified and tested to confirm high purity with RP-HPLC and SDS-PAGE, showing and single band with apparent molecular weight of approximately 8.5 kDa. In immunoblotting assay was detected a band corresponding to purified recombinant polcalcin. By indirect ELISA, eight of twenty sera analyzed (40%) showed positive response to purified recombinant polcalcin.
Conclusion: Polcalcin from *Salsola kali* pollen has been identified and described as a minor allergen with high identity of sequence with polcalcins from other relevant allergenic species, thus it should be involved in cross-reactivity with other pollen sources. This new allergen will be included in the official site for the systematic allergen nomenclature.

1408
Cloning and characterisation of Alt a 15, a novel cross-reactive allergen from *Alternaria alternata*

Gabriel, M[1,2]; Postigo, I[1]; Gutiérrez-Rodríguez, A[1]; Suñén, E[1]; Guisantes, JA[1]; Fernández, J[3]; Tomaz, C[2]; Martínez, J[1]
[1]Department of Immunology, Microbiology and Parasitology, Faculty of Pharmacy and Laboratory of Parasitology and Allergy, Lascaray Research Centre, University of the Basque Country, Vitoria-Gasteiz, Spain; [2]Department of Chemistry and CICS-UBI - Health Sciences Research Centre, University of Beira Interior, Covilha, Portugal; [3]Allergy Section, University General Hospital of Alicante and Department of Medicine, University Miguel Hernández, Alicante, Spain

Background: *Alternaria alternata* is one common environmental allergenic fungi that has been clinically and epidemiologically associated with severe asthma and life-threatening acute exacerbations of asthma. Although an important role in physiopathogenesis of asthma has been clearly attributed to serine protease-specific activity of *A. alternata extracts* in various

models, the recognition of this *A. alternata* protein as an allergen and its allergological relevance remains unstudied. The aims of this study were to clone and express the recombinant *A. alternata* serine protease (Alt a 15), and to test its relevance in *Alternaria alternata* sensitisation.

Method: The complete coding region for Alt a 15 was amplified by 5′ and 3′ rapid amplification of cDNA ends and PCR. The recombinant protein was produced in *Escherichia coli* and used in immunoblotting experiments. Fifty-nine sera from patients sensitised to *A. alternata* were selected. Immunoblotting and ELISA-inhibition assays were also performed.

Results: Recombinant Alt a 15 was expressed as a 65 kDa fusion protein which protein sequence presents high homology with Curvularia lunata major allergen, Cur l 4. IgE antibodies from A. alternata-sensitised patients bound to rAlt a 15 with a prevalence of 10.2%. A coincidence between patients apparently poly-sensitised to A. alternata and C. lunata and sIgE reactivity to rAlt a 15 was found. The extensive cross-reactivity between A. alternata and C. lunata serine proteases was confirmed by immunoblotting-inhibition assays.

Conclusion: Alt a 15 represents an important new cross-reactive allergen of A. alternata that can explain some cases of allergy to *Alternaria alternata* without Alt a 1 sensitisation and could be a reason for diagnostic errors initially made for allergies to *Alternaria*. This molecule might be suitable for improving the accuracy of the diagnosis and the understanding and management of IgE-mediated fungal diseases.

1409
High-throughput screening of T7 phage display and protein microarrays to complete allergenic protein panels from olive pollen and yellow mustard seeds

San Segundo-Acosta, P; Garranzo-Asensio, M; Martín-Pedraza, L; López-Rodríguez, JC; Abián-Saz, S; Batanero, E; Rodríguez, R; Villalba, M; Barderas, R
Complutense University of Madrid, Biochemistry and Molecular Biology I, Madrid, Spain

Type I allergy is a generalized health problem in industrialized countries, affecting about 30% of the population. Specific IgE production is a key event in the sensitization process against specific allergens. This phenomenon can be exploited by high-throughput screening to identify new allergens by combining T7 phage display and protein microarrays. Phage display technologies allow for the construction of phage libraries displaying cDNA from biological sources. Immobilization of IgEs from patients sensitized against those specific sources makes possible the isolation of phages displaying allergenic peptides. The allergenic potential of the phages is then assessed after printing the enriched phage library on nitrocellulose microarrays and probing them with sensitized patient's sera. We constructed two T7 phage libraries, displaying cDNA synthesized from mRNA isolated from yellow mustard seeds and olive pollen, respectively. Both libraries were iteratively biopanned in solution using mustard and olive-specific IgE to enrich them in IgE immunoreactive phages displaying allergens. After biopanning, 768 monoclonal phages of each library were printed on 20 nitrocellulose microarrays, and probed with sera from both sensitized patients. In total, we found 54 phages displaying allergenic peptides. Their immunoreactivity was analyzed by *dot blot* and ELISA. The cDNA inserted in each phage was amplified by PCR and sequenced to identify unique phages. Then, we designed specific oligonucleotides to amplify the complete cDNAs of the most reactive allergens displayed on phages. We have been able to clone one complete and three partial cDNAs encoding for potential allergenic proteins from mustard seeds. The complete cDNA clone codifies for a 80-amino acid protein (9.12 kDa and pI ~12), whose deduced amino acid sequence possess sequence identity with TATA binding-like and Cytochrome P450-like proteins especially at its C-terminal end. Regarding olive pollen allergens, we have cloned a partial cDNA encoding the C-terminal end of a protein with sequence identity with the PLAC8 superfamily. The newly identified allergens from olive pollen and mustard seed will be expressed as recombinant allergens in heterologous systems. Recombinant variants, exhibiting the functional activities of the natural allergens, will be used for the development of more accurate molecular diagnosis and to further improve olive and mustard therapeutic allergic approaches.

1410
The mite allergen Blo t 2 is expressed with a signal peptide as a complex mixture of isoforms in *Blomia tropicalis*

Urrego, J[1,2]; Ponte, J[2]; Wallner, M[1]; Alcântara-Neves, N[2]; Pinheiro, C[2]; Briza, P[1]; Ferreira-Briza, F[1]
[1]Department of Molecular Biology, University of Salzburg, Salzburg, Austria; [2]Instituto de Ciências da Saúde, Federal University of Bahia, Salvador, Brazil

Background: *Blomia tropicalis* is an important source of allergens associated with allergic asthma in tropical and subtropical regions. The prevalence of positive skin pick test to this mite in asthmatic patients from Brazil is around 83% to 93,7%. However, the clinical importance of group 2 allergens from this mite species is still under debate. Until now only rare information of Blo t 2 is available, most of it obtained at the transcript level.

Method: *Blomia tropicalis* extracts were prepared from 20 different mite breeds collected and cultured in Salvador, Bahia, Brazil. Mite extracts were prepared using phosphate buffered saline and thereafter proteolytically digested with a set of distinct proteases (i.e. trypsin, chymotrypsin, Glu C, or the respective combinations thereof). Peptides were analyzed by liquid chromatography/tandem mass spectrometry (LC-MS/MS). Prior to analysis peptides were separated on an in-house monolithic reversed-phase (RP)-column. The data was analyzed with Proteome Discoverer 1.4 software and Peaks Studio 7, and searched against the Uniprot protein database.

Results: Using MS analyses, we were able to identify Blo t 2 at the proteome level and quantify its relative abundance in aqueous extracts of 20 Blomia tropicalis breeds. Within the sequence of Blo t 2, we identified 8 diagnostic peptides as specific markers for Blo t 2 isoforms. In general, we obtained sequence coverage rates of 50 - 88.5% of Blo t 2 in our mite extracts. According to the published sequence, we could not find a matching peptide for the first 17 amino acids, suggesting the presence of a signal peptide on Blo t 2. This finding was confirmed by the signal peptide prediction software SignalP 4.0.

Conclusion: We successfully identified Blo t 2 at the protein level and were able to quantify their relative abundance in *Blomia tropicalis* extracts. In addition, we found for the first time that Blo t 2 is expressed with a signal peptide, which is cleaved in the mature protein. Our data provides the basis for recombinant production of Blo t 2 for allergy diagnosis as well as the rational design of Blo t 2 derivatives applicable in therapeutic setups.

1411
Sensitization phenotypes based on protein-groups and associations to allergic diseases in children; new perspectives of component resolved diagnostics

Schoos, A-MM[1,2]; Kattan, JD[1]; Gimenez, G[1]; Sampson, HA[1]
[1]Division of Allergy and Immunology, Department of Pediatrics, Jaffe Food Allergy Institute, Icahn School of Medicine at Mount Sinai, New York, USA; [2]Copenhagen Prospective Studies on Asthma in Childhood, Faculty of Health and Medical Sciences, University of Copenhagen & Danish Pediatric Asthma Center, Gentofte Hospital, University of Copenhagen, Gentofte, Denmark

Background: Component resolved diagnostics provide an opportunity to study allergic sensitization in a new way where

different phenotypes can be created based on biologically meaningful allergenic protein-groups. The objective of this study was to explore how sensitization to allergenic protein-groups is associated with asthma and allergic rhinitis in childhood.

Method: Allergic sensitization to 112 components was measured utilizing the ImmunoCAP Immuno Solid-phase Allergen Chip® (ISAC) in 269 children from the Mount Sinai Pediatric Allergy Clinic, a university-based outpatient practice. Fifteen protein-groups were extracted from these components (PR-10, pectate lyase, tropomyosin, nsLTP, profilin, cysteine protease, NPC2 family, lipocalin, albumin, Ole e 1 homologue, beta expansin, grasses, molds, weeds and trees). History of or current asthma and allergic rhinitis was registered by questionnaire. Associations between protein-groups, asthma, and allergic rhinitis were determined using logistic regression. Results were adjusted for gender and age and for multiple testing using Bonferroni correction.

Results: There was a significant association between sensitization to components in the lipocalin protein-group and asthma (aOR=2.47 [1.49;4.10], $P = 0.0004$). None of the protein-groups that mainly included house dust mites were associated with asthma (aOR cysteine protease=1.72 [0.90;3.30], $P = 0.10$ and NPC2 family=1.51 [0.75;3.06], $P = 0.25$). Similarly, we found significant associations between PR-10, pectate lyase and grass pollen protein-groups and allergic rhinitis, with PR-10 showing the strongest association (aOR=4.31 [2.37;7.82], $P < 0.0001$).

Conclusion: Sensitization phenotypes based on protein-groups is a novel and meaningful approach when analyzing associations to allergic diseases. Asthma was associated with the lipocalin protein-group and allergic rhinitis was associated with the PR-10, pectate lyase, and grass pollen protein-groups.

1412
What is the impact of genetic transformation on wheat allergenicity?

Lupi, R[1]; Masci, S[2]; Pineau, F[1]; Deshayes, G[1]; Tranquet, O[1]; Moneret-Vautrin, DA[3]; Denery-Papini, S[1]; Larré, C[1]
[1]INRA, Nantes, France; [2]University of Tuscia, Viterbe, Italy, [3]Faculty of Medicine-Nancy, Epinal, France

Background: Wheat allergy occurs by inhalation (baker's asthma) and ingestion (food allergy), but may also develop by contact in some cases. The responsible allergens of wheat are proteins accounting for about 10–15% of the grain dry weight. Wheat proteins are divided into two groups: the salt soluble fraction (albumins/globulins) and the gluten proteins (gliadins and glutenins). This latter group is responsible for celiac disease and also for food allergy, whereas the albumins/globulins are involved in baker's asthma and in some food allergy. Genetic modification (GM) technology for crop improvement has recently emerged and its impact on allergenicity must be evaluated, as recommended by the Codex Alimentarius.

Method: Following this recommendation, we first compared two GM lines with their parents using an allergenomic approach then in a second step we aimed at comparing the amount of allergenic polypeptides in these GM wheats, their untransformed genotypes and those measured among twenty commercial cultivars, either durum or bread wheats. In order to characterize the accumulation of allergenic proteins in wheats, sera from children and adults with clinically documented wheat allergy were used. The investigation is focused mainly on the soluble protein fraction of wheat.

For the comparison of GM lines with their natural counterparts, 2D immunoblot followed by mass spectrometry analysis and protein identification was set up. ELISA tests were performed on the whole set of genotypes.

Results: Few differences at molecular and quantitative levels were revealed between the GM lines and their counterparts. Two new IgE-binding proteins were detected for one GM line[a]. We also observed that the genetic transformation may impact IgE reactivity, either in a positive or in a negative way[b].

Conclusion: This study leads us to conclude that a wide variation exists in the amount of allergenic polypeptides among durum and bread wheat cultivars, and that the differences observed between GM wheats and their parents are within the range of these 20 cultivated wheats.

a: Lupi R. et al J. of P. (2013) 80, 281–291
b: Lupi R. et al J. C. S. (2014), http://dx.doi.org/10.1016/j.jcs.2014.02.009

1413
Anaphylaxis to porcupine meat

Potter, P[1]; Van Rooyen, C[2]; Fenemore, B[3]
[1]Allergy Diagnostic & Clincial Research Unit, University of Cape Town Lung Institute, Groote Schuur, South Africa; [2]Pretoria Ampath Pathology, Arcadia, Pretoria, South Africa; [3]Allergy Diagnostic & Clincial Research Unit, University of Cape Town Lung Institute, Mowbray, South Africa

Background: Allergy to porcupine, the largest living rodent, has not been previously reported.

Method: A 31 year old farmer, immediately after eating a piece of barbecued porcupine, developed severe angioedema of the mouth, eyes and face, followed by diffuse urticaria and bronchospasm requiring urgent hospitalization and treatment of anaphylaxis. The patient was a keen hunter who kept mongooses as pets and had also kept mice and rats as pets as a child. Other known allergies were to horses and crustaceans and an oral allergy syndrome to fresh melons, avocado, almond and carrots.

Results: A 31 year old farmer, immediately after eating a piece of barbecued porcupine, developed severe angioedema of the mouth, eyes and face, followed by diffuse urticaria and bronchospasm requiring urgent hospitalization and treatment of anaphylaxis. The patient was a keen hunter who kept mongeese as pets and had also kept mice and rats as pets as a child. Other known allergies were to horses and crustaceans and an oral allergy syndrome to fresh melons, avocado, almond and carrots. A single strong 68 kDa IgE binding band was found to an extract of porcupine meat on Western blotting. Similar IgE binding was also found on immunoblot of proteins prepared from Impala and Wildebeest.

Conclusion: This is the first reported case of anaphylaxis following ingestion of porcupine meat. The patient may have been sensitised following previous exposure to other rodents as a hobby.

1414
Immunoproteomics is complementary to classical diagnostic techniques

Longé, C[1]; Alter, M[1]; Bouakkadia, H[2]; Selva, M-A[3]; Couderc, R[3]; Vaquin, C[4]; Amat, F[5]; Just, J[5]; Boursier, C[6]; Sutra, J-P[7]; Sénéchal, H[1]; Poncet, P[1,8]
[1]Armand Trousseau Children Hospital, AP-HP, Biochemistry Department, Allergy & Environment, Paris, France; [2]Badji Mokhtar University, Biology, Annaba, Algeria; [3]Armand Trousseau Children Hospital, AP-HP, Biochemistry Department, Paris, France; [4]Armand Trousseau Children Hospital, AP-HP, Dermatology, Paris, France; [5]Armand Trousseau Children Hospital, AP-HP, Asthma and Allergy Center, Paris, France; [6]Paris-Sud 11 University, IFR141-IPSIT, Trans-Prot Proteomics, Paris, France; [7]Armand Trousseau Children Hospital, AP-HP, Biochemistry Department, Allergy & Environment, Paris, France; [8]Pasteur Institute, Infections & Epidemiology, Paris, France

Background: Food allergy together with atopic dermatitis is characteristics of the « atopic march » in newborn. GUI is a 6-month old male newborn consulting in the General Pediatric department in Armand Trousseau Children Hospital in Paris, France, for a generalized eczema.

Method: The evaluation of total and specific IgE were performed using ImmunoCap technology simple and multiarray. Further immunoproteomics analysis were carried out using electrophoretic migration of water soluble and non-soluble proteins from peanut in 1 and 2dimension (D) followed by western blot with patient's serum. IgE binding peanut proteins were identified

by mass spectrometry analysis and data bank searches.

Results: Total IgE level was high and the newborn was shown to be sensitized to egg, cow milk, fish and wheat. Specific IgE to total peanut extract was high while barely positive to negative with individual recombinant molecular allergens Ara h 1, 2, 3, 8, 9. IgE reactivities (mainly 60 kDa proteins in molecular mass and around isoelectric point of 6.0) were found in western blots 1D with peanut proteins extracted in detergent and not in aqueous conditions. Two D analysis of a non water soluble peanut extract followed by western blots confirmed the results obtained in 1D and mass spectrometry experiments allowed the identification of Ara h 1 and Ara h 3 as major allergens recognized in the extract by the patient's serum IgE.

Conclusion: In this case report the extraction of proteins in detergent was determinant to evaluate the IgE peanut reactivities in immunoproteomics. The high IgE reactivity obtained with the total peanut extract in simple array ImmunoCap contrasted with the low reactivities to the recombinant molecular allergens. This could have been indicative of the existence of a new allergen. However immunoproteomics results obtained with native proteins extracted in detergent identified Ara h 1 and Ara h 3 as main allergens recognized by the patient's IgE. This result suggests that, for this patient, protein folding, glycosylation and epitope structure is preserved/appropriate in the non water soluble fraction of peanut. Therefore, immunoproteomics analysis is complementary of the classical diagnostic techniques.

1415
Evaluation of structure and allergenicity of bovine allergen β-lactoglobulin oligomers induced by metal ions

Li, X[1,2]; Xie, X[1]; Zhou, J[1]; He, S[1]; Meng, X[1]; Chen, H[1]
[1]Nanchang University, State Key Laboratory of Food Science and Technology, Nanchang, China; [2]Salzburg University, Department of Molecular Biology, Salzburg, Austria

Background: β-lactoglobulin belongs to the retinol binding family of proteins and is the major protein component in bovine whey. It is reported about 82% of cow's milk-allergic patients are sensitive to β-lactoglobulin. The aggregation of β-lactoglobulin is a complex process under a wide range of temperature, pH and metal ions strength conditions. Moreover, the mechanism of metal ions stimulates aggregation of β-lactoglobulin depends on their ability in acting as bridges between proteins.

Method: Bovine β-lactoglobulin was purified by SephadexG-75 combined with DEAE-Sepharose Fast Flow, and identified by SDS-PAGE and mass spectrometry, respectively. Different parameters related to formation of oligomer were investigated including temperature ranging from 40°C to 75 °C, heating time from 0.5 to 2 h, pH from 5.55 to 8.04 and the ratio of metal ions to protein concentration. The particle size of oligomers was monitored by Laser Particle Size and the morphological characteristics was observed by scanning electron microscope. Moreover, the free sulfhydryl content was detected by Ellimen' reagent and secondary structure was defined by CD spectrum. The digestibility change of β-Lg oligomers were compared by simulation of gastrointestinal digestion in vitro and IgG and IgE binding capacity of oligomers were evaluated by competitive ELISA and western-blotting.

Results: The oligomers of β-lactoglobulin were dominated when heated for 0.5 h at 70 °C, with 1:1 of metal ions and protein concentration ratio with pH 7.0. The average particle size of β-Lg oligomers induced by Cu^{2+}, Ca^{2+}, Zn^{2+} and Mg^{2+} were 372 nm, 1236 nm, 1167 nm and 315 nm, respectively, and the free sulfhydryl contents were 0.026, 0.04, 0.033, 0.04 mM, respectively. With respect to digestion ability, monomer and oligomers of β-Lg showed stronger resistance to pepsin than that of trypsin. As for the allergenicity, IgG binding capacity of oligomers was as follow, $Zn^{2+}>Cu^{2+}>Mg^{2+}>Ca^{2+}$, while IgE binding capacity was as follow $Cu^{2+}>Ca^{2+}>Zn^{2+}>Mg^{2+}$.

Conclusion: The particle size of β-Lg oligomers and free sulfhydryl contents significantly different due to the distinguished mechanism induced by different metal ions and Ca^{2+} and Mg^{2} have significant positive effects on decreasing the allgergic risk as nutrients as well.

1417
The SQ® grass sublingual immunotherapy-tablet is well tolerated when administered with concomitant additional allergy immunotherapy

Wolf, H[1]; Keller, M[2]; Keller, W[2]; Schnitker, J[3]; Wüstenberg, E[4,5]
[1]ALK-Abelló Arzneimittel GmbH, Clinical Development, Hamburg, Germany; [2]HNO-Gemeinschaftspraxis, Donaueschingen, Germany; [3]Institut für angewandte Statistik GmbH, Bielefeld, Germany; [4]ALK-Abelló Arzneimittel GmbH, Medical Department, Hamburg, Germany; [5]Universitätsklinikum C.G.Carus, TU Dresden, Clinic for Otolaryngology, Dresden, Germany

Background: The SQ® grass SLIT-tablet is well tolerated according to results from controlled clinical trials and studies on real-life application. Objective of our study was to investigate the tolerability of the SQ® grass SLIT-tablet in patients concomitantly treated with additional AIT(s).

Method: In a non-interventional, open-label, observational study in adults and children from 5 years of age the safety and tolerability of the SQ® grass SLIT-tablet (GRAZAX®, *Phleum pratense* 75 000 SQ-T / 2800 BAU, ALK, Denmark) was assessed in patients who received a concomitant subcutaneous or sublingual AIT (SCIT or SLIT). Tolerability was assessed at first administration of the SQ® grass SLIT-tablet and after 1–3 months treatment according to the first visit for follow-up prescription. Patients recorded in a diary the applications of the SQ® grass SLIT-tablet and concomitant AIT(s) and side effects with date, time, symptoms, severity and actions taken. Adverse events (AEs) and adverse drug reactions (ADRs) were coded using the Medical Dictionary for Regulatory Activities (MedDRA).

Results: Data for 181 patients treated with the SQ® grass SLIT-tablet from January 2012 to January 2014 in 48 allergist′s practices were recorded, of which 160 (85.6% adults, 14.4% children and adolescents) could be evaluated with regard to tolerability for combination with a concomitant AIT. Predominant additional AITs were tree pollen (63.1% of patients) and house dust mites (35.6%); 18.8% of patients received a concomitant SCIT, 75.0% SLIT, and 6.3% two SCITs). Upon combined treatment, AEs were reported in 58 patients (36.3%) and ADRs in 49 patients (30.6%). ADRs possibly related to the concomitant AIT were recorded in 18 patients (11.3%). In the entire study population of 181 patients AEs were reported in 66 patients (36.5%) and ADRs in 57 patients (31.5%), with oral pruritus, oedema mouth, paraesthesia oral and throat irritation as most frequent reactions (>5% of patients). Significant AEs were recorded in 25 patients (SAE in 1 patient, unlikely related to the SQ® grass SLIT-tablet, discontinuation of treatment (8.3% of patients), need for medical measures (9.9%)). The overall tolerability was assessed as good or very good by 91.0% of patients and 91.6% of physicians.

Conclusion: No increase in frequency of AEs compared with data from previous studies or change in the tolerability profile was observed when the SQ® grass SLIT-tablet was administered with a concomitant SCIT or SLIT.

1418
Improving the safety of subcutaneous immunotherapy: are thirty minutes of post injection waiting time enough and if not what can we do about it?

Tziotou, M[1]; Zande, M[2]; Syrigou, E[2]; Sinaniotis, A[2]
[1]National & Kapodistrian University of Athens, 2nd Pediatric Clinic, Allergy Unit, Athens, Greece; [2]Sotiria General Hospital, Department of Allergy, Athens, Greece

Background: Subcutaneous allergen immunotherapy is an effective and safe treatment. However, systemic reactions may occur. International guidelines propose a 30 minutes post injection waiting period in order to prevent these reactions from happening outside the clinic. Formal pharmacokinetic studies are not possible for allergen extracts, either depot or aqueous. The purpose of this study was to examine whether systemic reactions occur within the recommended 30 minutes waiting period and if there are differences between depots and aqueous extracts, regarding the time of occurrence of systemic reactions, irrespective of allergen composition and patient related risk factors.
Method: We retrospectively reviewed the medical records of 138 patients who initiated subcutaneous immunotherapy between 2011 and 2013. Depot extracts were represented by commercially available European physically modified aeroallergens, while aqueous extracts were represented by commercially available hymenoptera venom allergens. The WHO grading system was used for the evaluation of the severity of systemic reactions.
Results: 64 patients initiated subcutaneous immunotherapy with aqueous extracts (venom immunotherapy-group A) and 74 with depot extracts (aerollergen immunotherapy-group B). There were no statistically significant differences in patients' characteristics between the two groups. 23% of patients in group A and 28% of patients in group B experienced a systemic reaction. In group A 62% of reactions were grade I and 38% grade II, whereas in group B 50% were grade I and 50% grade II ($P = 0.343$). In group A, 90% of reactions occurred in the first 30 minutes after the injection and no reaction occurred beyond 60 minutes. On the other hand, in group B, 36% of reactions occurred within the first 30 minutes, 31% 31–60 minutes after the injection and 33% beyond 60 minutes ($P < 0.0001$). There was also a tendency for more severe, grade II, systemic reactions to occur in the first 30 minutes in group A and beyond 30 minutes in group B.
Conclusion: 64% of systemic reactions following subcutaneous immunotherapy with aeroallergen depot extracts occur beyond the proposed 30 minutes post injection waiting time, while 90% of systemic reactions during venom immunotherapy with aqueous extracts fulfill the precautions stated by international immunotherapy guidelines. Extending the proposed post injection waiting time for aeroallergen depot extracts could improve the safety of allergen immunotherapy.

1419
Sublingual allergen specific immunotherapy and standard pharmacotherapy in children with allergic rhinitis and asthma

Filipovic, I[1,2]; Caminati, M[3]; Filipovic, D[4]; Stojanovic, M[5]; Zivkovic, Z[6]
[1]Sanofi Pasteur, Belgrade, Serbia; [2]Faculty of Medical Sciences, University of Kragujevac, Immunology, Kragujevac, Serbia; [3]Verona University Hospital, Allergy Unit, Verona, Italy; [4]Institute for Emergency Medicine, Belgrade, Serbia; [5]Clinical Center of Serbia, Allergology and Immunology, Belgrdae, Serbia; [6]The Centre for Pediatric Pulmonology and TB, Medical Centre "Dr Dragisa Misovic", Belgrade, Serbia

Background: Current treatment for children with asthma and allergic rhinitis include: the allergen avoidance, standard pharmacotherapy and immunotherapy. Due to limitations of standard pharmacotherapy which can only treat symptoms, nowadays immunotherapy starts to play a very important role in treatment of allergic diseases. Immunotherapy is the only treatment with the capability to reorient the natural course of immune response in patients with allergic diseases and in that way to prevent new sensitization and development of other allergic diseases. The aim of our work was to analyze the pharmacotherapy and consequtive outcome in pediatric patients on SLIT.
Method: 34 children (58.8% girls and 41.2% boys), average age 13.8 were included in the study which was conducted in the Centre for Pediatric Pulmonology and TB, Medical Centre "dr Dragisa Misovic", Belgrade. 7 (20.6%) patients were sensitized on Dermatophagoides pteronisimius (DP), 9 (26.5%) on pollens and 18 (52.9%) patients were polisensitized). According to the national and international guidelines and WHO position paper beside the symptom score the drug score is one of the main markers of clinical efficacy of SLIT. During the study procedure (2 years of follow up period) we asked patients to fill in the daily dairy on the medication usage.
Results: Our results showed that there is a significant statistical differences compering the usage of antihistaminic drugs in three different periods of SLIT treatment ($\chi^2 = 32\,774$, $P < 0.001$). Usage of SLIT also leads to the significant statistical reduction of inhalation corticosteroids in daily treatment. The usage of intranasal corticosteroids was significant statistically minimized after two years on SLIT ($\chi^2 = 30\,785$; $P < 0.001$). We also marked a significant statistic decrease of β2 agonist usage during the study (Cochrane's $Q = 28\,783$; $P < 0.001$). The patients on SLIT minimized the usage of LTRA and fixed combination during the procedure (Cochrane's $Q = 28\,783$; $P < 0.001$ and Cochrane's $Q = 25\,200$; $P < 0.001$). During the study we observed significant statistic reduction in all groups of drugs (both controllers and relievers.
Conclusion: Daily treatment with a great number of different groups of drugs for a long period is usually a very uncomfortable and inconvenient especially for children sometimes with not satisfied compliance. SLIT can reduce the usage all groups of drugs for AR and asthma: antihistaminic, LTRA, β2 agonist, INCS, ICS and fixed combinations.

1420
Safety and tolerability of immunotherapy in patients sensitised to Ole e 7 minor allergen of olive pollen

De Luque Piñana, V; Bellido Linares, V; Rubiano Sosa, C; Alcaraz Perez, C; Lopez Ruiz, C; Guardia Martinez, P
Hospital Universitario Virgen Macarena, UGC Intercentros de Alergologia de Sevilla, Sevilla, Spain

Background: Nowadays, safety and effectiveness of specific immunotherapy (SIT) is widely known. This fact has special interest in pollinosis patients, such as olive pollen allergy, in which sensitization to minor allergen Ole e 7 has been related to poorer tolerance to SIT. Ole e 7 is a lipid transport protein (LTP). Being a minor allergen is usually not quantified in most of the extracts used in SIT. Progress in molecular diagnostics has allowed classify patients by risk or probability of developing adverse reaction to SIT due to sensitization profile.In this study we check a group of allergic patients to olive pollen (in some cases also with others allergens), all of them sensitized to Ole e 7, in order to assess safety and tolerability of clustered up dosing pattern with modified polymerized olive extracts.
Method: We reviewed patients sensitised to Ole e 7 referred to Immunotherapy Unit of our Service in the last 2 months. A total of 29 patients were analysed, 19 women and 10 men with a mean age of 21.2 (range 8–50 years). All of them were diagnosed of allergic rhinoconjunctivitis, and 17 had allergic bronchial asthma coexistence.7 patients were diagnosed of pollinosis more

then 10 years ago, and the rest a mean time of 3.35 years. Mean measure of specific Ig E to Ole e 7 was 16.17 (range 0.35 to 66.7).All of them were undergoing modified polymerized extracts, and we used a cluster up dosing schedule performance in one visit: two doses (0,2 + 0,3 ml) separated 30 minutes or a single dose (0,5 ml) depending on the extract used.

Results: Good tolerance was found in 100% of patients undergoing SIT. No acute or late systemic reactions were observed.

Conclusion: Progress in the modified physical and chemical polymerized extracts has increased tolerance and safety profile of extracts used in SIT. In this subgroup of sensitised patients to Ole e7, although this fact is related to increased risk of adverse reactions, we found that the tolerability profile of modified polymerized extracts was very good and similar to population not sensitized to Ole e 7.

1421
Tolerance of administration of sublingual extract peach immunotherapy, compared with conventional regimen

de Luque Piñana, V; Lopez Ruiz, C; Gonzalez Montaño, MD; de la Calle Toral, A; Guardia Martínez, P
Hospital Universitario Virgen Macarena, Sevilla, Spain

Background: Allergy to fruits is the most frequent food allergy in adolescents and adults Worldwide.

The clinical presentation comprises systemic reactions mainly generalized urticaria and anaphylaxis, in approximately one-third of the patients, and OAS in the remaining.

The major allergens involved in this so called Mediterranean pattern are non-specific lipid transfer proteins (LTP), with a rate of sensitization of around 70%.

There is an specific sublingual immunotherapy with a Pru p 3 quantified peach extract that can be a promising therapeutic option that could modify the clinical reactivity of the patients to the intake of peach and the underlying immunological response with an overall good tolerance.

Method: Check tolerance of administration of sublingual extract peach immunotherapy, compared with conventional regimen recommended by the manufacturer.

It includes patients referred for sublingual administration beginning of peach extract during 2014. Of a total of 20 patients: 15 women, five men with a mean age of 29.5 years. 12 patients referred allergy to nuts, 14 to Rosaceae fruits, of which the most frequently involved was the peach (14), followed by apple (8), and among the most common legumes was the peanut (7) and and other plant foods like lettuce involved (3).

a group of 12 randomized patients doses of sublingual immunotherapy regimen was administered two days until reaching maintenance dose (first day dose vials 1, 2 and 3 corresponding to 0.4, 2 and 10 MCRG / ml PRUP p3 and the next day dose vial of 50 micgr / ml). In another group of 8 patients rush pattern is performed in a single day with increasing doses micgr vial 50 / ml of P3 to reach PRUP maximum dose.

Results: All patients maintenance dose is reached, presenting only local reactions (oral itching), self-limiting in its entirety without needing treatment.

Conclusion: Sublingual immunotherapy with peach has proved to be safe as no serious adverse events were observed. However, the patients that presented LRs in the oral cavity, most of them consisted of mild oral itching and were well accepted and were also similiar to those reported in the literature with the conventional dosage. We think this new pattern of rapid administration of the extract for SLIT peach that achieves therapeutic doses in one day, a saving in direct and indirect costs of this type of immunotherapy.

1422
Adrenaline auto injector experience of children receiving immunotherapy in a single centre

Bostanci, I; Ertugrul, A; Corut, N; Ozmen, S; Keles, S; Seymen, H
Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Pediatric Allergy Immunology, Ankara, Turkey

Background: Allergen immunotherapy (AIT) has been shown to be an effective treatment for respiratory allergies and hymenoptera venom allergy. AIT aims development of immuntolerance by administering increasing amounts of specific allergens. Administering these allergens may lead to development of hypersensitivity reactions. Self-injectable epinephrine is an important life-saving treatment in patients with anaphylaxis associated with AIT.

Method: A questionnaire consisting of questions about adrenaline auto-injector (AAI) experience in AIT patients was applied to parents of these patients. Demographics and clinical features, AAI availability and requirement, family education and knowledge of AAI were questioned.

Results: Fully completed surveys from 54 patients (66.7% male; 72.2% mono-sensitized, 90.7% SCIT) were analysed. Mean duration of SIT was 25.2 months with different allergens; venom allergy (11.1%), grass allergy (38.9%), grass and cereal allergy (33.3%), and house dust mite (13%), grass, cereal and olive (1.9%), ash tree and olive (%1.9). AAI was prescribed to 51.9% of the patients but 67.8% of these have still AAI available and only 21% of the patients carry their AAI with them. 22.2% of the patients defined local reaction after SCIT. Among all patients none of them needed to use AAI after immunotherapy administration, but only one of the patients with the venom allergy was experienced anaphylaxis and was required AAI admınıstration due to bee sting.

Conclusion: All AIT patients that have been experienced systemic reactions and Ig E mediated reactions previously and patients with venom allergy should be prescribed AAI definitely. But the patients on the other side is still open to debate.

1423
The usefulness of immunotherapy

Licari, A[1]; De Amici, M[1]; Marseglia, A[1]; Caimmi, S[1]; Caimmi, D[2]; Trovamala, V[1]; Madè, A[1]; Torre, C[1]; Desmet, N[1]; Marseglia, GL[1]
[1]Foundation IRCCS Policlinico San Matteo, Department of Pediatrics, Pavia, Italy; [2]CHRU de Montpellier, Allergy Unit and Cystic fibrosis Center, Montpellier, France

Background: In the last years the prevalence of allergic diseases has increased in industrialized country. The great part of allergic reaction derive from IgE antibodies for protein recognized from immunologic system (antigens), defined allergens. All allergens are proteical component or glycoproteins usually harmless for our body, than the allergy is considered an inadequate response of our immunological system to these proteins. In our case were analyzed patients referred to IRCCS Policlinico San Matteo of Pavia that are sensitized for certain type of grasses than was carried out a therapy which was observed its effectiveness trough follow-up to see if there was an improvement in symptoms, to understand whether or not to continue with the therapy.

Method: At examined patients was made to fill in a questionnaire about severity of their symptoms how rhinitis, conjunctivitis and asthma using score from 0 to 3 for the severity of symptoms for the first two disease and the values of fcv, fev, fef for asthma. Completed the clinical part, specific IgE analysis was carried out for each allergen, in our case grasses. Is used a tests for the activation of basophils CD63 with citofluorimetry. The results of the exams are valued also drawing graphs with the values of IgE triggered by allergen found in the whole patient and its dilutions, eval-

uating the lowering of the concentration of IgE in time.

Results: For the total of patients on which it was decided to attend with immunotherapy in order to alleviate the symptoms of allergy was fill again the table of the clinical symptoms to understand if there is an improvement of symptoms and then continue with immunotherapy. Their results are: on 11 patients that we considered also with their follow-up, thanks to therapy for the first year one patient gets better than worse for rhinitis that for conjunctivitis but not for asthma which continued to get better; for another one remain the same all the symptoms except asthma that gets better; for another patient get better only conjunctivitis symptoms while others remain the same or get worse; for three patients get better all symptoms but we don't have successive values about the follow-up; for another three all symptoms get better and for only two patients we verify a worsening of all symptoms.

Conclusion: This study, despite the immunotherapy is expensive for the treatment of allergic disease, shows that there is an improvement in the great part of cases.

1424
Risk factors for systemic and local reactions to subcutaneous allergen immunotherapy

Nacaroglu, HT[1]; Erdem Bahceci, S[1]; Sumer, O[1]; Karaman, S[1]; Unsal Karkıner, CS[1]; Dogan, D[1]; Asilsoy, S[2]; Altınoz, S[1]; Gunay, I[1]; Can, D[1]
[1]Dr Behcet Uz Children's Hospital, Division of Pediatric Immunology and Allergy, Izmir, Turkey; [2]Dokuz Eylul University Hospital, Division of Pediatric Immunology and Allergy, Izmir, Turkey

Background: Local, and especially systemic, reactions are important problems in subcutaneous immunotherapy (SCIT). Local reactions develop in 0.7–4% of all injections and systemic reaction develops in 0.2%. The current study aimed to evaluate the frequency and risk factors of reactions developing in patients undergoing SCIT.

Method: Local and systemic reactions developing after 14 308 injections between 2003 and 2013 were retrospectively evaluated in the current study. The grading system for systemic reactions that was recommended by the World Allergy Organization (WAO) was used. The type of allergic disease, the allergens producing sensitivity, the vaccine content, the adjuvant content, and the effects of treatment phase on frequency of adverse effects were investigated.

Results: Out of 329 patients included, there was local reaction in 11.9%, large local reaction in 6% and systemic reaction in 4.7%; local reactions were observed in 0.38% of all injections, whereas a systemic reaction was observed in 0.1% of all injections. Local reactions were frequent at the initial phase and systemic reactions were frequent at the maintenance phase ($P = 0.01$). Adverse reactions were more common in patients vaccinated (SCIT) with multiple allergens and house-dustmites ($P = 0.002$). No statistically significant difference was found between the content of the adjuvant and the frequency of adverse effects ($P = 0.319$).

Conclusion: The frequency of local and wide local reactions during subcutaneous immunotherapy were lower than expected. Although systemic reactions are frequently seen, no fatal reaction was observed in the current study. Mite immunotherapy and multiple allergen use increase the risk of reaction.

1425
Safety evaluation of immunotherapy using high doses of polymerized allergen extracts

Guzmán-Fulgencio, M; Caballero, R; Lara, B; Mena, M; Subiza, JL; Fernández-Caldas, E; Casanovas, M
Inmunotek S.L, Madrid, Spain

Background: Allergen extracts chemically modified with glutaraldehyde show a significant reduction in specific IgE binding capacity. This allows the administration higher doses in a shorter period of time.

The objective of this study was to evaluate the safety of immunotherapy treatments containing 3 times the conventional dose of the modified allergen extracts used in normal clinical conditions

Method: The study included a total of 343 patients, 174 men and 169 women (age range 4–69 years, mean 26). From these, 241 patients (121 men and 120 women) were treated with a mite mixture containing D. pteronyssinus and D. farinae and 102 (53 men and 49 women) were treated with grass pollen. The treatment was a set containing vials at a concentration of 30 000 TU/mL. Major allergens: Dermatophagoides 12 μg/mL of group 1 and 6 μg/mL of group 2 (measured by monoclonal antibodies); grasses 73.8 μg/mL of groups 1 + 5 (measured by means of scanning densitometry). Two administration schedules were used: conventional and rush. Conventional schedule: the first day patients received 0.2 mL (6000 TU) followed by the maintenance dose after 7 days. Rush schedule: the first day they received 0.2 mL (6.000 TU) followed by 0.3 mL (9.000 TU) after 30 min. Maintenance dose was 0.5 mL every 4 weeks for both schedules.

Safety was evaluated registering all adverse events related to the administration of these preparations and were graded according the EAACI criteria

Results: A total of 2715 injections were administered (mean of 7.9 per patient). Local reactions were 33 immediate and 10 delayed. Systemic reactions were 4 immediate and 9 delayed (8 of grade I and 1 of grade II).

Conclusion: The chemical modification of allergen extracts allows the administration of higher doses in a short period of time with a high degree of safety. This fact could expedite the clinical benefit. The significant reduction in the number of injections and in the time needed to achieve the maximum dose provides better compliance and cost-effectiveness.

1426
51 systemic reactions in 15 year follow up after subcutaneous immunotherapy injections

Erdem Bahceci, S[1]; Karaman, S[1]; Nacaroglu, HT[1]; Unsal Karkıner, CS[1]; Gunay, I[1]; Asilsoy, S[2]; Altınoz, S[1]; Dogan, D[1]; Can, D[1]
[1]Division of Pediatric Immunology and Allergy, Dr Behcet Uz Children's Hospital, Izmir, Turkey; [2]Division of Pediatric Immunology and Allergy, Dokuz Eylul University Hospital, Izmir, Turkey

Background: Although allergen immunotherapy is an effective treatment method used for more than 100 years in rhinitis, asthma and venom anaphylaxis, systemic reactions limit the use of this therapy. The systemic reactions (SRs) related to subcutaneus immunotherapy (SCIT) have been investigated according to their distribution of severity and risk factors.

Method: Retrospectively we evaluated 67758 injections applied in our Pediatric Allergy Department between 1999 and 2014, and all cases which developed SCIT-related systemic reactions were included to this study. Severity of SRs were graded according to the WAO's classification. Early onset was defined as beginning at the first 30 minutes, and delayed onset as beginning more than 30 minutes after injections. Risk factors related to the emergence of SRs were investigated.

Results: In 67758 injections 51 systemic reactions were seen in 39 patients (0.075%). 51.3% of SRs was grade 1; 38.5% grade 2; 7.7% grade 3 and 2.6% was grade 4. 41% of SRs was early onset and 59% delayed onset. Risk factors were determined as being in maintenance phase of SCIT in 76.9%, being uncontrolled asthma in 7.7%, being in the peak season of pollens in 56.4%, presence of previous reaction in 28.2% and presence of previous grade 1 reaction in 30.8%.

Conclusion: SCIT related SRs are generally in light intensity, however grade 4 reactions have been found more frequently. The frequency of serious SRs can be reduced by a carefull evaluation of the patient's previous reactions and illnesses.

1427
Repeated dose toxicity studies with vaccines containing natural allergenic extracts

Gomez, M; Ponte, A; Landeta, A; Madariaga, B; Asturias, J; Martinez, A
Bial-Arístegui, R&D Department, Zamudio, Spain

Background: Non-clinical data on safety of vaccines containing native allergenic extracts are rarely found on literature. Assessment of toxicity of vaccines for allergen immunotherapy should be done in spite of their well-established use and in spite of the fact that environmental exposure to constituents of native allergenic extracts is unavoidable. In the case of subcutaneous immunotherapy (SCIT) depot preparations containing aluminium adjuvants, the need for a safety evaluation is increased further.
Method: SCIT depot vaccines (Allergovac) containing alum-adsorbed extracts from a range of relevant common aeroallergen groups (*Dermatophagoides pteronyssinus, Phleum pretense, Parietaria judaica, Olea europaea* and *Alternaria alternata*) were subjected to a 28-day subcutaneous toxicity study in the Wistar rat followed by a 2-week recovery period. Local tolerance was assessed by histological examination. IgG specific antibody responses towards the immunizing allergens were also determined. Vaccines were administered subcutaneously once a week. Four treatment groups were used, receiving saline, depot diluent and two allergen concentration level of finished vaccine preparations.
Results: In any of the studied cases no mortality was recorded during the treatment or recovery periods. No test-item-related clinical signs were recorded throughout the treatment period. Nodules at the injection sites were recorded in the test-item- and adjuvant-treated animals. A slight increase in body temperature was recorded in some animals. The administration of vaccines did not cause other macroscopic findings, or differences in organ weights. No relevant differences between groups were recorded in the IgG levels.
Conclusion: Repeated dose (sub-acute) toxicity studies done by subcutaneous administration of depot vaccines from five common aeroallergens to Wistar rats once a week for 4 weeks (a total of five administrations) did not cause toxicological findings, thus confirming the safety profile of these preparations. The signs observed at the injection site were caused by the adjuvant (aluminum hydroxide).

1428
Safety of inmunotherapy treatments containing mixtures at optimal doses of each modified allergen extract

Caballero, R; Lara, B; Guzmán-Fulgencio, M; Mena, M; Subiza, JL; Fernández-Caldas, E; Casanovas, M
Inmunotek S.L, Madrid, Spain

Background: Immunotherapy in polysensitized patients is an important issue. Normally, patients receive allergen mixtures, which affect the final concentration of each extract. Glutaraldehyde modified allergen extracts show a significant reduction in specific IgE binding capacity and in the intrinsic proteolytic activity. These properties allow mixing allergen extracts without modifying the final concentration of each component and without proteolytic degradation.

The objective of this study was to evaluate the safety of rush administration of immunotherapy treatments containing mixtures of different modified allergen extracts, keeping each extract at its optimal concentration (without dilution factor).
Method: The study included 1216 patients, 663 men and 553 women (age range 5–70 years, mean 27). All were treated with mixtures of modified allergen extracts: 284 with mites and pollen, 29 with cat dander and mites and/or pollen and 903 with a mixture of allergenically unrelated pollens. The concentration of each allergen extract was 10 000 TU/mL. Major allergens: *Dermatophagoides* 4 μg/mL of group 1 and 2 of group 2; grasses 24.6 μg/mL groups 1 + 5, *Olea*, 24 μg/mL of Ole e1.

The rush administration schedule consisted of: the first day 0.2 mL followed by 0.3 mL after 30 min; the maintenance dose was 0.5 mL each 4 weeks.

Safety was evaluated registering all adverse events related to the administration of these preparations and were graded according the EAACI criteria.
Results: A total of 6879 injections were administered (mean: 5.6 per patient). Local reactions were: 17 immediate and 22 delayed. Systemic reactions were all of grade I: 34 immediate and 19 delayed.
Conclusions: Modified allergen extracts allow the administration of optimal doses of each allergen extract in mixtures using a rush schedule with a high degree of safety. It allows the treatment of polysensitized patients in single treatment sets and without increasing the number of injections. These factors could significantly improve the treatment of clinically relevant polysensitized patients reducing costs and time.

1430
Single center pilot study of small amount induction oral immunotherapy to persistent severe milk allergy

Yanagida, N[1]; Sato, S[2]; Nagakura, K[1]; Okada, Y[1]; Asaumi, T[1]; Ogura, K[1]; Ebisawa, M[2]
[1]Sagamihara National Hospital, Kanagawa, Japan; [2]Sagamihara National Hospital, Clinical Research Center for Allergy and Rheumatology, Kanagawa, Japan

Background: Many of the milk immunotherapies are set at a target volume of 100 mL~200 mL. However, with milk allergies, if a removal of allergies against approximately 3 mL is possible, then 10 g of butter can be ingested, and a large improvement in the quality of life may be possible.

The aim of this study is to investigate the efficacy and safety of small amount induction oral immunotherapy (SOIT) (UMIN000011202), which is an oral immunotherapy set at 3 mL of milk, which is a lower target volume than what is conventionally used.
Method: This study was a single center pilot study. Subjects were children with milk allergies above age 5, who exhibited clearly positive symptoms by OFC against 3 mL of pasteurized milk. A comparison was made between the SOIT group where the treatment was performed, and the Control group where an oral food challenge test (OFC) was simultaneously performed. The SOIT group was admitted to hospital for 5 days for build-up. At home, the volume was gradually increased by 0.2~0.5 mL up to a maximum of 3 mL, every five days. The primary end point was the acquiring tolerance against 3 mL or 25 mL of pasteurized milk after one year. The secondary end point was the symptom induction rate of the SOIT group.
Result: The proportion of tolerant to 3 mL after one year was 58.3%(7/12) in the SOIT group, and 10.0%(1/10) in the Control group, and this difference was statistically significant ($P = 0.031$). Of the 7 subjects where tolerant to 3 mL was confirmed in the SOIT group, 4 subjects could intake as much as 25 mL. A significant decrease casein-specific IgE levels was seen between commencement and after 12 months ($P = 0.033$) in SOIT group.The SOIT group consumed milk 56 times when admitted to the hospital, and 3739 times as an outpatient. The symptom induction rate per intake was 57.1% in hospital and 19.5% at home, of which: mild symptoms were 23.2% in hospital and 17.5% at home, moderate symptoms were 23.2% in hospital and 2.0% at home, and severe symptoms

were 0% in hospital and 0.03% at home. Adrenaline was used in one case. 2.5 mL was taken at home, and a cough occurred.
Conclusion: SOIT seemed to be effective to acquire tolerant to 3 mL and 25 mL of milk and severe symptoms were rare. This indicates that for the improvement of food allergies, continuing the intake of small amounts without increasing above a certain level can be as effective. A prospective randomized control trial with a larger sample size will be awaited in the future.

1431
Oral induction of tolerance to Rosaceae if dual sensitization of PR-10 and LTP

Bradatan, E[1]; Vandezande, LM[2]; Van der Brempt, X[2]
[1]Centre Hospitalier Regional, Pediatrics, Namur, Belgium; [2]Allergopôle, Clinique Saint-Luc, Namur, Belgium

Background: Allergy Betulaceae is frequently associated with oral allergy syndrome Rosaceae. This is most often cross reactions via the PR-10. Sensitization to LTP associates rarely there. The symptoms reflect these two phenotypes is simple oral allergy syndrome (itching and local edema) or (association with) general symptoms. SLIT birch is effective on respiratory symptoms but little food improves symptoms.
Objective: Oral induction of tolerance to fruits,with the goal to reduce the risk of severe reaction and improve the quality of life of patients who developed anaphylaxis after consumption of peach, soy, pear, and apple.
Methods: Five children (age 4–17 years) allergic to birch cross with food allergy who had never undergone specific immunotherapy were included. They all had respiratory symptoms and an oral syndrome (apple, pear, peach, soybean, hazelnut), but also a history of severe anaphylactic reactions in relation to the Rosaceae. Skin prick tests and RAST were performed.
Results: Five patients had concurrent sensitization LTP and PR-10 proved by RAST(rBet v 1 and rPru p 3). Oral food challenge with fruits (apple n = 3, n = 1 pear, peach n = 1) were performed at the beginning of treatment (OIT) and after 8 months. Cumulative reactogenic doses after the first TPO ranged from 2 g to 12 g. An OIT with apple, pear or peach as the case has been started after the first OFC with increasing dose in steps of 2 to 3 weeks. After 8 months on average, all patients tolerate 120 grams of fruit (some side reactions limited to a mild oral syndrome). The maintenance of tolerance has been provided by fruit consumption 2x / week. Then a gradual reintroduction of other Rosaceae was proposed. In two patients (ages 8 and 14) the interruption of the administration of the food for respectively 2 and 3 months resulted in a recurrence (respectively oral syndrome and facial edema).
Conclusion: In these 5 children sensitized to LTP and PR-10, the OIT was achieved without serious side effects. Consumption of a sufficient dose of fruits is strongly recommended, at least 2 times by week to maintain tolerance.

1432
Oral immunotherapy (OIT) with egg white: immunological changes

Pereira, MJ; Lizaso, MT; Arroabarren, E; Echechipía, S; García, BE; Tabar, AI
Complejo Hospitalario de Navarra, Allergy Department, Pamplona, Spain

Background: Hen's egg is one of the most frequent causes of food allergy in children. Our aim was to describe the immunological evolution of specific IgE (sIgE), specific IgG4 (sIgG4) and the ratio between them, during the first year of OIT and the relationship with tolerance.
Method: OIT was performed using dehydrated egg white (EW). During 2 years, we included 76 pediatric, patients (Boys 40, Girls 36), median age 8.92 years (7.2–11.42 IQR), sensitized to EW, Ovoalbumin (OVA) and/or Ovomucoid (OM), fulfilling the following inclusion criteria: Positive oral challenge (n = 64), some recent reaction < 12 months (n = 10) and/or specific (EW or its proteins) sIgE>50 KU/L (n = 2).

Doses were administered increasing weekly. During the maintenance period was administrated three eggs per week. Serum sIgE and sIgG4 (EW, OVA, OM) were measured with CAP at the different times: Baseline (T0), at maintenance after 3, 6 and 12 months (T3, T6, T12). The number of reactions along OIT and the duration of updosing phase were considered as a measure of tolerance. Non-parametric tests were used to analyzed the results (Kendall, Wilcoxon, Kruskal - Wallis, Rho Spearman).
Results: The median sIgE (KU/L) decreased significantly from T0 (EW: 5.04; 1.76–10.7; OVA: 2.75; 0.99–5.95; OM: 3.11; 1.02–11.65) to 3, 6 and 12 months (EW: 2.05; 0.76–2.38; OVA: 0.78; 0.36–2.38; OM: 1.72; 0.66–6.08) ($P < 0.05$).

The median sIgG4 (mg/L) increased significantly from T0 (EW: 0.19;0.01–0.93; OVA: 0.12;0.01–0.84; OM:0.10; 0.01–0.29) to 3, 6 and 12 months (EW:6.31;1.27–21.48; OVA: 6.8;1.49–17.23; OM: 3; 0.83–10.05) ($P < 0.05$). sIgE/sIgG4 ratio to EW, OVA and OM shown a similar pattern. Adverse effects were frequently reported: 49/76 patients at the updosing phase, 24/73 at T1, 22/67 at T3, 15/44 at T6 and 1/24 at T12. Correlation between length updosing phase and sIgE basal to EW (r = 0.34), OVA (r = 0.32) and OM (r = 0.27) was found ($P < 0.05$). No other significant variable related with tolerance were detected.
Conclusion: We observed immunological changes associated with desensitization in OIT. Exist a correlationship between the value of basal sIgE (to EW, OVA and OM) and the time required to achieve the maintenance phase.

1433
Oral allergy syndrome recurring in the first year of allergen specific immunotherapy

Dumitrescu, NV; Cretu, ID; Tudose, AM; Albert, K
Clinical Hospital 'Nicolae Malaxa', Bucharest, Romania

Background: Allergic rhinoconjunctivitis is a widespread health problem with an important impact on the patient's quality of life. OAS -Oral allergy syndrome (or fruit - pollen syndrome) is usually caused by cross-reactive epitopes found in both pollen and raw fruits, nuts and vegetables and occur in aeroallergen induced disease. Allergen specific immunotherapy is the only immune modifying treatment that could prevent the natural progression of allergic disease and SLIT (sublingual immunotherapy) is one of the most common types of immunotherapy with superior adherence and safety profile.
Method: A 31 years old male patient with history of moderate- severe rhinoconjunctivitis symptoms (nasal, eyes and throat itching, sneeze, conjunctival hyperemia, watering eyes, peri-orbital edema) manifested every late summer - early autumn in the previous five years. In Romania, this period of the year is the pollinating season of weeds, especially plants in the *Asteraceae* family.
Results: *In vitro* and *in vivo* tests showed dominant sensitization of the patient to *Ambrosia* sp. pollen. *Ambrosia* specific immunotherapy was started and during the first year of the treatment the patient had good clinical response regarding the intensity of the initial symptoms but with onset of oral allergy symptoms triggered by consumption of melons and bananas.
Conclusion: Sublingual immunotherapy is administrated directly to the oral mucosa and determines in most of the cases, the allergen tolerance. However, in other cases it is possible to aggravate or induce allergy symptoms and rarely including OAS manifestations.

Poster Session Group III - Green TPS 50
Atopic dermatitis

1434
Dominancy of *Staphylcoccus spp.* in the skin of atopic dermatitis patients compared to healthy subjects through metagenomic analysis

Kim, M-H[1]; Rho, M[2]; Min, T-K[3]; Cho, Y-J[4]; Pyun, BY[3]; Kim, Y-K[5]
[1]Ewha Womans University Medical Center, Seoul, Korea; [2]Hanyang University College of Medicine, Computer Engineering, Seoul, Korea; [3]Soonchunhyang University College of Medicine, Pediatrics, Seoul, Korea; [4]Ewha Womans University Medical Center, Internal Medicine, Seoul, Korea; [5]Ewha Womans University Medical Center, Ewha Institute of Convergence Medicine, Seoul, Korea

Background: *Staphylococcus aureus* is known to be the most frequent cause of skin infection or aggravating factor in atopic dermatitis patients. The colonization rate of *S. aureus* reaches to 90% of atopic dermatitis patients, which is much higher than in the healthy subjects. Until now, bacteria could be identified only through the bacterial culture technique, by which only 1% of total bacteria can be identified. Here, we performed metagenomic analysis to determine major colonizing bacteria in the skin of atopic dermatitis patients vs. healthy control subjects.
Method: Seventeen patients with atopic dermatitis and 6 healthy control subjects were enrolled. Skin washing fluids were obtained from the moistened gauze which loaded on the skin lesion in the cubital fossa of atopic dermatitis patients and on the same part of normal controls. After genomic DNA was extracted from the skin washing fluids, 16s ribosomal DNA was amplified using the universal primer, sequenced through the next generation sequencer, and then the sequenced data was analyzed using bioinformatics.
Results: *Staphylococcus spp*. was dominant in the skin from atopic dermatitis patients, while it was undetectable in the control subject skins. The mean proportion of Staphylococcus in the total bacterial DNA of atopic dermatitis patients was 68%, however that was 0% in normal controls. The following frequent bacteria were *Pseudomonas* and *Streptococcus* spp., and their proportions were 11% and 10% in the patients vs. 2% and 1% in the controls, respectively. On the other hand, Alcaligenaceae family and *Sediminibacterium spp*. were the most frequent bacteria in the skin of the controls, and their proportions were 39% and 13% in the controls vs. 0% and 0% in patients, respectively.
Conclusion: Staphylococcus is the predominant colonizer in the atopic dermatitis skin through the metagenomic analysis of bacterial DNA.

1435
The effect of airborne toluene on skin barrier function in atopic dermatitis

Park, M[1]; Lee, J[2,3]; Kim, Y[3,4]; Kim, H[3]; Han, Y[3,4]; Lee, J-O[3,4]; Ahn, K[2,3]
[1]Sungae General Hospital, Pediatrics, Seoul, Korea; [2]Samsung Medical Center, Pediatrics, Seoul, Korea; [3]Samsung Medical Center, Environmental Health Center for Atopic Diseases, Seoul; [4]Samsung Biomedical Research Institute, Seoul, Korea

Background: To control atopic dermatitis (AD), proving the relationship of air pollutants and AD is important. This study is to evaluate the effect of airborne toluene to skin barrier function in children with AD.
Method: We enrolled patient aged 5–18 with AD and normal healthy children. Provocation test was performed by stimulating 2 different areas of normal-appearing skin on the forearm with airborne toluene and placebo. We measured transepidermal water loss (TEWL), skin pH and water content of stratum corneum at baseline, 1 and 2 hours of exposure, and calculated percentage change from baseline. Datas were analyzed using the Wilcoxon signed rank test and Mann-Whitney U test.
Results: Test was performed to the 32 AD patients and 15 controls. The level of TEWL was elevated in AD group after exposure 2 hours to both toluene and placebo. Skin pH showed no significant change to both toluene and placebo in both group. The level of water content of stratum corneum lowered after 2 hours exposure to toluene in both AD group and control group ($P < 0.05$). The percentage change of water content of stratum corneum was higher when exposure to toluene than placebo in both group. There are no significant differences between AD group and control group. The percentage change of TEWL was higher when exposure to toluene in AD with family history of AD ($P < 0.05$).
Conclusion: Toluene exposure causes skin barrier dysfunction in both control and AD patient, but not prominent in AD.

1436
Interaction between mold exposure and IL13 polymorphism increases the risk for atopic dermatitis in atopic children through down-regulation of skin barrier protein

Shim, JY[1]; Kang, M-J[2]; Kim, HK[2]; Hong, S-J[3]; The Group of Allergic Disease Standardization
[1]Sungkyunkwan University School of Medicine, Pediatrics, Seoul, Korea; [2]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [3]Asan Medical Center, University of Ulsan College of Medicine, Pediatrics, Seoul, Korea

Background: Both environmental and genetic factors contribute to increasing numbers of children with atopic dermatitis (AD). Mold exposure and IL13 polymorphism are known to be risk factors for allergic diseases. Filaggrin is a key protein for the integrity of skin barrier, and skin barrier dysfunction is considered as the mainstay of AD. We investigated the association between mold exposure and IL13 polymorphism on current AD in Korean adolescents and the expression of filaggrin in mycotoxin patulin-treated AD mouse model.
Methods: A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to investigate the prevalence of AD, and *IL13 + 2044G/A* polymorphism were analyzed in 520 middle school students. Mice were treated with patulin, and the expression of filaggrin was assessed from the mice skin using immunohistochemical staining.
Results: Prevalence of current AD was 8.2%. After controlling for potential confounders, exposure to visible mold during infancy was associated with current AD in subjects with *IL13 + 2044G/A* polymorphism. However, the interaction between exposure to visible mold and *IL13 + 2044G/A* polymorphism was only found in subjects with atopy, not without atopy. The expression of filaggrin from the skin of patulin-treated mice decreased significantly compared to control mice.
Conclusion: Mold may contribute to atopic dermatitis in atopic children with *IL13 + 2044G/A* polymorphism, partly by down-regulation of skin barrier protein.

1437
Chromosome 11q13.5 variant as a risk factor for atopic dermatitis in Polish children population

Debinska, A; Danielewicz, H; Drabik-Chamerska, A; Kalita, D; Boznanski, A
1st Department and Clinic of Paediatrics, Allergology and Cardiology, Wroclaw Medical University, Wroclaw, Poland

Background: Atopic dermatitis is a chronic inflammatory skin disease with multifactorial etiology and a strong genetic basis. Apart from filaggrin (FLG), the genes influencing atopic dermatitis are largely unknown. A single nucleotide polymorphism on chromosome 11q13.5 (rs7927894) was currently identified in GWASs as novel susceptibility loci of atopic dermatitis. The aim of the study was to evaluate the association of this genetic variants with atopic dermatitis and to investigate its possible interaction with FLG null mutations in Polish children population.
Method: Of 188 children younger than 2 years of age were screened for the variant of allele of rs7927894 on chromosome 11q13.5 and for the 4 most prevalent FLG mutations. All subjects were selected using a detailed questionnaire that included questions on symptoms of atopic dermatitis and blood samples for total and specific IgE measurement were obtained. Atopic dermatitis cases were diagnosed according to the criteria of Hanifin and Rajka and skin examination. The variant of allele rs7927894 and all FLG mutations were genotyped by real-time PCR assays with subsequent melting curve analysis using a SimpleProbe® probes.
Results: The rs7927894[T] allele was found to be significantly higher in the atopic dermatitis group when compared with controls ($P = 0.009$). In dominant model adjusted for potential confounders, rs7927894[T] allele was associated with significantly increased risk for atopic dermatitis (OR 2,21; 95%CI; 1,14, 4,28; $P = 0.015$). Both allergic and non-allergic patient groups had rs7927894 T allele significantly more frequently than the control group, however, the frequency of alleles did not differ in these two groups. There was no significant association between rs7927894 variant and atopic dermatitis severity. After stratification for FLG mutations previously identified in this population, significant association between the rs7927894[T] and atopic dermatitis was seen only in group without FLG mutations. Furthermore, when rs7927894 variant and FLG mutations were consider together, the risk of atopic dermatitis was the most increased in the subjects who combined both rs7927894 [T] allele and at least one FLG mutation (OR 9,90; 95%CI; 1,81; 71,12).
Conclusion: Our results indicate that the rs7927894 variant on the chromosome 11q13.5 may play a role in the development of atopic dermatitis, but this effect seems to be independent of allergic sensitization and may be modulated by gene-gene interactions.

1439
A rare exacerbator of atopic dermatitis: chicken allergy in an infant

Yavuz, ST[1]; Koc, O[2]; Selcuk, A[3]; Gülec, M[3]; Gok, F[2]
[1]GATA School of Medicine, Ankara, Turkey; [2]Department of Pediatrics, GATA School of Medicine, Ankara, Turkey; [3]Department of Adult Allergy and Immunology, GATA School of Medicine, Ankara, Turkey

Introduction: Atopic dermatitis is a frequent disease in infancy and nearly half of the cases are worsened by certain foods in sensitized infants. Most common foods associated with atopic dermatitis in our population are cow's milk, hen's egg, peanut, treenuts, wheat, soy and beef. Herein, we report infant with atopic dermatitis associated with chicken allergy which is a relatively rare cause of food allergy in childhood.
Case report: A 3-month old boy admitted to our outpatient department suffering from pruritus and erythematous lesions in his cheek. Physical examination revealed dry skin and widespread eczematous lesions in his body and he was diagnosed with atopic dermatitis. He was exclusively breast-fed. A skin prick test with most common food allergens including cow's milk, hen's egg, peanut, treenuts, wheat and soy was performed and resulted as negative. As his mother carefully noticed and reported the exacerbation of the eczematous lesions after chicken consumption, we performed a skin prick test and there was a 8X9 mm. edematous reaction with ertyhema. He was prescribed topical steroids and his lesions recovered with chicken elimination from the mother's diet. After two weeks of uneventful period, his mother started chicken consumption and the lesions exacerbated in two days. He was diagnosed with chicken allergy and elimination of chicken from the mother's diet was re-initiated. He is still asymptomatic and under regular follow-up for six months.
Conclusion: Along with the leading causes of food allergy associated with atopic dermatitis in childhood, rare foods may cause allergic reactions in children. Skin prick test panels should also include the foods particularly suspected after the interview with mothers of breast-fed children along with the most common incriminated food allergens.

1440
Symbiotic adjuvant therapy in atopic dermatitis

Rial Prado, MJ; López Rico, R; Parra Arrondo, A; Pérez Quintero, O; Meijide Calderón, A
CHUAC, Allergy and Clinical Immunology, A Coruña, Spain

Background: Atopic dermatitis is a disease with a lot of clinical interest because it is the point of attachment between allergic diseases and autoimmune diseases. In the intrinsic atopic dermatitis the effector cells belong to the innate immunity and the allergen specific TH2 cells are added in extrinsic atopic dermatitis. Probiotics and synbiotics favor the expression of anti-inflammatory Th1 cytokines which produces therapeutic benefits in patients with atopic dermatitis as revealed by recent meta-analysis.
Method: Five patients (3 women and 2 men) suffering from moderate atopic dermatitis aged between 16 and 28 years were treated with *Bifidobacterium lactis* BS01, *Lactobacillus rhamnosus* LR05 and prebiotic fructo -oligosaccharides (2x10 ^ 9 CFU) once daily in a period of four months added to their previously scheduled topical treatment. SCORAD index and dermatitis quality of life test (DQL) prior to treatment and four months after treatment were analyzed.
Results: After 4 months of treatment we objectified clinical improvement by reducing the SCORAD index (average of 6 points) and better results in DQL test in 4 of the 5 patients. Previously scheduled medical treatment remained unchanged and no side effect was observed in any of the patients treated.
Conclusion: The fact that in most of our patients treated, obtained clinical improvement and in quality of life without adverse effects, support the results of recent studies that conclude that the use of probiotics in diary clinical practice is a safe coadyuvant and possibly effective in the treatment of atopic dermatitis.

1440-A
The clinical experience of intravenous immunoglobulin in severe atopic dermatitis

Lee, J-H; Kang, H-J; Jwa, H-J
Pediatric, College of Medicine, Chungnam National University, Taejeon, Korea

Background: Atopic dermatitis is a condition that can be chronically relapsed despite of many treatment. Continuous medication of high dose predinisolone to treat the refractory atopic dermatitis results in developing the serious side effects. So

there is a need for alternative treatment in severe atopic dermatitis. Many trials have been done on steroid-resistant atopic dermatitis to spare the steroid. Intravenous immunoglobulin (IVIG) treatment has been shown to be effective in the treatment of steroid-dependent atopic dermatitis.
Method: Seven children with severe atopic dermatitis resistant to conventional treatment were included in this study. IVIG (1 gm/kg) was infused for 10 hours slowly, and total 5 or 6 times every 4 weeks. The severity and extent of atopic dermatitis were evaluated by SCORAD index at 0, 4, 8, 12, 16, 20 and 24th week of IVIG therapy. The frequency of steroid requirement to control, and also the profiles of blood eosinophils and levels of serum IgE were evaluated at the each day of IVIG therapy monthly.
Results: The SCORAD indices were improved significantly at forth IVIG infusion time without any side effects of IVIG except mild fever. And also the total dosages of steroid requirement were decreased during the treatment with IVIG. The number and percentage of blood eosinophils were increased initially and decreased later, but the levels of serum IgE were not changed after treatment.
Conclusion: Adjunctive therapy with IVIG in chronic severe atopic dermatitis is effective on reducing the clinical symptoms and signs, and sparing the steroid therapy.

1441
IgE - antibodies to the yeast's *Malassezia spp* and *Mn superoxide dismutase* in patients with atopic dermatitis is a hallmark of severity of AD and polysensitisation

Turlapova, E
Clinical Allergology Department, Mechnikov's Research Institute, Moscow, Russian Federation

Background: It is well known the role of yeast *Malassezia spp* as a triggering factor in atopic dermatitis (AD).
Aim: To analyze the clinical relevance of IgE-antibodies to *Malassezia spp* allergen in children and adults with AD. Patients. There were 133 patients (pts) with different severity of AD and head and neck skin lesions observed. The patients were divided into four age groups: 43 pts from 1 to 5 years, 38 pts from 6 to 15 years, 18 pts from 16 to 25 years, 34 pts from 26 to 55 years. The severity of AD was estimated by means SCORAD.
Method: The presence and level of IgE-aB to Malassezia spp, allergen components and the level of total IgE in the sera were measured by ISAC and ImmunoCAP technology.
Results: The SCORAD in observed pts varied from 45 to 80 scores; (Me: 62 ± 14,5). IgE-aB to Malassezia spp were identified in 42,85% (56 pts) of all pts with AD. The positive IgE-aB to yeasts were found out in the sera of 25% of children up to 5 years and in every second adult patient with AD. There was strong correlation between the level of total IgE and IgE-antibodies to Malassezia. ($P < 0,05$). There was positive correlation between the SCORAD and presence of IgE-aB to Malassezia spp. in the sera. In 24 pts with highly positive serum to Malassezia the ISAC ImmunoCap were tested with the purpose to reveal IgE-aB to fungal allergen component r Asp 6 - Mn superoxide dismutase. 7/24 serum positive to Mn superoxide dismutase (ISU-E: 3 -53; Me: 23,5 ± 13,4). There was highly positive effect due to antifungal therapy in these pts.
Conclusions: The presence of IgE-aB to *Malassezia spp* in the sera of pts is an objective prognostic symptom for the chronic course of AD. The severity of AD correlates with the presence of antiyeast IgE - aB. The IgE -aB to fungal Mn superoxide dismutase (highly cross - reactive with human Mn superoxide dismutase synthesized from keratinocytes) is a hallmark of autoimmune inflammation. All pts. with IgE-aB to Malassezia were polysensitized to pollen, mites, fungi in different variation.

1442
Sensitization to soy allergens in children with atopic dermatitis

Cudowska, B[1]; Marcinkiewicz, S[2]; Kaczmarski, M[1]
[1]Department of Pediatrics, Gastroenterology, Allergology, Medical University of Bialystok, Bialystok, Poland; [2]Department of Developmental Medicine and Pediatric Nursing, Medical University of Bialystok, Bialystok, Poland

Background: The primary soy allergy concerns mainly infants and young children allergic to cow′s milk protein; the secondary is a kind of cross-allergy to birch pollen allergens. The aim of the study was to evaluate the prevalence of soy sensitization in children with atopic dermatitis, its impact on the course of the disease and the co-occurrence with sensitization to other food and airborne allergens.
Method: A group of 61 children aged from 5 months to 16 years with atopic dermatitis were diagnosed with skin and atopy patch tests, specific IgE. In 18 of them (29%) allergy to soy was confirmed. The remaining patients were qualified to the control group.
Results: There were no statistically significant differences between the prevalence of allergic rhinitis and asthma in the study and the control group ($P = 0.672$ and $P = 0.829$) and between the degree of severity of skin lesions, total IgE and peripheral blood eosinophilia. A statistically significant ($P = 0.0021$), a positive correlation ($r = 0.8185$) between the concentration of total IgE and specific IgE to soybean has been stated. IgE-mediated allergy to soy was found in 53% of patients; delayed in 72% of children. More than 50% of the patients were allergic to other cereals, 40% to milk, and over 60% to tree and grass pollen.
Conclusions: Allergy to soy is an important clinical problem and affects more than 30% of children with atopic dermatitis. It most often coexists with hypersensitivity to other airborne allergens of plant origin. Atopy seems to be the predisposing factor to soy allergy.

1443
Controlled exposure to grass pollen in an environmental challenge chamber induces a worsening of cutaneous symptoms in patients with atopic dermatitis

Heratizadeh, A[1]; Badorrek, P[2]; Kapp, A[1]; Niebuhr, M[1]; Roesner, LM[1]; Karch, A[3]; Erpenbeck, VJ[4]; Loesche, C[4]; Jung, T[4]; Krug, N[2]; Hohlfeld, JM[2]; Werfel, T[1]
[1]Division of Immunodermatology and Allergy Research, Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany; [2]Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany; [3]Hannover Medical School, Institute for Biostatistics, Hannover, Germany; [4]Novartis Pharma AG, Basel, Switzerland

Background: Inhalant allergens may act as a trigger factor of atopic dermatitis (AD). In case reports and interventional studies on bronchial or nasal allergen provocation with inhalant allergens a deterioration of skin symptoms in a subgroup of AD patients has been described. Aside from this atopy patch tests (APT) with inhalant allergens revealed a high diagnostic specificity with regard to the patients' history. However, a diagnostic tool testing the clinical relevance of inhalant sensitization in patients with AD by provocation as near as possible to 'true life' conditions is not available. The aim of this single center, double-blind, placebo-controlled study was to assess the cutaneous reactions to grass pollen in adult patients suffering from AD with accompanying IgE-sensitization to grass pollen allergen. For this purpose, AD patients were exposed to grass pollen in an environmental challenge chamber (ECC).
Method: On two consecutive days sensitized patients were challenged with either 4000 pollen grains/m^3 of *Dactylis glomerata* pollen (verum) or clean air (placebo). Prior to the challenge, on each challenge

day (Day 1 and 2) and also during a follow-up period (Day 3–5) the severity of AD was assessed by objective SCORAD (primary endpoint). Additionally, air-exposed and textile covered skin areas were separately scored by IGA and 'local SCORAD'. By 'local SCORAD' two representative target lesions – one textile covered and one air-exposed – in each patient were evaluated. As biomarker of the disease activity serum CCL17 levels were determined by ELISA.

Results: In patients exposed to grass pollen a significantly higher increase in objective SCORAD from pre-challenge to post-challenge Day 3 in the verum group compared to the placebo group was observable ($P = 0.010$). Of note, a significant worsening of air-exposed rather than of textile covered skin occurred. A trend towards an increase of CCL17 serum levels in grass pollen exposed patients was obvious.

Conclusion: By this proof-of-concept study, effects of an inhalant allergen on cutaneous symptoms in selected AD patients could clearly be demonstrated. Our results support the need for allergen avoidance as a preventive measure in these patients. Aerogen allergen challenge by means of an ECC might represent a useful procedure also for research on therapeutic agents in AD.

1444
Phenotypes of atopic dermatitis in school children are associated with allergic march

Lee, E[1,2]; Lee, SH[2]; Kwon, J-W[3]; Yu, H-S[2]; Kang, M-J[2]; Yang, S-I[1]; Kim, HY[4]; Seo, J-H[5]; Kim, B-J[6]; Kim, HB[7]; Lee, SY[8]; Kwon, H-J[9]; Hong, S-J[1]
[1]Department of Pediatrics, Childhood Asthma Atopy Center, Research Center for Standardization of Allergic Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [2]College of Medicine, Ulsan University, Asan Medical Center, Seoul, Korea; [3]Seoul National University Bundang Hospital, Seung Nam, Korea; [4]Pusan National University Yangsan Hospital, Yangsan, Korea; [5]Korea Cancer Center Hospital, Seoul, Korea; [6]Inje University Haeundae Paik Hospital, Inje University College of Medicine, Pusan, Korea; [7]Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea; [8]Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea; [9]Dankook University College of Medicine, Cheonan, Korea

Background: Atopic dermatitis (AD) is characterized by heterogeneous clinical spectrum and some forms of AD are associated with the initial step of allergic march. Identification of determinants of allergic march is of crucial important for understanding the pathophysiology and prevention of allergic march. The aim of this study was to determine AD phenotypes in children aged 6–13 years in its association with allergic march and to identify the characteristic features of these subjects.

Method: A total of 242 children diagnosed with AD ever and AD symptoms during the last 12 months were included from the first survey of Children′s Health and Environmental Research survey ($n = 2491$). This study is a prospective follow-up study of 2 years interval for 4 years. Latent class analysis was used with variables such as personal characteristics, onset age of AD, treatment during the last 12 months, positivity on skin prick tests (SPTs), total serum IgE levels and eosinophil (%). After 4 years, SPTs, lung function tests, methacholine provocation tests, and blood tests including IgE and eosinophil were performed. Differences in the polymorphisms of immune related and reactive oxygen genes were evaluated.

Results: We identified 4 AD phenotypes in this study. Groups were characterized as 'early onset with low atopy' (26.4% of sample, Group 1), 'early onset with high atopy and high eosinophil' (48.3%, Group 2), 'late onset with low atopy' (9.9%, Group 3), and 'late onset with high atopy and normal eosinophil' (15.3%, Group 4). At enrollment, children in group 2 showed highest prevalence of sensitization, even to multiple allergens. After 4-year follow-up, although both groups 2 and 4 showed persistently elevated IgE levels, only group 2 showed elevated eosinophil percentage, higher prevalence of new onset of bronchial hyperresponsiveness (BHR) (12.3%) and asthma diagnosis (10.0%) and positive skin reactivity, compared to group 4.

Conclusion: High atopy combined with high eosinophil percentage and earlier and multiple sensitization might be linked to new development of BHR and asthma, suggesting the presence of allergic march phenotype in AD.

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1445
Analisys of total and specific IgE against dermatophagoides pterronissimus and interleukin-4 in patients with atopic eczema

Prnjavorac, B[1]; Bego, T[2]; Malenica, M[2]; Dujić, T[2]
[1]General Hospital, Internal Medicine, Tešanj, Bosnia and Herzegovina; [2]Faculty of Pharmacy, Sarajevo, Bosnia and Herzegovina

Background: Atopic eczema is very common disease in general population. Nevertheless atopic eczema is skin disease the most common sanitation is with respiratory allergens. Among them home dust mite and dermatophagoides pteronissimus are the most common allergen accused for atopic eczema. It′s known for long time that′s Interleukin-4 (IL-4) is the most important for switching synthesis of IL-4 by plasma cells toward synthesis of IgE, among other immunoglobulins. So, IL-4 is one of most important factor for development of atopic eczema.

Method: Total IgE was measured by Enzyme immunoassay sandwich method, with final fluorescent detection with 'ELFA method', so combines of two-step method. Specific IgE was measured using method of adsorption to 'sandwiches' with previously performed antibody coated plats. Il-4 was measured using open ELISA method. Skin provocation tests were performed according to method described in Manual of Clinical Laboratory Immunology. Statistical analysis was performed using statistical package Statistica for Windows, with multiple-correlation test and descriptive statistics.

Results: In study 30 patients were included, 20 female (67%) and 10 male (33%), with mean age 29.13 years (SD 20.3). Mean concentration of total IgE was 419 IU/ml (SD 860), with very high dispersion of results from 1.97 to 4420 IU/ml. Mean concentration of specific Age against dermatophagoides pteronissimus was 31.26 IU/ml (SD 45.59). Mean level of IL-4 was 51.42 pg/ml (SD 10.32). Using test of multiple correlation we showed statistical significant correlation between specific IgE and IL-4 concentration at level of significance $P < 0.05$. Concentration of specific IgE againt dermatophagoides pteronissimus was in correlation with intensity of skin reaction at level of $P < 0.05$, so.

Conclusion: In patients with atopic eczema significant correlation between level of specific IgE against dermatophagoides pterronissimus and concentration and IL-4 was seen. Blood level of IL-4 and intensity of skin test was present, so.

1448
Inflammatory cytokines balance and correlation with total IgE level in the patients with atopic dermatitis

Hamad, MA[1]; Mitskevich, N[2]; Machavariani, K[3]
[1]Petre Shotadze Tbilisi Medical Academy, Tbilisi, Georgia; [2]Department of Immunology and Microbiology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia; [3]Department of Allergy and Clinical Immunology, Tbilisi State Medical University, Tbilisi, Georgia

Background: Atopic dermatitis (AD) is a chronic relapsing inflammatory skin dis-

ease. AD is increasing in prevalence around the world. Intensive research is ongoing to understand the mechanisms involved in the development of AD and offer new treatment options for patients suffering from AD. New data support the participation of ILs (interleukins) in the pathophysiology of AD, and its significance of cytokines, comparative characteristics of inflammatory cytokines profiles balance in relation to atopy and Total IgE level.

Method: Patients with Atopic Dermatitis, Contact Dermatitis (CoD) (as a control) and Healthy control groups were randomly selected at the Center of Asthma, Allergy and Clinical Immunology at TSMU. In peripheral blood was detected T CD4+, CD8+ lymphocytes by flow cytometry using Becton Dikinson′s monoclonal antibodies. The serum levels of IgE (total), IFNγ, TNFα, IL4, IL5, IL10, IL13 were measured using ELISA, R&D System kits, Germany, at the lab of Immunology and Microbiology at TSU. Statistic processing – One-Way ANOVA analysis.

Results: The following cytokines concentrations – TNFα, IL-5, IL13 – in AD patients were significantly higher than in healthy control group ($P = 0.01$). IL6, TNFα concentrations in the atopic patients were higher than those in the CoD patients without atopy ($P < 0.05$). IFNγ levels did not differ depending on the presence of atopy [17.3 pg/ml (1; 33.6)]. IL4, IL5, IL13 levels were higher in subjects with an atopy compared with those without this condition [0 pg/ml (0; 20.8)]. This difference was statistically significant (Mann–Whitney test, $P = 0.01$). Cytokine levels that have been studied correlated with each other as it follows – IFNγ levels correlated with IL10 and IL13 levels ($P = 0.05$), IL5 levels correlated with IL6 levels ($P < 0.001$), and other statistically significant correlations between the eight cytokines have not been observed in patients with CoD. The numbers of CD4+ and CD8+ T cells were without any specific changing.

Conclusion: According our study was shown that AD is not specifically characterized only by increasing level of Th2 profile cytokines in the peripheral blood. There is a combination of mixed Th1/Th2 profiles. Not all of the patients with AD and CoD have the same profile of ILs. The present findings have demonstrated that the patients with CD were impaired in cellular immunity. Total Ig E level and certain etiological factors relatively specifically modulate the immune response of AD.

1449
The effects of intramuscular injection of autologous immunoglobulin on clinical severity and serum IgE concentration in patients with atopic dermatitis

Nahm, D-H[1]; Kim, M-E[1]; Cho, S-M[1]; Jeon, S-Y[2]
[1]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea; [2]Yonsei-Ajou Pediatric Clinic, Gwangju-Si, Korea

Background: The management of patients with atopic dermatitis (AD) is frequently difficult for both patients and physicians. We hypothesized that repeated intramuscular injections of autologous immunoglobulin can induce clinical improvements in patients with AD by stimulating an active immune response to antigen binding sites of pathogenic antibodies, thereby correcting immune dysfunction.

Method: To test this hypothesis, 17 adult patients with severe AD were treated by intramuscular injections of 50 mg autologous immunoglobulin (mainly IgG with purity ≥97%) twice a week for 4 weeks. Autologous immunoglobulin was purified from autologous plasma by affinity chromatography using Protein A. The standardized clinical severity scoring system for AD (SCORAD) value and serum IgE concentration were measured at baseline, 4, 8, and 12 weeks.

Results: The SCORAD values significantly decreased from 66.8 ± 10.8 (mean ± SD) at baseline to 52.1 ± 12.2 at 4 weeks, 52.2 ± 16.4 at 8 weeks, and 50.5 ± 17.3 at 12 weeks (Wilcoxon signed-rank test, $P < 0.005$). The serum IgE concentrations significantly decreased from 18044.1 ± 20049.6 kU/l at baseline to 14960.0 ± 17442.8 kU/l at 4 weeks, 15055.1 ± 16424.0 kU/l at 8 weeks, and 14117.7 ± 16581.0 kU/l at 12 weeks ($P < 0.05$). No significant side effects were observed.

Conclusion: Repeated intramuscular injections of autologous immunoglobulin significantly decreased clinical severity and serum IgE concentration in patients with severe AD. Further studies are required to evaluate the clinical significance of these findings.

Poster Session Group III – Green TPS 51

Urticaria and angioedema

1450

Correlation of clinical history in patients with chronic spontaneous urticaria (CSU) and diagnostic tests for inducible urticarias

Amaya, E; Acevedo, AM; Celis, AM; Caraballo, D; Cardona, R; Sanchez, J
University of Antioquia, Medellin, Colombia

Background: To date, there is scarce literature on the frequency of inducible urticarias based on provocation tests with physical stimuli.
Objective: To evaluate the frequency of inducible urticarias in patients with chronic spontaneous urticaria compared with a healthy control group in whom provocation tests were performed.
Methods: A multicenter study involving people older than 12 years diagnosed with chronic spontaneous urticaria and a control group with no current or past history of urticaria were performed. All subjects underwent the tests based on the guidelines suggested by the EAACI. Tests were dermographism, pressure, ice cube test, water and exercise.
Results: A total of 245 patients with CSU and 127 controls were included in the study. Among patients with urticaria 89 (36.3%) had at least one positive provocation test and seven in the control group (5.5%). According to provocation tests performed in the group with CSU ($n = 245$), symptomatic dermographism was the most common inducible urticaria (24.8%) followed by cold contact urticaria (13.4%), delayed pressure urticaria (7.3%), cholinergic urticaria (2%) and finally aquagenic urticaria (0.4%). The frequency of false positives in the control group ($n = 127$) was quite low: symptomatic dermographism (3.9%), cold contact urticaria (0.7%), delayed pressure urticaria (0%), cholinergic urticaria (0.7%) and aquagenic urticaria (0%). The self-report was statistically significant with provocative test for dermographism and pressure ($P < 0.05$). It was found that 29 subjects (11.8%) had at least two positive provocation tests.
Conclusion: Symptomatic dermographism and cold contact urticaria are the most frequent inducible urticarias in patients with CSU. Provocation tests are useful tools for identifying different stimuli can induce urticaria and frequency of false positives is low, which makes this test a very sensitive tool.

1451

Effect of omalizumab over a 6-month treatment period on angioedema and quality of life associated with refractory chronic idiopathic/spontaneous urticaria (CIU/CSU): subgroup analyses focused on the presence of baseline angioedema

Maurer, M[1]; Spector, S[2]; Bernstein, J[3]; Gabriel, S[4]; Karagiannis, T[4]; Kianifard, F[4]; Mendelson, M[4]
[1]Department of Dermatology and Allergy, Charité Universitätsmedizin, Berlin, Germany; [2]Division of Clinical Allergy and Immunology, UCLA Medical Center, Los Angeles, United States; [3]Allergy Section, Division of Immunology, Department of Internal Medicine, College of Medicine, University of Cincinnati, Cincinnati, United States; [4]Novartis Pharmaceuticals Corporation, East Hanover, United States

Background: Approximately 40–50% of patients with CIU/CSU report angioedema associated with urticaria. Angioedema negatively impacts health-related quality of life. The course of angioedema over the first 12 weeks of treatment in an omalizumab trial has been reported previously. Here we examined angioedema and Dermatology Life Quality Index (DLQI) scores over 24 weeks in a subgroup who had angioedema at baseline.
Method: Data were retrospectively analysed from GLACIAL, a trial of omalizumab in patients with CIU/CSU who remained symptomatic despite H_1-antihistamine therapy (up to 4× approved dose), and either H_2-antihistamines or leukotriene receptor antagonists, or all three drugs combined (refractory CIU/CSU). Patients were treated with omalizumab 300 mg or placebo by subcutaneous injection every 4 weeks over 6 months. For patients who reported baseline angioedema (presence during the 7 days prior to enrolment) and had non-missing data, the number of patients and days per week with angioedema were examined as was the change from baseline to Week 24 in overall DLQI score.
Results: Of 335 patients, 178 (53.1%) had baseline angioedema ($n = 137$ and 41 in the omalizumab and placebo groups, respectively). Patients with angioedema reported a mean (standard deviation, SD) CIU/CSU duration of 7.9 (9.6) years.

A response to omalizumab was observed after the first injection (baseline). At Week 2 post-dosing, 57.5% (73/127) of patients who received omalizumab 300 mg and 31.6% (12/38) of placebo patients were angioedema-free. The proportion of patients who were angioedema-free was 70.5% (79/112) and 55.2% (16/29) at Week 12 and 77.4% (82/106) and 56.0% (14/25) at Week 24 in the omalizumab 300-mg and placebo groups, respectively. A reduction in the mean number of angioedema days per week (SD) was also seen – omalizumab: baseline, 3.7 (2.2, $n = 137$); Week 12, 1.0 (2.0, $n = 33$); Week 24, 0.7 (1.6, $n = 24$) and placebo: baseline, 3.3 (1.9, $n = 41$); Week 12, 1.2 (1.7, $n = 13$); Week 24, 1.5 (2.1, $n = 11$). The mean change from baseline (SD) in overall DLQI score at Week 24 was −10.31 (7.26, $n = 105$) with omalizumab 300 mg and −8.68 (9.68, $n = 22$) in the placebo group.
Conclusion: Omalizumab is an option for reducing the number of angioedema days associated with refractory CIU/CSU, which also has an impact on improving patient quality of life.

1452

ASSURE-CSU, burden of illness study in CSU patients: demographics and clinical characteristics from UK, Canada and Germany

Wellar, K[1]; Grattan, C[2]; Hollis, K[3]; McBride, D[3]; Radder, C[3]; Balp, M-M[4]; Tian, H[5]; Chapmann-Rothe, N[6]; Chiva-Razavi, S[7]; Halliday, A[8]; Sussmann, G[9]; Naconechna, A[10]
[1]Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany; [2]Dermatology Department, Norfolk and Norwich University Hospital, Norwich, United Kingdom; [3]RTI Health Solutions, North Carolina, United States; [4]Novartis Pharma AG, Basel, Switzerland; [5]Novartis Pharmaceutical Corporation, East Hanover, NJ, United States; [6]Novartis Pharma GmbH, Nuremberg, Germany; [7]Novartis Pharmaceuticals Canada Inc, Quebec, Canada; [8]Novartis Pharmaceuticals UK Limited, Frimley, United Kingdom; [9]Division of Allergy and Clinical Immunology, University of Toronto, Toronto, Canada; [10]Department of Immunology, Hull Royal Infirmary, Hull and East Yorkshire NHS Hospital Trust, Yorkshire, United Kingdom

Background: Chronic spontaneous urticaria (CSU) is defined as the occurrence of itchy wheals, angioedema or both lasting 6 weeks or more due to known or unknown causes. Very little real-world evidence is available

quantifying the disease burden of CSU. ASSURE-CSU is the first multinational study designed to quantify the humanistic and economic burden of CSU in seven countries.

Method: Data were retrieved through retrospective patient medical record abstraction, cross-sectional patient survey, and 7-day patient diary and included demographics, clinical characteristics, quality of life, healthcare resource utilization, and work productivity. Adult CSU patients with a clinician-confirmed/guideline defined diagnosis of CSU, having failed on at least one course of H_1-antihistamines, and been symptomatic for ≥12 months despite treatment were included. Here we present demographics and main clinical characteristics reported in the medical charts for the UK, Canadian and German cohorts. Data were analysed using descriptive statistics.

Results: The mean (SD) age at enrolment for the UK (n = 83), Canada (n = 99), and Germany (n = 100) cohorts was 49.7 (15.4), 50.8 (15.0) and 45.6 (15.4) years, respectively, with a higher proportion of women and Caucasians. Mean (SD) CSU duration between diagnosis and enrollment was 57.3 (82.30), 62.0 (81.91) and 67.4 (92.57) months. At diagnosis, 49.4%, 42.4% and 36.0% had severe disease while 31.3%, 30.3% and 24.0% had moderate disease. Disease severity was assessed by physicians using mostly the flare characteristics, presence of angioedema, medication requirements, and in less cases UAS7 score. Angioedema at diagnosis was reported in 53.0%, 41.4% and 19.0% of patients, among whom the mean (SD) number of angioedema episodes in previous 12 months was 23.8 (16.0), 12.4 (14.3) and 9.1 (11.3). At enrolment, asthma, allergic rhinitis and history of allergic diseases were the major comorbidities recorded in CSU patients.

Conclusion: This analysis shows that CSU patients refractory to anti-H_1s have long disease duration with similar disease profile among the three countries. Angioedema episodes are reported frequently. Despite the availability of validated disease severity assessment tools, these are not widely used in either of the countries.

1453
Chronic urticaria and angioedema – a retrospective analysis of treatment with high dose antihistamines in a tertiary centre

van den Elzen, MT; van Os-Medendorp, H; Laheij-de Boer, A-M; Röckmann, H; Bruijnzeel-Koomen, CAFM; Knulst, AC
Dermatology/Allergology, UMC Utrecht, Utrecht, The Netherlands

Background: The prevalence of chronic urticaria and angioedema is high. In many patients treatment with second generation antihistamines (sgAH) fails even in high dosages (up to fourfold) as recommended in recent guidelines due to the excellent safety profile. Other alternative therapies are associated with significant side-effects (cyclosporine A) or not reimbursed (omalizumab).

So far there is no literature on the efficacy and safety of increasing antihistamines higher than fourfold, however experts in the field have some experience.

Method: A retrospective study was performed. Outcome measures were efficacy and safety of treatment with antihistamines in terms of patient satisfaction, disease activity, and side effects. Data regarding demographic, diagnostic, and therapeutic characteristics was extracted from the medical records of adults with chronic urticaria and/or angioedema.

Results: A total of 200 patients were included; 136 (68.0%) were female, the median age was 46 (range 19–86). 30.0% had urticaria only, 24.5% had angioedema only, and 45.5% had both. A majority (n = 170) was treated with antihistamines, dose increase up to fourfold was necessary in 114 patients (57%) in 56 out of these 114 eliciting insufficient andand in 25 acceptable results (effect unknown in 33 patients); 47 of these 56 patients were treated with ≥5 tablets daily mostly by combining two sgAHs (median 6, ranging up to 12). Data of 27 patients showed insufficient effect in 29%, acceptable results in 54%, and 17% became completely asymptomatic (effect unknown in 23 patients).

The most frequently prescribed sgAH were levocetirizine (72%), desloratadine (55%) and fexofenadine (23%). First generation antihistamines (fgAH) were prescribed usually in addition to sgAH in 84 patients (49%).

Side effects were reported in 57 (34%) of patients treated with sgAH and 8 (9.5%) with fgAH and consisted mostly of fatigue (70%). Increase in dose ≥5 did not lead to an increase in side effects compared with dosages up to 4. No serious adverse events were reported.

Conclusion: First results show that the use of antihistamines in dosages ≥5 tablets daily can lead to satisfactory results in patients with insufficient response to fourfold dosages without an increase in side effects. These results suggest a possible extra treatment option for refractory chronic urticaria. It may prevent the medical need for add-on therapies in some cases, particularly in case of side effects or when other therapies are not available.

1454
The role of *Blastocystis hominis* in acute/chronic urticaria and pruritus

Karabiber, E; Özdemir, E; Karakaya, G; Kalyoncu, AF
Allergy and Immunology, Hacettepe University Medical Faculty, Ankara, Turkey

Background: Acute/chronic urticaria/pruritus are a group of diseases admitted to allergy and immunology clinics frequently. It is difficult to find the etiology in most patients. In clinical practice, it is not always possible to perform tests for parasitic and viral infections. The aim of this survey was to show the role of intestinal parasites, especially *Blastocystis hominis*, in the etiology of urticaria/pruritus.

Method: The data is retrospectively obtained from the records of patients with acute-chronic urticaria/pruritus who were admitted to our clinic between 1 June and 1 December 2014.

Results: A total of 391 patients were diagnosed as acute-chronic urticaria/pruritus during this period. Stool microscopic examination was performed in these 285 patients at least once. The median age of 285 patients was 36 and 63.5% of these patients were women. The diagnosis was chronic urticaria in 162 patients, chronic pruritus in 62, acute urticaria in 31 and acute intermittant urticaria in 30. Stool examination results were positive in 92 patients and among these 71 (%78.9) were positive for *B. hominis*. Stool examination results were positive in 40.3%, 28.4%, 32.3% and 36.7% patients with chronic pruritus, chronic urticaria, acute urticaria and acute intermittent urticaria, respectively. Oral metronidazole treatment, 4 × 500 mg for 10 days, was offered to 77 patients. The clinical response could have been assessed in 30 patients. There was complete response, partial response and no response in 12, 9 and 9 patients, respectively. The complete response was seen in 3, 1, 4 and 4 patients with acute urticaria, acute intermittent urticaria, chronic urticaria and chronic pruritus, respectively.

Conclusion: The role of *B. hominis* in acute/chronic urticaria and pruritus is not clear. In a survey from Turkey, the prevalence of *B. hominis* in healthy people was 11,6% and there were no statistically significant differences between patients with urticaria and healthy group. In our study, it is a disadvantage not to have a control group; but it seems remarkable that 40% of 30 patients had benefited from antiparasitic treatment. This preliminary study showed that the stool examination might be useful in the etiologic evaluation of the patients with acute/chronic urticaria and pruritus and may have positive effects on prognosis. Prospective controlled trials are

needed to disclose the role of *B. hominis* in these group of patients.

1455
Icatibant treatment for non-histaminergic angioedema acute attacks in two emergency hospital departments

Martinez Virto, AM[1]; Jacob, J[2]; Rivera Nuñez, A[1]; Carrizosa, M[2]; Torres Santos-Olmo, R[1]; Quintana Diaz, M[1]
[1]Hospital Universitario La Paz, Madrid, Spain; [2]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain

Background: Angioedema is a relatively common reason of emergency department visits. Angioedema is due to different pathogenetic mechanisms with the same clinical manifestations. Around 80% of angioedemas are result of histamine release and in a lower percentage of cases bradykinin is the main mediator. Bradykinin-mediated angioedemas are generally unresponsive to corticosteroids and H1 antagonists. Icatibant is a selective bradykinin-2 receptor antagonist that blocks the vascular effects of bradykinin. ACE-induced angioedema and acquired angioedema are bradykinin- mediated angioedemas where Icatibant is not indicated and its use is off-label and requires signed informed consent for its administration. We describe the use of Icatibant in bradykinin-mediated angioedemas without previous diagnosis in two hospital emergency departments.
Method: We retrospectively analyzed angioedemas treated with Icatibant following our protocol in Bellvitge hospital and Universitary La Paz hospital emergency departments during 2012–2013. Epidemiological data, safety data and Icatibant label and off-label use are analyzed.
Results: Thirty five episodes of angioedema were treated with Icatibant in 28 patients (median age: 65 ± 2 years; 62% males); 85% of episodes were orofacial attacks, 5.7% in extremities and 2.8% abdominal attacks. 62.8% had previous attacks of angioedema. All attacks were treated with corticosteroids and H1 antagonist without response and Icatibant following emergency protocol for angioedema at the two hospitals. Second dose were needed in seven patients. Non adverse events were observed.

Diagnosis of Angioedemas treated with Icatibant was: 22.85% idiopathic angioedema, 14.28% acquired angioedema and 37.14% ACE-induced angioedema.
Conclusion: Icatibant for non-histaminergic angioedema in emergency department were effective and well tolerated. Orofacial location was the most common location. The first frequent cause of angioedema treated with Icatibant was ACE-induced angioedema and the second one was idiopathic angioedema.

1456
Plasmapheresis as a choice of treatment for patients with severe chronic spontaneous urticaria

Zilenaite, E; Stankeviciute, R; Chomiciene, A; Blaziene, A; Griskevicius, A; Audzijoniene, J
Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania

Background: Due to lack of evidence and high costs plasmapheresis is considered as a second line treatment for spontaneous chronic urticaria (CU). It is usually used in patients with severe urticaria when treatment with antihistamines and corticosteroids is not effective. The aim of this study was to compare the patient's, in which plasmapheresis was used, profiles and determine its effectiveness.
Method: We reviewed the records of CU patients, who were treated by plasmapheresis in Vilnius University Hospital (Lithuania) for 4 year period (2010–2014).
Results: Records of 55 CU patients treated by plasmapheresis were reviewed. Most of the patients were women (85.5%). The mean age of participants was 47 years old (SD ± 16.3) ranging from 20 to 70. The majority of patients (89.1%) experienced both hives and angioedema episodes. All patients before plasmapheresis were treated with high doses of antihistamines and the majority of them got corticosteroids. The time duration before initiating plasmapheresis varied greatly, from 1 to 120 months (the mean 22, 19 months, SD ± 31.8). In 31 patients autologous serum skin test (AST) was performed. It was positive in 15 (48.4%) and negative in 16 (51.6%) patients. Anti-thyroid peroxidase antibodies (ATPO) concentration was elevated for 24 patients of 39 (61.5%). 22 (40%) patients experienced clinical improvement after plasmapheresis, in 2 (3.6%) patients urticaria disappeared, 1 (1.8%) patient had no clinical effect, no data was found for 30 patients.
Conclusion: We could speculate that treatment resistant CU is common in patients with autoimmune form of the disease and plasmapheresis may be considered as additional choice of treatment.

1457
Omalizumab in chronic spontaneous urticaria: initial experience from a specialized center in São Paulo, Brazil

Ensina, LF[1,2]; Machado, LMO[1]; Andrade, DM[1]; de Lacerda, AE[1]; Camelo-Nunes, IC[1,2]; Solé, D[1]
[1]Allergy, Immunology and Rheumatology, Federal University of Sao Paulo, Sao Paulo, Brazil; [2]Allergy and Clinical Immunology, University of Santo Amaro, Sao Paulo, Sao Paulo, Brazil

Background: Chronic spontaneous urticaria (CSU) severely affects quality of life. Many patients with CSU do not have responses to therapy with H1-antihistamines even at high doses. The current EAACI/GA2LEN/EDF/WAO treatment guidelines for the management of urticaria recommend omalizumab as a third line therapy for these patients. The aim of this study was to evaluate the clinical response to omalizumab in patients with H1-antihistamines refractory CSU.
Method: We retrospectively analysed the clinical course of patients with severe recalcitrant CSU that were treated in our department with omalizumab off label every four weeks. The clinical response to omalizumab was classified in: complete (no hives and no itching), partial (significant improvement of hives and pruritus) and no response.
Results: Fifteen patients (13 females, median age 41 years) have been treated, all but one with 300 mg of omalizumab as a starting dose. Eleven patients had a complete response, two had a partial response and only one was a non-responder. This one is currently being treated with cyclosporine successfully. Of those with complete response, one is still taking H1-antihistamines (fexofenadine 720 mg/day), all the others stopped antihistamines and/or corticosteroids within the first month of therapy with omalizumab. After 6 months of treatment we decreased the dose in six of the responders to 150 mg, but three relapsed after one or two months. One of the patients who is under remission with 150 mg is taking the drug every 6 weeks. One patient started with 75 mg of omalizumab and was able to maintain his urticaria controlled with this dose. There were no reported adverse reactions attributable to the drug.
Conclusion: Omalizumab is an effective and safe treatment for refractory CSU. Treating CSU with omalizumab requires an individual approach, as doses and intervals needed to maintain a good response may be different from patient to patient.

1458
'Internal disease pattern' in patients with chronic urticaria

Voronova, M[1]; Bodnya, O[2]
[1]Allergy, State Hospital No. 52, Moscow, Russian Federation; [2]Allergy, Russian Medical Academy of Postgradyat Education, Moscow, Russian Federation

Any disease, in addition to its impact on original mental processes, states, psychological properties of the 'premorbid personality', induces formation of an 'internal disease pattern' (IDP). It is possible that it is the IDP that determines a patient's attitude toward disease, the estimation of his own state, and as a result, the patient's commitment to the prescribed therapy. We have examined 67 patients with CU at the age of 24–65 years (mean age 42 ± 3.5); 25 males, 37 females. Patients were divided into two groups depending on severity of the disease (urticaria). Patients with severe (30 patients) and moderate (37 patients) CU were enrolled in the study. All patients received a background therapy with antihistamines. The psychological status of patients was assessed using self-administered validated questionnaires, including Taylor Manifest Anxiety Scale and Beck's depression inventory. The anxiety scale contains a built lie scale to assess the reliability of the responses. Commitment to therapy during the past six weeks, care-seeking and treatment were evaluated based on an analysis of outpatients' cards.

In the group with moderate severity of the disease (CU) high levels of anxiety (38 ± 2), have been reported; levels of depression made 19 ± 3 points. It is noteworthy that patients in this group scored low on a built-in lie scale, their commitment to treatment kept high, only 3 (6.6%) patients skipped medication or avoided treatment. In the group of patients with severe CU anxiety and depression levels were lower making 21 ± 1.5 and 7 ± 1 points, respectively. However, the fact that 21 (70%) patients enrolled for the survey scored more than 6 points on the built-in lie scale makes the results of anxiety and depression assessments doubtful. The same patients have shown low levels of compliance and repeated omission of medication intake, repeated requests to replace the administered drug and refusal of treatment.

The presently obtained results for the group of patients with the moderate CU disease agree with the worldwide concept of mental change in those patients marked by increasing anxiety and depression. The results for the group of patients with severe CU raise questions about the origins of such a variant of clinical course of the disease. It is possible that by those patients a special IDP is forming marked by denial of the very fact of disease and as a consequence, reduced compliance, poor commitment to treatment, and, accordingly, to a more grave condition.

1459
Environmental factors in inducible urticaria

Celis, AM; Amaya, E; Acevedo, AM; Caraballo, D; Cardona, R; Sanchez, J
University of Antioquia, Medellín, Colombia

Background: It has been observed that frequency of inducible urticaria varies significantly among different populations. However, there is scarce studies how environmental factors could explain these variations.
Objective: To compare frequency of inducible urticaria in two populations of patients with Chronic Spontaneous Urticaria (CSU) exposed to different environmental conditions and as secondary aim, we compared the severity of symptoms and the impairment of quality of life.
Methods: A total of 175 patients with CSU from Medellin (located at 1600 m above sea level, average temperature is 22°C (72°F) and relative humidity typically ranges from 54% at night and 87% at day. Of 76 patients from Bogota (located at 2600 m above sea level, average temperature is 14°C (58°F) and relative humidity of 76%) were included. (ClinicalTrials.gov: NCT01940393). All patients were evaluated using challenge testing with: cold, dermographism, water, exercise, and pressure. In all patients the severity of symptoms (UAS score) and the quality of life (DLQI score) were evaluated.
Results: We observed that patients who living altitudes around 1500 m above sea level had a significantly higher frequency of symptomatic dermographism ($P = 0.03$ OR 2.1 IC 1–4.4), cold urticaria ($P = 0.02$ OR 3.3 IC 1.125–9.8). There was no significant difference for urticaria pressure ($P = 0.3$), exercise ($P = 0.15$) or aquagenic ($P = 0.53$).
Conclusion: Environments factors such as temperature and altitude could influence in the development of some inducible urticaria like symptomatic dermographism and cold contact urticaria. Multicenter studies are required to confirm this results in different regions and to characterize better the underlying pathophysiologic mechanism of the inducible urticaria and different factors such as epigenetics of every population should also be studied.

1460
Hair loss in patients with chronic spontaneous urticaria treated with omalizumab: an under-reported, transient side effect?

Chioti, AG; Konstantinou, GN
Department of Allergy and Clinical Immunology, 424 General Military Training Hospital, Thessaloniki, Greece

Introduction: Omalizumab, a monoclonal antibody that binds free IgE antibodies, has been recently approved for treating patients with chronic spontaneous urticaria (CSU) with inadequate response to H1-antihistamine treatment. As expected with all medications, omalizumab has been associated with a few side effects. Hair loss is listed among them in the Summary of Product Characteristics, but there are no available data to estimate its frequency. We describe for first time three patients treated with omalizumab for CSU that experienced hair loss.
Cases description: Three women, 38, 62 and 70 years old, suffering from refractory to H1-antihistamine treatment CSU for 6, 5 and 3 months, respectively, were referred to our Specialized Urticaria Center for evaluation and treatment. At initial assessment their Urticaria Control Tests (UCT) were 5, 6 and 6 and their urticaria activity scores summed over a week (UAS7) 25, 27 and 30, respectively. At the second administration of omalizumab (four weeks after the first one) these patients described hair loss that significantly affected their quality of life. This information was retrieved from their Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) responses. Despite this side effect, all patients agreed to continue omalizumab regular administration. Hair loss appeared to be transient, lasting up to four months. All cases finally benefited from omalizumab continuation.
Conclusion: Hair loss seems to be transient in cases with CSU treated with omalizumab that finally seem to benefited from this treatment. The CU-Q2oL is a very helpful clinical tool to assess CSU.

1461
Recurrent angioedema due to acquired C1 inhibitor deficiency with late onset and good response to attenuated androgens

Leru, PM[1,2]
[1]Colentina Clinical Hospital, Bucharest, Romania; [2]Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Background: Angioedema due to acquired C1inhibitor deficiency (ACID) is a rare disease that may look like hereditary angioedema, but without family history and with

onset after the age of 40 years. Most of the cases are secondary to malignant tumors, usually lymphoma or autoimmune disorders, such as systemic lupus erythematosus, but others remain idiopathic and may rise severe clinical problems. We report a case of a 73 years old woman with recurrent angioedema since age of 66, considered first to be induced by angiotensin-converting -enzyme inhibitor (ACEI) treatment for mild hypertension. She had continuous evolution during 7 years after ACEI discontinuation and progressive aggravation in the last year. The C1 inhibitor (C1INH) plasma level was significantly decreased, with low activity ranging from 58% to 4% and constantly low C4 plasma level. The patient had no relevant medical history and took no medication since at least 2 years, when episodes of angioedema became more frequent and severe. She had no clinical signs between attacks. Angioedema was painful, not accompanied by urticaria, located variably to face, neck, arms or buttocks and usually lasted 72 h irrespective corticosteroids and antihistamines treatment. The frequency of attacks increased from one at two-three months to almost weekly. The last angioedema attack was more severe and prolonged, accompanied by respiratory symptoms and laryngeal edema. The extended medical evaluation included complete blood tests for inflammation, allergy, autoimmunity and cancer. Full body CT scan and bone marrow examination were normal. No genetic test could be performed. Since no pathogenic therapy with C1INH, icatibant or ecallantide was available, we first initiated daily prophylactic treatment with tranexamic acid for three months, with no amelioration. During the last severe attack we have switched to danazol, with 400 mg the initial dose, reduced to 200 mg after one week and then to 100 mg daily. The clinical evolution after three months was very good, no angioedema attack occurred since introduction of danazol. C1INH and C4 plasma levels increased after two weeks treatment and became normal after one month.

Conclusion: This case is illustrative for various clinical presentations of recurrent angioedema due to acquired C1 INH deficiency, that may have no clear cause for many years and also for therapeutic value of attenuated androgens as possible effective prophylactic choice.

1462
A case of Hypocomplementemic urticarial vasculitis syndrome (HUVS) with high serum IgG4 immunoglobulins: a steroid-free clinical management

Tontini, C[1]; Cognigni, M[1]; Marinangeli, L[1]; Marchionni, A[1]; Sielli, MC[1]; Zoli, A[2]
[1]Servizio di Immunologia Clinica e Tipizzazione Tissutale, Università Politecnica delle Marche, Ancona, Italy; [2]Servizio di Immunologia Clinica e Tipizzazione Tissutale, Ospedali Riuniti Ancona, Ancona, Italy

Background: A 47-year old female patient came to our clinic for a 2-year history of diffuse urticarial papules, angioedema and low serum complement fractions. Her lesions were painful more than itchy, with residual brown pigmentation on remission and associated with diffuse arthralgias and swelling. Complement fractions were markedly decreased (C3 = 32 mg/l; C4 = 4 mg/l; C1q = 56 mg/l; C2 = 11 mg/l) with no alterations in functional and quantitative C1-Inhibitor protein. Acute phase reactants were constantly within normal range, with no evidence of serum anti-C1q, anti-nuclear or anti-dsDNA antibodies. Biopsy of skin lesions showed a vasculitic pattern, with neutrophilic inflitrates, suggesting Hypocomplementemic Urticarial Vasculitis Syndrome (HUVS). On further analysis IgG subclass assay showed high serum IgG4 (IgG4 = 490 mg/dl), with an increasing trend over time. Renal and cardiac function were unaffected, pulmonary assessment showed minimal obstructive disease. She was treated for 2 years with low dose dexamethason and anti-histamines with little benefit. Steroid choice was restricted due to reported side effects to different molecules and low tolerance to higher doses; anti-histamines alone were completely uneffective.

Method: Hydroxychloroquine and high-dose dexamethason were prescribed, with no relief in cutaneous symptoms, nor arthralgia. Cyclosporin was started at 3 mg/kg dose and dexamethason slowly tapered until suspension, with close clinical and biochemical monitoring.

Results: Cutaneous lesions, angioedema and arthralgias improved within 2 months of the new treatment, without any adverse events, though complement fractions and IgG4 levels did not vary. The patient is currently on a steroid-free regimen; no major cutaneous relapses nor further organ involvement were detected in a 6-month follow-up.

Conclusion: HUVS is a rare vasculitis that shares multiple similarities with Systemic Lupus Erythematosus, though being a separate entity. Few cases are reported in literature with different therapeutic approaches; remission with high dose steroid is frequently observed. Cyclosporin treatment is a feasible steroid-sparing option in managing cutaneous involvement in HUVS, but close monitoring is needed. The association with increased IgG4 immunoglobulin has been reported, but clinical and pathological significance is still unclear.

1463
Omalizumab in the treatment of chronic spontaneous urticaria in 9-year-old boy with diabetes mellitus

Jesenak, M[1,2]; Banovcin, P[1]; Petrovicova, O[1]; Ciljakova, M[1]
[1]Department of Paediatrics, Center for Diagnosis and Treatment of Primary Immunodeficiencies, Jessenius Faculty of Medicine, Comenius University in Bratislava, Martin, Slovakia; [2]Department of Pulmonology and Phthisiology, Jessenius Faculty of Medicine, Comenius University in Bratislava, Martin, Slovakia

Background: Chronic spontaneous urticarial (CSU) represents a big challenge regarding diagnostic approach a treatment strategy. Many drugs were tested in the treatment of CSU, but the most important are modern antihistamines (in higher doses). The last introduced add-on therapeutic option for patients with refractory CSU is monoclonal antibody against IgE – omalizumab. However, the experiences in children are scarce.

Methods: We report the case of 9-year-old boys with refractory chronic spontaneous urticarial treated initially by standard anti-allergic therapy (including cyclosporine A) followed by the application of anti-IgE therapy due to the persistence of the urticarial symptoms and contraindication for corticosteroids (diabetes mellitus).

Case description: The history of the patients contains autoimmune thyroiditis and diabetes mellitus from the age of 7. Three months after the diagnosis of diabetes mellitus, patient started to suffer from severe generalized urticarial. After exclusion of the possible triggers, the diagnosis of chronic spontaneous urticaria was established. Specific IgE against broad panel against food, drug and inhalant allergens (including also component resolved diagnosis), serum tryptase, and eosinophilic cationic protein gave negative results. Basophil-activation test with different forms of insulin was also negative. Concentration and function of diaminooxidase were within normal range. Because combined anti-allergic therapy including cyclosporine was not successful and CSU had significantly impact on quality of life, we decided to start add-on therapy with omalizumab. After 4 months of omalizumab application, weekly urticarial activity score (UAS7) declined from 34 to 6 and the control over CSU was finally achieved. Through the whole treatment period, we did not observe any significant changes.

Conclusions: Omalizumab was recently approved for the treatment of chronic spontaneous urticaria in patients older than 12 years. However, the number of paediatric patients treated by omalizumab due to urticaria is still very small. We confirm the clinical efficacy and safety of anti-IgE therapy in 9-year-old diabetic boy with insufficient clinical response to combined anti-allergic or immunosuppressive therapy. Therefore, omalizumab could be considered as a therapeutic alternative in paediatric diabetics with refractory urticaria, where the application of corticosteroids should be avoided.

1464
Montelucast in the treatment of chronic spontaneous urticaria: management and quality of life

Davidouskaya, Al[1]; Ruzanau, DY[2]
[1]Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus; [2]Gomel State Medical University, Gomel, Belarus

Background: Now there is no curative treatment of chronic spontaneous urticaria (CSU). Typically, current therapy includes a hypo-allergenic diet, H1-blockers and emergency care in cases of acute episodes. The aim of our study was to assess the course of the disease and quality of life of patients with CSU which was assigned montelukast.
Method: Within 6 months we observed 11 adult patients (10 women and 1 men aged from 26 to 48 years old) with CSU. All patients were assigned montelukast 10 mg a day. Also a retrospective analysis of the frequency of episodes of CSU in the previous 6 months was conducted. In addition validated separate questionnaires of health-related quality of life (HRQL) were used. Questions were divided into three main groups: food anxiety (FA), dietary limitation (DL) and emotional impact (EI).
Results: A 6 months before the therapy all patients had 2 to 8 episodes CSU (average 4 ± 2.1), three of them were hospitalized twice and received systemic corticosteroids intravenously. In 40% of cases the cause of the acute episode has not been installed. While in 60% of cases, the probable cause was an error in diet. These patients had significantly greater FA and DL score. However, EI score no difference and not depended on the reasons and frequency of acute episodes.

During the follow-up period after the appointment of montelukast frequency of episodes of urticaria decreased significantly (2 ± 1.1 to 6 months). Side effects of therapy were not observed. Indicators of HRQL improved in EI score ($P = 0.024$) in all patients. At the same time, the results of FA score and DL score did not change significantly, which is probably due to a long history and continuously receivership character of CSU.
Conclusion: Thus, the inclusion in the CSU therapy montelukast allows not only to achieve clinical results, but also to improve the HRQL of patients by emotional impact score.

1465
Atopy and autoimmunity. Risk factors in the chronic spontaneous urticaria?

Acevedo, AM; Celis, A; Amaya, E; Cardona, R; Sanchez, J
University of Antioquia, Medellín, Colombia

Background: Chronic Spontaneous Urticaria (CSU) is acomplex disease with many etiologic factors. IgG anti-FCεRI autoantibodies are seen in 30% to 60% and IgG anti-IgE autoantibodies. Some studies demonstrated that 50% of patients with CSU had atopy[1]. Some studies have considered that Atopy orautorreactivity among patients with CSU, could be a risk factor, however these hypothesis are still controversial and have not been studied if these two factors may have a synergistic effect.
Objective: To evaluate whether the presence of Atopy or autorreactivity (self-reactivity) is associated with the severity of symptoms in patients with CSU.
Method: A total of 245 CSU were included and 127 controls (ClinicalTrials.gov identification: NCT01940393). House dust mites sensitization was evaluated by prick test (main source of atopy in the tropics) and forautorreactivity we used the autologous serum test. Severity of symptoms (CUS score) and its involvement in the quality life (DLQI score) was evaluated in patients with CSU.
Results: Sensitization was significantly higherin CSU group vs control group (42% vs 29%) and autoreactivity (39% vs 28%; $P = 0.01$ and $P = 0.049$ respectively) giving both states a significant risk factor (OR 1.823 CI 1.153–2.887 and 1.650 OR IC 1–2.722 respectively). In logistic regression analysis, we observed that the two variables have no significant covariance. We observed no association between atopy and self-reactivity with CSU score or DLQI score.
Conclusion: Different factors could interact in the pathogenesis of chronic urticaria but the effect of each factor is still not completely clear. We confirmed that Atopy and autorreactivity, are two independent risk factors associated with the presence of CSU, however these factors are not associated with the severity of symptoms or degree of impact on quality of life.

1466
Coagulation and fibrinolytic parameters in patients hospitalised due to acquired angioedema

Lukaszyk, M; Lukaszyk, E; Budny, W; Skiepko, R; Zietkowski, Z; Bodzenta-Lukaszyk, A
Department of Allergology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland

Background: Acquired angioedema (AAE) is characterized by localized, self-limiting swelling of the skin and/or of the mucous tissues of the upper respiratory and gastrointestinal tracts. In recent years considerable attention has been paid to relations between coagulation and angioedema. Low levels or faulty C1-esterase inhibitor may lead to uncontrolled activation of different systems: fibrinolytic, kallikrein and complement. The aim of this study was to investigate certain coagulation and fibrinolysis parameters as well as platelet function in the group of patients with AAE.
Method: The study included 14 men and 50 women, aged between 22 and 81 years hospitalized due to acute attacksof angioedema with and without wheals. The following parameters were evaluated: C1-INH activity and serum concentration, C3 and C4 complement components concentration, angiotensin I converting enzyme (ACE) activity, total complement concentration, fibrinogen, D-dimer, CRP concentrations as well as certain blood platelet function parameters – platelet count, mean platelet volume (MPV) and platelet hematocrit (PCT).
Results: In patients with angioedema accompanied by urticaria platelet count and PCT were significantly higher ($P = 0.009$ and $P = 0.005$ respectively), although in laboratory ranges. Moreover only in the group of patients hospitalized due to angioedema without wheals C1-INH serum concentration correlated with certain coagulation parameters: PT index ($r = 0.43$), fibrinogen ($r = 0.37$), APTT ($r = -0.43$), INR ($r = -0.49$); C1-INH activity correlated with C4 complement component concentration ($r = 0.55$). In patients suffering from angioedema with wheals there was a positive correlation between CRP and C1-inhibitor serum concentration ($r = 0.6$) and total complement concentration ($r = 0.66$). No significant correlations in other parameters within both patient groups were found.
Conclusion: The evaluation of coagulation casacade biomarkers in patients with AAE may be useful for the better understanding pathogenetic mechanisms underlying illnesses as well as be of help in the disease management.

Poster Session Group III – Green TPS 52

Food Allergy – Epidemiology

1467
New allergens associated to severe symptoms of the tomato-allergic patients

González, M[1]; Martín-Pedraza, L[2]; Villalba, M[2]; Somoza, ML[3]; Blanca-López, N[3]; Perez, D[3]; Canto, G[3]; Torres, MJ[4]; Molina, A[1]; Rodríguez, R[2]; Blanca, M[4]; Mayorga, C[1]
[1]IBIMA, Málaga, Spain; [2]Biochemistry and Molecular Biology Department, University Complutense Madrid, Madrid, Spain; [3]Allergy Service, Infanta Leonor Hospital, Madrid, Spain; [4]UMA, Allergy Unit, IBIMA, Regional University Hospital of Malaga, Málaga, Spain

Background: Tomato become one of the worldwide most consumed vegetables, but accompanied by an increasing risk of inducing allergic symptoms in certain patients. Most of tomato allergens have been described in the peel and pulp of this fruit. Seed-specific allergens identification in certain foods has improved the sensitivity and clarified the diagnosis of certain food allergies.

The aim of this study was to identify allergens in tomato seeds associated to the severe symptoms in patients allergic to tomato.

Method: Sample from 22 well-defined tomato allergic patients were used. Tomato seed proteins were purified by HPLC-chromatographic procedures. Mass spectrometry, immunoblotting, enzyme-linked immunosorbent assays, basophil activation tests and IgE-inhibition experiments were used for their biochemical and immunological characterization.

Results: A protein band of 12-kDa was identified in 71.4% of patients with severe symptoms and only in 9% with mild symptoms. Proteins were purified from tomato seeds to homogeneity. They present homology to class-1 and class-2 non specific lipid transfer proteins (nsLTP). Both allergenic nsLTPs, named Sola l 6 and Sola l 7, display different structural characteristics with respect to their counterparts from the tomato peel and other foods. The allergens retain the ability to bind serum IgE from tomato allergic patients, induce IgE cross-linking in effector circulating basophiles and display IgE cross-reactivity with homologous allergens from peanut and sunflower seeds.

Conclusion: Sola l 6 and Sola l 7 are two novel allergens from tomato seeds that belong to the nsLTP family class-1 and class-2 that might be useful to clarify the diagnosis of the tomato allergic patients with severe symptoms.

1468
Prevalence of skin sensitization to food panallergens (profilin and LTP) in adult patients from Madrid, Spain

Ramos, T; Vega, F; De Sousa, D; Mugica, V; Blanco, C
Allergy Department, Hospital Universitario de La Princesa, Madrid, Spain

Background: Profilins and lipid transfer proteins (LTP) are two panallergen families involved in food allergy. We have studied the prevalence of sensitization to both of them in our area.

Method: Skin tests were performed with commercial extracts of palm tree profilin and peach LTP (ALK-Abelló), in 5297 first-visit patients seen in our Allergy department. A diameter greater or equal than 3 mm was considered a positive result. Allergic symptoms were recorded. Sensitization prevalence was estimated, as well as possible statistical associations and odds ratios.

Results: In our population, profilin and LTP skin sensitization prevalence was 12.9% and 8.7%, respectively. Among them, 165 (i.e. 3.1%) showed co-sensitization to these two panallergens. Patients who were sensitive to profilin showed a risk (odds ratio) of 4.6 to be co-sensitized to LTP. Profilin-LTP association was statistically significant ($P < 0.001$). Regarding allergy symptoms, LTP skin sensitization was significantly associated with bronchial asthma and anaphylaxis, while profilin sensitization was only associated with the presence of asthma.

Conclusion: We have found a high prevalence of food panallergen sensitization in our area, and a significant association between sensitization to profilin and LTP has been demonstrated. Both panallergens showed significant association with asthma, but only LTP is linked to anaphylaxis.

1469
Food hypersensitivity phenotypes among Swedish schoolchildren reporting partial avoidance of milk

Winberg, A[1]; West, CE[1]; Strinnholm, Å[2]; Nordström, L[1]; Hedman, L[2]; Rönmark, E[2]
[1]Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden; [2]The OLIN Unit, Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Background: Reported hypersensitivity to cow's milk is common among children and adolescents and comprises different phenotypes. However, these phenotypes have not been thoroughly defined. The aim of the study was to investigate the symptom phenotypes underlying reported hypersensitivity to cow's milk and partial milk avoidance among Swedish schoolchildren.

Method: In a population-based cohort of 11- to 12-year-old children, the parents of 2612 (96% of invited) returned a questionnaire. Of the children who reported partial avoidance of milk due to perceived hypersensitivity and no physician diagnosed celiac disease, $n = 180$ (93.3% of invited) participated in a structured telephone interview. Specific IgE and a celiac screening test were analyzed in children participating in the interview and in a random sample of children ($n = 695$) from the entire cohort. According to results from the structured interview and blood analyses, children were categorized into phenotypes of food hypersensitivity according to preset criteria.

Results: In this cohort of 11- to 12-year olds, 9.5% reported partial avoidance of milk due to perceived hypersensitivity. According to test results, the children in the study were categorized with the following phenotypes; milk allergy (0%), outgrown milk allergy (21%), lactose intolerance (36%), and unclear (12%). At the time of the interview, 30% of the children were no longer on an elimination diet. A physician diagnosis of food hypersensitivity was reported by 67% of children with an outgrown allergy phenotype and by 37% of children with a lactose intolerance phenotype. None of the children had performed a diagnostic oral challenge.

Conclusion: Among Swedish 11- to 12-year-olds partially avoiding milk the most common symptom phenotypes were lactose intolerance and outgrown milk allergy. Self-diagnos of the food hypersensitivity

was common as was cancellation of the elimination diet.

1470
Eosinophilic esophagitis and allergy: evaluation of 50 Portuguese patients and comparison between paediatric and adult age

Marcelino, JL; Aguiar, R; Duarte, F[1]; Costa, AC; Pereira-Barbosa, MA
Immunoallergology Department, Hospital de Santa Maria, CHLN, E.P.E., Lisbon, Portugal

Introduction: Eosinophilic oesophagitis (EoE) is a chronic,immune-mediated inflammatory disease,characterized by symptoms of oesophageal dysfunction and histological eosinophil-predominant inflammation.Albeit many recent studies, little information exists on the Portuguese population and differences between children(Ch, age < 18 years) and adults(Ad).
Methods: Retrospective analysis of patients with EoE diagnosis followed in our Department (February/09–March/14).They were divided into Ch and Ad, according to age at diagnosis, and characterized by: demographic data; allergic history; clinical, laboratorial (peripheral eosinophils and total IgE), endoscopic and histological features and sensitization profile-specific IgE (sIgE), prick, prick-prick and patch tests.

SPSS was used: Binomial test, Chi-square, Fisher and Mann–Whitney.
Results: Of 50 patients, 80% are male ($P < 0.01$), with average age 21 ± 15 years (4–70). 88% Ch ($P < 0.01$) and 48% Ad had prior rhinoconjunctivitis and 76% Ch ($P < 0.01$) and 20% Ad asthma. Both are more frequent in Ch than Ad ($P < 0.01$).

The most frequent onset symptom is dysphagia (44%) in Ch and impaction (44%) in Ad. Dysphagia and impaction are the most common symptoms in Ch (56% and 52%) and Ad (46% and 86%). Symptoms of anorexia, abdominal pain, chocking, food refusal were more common in Ch (32%) than Ad (0%; $P < 0.01$).

sIgE for mites, pollens and food are positive in 68%, 52% and 64% of Ch and 12%, 16% and 24% of Ad. They also are more frequent in Ch than Ad ($P < 0.01$). Patch tests are most frequently positive for: Shellfish (48% Ch, 44% Ad), meat (24% Ch, 20% Ad), egg (16% Ch, 48% Ad) and cereal (12% Ch, 4% Ad). Overall, the most frequent food sensitization are: Shelfish 56%, nuts 32%, milk 28%, egg 22%, meat 22%. Sensitization to food exists in 76% Ch and 80% Ad; to aeroallergens in 92% Ch and 68% Ad; and to either in 96% Ch and Ad.

Endoscopy is normal in 4% of Ch and Ad. Furrows was observed in 80% Ch, 28% Ad and white plaques in 40% Ch, 32% Ad. Furrows were more frequent in Ch ($P < 0.01$). Microabscesses exist in 32% Ch and 12% Ad.
Conclusion: There's a predominance for the male gender.Ch have a higher aeroallergen sensitization and respiratory allergic disease than Ad. Whether due to their increased prevalence in Ch or to EoE pathogenesis in Ch is unknown. The most common:
1) positive patch test is to shellfish;
2) symptoms are impaction and dysphagia. Unspecific symptoms are more common in children;
3) endoscopic abnormalities are white plaques and furrows (when present, EoE should always be excluded). Furrows are more characteristic of Ch.

1471
Fish and shellfish allergy: an in-depth investigation of adults in the UK

Moonesinghe, H[1]; Mackenzie, H[1]; Chin, YT[2]; Skypala, I[3]; Dean, T[1,4]; Turner, PJ[5]; Venter, C[1,4]
[1]University of Portsmouth, Portsmouth, United Kingdom; [2]University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; [3]Royal Brompton and Harefield Hospital NHS Foundation Trust, London, United Kingdom; [4]David Hide Asthma and Allergy Research Centre, Isle of Wight, United Kingdom; [5]Paediatrics (Allergy & Immunology) and MRC & Asthma UK Centre in Allergic Mechanisms of Asthma, Imperial College London, London, United Kingdom

Background: Fish and shellfish allergy is a leading cause of anaphylaxis. There is limited data describing the characteristics and management of fish/shellfish allergy, in particular with reference to clinical cross-reactivity between species. We sought to describe the clinical characteristics of fish and/or shellfish allergic adults in the UK.
Method: We contacted adult patients (>16 years) with a record of fish and/or shellfish allergy from three UK allergy clinics, as well as members of a patient support group (Anaphylaxis Campaign). Participants were asked to complete a questionnaire covering: history of atopy, existing food allergies, dietary advice and HRQL. For those participants recruited via allergy clinics, additional relevant information such as skin prick tests, specific IgE and food challenge information was extracted from their medical notes.
Results: A total of 111 participants were recruited; 48 from NHS allergy clinics and 63 from The Anaphylaxis Campaign. A proven fish, crustacean and mollusc allergy was reported in 54%, 63% and 34% of the participants respectively, with 47% overall reporting a proven allergy to both fish and shellfish. 78% had evidence of co-existent atopic disease, 33% developed symptoms after inhalation of seafood vapours, and at least 15% of fish allergic adults were able to tolerate the implicated fish in tinned form.
Conclusion: This is a novel study describing clinical characteristics of fish and shellfish allergy in an adult population in the UK. In agreement with a large case series of seafood-allergic children, we found that
(1) fish and shellfish allergy often co-exist;
(2) seafood-allergic individuals frequently have other atopic conditions;
(3) the clinical phenotype with regards to reactivity to vapours, tolerance of tinned fish varies between individuals.

1472
Impact of hygiene factors on childhood food allergy and asthma

Gupta, RS[1]; Singh, AM[1]; Walkner, M[2]; Smith, BM[1,3,4]; Caruso, D[5]; Wang, X[5]; Pongracic, JA[1]; Marchisotto, MJ[6]; Greenhawt, M[7]
[1]Northwestern University Feinberg School of Medicine, Chicago, United States; [2]Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, United States; [3]Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innsbruck, Austria; [4]Innovation for Complex Chronic Healthcare (CINCCH) Edward J. Hines, Jr. VA Hospital, Hines, United States; [5]Johns Hopkins Bloomberg School of Public Health, Baltimore, United States; [6]Food Allergy Research & Education, Inc, New York City, United States; [7]Division of Allergy and Clinical Immunology, University of Michigan Medical School, Ann Arbor, United States

Background: Childhood food allergy and asthma are increasing. Although the exact mechanism of this increase is not known, it has been hypothesized that hygiene factors including microbial exposure, maternal child factors and pet exposure may play a role. This study compares the effect of these hygiene factors on the development of food allergy and asthma.
Method: Parents with at least on food-allergic child were asked to complete a baseline survey detailing their child's history of antibiotic use, infections, maternal child health characteristics, and pet exposure.
Results: History of skin infection was the only hygiene exposure variable that showed a significant association with the development of food allergy (8% vs 2%; $P < 0.01$). Multiple factors including, antibiotic use, common cold, RSV, Bronchitis, Pneumonia, skin infection, out-of-home childcare, and owning a cat, were significantly associated with the development of asthma. Children had higher odds of developing food allergy if they had a skin infection in the first year of life (OR 4.13; 2.18–7.81). Children had higher odds of developing asthma if they had RSV (OR 2.70; 1.88–3.89) during their first year;

or if they spent time in a childcare center (OR 1.23; 0.90–1.68). Children with cats had lower odds of developing asthma (OR 0.53; 0.36–0.79).

Conclusion: Although multiple hygiene factors were associated with the development of asthma, only a history of skin infections significantly increased the development of food allergy. Understanding the role of hygiene factors in food allergy and asthma is critical to determining potential triggers.

1473
The prevalence of food allergy is similar between school-age children living in rural and urban areas in Guangdong, China

Zhao, JF; Xian, M; Feng, ML; Wei, NL; Yang, ZW; Li, J
The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

Objective: The epidemiology of food allergy (FA) confirmed by skin-prick tests (SPTs) and serum specific IgE (sIgE) in China is limited. The aim of our study was to investigate and compare the prevalence of FA among school-age children in GuangZhou urban area and Shao Guan rural area.

Method: The screen questionnaires enrolled 5836 school-age children living in Guang Zhou and 5596 school-age children living in Shao Guan, China. The following case-control study selected 402 (included 189 children confirmed as FA according to self report and medical diagnosis, and 213 randomly selected healthy children) school-age children living in Guangzhou urban area as Guang Zhou group, and 349 (included 124 children confirmed as FA according to self report and medical diagnosis, and 225 randomly selected healthy children) school-age children living in Shao Guan rural area as Shao Guan group, they underwent standardized detail questionnaires, SPTs with 18 common food allergens. Blood samples were collected from the 751 school-age children for sIgE measurements against 27 common food allergens. The prevalence of FA recorded in detail questionnaires, responses of SPTs and sIgE in children from Guang Zhou and Shao Guan were compared.

Results: Based on standardized detail questionnaires, the prevalence (31.1% vs 16.3, $P = 0.000$) of FA in Guang Zhou higher than that in Shao Guan. Positive rate of food allergen SPT (11.7% vs 5.2%, $P = 0.01$) and sIgE (29.8% vs 18.9%, $P = 0.01$) in children in Shao Guan was significantly higher than in Guangzhou. Based on the results of SPT/sIgE and medical history reported in detail questionnairs, shrimp (0.31% for GuangZhou vs 0.31% for Shao Guan, $P = 1.000$), crab (0.018% vs 0.019%, $P = 1.000$), egg (0.018% vs 0.00%, $P = 1.000$), milk (0.018% vs 0.019%, $P = 1.000$) and peach (0.00% vs 0.019%, $P = 0.481$) are the main food allergens in the two areas. There was no significant difference in the prevalence (0.34% vs 0.37%, $P = 0.872$) of food allergy in children among the two areas.

Conclusions: Based on the results of SPTs/sIgE and medical history, there was no significant difference in the prevalence of food allergy in children between urban GuangZhou and rural ShaoGuan in Guangdong.

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1474
Fennel (*Phoeniculum vulgare*): a major allergen of the Mediterranean diet

Di Giacomo, M[1]; Giliberti, LA[1]; Nico, A[1]; Vacca, M[1]; Lotti, A[1]; Rossi, MP[1]; Bellotti, A[2]; Taurino, ML[2]; d'Elia, L[2]; Damiani, E[1]; Rossini, M[3]; Fumarulo, R[3]; Caiaffa, MF[2]; Macchia, L[1]
[1]School of Allergology and Clinical Immunology, University of Bari Aldo-Moro, Bari, Italy; [2]School of Allergology and Clinical Immunology, University of Foggia, Foggia, Italy; [3]Department of Clinical Pathology, University of Bari Aldo-Moro, Bari, Italy

Background: Unlike celery (*Apium graveolens*), fennel (*Phoeniculum vulgare*), another plant allergen of the *Apiaceae* family, has been rarely studied.

This project aims at estimating the occurrence of this allergy, in a population with a typically Mediterranean Diet, from Apulia-Southern Italy and characterizing the proteins responsible for fennel allergy, from the biochemical point of view.

Method: Out of a recent series of 189 food allergy patients, we studied 57 patients with a clear-cut fennel allergy diagnosis. The investigation was performed by: (i) quantitative skin prick tests with a commercial extract marketed by Lofarma, Milan, and with an in-house semi-purified fennel extract; (ii) quantitative prick by prick with raw fennel and microwave oven-heated fennel (10′, 2450 MHz); (iii) CAP RAST for fennel. Moreover, sera from 36 patients were analyzed by Immunoblotting, upon SDS-PAGE of the semi-purified fennel extract.

Results: The average areas of the wheals generated by SPT and prick by prick were measured. The semi-purified extract elicited an average wheal area of 59 ± 48 mm^2, in comparison to 26 ± 19 mm^2 for the commercial extract. The raw fennel prick by prick area was 40 ± 41 mm^2, whereas that obtained with microwave oven-heated fennel was 38 ± 32 mm^2. This latter result indicates that the allergens implied in fennel allergy are thermo-resistant.

As for RAST, the average value in 41 patients studied was 1.86 ± 2.22 kU/l. Four patients were RAST-negative.

SDS-PAGE and Immunoblotting analysis suggest that all 36 sera studied (100%) reacted with a protein doublet with a molecular weight in the range of approx. 65 kDa; 4 sera (11%) recognized a 47 kDa band; 6 sera (17%) a band in the range of 34-47 kDa; 10 sera (28%) a 34 kDa band; 6 sera (17%) a 27 kDa band; 6 sera (17%) a 18 kDa band; and, finally, 7 sera (19%) reacted with a band < 18 kDa. Thus, a putative major antigen was detected, along with other secondary allergenic proteins.

Conclusion: Fennel can be considered a major food allergen in those Countries where the Mediterranean Diet prevails, since it is implied in approx. 30% of all food allergy cases. Immunoblot investigation is revealing the pattern of allergic fennel proteins.

1475
Clinical pattern of Pru p 3 food allergy: influence of plane tree pollinosis

García-Moral, A[1]; Sánchez-López, J[1]; Díaz-Perales, A[2]; Pascal, M[3]; Valero, A[1]; Bartra, J[1]
[1]Allergy Section, Pneumology Department, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain; [2]Center for Plant Biotechnology and Genomics, Polytechnic University of Madrid, Madrid, Spain; [3]Immunology Department, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain

Background: Lipid transfer protein (LTP) food allergy is known to be less severe in context of pollinosis. Most patients suffer from Pru p 3 allergy in context of Plane tree pollinosis. The aim of the study was to describe the influence of Plane tree pollinosis on the clinical and molecular expression of LTP food allergy.

Method: Patients allergic to plant food who were monosensitized to LTP were selected and classified in two groups: patients affected by plane tree pollinosis (Group A) or not suffering from any pollinosis (Group B). Symptoms due to respiratory allergy and to food allergy, as well as culprit food and molecular sensitization pattern were recorded. Skin prick test (SPT) to a standard pannel to inhalants, plant food, and culprit food were performed. Allergen components to Platanus (Pla a 1, Pla a 2, Pla a 3), Pru p 3 and Art v 3 were evaluated by SPT and/or Specific IgE by a commercial microarray panel.

Results: Fifty-three subjects, age 37 ± 10.8, women 40/53 (75.5%). 32/53

(60.4%) group A, 21/53 (39.6%) group B. Regarding group B: 100% of patients had Rhinitis, 40% concomitant asthma. Number of culprit food: A: 3 (2–5) vs B: 3 (2–6). Oral allergy syndrome: (A:41.3% vs B:57.0%), Contact Urticaria (A:34.4%/B:48.2%), Urticaria/Angioedema (A:41.0%/B:33.1%), Gastrointestinal (A:41.1%/B:33.0%), anaphylaxis (A:38.0%/B:52.6%).

Molecular sensitization pattern in A/B: Pla a 1:59%/0%, Pla a 2:75.0%/5%, Pla a 3:66.6%/26.3%, Art v 3:44.1%/38.4%, Ara h:9 31.1%/33.6%, Cor a 8:50.2%/:33.8%, Jug r 3:50.9%/43.8%. Sensitization to Pru p 3 as a unique LTP: A:28.4% vs B:43.5%. To >1 LTP: A:72.6% vs B:58.4%. Sensitization to >2 LTP: A:8.0%/B:34.3%. To > 3 LTP: A:29% vs B:24%. To the 5 food LTP evaluated: A: 16.0% vs B: 0%.

Conclusion: Plant food allergy caused by LTP occurs with lower prevalence of anaphylaxis and follows a broader recognition profile of LTP when given in context of Plane tree pollinosis.

Pla a 1 and Pla a 2 are recognized in 90% patients with plane tree pollinosis. An isolated sensitization to Pla a 3, in the absence of Pla a 1/Pla a 2, can also induce a pollinosis in patients allergic to plant food due to LTP.

Most of the patients with plant food allergy are sensitized to more than one LTP.

When affected by pollinosis, the pattern of sensitization to LTPs is wider.

1476
Severe allergic reactions to Anacardiaceae in infants (birth to age 2 years)

Konstantinopoulos, AP; Savvatianos, S; Mitsias, D; Karantoumanis, D; Koutsalitis, D; Psomiadou, M; Tziotou, M; Tzeli, K; Manousakis, E; Papadopoulos, N
Allergy Department, 2nd Pediatric Clinic, University of Athens, Athens, Greece

Background: Tree nut allergy is characterized by a high frequency of life-threatening reactions. The prevalence of cashew and pistachio nut allergy, in particular, is rising, according to recent studies. Concurrently, anaphylaxis is increasingly reported in infants and young children, with foods being the most common triggers.

Method: A retrospective study was performed over a 5-year period (2008–2013). Medical record databases of patients referred to our department for food allergy evaluation were screened for the diagnosis of clinical allergy to cashew and/or pistachio nut. Information on the patient's age at the first reaction to cashew/pistachio was collected. Reported consumption of any of the two nuts, prior to first reaction, was recorded. Diagnosis was based on history, symptoms, skin prick testing, sIgE and exclusion of other causes. Oral food challenges were not performed, because of the very young age.

Results: Out of 103 children diagnosed with clinical allergy to cashew/pistachio (m/f: 69/34), with median age 4.5 years, at their first reaction, 30 were infants (m/f: 22/8), having had their first reaction reported, by the age of 2 years. Systemic reaction was reported for 22/30 of the infants. The rest (8 infants) had reactions limited to urticaria/angioedema. Consumption of cashew/pistachio prior to the first reaction could only be confirmed for 2 infants. Data revealed that minimal quantity, only traces of cashew/pistachio nut elicited reaction to 16/30 of the infants.

Conclusion: Awareness of anaphylaxis in infancy should intensify, in order to improve clinical diagnosis, management, and prevention of recurrences. Minimal amounts of cashew/pistachio nut allergen may cause a severe allergic reaction, suggesting high potency. Anacardiaceae appear to have an escalating impact on food allergy and anaphylaxis.

1477
Natural course of food allergy at the end of the 4 years of age: results of birth cohort study from Turkey

Karakoc, G[1]; Karagoz, D[2]; Altintas, D[1]; Yılmaz, M[1]; Duyuler, G[1]; Kont, A[1]
[1]Faculty of Medicine, Cukurova University, Adana, Turkey; [2]Faculty of Medicine, Baskent University, Adana, Turkey

Background: Food allergy (FA) is the most common allergic disorders during childhood. In this birth cohort study we aimed to determine the prevalence of and natural course of FA in southeast Turkey.

Method: Adana Pediatric Allergy Research (ADAPAR) birth cohort study was derived from 1377 infants who were born in Cukurova University, Medical Hospital, Adana, Turkey between 2010 and 2011 to determine prevalence of FA in the first year of life. Food allergic children were reevaluated at the end of the 4 years of age .The diagnosis of FA was based on clinical symptoms, skin prick test and specific IgE results and confirmed with oral food challenge(OFC).

Results: Food allergy was confirmed with OFC in 33 cases (2.4%) in the first year of life. Cow's milk was the major cause of FA and determined in 20 children (1.45%), followed by egg allergy (17 cases, 1.2%). Skin symptoms were the major clinical features (74%). Family history of atopy as identified an important risk factor for FA (ORs 18.90, 95% CI 1.59–224.05; $P = 0.020$). Duration of breastfeeding and cord blood IgE levels were not identified as risk factors. At the end of the 4 years FA was found to be persist in 3 of 20 children (15%) whereas in 2 of 17 egg allergic children (11.7%). Inhalant allergen sensitivity was developed in three children (9%).

Conclusion: Although FA is the most common during infancy, usually many children outgrew their FA in first 3 years. Similarly, in our birth cohort study we found that almost 85% of children developed tolerance. We assume that early distinct elimination and close monitoring may affect this result.

1478
Natural course of our patients with egg and cow's milk allergy: single clinical experience

IŞIK, S; Çağlayan-Sözmen, Ş; Asilsoy, S; Anal, Ö; Karaman, Ö; Uzuner, N
Pediatric Allergy and Immunology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

Background: IgE-mediated egg and cow's milk allergy are most common forms of food allergy in childhood and usually present in the first few years of life. Cow's milk and egg allergy generally has a good prognosis and is expected to resolve in the majority of children by school age. However, a recent study suggested that the natural history of milk allergy might change over time, with slower rates of resolution and in a higher proportion of children, persisting into adolescence and even adulthood. We aimed to investigate the natural course of our patients with cow's milk and egg allergy followed up between years 2010 and 2014.

Material and Methods: Eighty two infants and children (mean age: 7.8 ± 6.4 months) with cow's milk and egg allergy were evaluated retrospectively. 31.7% ($n = 26$) of the patients had both milk and egg allergy; 10.9% ($n = 9$) of the patients had only egg, and 57.3% ($n = 47$) of the patient had only milk allergy. All children were examined for specific IgE and skin prick test to milk and egg.

Results: First presenting symptoms of the patients were urticaria (61%), anaphylaxis (15.9%), atopic dermatitis (30%) and colitis (2.4%). Milk allergy had resolved in 49 (67.1%) subjects at a mean age 21.8 ± 20.6 months and egg allergy had resolved 29 (85.1%) subjects at a mean age 8.7 ± 18.1 months. The mean levels of egg white and milk specific IgE at first analysis and after resolution were determined 4.2 ± 12.1 ku/l, 9.1 ± 16.9 ku/l, 1.6 ± 4.4

ku/l, 11.3 ± 25.0 ku/l respectively. There were no correlation between presenting symptoms and resolution age.

Conclusion: Many food allergies such as milk and egg with onset in early childhood are outgrown later in childhood, although a minority of food allergy persists into adolescence and even adulthood. In our study majority of patients with egg and milk allergy had resolved in childhood in consistence with other reports. Altough there were no association between initial milk spesific IgE levels and resolution age of milk allergy, but initial egg spesific IgE level had strong association with egg allegy resolution age.

1479
Oral allergy syndrome in birch-sensitized children in Western Siberia

Fedorova, O[1]; Fedotova, M[1]; Petrovskiy, F[2]; Evdokimova, T[3]; Fernandez-Rivas, M[4]; van Ree, R[5]; Ogorodova, L[1]; Kamaltynova, E[1]
[1]Siberian State Medical University, Tomsk, Russian Federation; [2]Khanty-Mansiysk State Medical Academy, Khanty-Mansiysk, Russian Federation; [3]Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation; [4]Hospital Clinico San Carlos, Madrid, Spain; [5]Academic Medical Center, Amsterdam, Netherlands

Introduction: Oral allergy syndrome (OAS) is defined as the symptoms of IgE-mediated immediate allergy localized in the oral mucosa and usually developed due to pollen-food cross-reaction. Birch pollen is one of the most common pollen allergens in Western Siberia.

Purpose: To estimate the prevalence of OAS and its characteristics in birch-sensitized patients with pollen syndrome.

Material: The cross-sectional study in random samples of children aged 7–10 years from the Tomsk Oblast, Western Siberia, Russia, was performed (EuroPrevall-INCO study, FP6- FOOD-CT-2005-514000). The study included screenning and case-control stages. The total sample of birch-sensitized patients with pollen syndrome (n = 42) was selected from case-control sample.

Methods: The standardized screening questionnaires were used at the screening stage. The case-control stage included the completion of a clinical questionnaire, skin-prick test (ALK-Abelló, Spain) and serum specific IgE measurement (ImmunoCAP, Phadia, Sweden). OAS was defined as the typical clinical symptoms within 2 h after food ingestion together with specific IgE ≥ 0.35 kU/l and/or positive skin-prick test to the same food (mean diameter of wheal ≥3 mm). Birch sensitization was defined by specific IgE measurement (≥0.35 kU/l) and/or positive skin-prick test (mean diameter of wheal ≥3 mm).

Results: There were 38.09% of children who has OAS among birch-sensitized patients with pollen syndrome (n = 16, mean age: 9.04 ± 1.22 years). The boys and girls ratio was 1:1. Symptoms of OAS were developed after eating apple – 75%, carrot – 43.75%, peach – 40%, peanut – 40%, hazelnut – 25%, walnut – 16.67%. In 25% cases OAS occurs immediately – within less than 5 min after food intake, in 50% – within 30 min and in 25% – in 30–60 min. In 31.25% children OAS was combined with rhinitis and/or conjunctivitis; in 12.5% cases occurs angioedema, caused by carrot consumptions.

Conclusion: The prevalence of OAS is 38.09% in birch-sensitized patients with pollen syndrome in Western Siberia. The main food cross-reactive allergens are: apple, carrot, peach, peanut, hazelnut, walnut. The severe reactions (angioedema) are associated with allergy to carrot.

1480
Frequency of sensitization to corn in patients of the National Institute of Respiratory Diseases

Ruiz Morales, RD; García Cruz, MDIL; Ramírez Jiménez, F; Pavón Romero, GF; Camacho Ordóñez, N; Sánchez de la Vega Reynoso, P; Pérez Estrella, Z; Terán, LM
Allergy and Immunogenetics, National Institute of Respiratory Diseases, Mexico City, Mexico

Background: Corn is one of the main foods in many countries; this allergy can be expressed as oral allergy syndrome, urticaria, rhinitis, bronchial, gastrointestinal symptoms or anaphylaxis. Over 10 corn proteins are related to allergic reactions. Zea m1, a β expansin, is the greatest pollen allergen. Zea m12, a profilin, found in food and pollen. Zea m 14 a lipid transfer protein (LTP), considered as a major food allergen. May have cross-reactivity with rice, wheat, barley, peach, cherry, grape and tomato.

Method: Patients were evaluated at Allergy and Immunology Department with suggestive symptoms of food allergy, they underwent skin tests with fresh foods, airborne allergens; questionnaire to determine functional gastrointestinal disorders was performed.

Results: Of 60 patients, 22 positive for corn (36.6%), 50% female, 50% male, mean age of 27.4 years, Ig E 567 IU/l, eosinophils of 472 cells/mm^3. 100% of patients had allergic rhinitis, 68.1% asthma and 100% positive to airborne allergens. About 63.6% of patients had gastrointestinal symptoms, mainly esophageal and 72.7% oral allergy syndrome. The 63.6% had positive skin test to corn, 54.5% to pollen and 18.1% had both. Also 54% of the patients had cross-reactivity with tomatoes, 45% with peach, 36.3% with wheat, and 31.8% with cherry.

Conclusion: The frequency of sensitization to corn is high in our population, which may be mediated by a profilin or LTP, producing mainly gastrointestinal symptoms. So, it is essential to perform skin test for corn, as well as taking into account the possible cross-reactivity with peach, tomato, wheat and cherry profilin or LTP.

1481
Food skin prick test results in the patients with urticaria

Ozseker, F; Bulut, I
Immunology and Allergy, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

Background: Food allergy is usual in children, but it's not same in adults. We evaluated food prick test results of the patient who had urticaria complaint admitted to our outpatient clinic.

Method: We evaluated retrospectively the food skin prick test results of the patients with urticaria admitted to the our outpatient clinic in the last 18 months. We made skin prick tests with 16 different commercial allergen extracts (ALK, Albello, Denmark) and fresh foods by prick to prick tests.

Results: In 70 of the 930 patients skin prick tests positive with foods. Female/Male ratio was 47/23, mean age was 40.47 ± 12.8 (18–78 years). The most frequent positive tests were hazelnut (n = 22), groundnut (n = 18), peach (n = 14), egg yolk (n = 14), cacao (n = 11), apple (n = 9), chicken meat (n = 9), Fishes (n = 7), cow milk (n = 7), respectively. In 26 patient multiple food tests were positive.

Conclusion: Food allergy is not frequent in the adults. However in the patients with urticaria food allergy kept in mind all the time. Nevertheless double blind placebo control food challenge test is the gold standard for diagnosis of food allergy; skin prick test may give some idea about allergy. If the patient history and skin prick test is compatible, elimination of the culprit food from diet can be satisfactory. When we look at the results nut is the first allergenic food that is suitable national eating habits.

1482
Prevalence of fruit allergen-free diets in school canteens in Hortaleza district, Madrid, Spain

Ortiz, JC[1]; Cabrera, M[2]; López-Gay, D[3]
[1]Health Service, Quality and Consumer Department, Madrid City Council, ImFINE Research Group, Universidad Politécnica de Madrid, Madrid, Spain; [2]Allergy Department, Los Madroños Hospital, Brunete, Spain; [3]Epidemiology Department, Public Health Area 4, Prevention and Health Promotion Section, Community of Madrid, Madrid, Spain

Background: In Spain, in children under 5 years of age, milk and eggs are the main food that induce allergies while in age up to 5 years, are fresh fruits and nuts, followed by crustaceans. In fresh fruits, melon, watermelon and bananas often induce reactions, especially in children allergic to grass pollen.
Objective: To estimate the prevalence of fruits allergen-free (FA-free) special diets in school canteens of a northern District in Madrid (Hortaleza), Spain.
Methods: A structured questionnaire on special diets was distributed to 86, 88, 89, 90 and 84 school canteens in different school years during the period 2009–2014. Special diet by means of FA-free diets was recorded on the basis of clinical reports by specialists.
Results: About 25% FA-free diets were reported in the last year of the surveyed schools with upward trend year on year ($P < 0.05$; total studied period 22%). Significant upward trend year on year were shown in kiwi, melon and watermelon-free diet prevalence but not in *rosaceae* family. The group of children 6–15 years old, was the most affected ($P < 0.05$) taking into account all fruit allergies during the studied period.
Conclusions: Prevalence of fruits allergen-free diets in the Hortaleza District schools is high, similar to the Spanish Alergológica 2005 report. Kiwi, melon and watermelon are the most prevalent allergens implicated. School canteens represent a good source of information on food allergy trends in children.

1484
Immunological differences between three clinical groups of peanut sensitized patients from northeast Slovenia

Homsak, M[1]; Berce, V[1]; Šilar, M[2]; Korošec, P[2]
[1]Department of Paediatrics, University Medical Centre Maribor, Maribor, Slovenia; [2]Laboratory for Clinical Immunology and Molecular Genetics, University Clinic of Pulmonary and Allergic Diseases, Golnik, Slovenia

Background: Peanut sensitization is common in children. Whole peanut specific IgE (sIgE) testing could not differentiate between sensitized and truly allergic patients. We describe the immunological pattern in three different clinical groups of peanut sensitized patients using molecular component diagnostic approach.
Method: Patients with positive sIgE to peanut were divided according to clinical picture after peanut exposure: patients with anaphylaxis belong to anaphylaxis group (AG), patients with milder symptoms like hives or angioedema belong to group with milder symptoms (MSG) and patients without reported symptoms were regarded as only sensitized (SZG). Clinical data were gathered from chart reviews. We analyzed sIgE to peanut recombinant allergens rAra h 1, 2, 3, 8 and 9.
Results: Included were 66 children from Slovenia. In the AG there were 12, in MSG 17 and in SZG 37 patients. Whole peanut sIgE levels were not different between groups. Patient in AG have significantly higher sIgE to rAra h 1 compared to MSG ($P = 0.03$) and to SZG ($P = 0.0001$). Between SZG and MSG there were no differences in rAra h 1. sIgE rAra h 2 levels were extremely higher in AG (median 34.6 kU/l) than MSG (median 0.46 kU/l; $P = 0.006$) and SZG (median 0.1 kU/l; $P < 0.0001$). Also there was difference between SZG and MSG ($P = 0.0003$). sIgE levels to rAra h 3 were higher in AG than SZG ($P = 0.0002$) and MSG ($P = 0.03$). There is no difference between MSG and AG. Interestingly, sIgE levels to rAra h 8 were higher in SZG and MSG groups compared to AG ($P = 0.04$). Testing of sIgE to rAra h 9 showed no differences. Patients in AG were polysentisized with 2–4 recombinant peanut allergens (in 92%), monosentisized were only 8% (all to rAra h 2). Patients in AG were all sensitized to rAra h 2 (100%), additionally in 75% to rAra h 1 and 67% to rAra h 3. MSG patients were polysensitized in 64%, from monosensitized part only to rAra h 2 (75%) and to rAra h 8 (25%). In contrast SZG patients were predominantly monosentisized (73%), 70% to rAra h 8, 15% to rAra h 9, to rAra h2 in 11% and in 4% to rAra h 1.
Conclusion: The sensitization pattern in Slovenian children showed the importance of rAra h 2, h 1 and h 3 components in peanut clinical allergy. Especially high sIgE to rAra h 2 and additionally high sIgE to rAra h 1 and/or h 3 are factors predicting anaphylaxis. Monosensitization to rAra h 8 is mostly connected with birch allergy.

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Case reports in food allergy

1486
A follow-up study of fruit allergy with latex sensitization in children

Shibata, R; Odajima, H
Pediatrics, Fukuoka National Hospital, Fukuoka, Japan

Background: Banana and kiwi allergy have been associated with latex sensitization or the latex-fruit syndrome. Fruit allergy in children may be tolerant with age as compared with fruit OAS of adults. We studied the children with fruit allergy and serological evidence of latex sensitization, and examined the clinical course and the change of the fruit and latex IgE antibody 6–7 years after the onset.
Method: Ten patients who the case developed fruit allergy (banana 8, kiwi 5, melon 5, apple 3) for early childhood (Average age 4.4 years old, boys 7: girls 3), and have latex IgE antibody positive (3 cases had history of latex allergy). The subjects underwent an accurate allergological evaluation (skin prick test with fruit and latex) and specific IgE to fruit, latex and recombinant allergens (rHev b 5, rHev b 6.01, rHev b 6.02, rHev b 8, rHev b 11) were measured by Immuno-CAP.
Results: Positive history cases of the IgE antibody-positive inside were banana 8/10 case, kiwi 5/8 cases, melon 5/7 cases, apple 3/4 cases, and 7 years later banana 4/9 cases, kiwi 5/8 cases, melon 2/1 cases, apple 2/2 cases. Five case had positive IgE antibody to rHev b 8 (profilin) and 3 case had positive to rHev b 6.02. The latex IgE antibody decreased in all cases (from 6.8 ± 9.9 to 0.55 ± 0.42 UA/ml).
Conclusion: The case showing IgE antibody positive to banana, kiwi and apple with age tended to be hard to be tolerant. There was many profilin rHev b 8 (profilin) antibody positive, but all cases revealed the fall of the latex IgE antibody.

1487
Allergy from cantaloupe seed

Alselahi, E
Pediatric Department, Amiri Hospital, Kuwait, Kuwait

Background: Food allergy is increasing world wide and nowadays we are facing cases having reaction to food that was not known to cause allergy, allergy to fruit is increasing and allergy to the seeds in fruits is increasing it seems. Here I diagnosed a case of allergy to cantaloupe seed. 11 year old boy came to our allergy clinic with histroy of reaction to cantaloupe seed.

After eating one piece he started to feel itchy in his throat with no other symptoms, his mother gave him antihistamine and brought him to our clinic. He used to eat cantaloup before with no problem, but he doesn′t like to eat it.
Method: Skin prick test was done to fresh cantaloupe fruit and it′s seed, also to the seed soaked in water for 1 day and dry seed as well. Also challenge to fruit was done at clinic
Results: Positive skin testing to fresh cantaloup and it′s seed around 6 mm and to the seeds slacked in water was 1 cm and dry seed 5 mm. He was asked to lick cantaloup seed and waited for 20 min with no symptom but when asked to have small piece of fruit he had lip swelling and throat redness and sensation of swelling.
Conclusion: Food allergy can be to any kind of food and not to the common food as used to be, lower the threshold of diagnosing the unusual food items. And skin testing bad challenge are the gold standard.

1488
Anaphylaxis to Yuzu (*Citrus junos*)

Lefèvre, S[1,2]; Jacquenet, S[3]; Richard, C[3]; Astafieff, K[4]; Peru, L[4]; Froelicher, Y[5]; Kanny, G[1]
[1]EA 7299, Université de Lorraine – Faculté de Médecine, Vandœuvre-lès-Nancy, France; [2]Hôpitaux Civils de Colmar, Colmar, France; [3]GENCLIS SAS, Vandœuvre-les-Nancy, France; [4]Jardin Botanique du Montet, Villers-les-Nancy, France; [5]Institut National de la Recherche Agronomique – Centre Corse, San Giuliano, France

Introduction: Yuzu (*Citrus junos*) is a hybrid of a mandarin (*Citrus reticulata)* and a lemon fruit (*Citrus ichangensis*). Citrus belongs to *Rutaceae* family, which composed of two sub-genus: *Eucitrus*, to which *Citrus reticulata* belongs and *Papedas* to which *Citrus ichangensis* belongs.

The consumption of yuzu is common in the Japanese food, where its peel is used as a condiment, and its juice for the flavouring. In France, there is a growing interest for this Citrus as a new culinary fashion.

Case report: We report the case of a 42 years old woman, with no atopic history, who has experienced two anaphylactic episodes after consumption of yuzu: once in bluefin tuna flavouring with yuzu juice, and 3 months later, eating a butter flavouring with juice and peel. She consumed other citrus fruits (lemon, orange, grapefruit, tangerine) without any reaction.

Skin prick tests (SPTs) were performed with juice, peel and pulp of commercially available lemon, orange, grapefruit, tangerine and yuzu, 2 cultivars of *Citrus junos* (B2 and 846), 2 cultivars of mandarin (*Citrus mandarina* and *Citrus reticulata*), *Citrus ichangensis* and food consumed during the culprit meal (tuna). Codeine 9% was used as positive control.

SPTs were positive with juice (8 mm) and peel (7 mm) of commercial yuzu, with juice of *Citrus junos* B2 (10 mm), juice (5 mm) and pulp (8 mm) of *Citrus mandarina*, negative to other Citrus and tested food.

Specific IgE (ImmunoCap, Thermofisher) to lemon, orange, grapefruit, tangerine, mandarin, rPru p3, tuna were negative (<0.10 kU/l).
Discussion: Food allergy to citrus is rare, despite the wide consumption of these fruits. Reported cases concern mainly orange and lemon. Three allergens has been identified: Cit s 1, Cit s 2 and Cit s 3 (1). Our patient presented a selective food allergy to yuzu and can consume other citrus fruits. It is interesting to note, as previously described with other fruits (2), that there is a difference of reactivity among cultivars. The most reactive is Yuzu B2 that is the most consumed fruits of this *Citrus*.
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1489
Difficult diagnosis cross-reactions mugwort – celery

Gocki, J; Bartuzi, Z
Allergy, Clinical Immunol. and Intern. Diseasess, Nicolaus Copernicus University, Bydgoszcz, Poland

Background: Cross-reactions between mugwort and celery and other vegetables are observed more frequently in Poland. They are often dangerous anaphylactic reactions after accidental ingestion of celery, which is a popular accessory in Polish cuisine.
Aim: The authors draw attention to the diagnostic difficulties associated with the diagnosis of mugwort-celery reactions even with the use of modern research techniques and many unexplained aspects of these reactions.
Method: A case of the patient 36 years old. Before 6 years ago was diagnosed with seasonal allergic rhinitis and conjunctivitis in the period from June to September. In addition, after ingestion of celery occurred of feet itching and pain of the abdomen. The skin tests performed were found positive reactions to mugwort. The patient was qualified for immunotherapy sublingual formulation of mugwort. Because of the side effects (abdominal pain) discontinued immunotherapy. Over the years observed intensification of allergic symptoms after ingestion: celery, kiwi, honey, parsley, peanuts, walnut and hazelnuts. The patient complained of severe abdominal pain, vomiting, itching of palate, oedema of the lips, eyelids, tongue, palate and urticaria, runny nose and nasal congestion. Repeatedly experienced anaphylactic reactions after consuming celery and nuts. Laboratory tests found no presence of specific IgE antibodies to food allergens and showed specific IgE to mugwort: >100 kU/l, plantain: 0.24 kU/l, hazel 0.2 kU/l, *D. pteronyssinus*: 0.19 kU/l. The diagnostics performed using allergen component ISAC revealed sIgE for nArt v 1 defensin family. sIgE antibody against Art v 1 is detected in 70% of patients allergic to mugwort. In IUIS allergen database this allergen is not considered to be food allergens. Artemisia belongs to the order *Asteraceae*, among which we find 3 food allergens belonging to the family of defensins: one in soybeans (Gly m 2) and two in peanuts (Ara h 12, Ara h 13). This could explain the cross-reactions with peanuts in our patient. Mugwort belongs to the *Asteraceae* and source *magnoliopsida*, which also include celery, hazelnut, walnut, and kiwi.
Conclusion: Perhaps among these species, there are unexplored allergens defensin family of proteins, which would explain the observed cross-reactions.

1490
LTP syndrome or multiple sensitisation?

Fernandes, R-A[1]; Carrapatoso, I[1]; Bartolome, B[2]; Pereira, C[1]; Todo-Bom, A[1]
[1]Imunoallergy Department, Coimbra University Hospital Centre, Coimbra, Portugal; [2]R&D Department, Bial-Aristegui, Bilbao, Spain

Background: We report the case of a 39-year-old woman who suffered from recurrent episodes of oral allergy syndrome (OAS), facial erythema and labial oedema with the ingestion of peach and walnut since the age of 4, when these foods were restricted from her diet. In her late twenties she began to have OAS, nausea, vomiting and diarrhoea after ingestion of soy, red fruits, chestnut and peanut. By 27, she had an anaphylactic reaction 2 h after eating breakfast, without identifying the triggering factor, but denying the possible influence of co-factors. Self-administered adrenaline was prescribed and she was advised to restrict all suspect foods. She had history of asthma and allergic rhinitis in early childhood.
Method: Skin prick tests (SPT) to aero- and food-allergens; serum specific IgE determinations (sIgE) to some plant foods and to Pru p 3 were performed. Molecular mass of IgE binding bands from suspected foods was calculated by means of SDS-PAGE immunoblotting. In order to study the presence of cross reacting IgE in the patient serum, we carried out a SDS-PAGE immunoblotting-inhibition assay using walnut extract as solid phase and Pru p 3 as inhibitor.
Results: SPT were positive to extracts from peach, walnut, cherry, peanut, chestnut, green beans and soy. Serum sIgE (kU/l) was positive to extracts from peach (1.32), walnut (2.8), cherry (1.47), peanut (0.67), chestnut (1.14), plum (2.56), tomato (0.52), green beans (2.02), soy (1.14) and to rPru p 3 (3.32). Immunoblotting assays to peach and walnut extracts revealed the presence of an IgE binding band of nearly 10 kDa. A strong IgE binding inhibition was detected in walnut extract (solid phase) when Pru p 3 was used as inhibitor. Immunoblotting assays to soy, green bean, cherry, plum and tomato revealed the presence of IgE binding bands of molecular weight similar to those found for peach and walnut. All these extracts revealed an IgE binding band of similar molecular mass of those found with patient serum, when anti-Pru p 3 rabbit serum was used in the IgE-Immunoblotting study. For chestnut and peanut the immunoblotting revealed the presence of bands with distinct molecular mass of those found for the other foods.
Conclusion: Immunoblotting and inhibition studies support the diagnosis of LTP syndrome involving the majority of foods. However, as atopic patients are prone to develop multiple sensitisation, other distinct proteins than LTPs seems to be involved in chestnut and peanut allergy.

1492
Tri a 19 and wheat exercised-dependent urticaria

Gomes, R; Loureiro, C; Pita, J; Todo-Bom, A
Immunoallergology, Coimbra University Hospital Centre, Coimbra, Portugal

Wheat allergy is one of the most common food allergy, and the most frequent related clinical finding is urticaria. The major proteins in wheat allergy are albumins, globulins, gliadins and glutenins. Gliadins, like Tri a 19, are the most common, particularly in wheat-dependent exercise-induced anaphylaxis (WDEIA), positive in 80% of the cases. As we know some co-factors may predispose or influence the hypersensitivity reaction like exercice, non-steroidal anti-inflammatories (NSAIDs) and prior alcohol intake.

The authors present two young patients, with recurrent urticaria, that the study revealed to be related to wheat, but exercise dependent. The aim of this presentation is reinforce the need for the clinic to be aware of such different cases, which may be responsible for a reduction in the patient′s quality of life.

We report a young 37 year old male (Case 1) and a 39 years old female (Case 2), both with multiple episodes of generalized pruritic erythematous maculopapular rash a few minutes after physical activity starts, with no other associated symptoms and with a good response to antihistamine. The exercise usually takes place after snack and both deny alcohol or NSAIDs intake prior to it.

For evaluation we performed full blood count, liver, thyroid and kidney function, prick (P) tests to commercial food extracts to fruits, vegetables, meat, fish, seafood, spices and flours (wheat, rye, oats and soy); prick-to-prick tests (PP), specific IgE and food challenge according to the results.
Case 1: Revealed only positive P and PP tests to wheat flour (histamine 6 mm; *P* = 5 mm and PP=8 mm). Specific wheat IgE = 22.5 kU/l; Tri a 19 = 45.7 kU/l. Wheat challenge was positive with exercise only.
Case 2: Revealed positive P and PP tests to wheat and rye flour (histamine 4 mm; Wheat – P = 4 mm and PP = 6 mm; Rye – P = 3 mm; PP = 4 mm). Specific wheat IgE = 8.2 kU/l; Tri a 19 = 8.86 kU/l. Wheat challenge was also positive with exercise only.

Taken this results they stop eating wheat at least 4 h before exercise, without further recurrence of urticaria.

Cases of wheat-induced urticaria dependent on exercice, with no criteria for WDEIA, are rare, particularly when associated to Tri a 19 sensitization. As we know continuous to exposure to the allergen can be dangerous, taking into account that these reactions can become more severe with continued exposure, and therefore required early diagnosis.

1493
Anaphylaxis due to peanut

Loloci, G[1,2,3]; Hoxha, M[4]; Nikolla, E[2]; Ibranji, A[3]
[1]Service of Allergy and Clinical Immunology, University Hospital Center 'Mother Theresa', Tirana, Albania; [2]Department of Allergy, 'Petro Nako' Hospital, Saranda, Albania; [3]Department of Allergy, University Hospital Center 'Zoja e Keshillit te Mire', Tirana, Albania; [4]Clininic of Allergy and Clinical Immunology, University Hospital Center 'Mother Theresa', Tirana, Albania

Background: Anaphylaxis is a severe, potentially life-threatening allergic reaction. Peanut allergy is the most common cause of food-induced anaphylaxis. It is recognized as one of the most severe food allergies due to its persistency, prevalence and potential severity of allergic reaction. Anaphylaxis usually occurs within minutes but can occur up to several hours after eating peanut products or peanuts. Prevalence of peanut allergy is 0.6–1.3%. It is believed that the incidence of peanut allergy exceeds 1% of the population. Fatal food anaphylaxis is most often caused by peanut (50–62%).

Case report: A 16 years old boy appeared in emergency room with dyspnea, generalized urticaria and hypotension. He referred that hasn't experienced such situation in the past. Also referred the first symptoms were tingling and numbness of lips and tongue, pruritis, generalized urticaria, dyspnea, dysphonia, dysphagia, abdominal pain and dizziness after consuming different foods such as pasta, tomatoes, green salad and chocolate (sugar, wheat flour, vegetable fat, coconut, palm, peanut, low fat, cocoa, powder, hazelnut, lactose, soya lecithin, salt, sodium hydrogen carbonate, clavouring). He had a history of 6 years with allergic rhinitis. Three years ago SPT performed for the inhalant allergens resulted positive to Wall Pellitory. The symptoms resolved with administration of 1/3 epinephrine 1 mg/1 ml s/c, prednisolone 125 mg i/v and antiH1 180 mg p.o. After 15 days we performed specific IgE for foods and resulted positive to Peanut.

Discussion: Peanuts cause serious food allergy in both adults and children. Peanut allergy usually begins in childhood and persists throughout life. Only 20% of young children will develop tolerance. Wall pellitory pollen has been recognized as an important allergen, causing symptoms of asthma, allergic rhinitis and allergic conjunctivitis. The major allergen of Wall Pellitory-Par j 2 and Peanut-Ara h 9 was identified as a lipid transfer protein (LTP). LTP are proteins stable to heat and digestion causing reactions also to cooked foods, often associated with systemic and more severe reactions in addition to OAS and responsible for systemic manifestations in food allergy.

Conclusion: We presented a case of a patient with anaphylaxis. Cross-reactivity between Wall Pellitory and Peanut and positive specific-IgE to Peanut lead us to the diagnosis of Anaphylaxis to Peanuts.

1494
An interesting case of laryngeal edema due to intake of ground nuts

Bulut, I; Ozseker, ZF
Immunology and Allergy, Süreyyapasa Chest Disease and Chest Surgery Training and Research Hospital, Istanbul, Turkey

Background: FTA, a 29 years old woman applied to our clinic, suspecting allergy against ground nuts. Medical history revealed that 4 months ago, the woman experienced hoarseness, itching in oral and throat region, swelling at toungue and throat, difficulty in swallowing that occured 3 h after intake of ground nuts.The patient had applied to an emergency service with these symptoms and recieved medical treatment. There was no history of asthma, rhinitis, urticaria or accompanying allergic comorbidities.

Method: Skin prick test was done with respiratory allergens panel and food allergen panel. No sensitization has been detected. A prick to prick test has been carried out with ground nut extract, along with a prick test done with ground nut press.

Results: In the latter one, a typical hyperemia accompanied an enduration zone 7 × 7 cm in diameter. This has been regarded as positive. On the other hand, no sensitization has been detected in the former test. The patient was issued an adrenalin autoinjection certificate and adviced to come for follow-up.

Conclusion: Food allergies similar to this case of ground nut allergy can be seen in aduult population, although not very frequently. This should be kept in mind when dealing with cases of urticaria, since failing to recognise this can lead to serious allergic reactions accompanied by laryngeal edema that can be life-threatening.

Clinicians should be aware of the clues that suggest a food allergy when taking medical history. We wanted to point this out with this case presentation.

1495
Hypersensitivity to banana and nuts through breastfeeding

Mendoza Parra, A; Montoro, A; de Vicente, T; de Mateo, MB; Fonseca, J; Nuñez, MA
Hospital Central de la Defensa, Madrid, Spain

Introduction: Several factors may act together or separately, at the onset of IgE-mediated food allergy such as: self-allergenic capacity of each food consumption frequency, age of introduction of foods, highly responsive IgE, the presentation of allergen behind the apparent first intake of food that explain the existence of minimal doses contacts by their passage through the placenta or breast milk protein allergy being cow's milk, egg and fish the most common and less often fruit and nuts.

Method: Girl 6 months old, exclusively breastfed, that after the first intake of banana mush naturally presents box patchy erythematous lesions on facial area without angioedema without dyspnea that disappear when treated with Dexcloferinamina. Refer the mother who had previously tolerated mashed potatoes, vegetables, pear and apple. Without introducing other foods. Acude to our center for evaluation and study.

Results: Negative skin tests vs standard battery of inhalants and alimentos. IgE Total: 37 kU/l. IgE specified banana 0.51 kU/l, eosinophil cationic protein: 26.9 μg/weakly positive mixed nuts. Milk fish egg negative.

Conclusion: IgE mediated food allergy is the most common in infants.The onset of symptoms after the first intake of foods other than milk, egg and fish have a low incidence not therefore be underestimated. The existence of contacts with minimal doses, for their passage through the placenta or breast milk is a method of sensitization in infants to consider in our daily practice and should corroborated with skin tests and specific IgE determination of blood.

1496
Persistent contact urticaria to raw potato in a child with a history of reactivity to ingested cooked potato and high potato – CAP levels: a case report

Georgountzou, A; Tzeli, K; Karantoumanis, D; Douladiris, N; Manousakis, M; Xepapadaki, P; Papadopoulos, NG
2nd Pediatric Clinic, Unit of Allergy and Clinical Immunology, National & Kapodistrian University of Athens, Athens, Greece

Introduction: IgE mediated allergy to potato is rare and most reactions in children result from ingestion of cooked potato, whereas contact urticaria is uncommon in this age group. Allergy to cooked potato is related to latex allergy and IgE mediated responses to several foods of plant origin. Sensitization to raw potato may also be related to pollen allergies.
Case report: A 4 year old boy presented to our outpatient allergy clinic reporting a history of immediate reactions (generalized urticaria) after ingestion of cooked potato at the age of 6 and 7 months. Upon pediatrician's advice the child was put on a potato-free diet ever since, and at accidental contact with raw potato at the age of 18 months had developed contact urticaria, which resolved within 30 min after ceasing contact and washing the skin. The child had no history of atopic dermatitis, respiratory or other food allergy but reported a positive family history of respiratory allergy. Specific IgE to potato levels were 21.8 kU/l with total IgE at 265 kU/l. The prick-to-prick (PTP) test with raw potato pulp was positive, with a maximal wheal diameter of 7 mm, whereas PTPs to cooked- boiled or fried- potato were negative. Skin prick tests to peach, profilin, grass mix and latex were negative, as well. Oral challenges to cooked and fried potatoes at ages 4.5 and 5 years old, respectively, were negative. Upon a follow-up period of twelve months the child has reported twice a mild, self-limiting sensation of pruritus of the trunk after ingestion of boiled potatoes, within the first month of potato reintroduction in his diet. He continues to eat cooked potatoes regularly, but he still exhibits contact urticaria to raw potato, as documented after recent accidental contact.
Conclusion: We report on a rare case of a boy in preschool age, strongly sensitized to potato, with transient reactivity to cooked ingested potato but persistent reactivity to raw potato, presenting as contact urticaria.

1497
Buckwheat: an emerging food allergen in the UK

Liau, JL; Khan, NL; Croom, AJ
Clinical Immunology and Allergy, University Hospital of Leicester, Leicester, United Kingdom

Buckwheat (*Fagopyrum esculentum*) is a pseudocereal with a short growing season and able to thrive in poor climatic conditions. It has been used as a food stuff for around 8000 years. First cultivated in the Balkan region its use has become geographically more widespread particularly in areas with poor growing conditions. It is a staple of the diet in some areas of the Far East e g. soba and naeng myun noodles in Japan and Korea respectively and found in typographic cuisines within Europe e.g. Breton gallettes, Dutch pofferties, and Italian pizzoccheri. Increasingly buckwheat is used as a gluten-free cereal substitute in 'free from foods'. It is now also gaining popularity in Europe due to its perceived health benefits; attributed to its being rich in flavonoids and soluble fibre. It is also used as a prebiotic. Buckwheat allergy is common in Japan and Korea (prevalence of 3.4% and 2.9% respectively); its prevalence across Europe has not been established although in one Northern Italian study it was thought to account for 7.3% of the confirmed diagnoses of food allergy. It can cause occupational asthma as well as anaphylaxis.

We report three patients with anaphylaxis due to buckwheat allergy. All had episodes after ingesting buckwheat in a popular breakfast biscuit; one patient had a second episode after eating a cake made with gluten-free flour. All 3 had eaten the biscuits without adverse effect for some time prior to the episodes of anaphylaxis. All patients were female with an age range of 38-58 years. One patient had asthma; two had no history of atopic disease. With the exception of the buckwheat all other ingredients of the biscuits had been eaten subsequently without problems.

The buckwheat-specific IgE levels in all three patients were elevated; skin prick testing was not performed. After diagnosis the patients were counselled about future avoidance and prescribed adrenaline autoinjectors.

It seems likely that all three of our patients were sensitised via ingestion of the buckwheat in the breakfast biscuits. Buckwheat is currently promoted for its putative health benefits and its increased inclusion in the UK diet reflects both this and its use as a gluten-free wheat substitute. This may result in increasing rates of sensitisation; clinicians should be aware of where buckwheat is found in the diet and its role as a trigger of anaphylaxis.

1498
Anaphylaxis caused by mushrooms. A case report

Verdeguer Segarra, O[1]; Bartolomé, B[2]; Peláez Hernández, A[1]; Ortega Sanchis, S[1]; Morales Rubio, C[1]
[1]Hospital Clinico de Valencia, Valencia, Spain; [2]Bial-Arístegui, Bilbao, Spain

Background: In certain cases of food allergy, the development of symptoms is dependent on the manner in which the food is prepared. Some allergens present in foods can be destroyed in the cooking process. As a result, if such processed foods are ingested, no symptoms manifest.
Method: A 34-year-old patient with a family history of AINES intolerance, immediately after eating sauce containing two types of raw mushrooms -Boletus edulis and Craterellus cornucopioides (Black Trumpet), presents an episode of lingual and uvula edema, sensation of pharynx obstruction, and dispnoea; all of which resolve spontaneously after a few minutes. Four months later, the ingestion of another kind of sauce containing Boletus edulis causes a similar episode, and requires an antihistamine. The rest of ingredients in the processed sauces have been tolerated afterwards, as well as both kinds of mushrooms when cooked.

Skin tests with both kinds of mushroom are carried out. Specific IgE is assessed by means of EAST method (Enzyme AllergoSorbent Test). Specific IgE-binding protein molecular mass is studied by SDS-PAGE immunoblotting method performing electrophoresis under reducing and non-reducing conditions.
Results: Skin tests with Black Trumpet extract proved positive ++++; with Boletus edulis extract – positive +++.

Prick-prick with Black Trumpet – positive +++; with Boletus edulis – positive +++.

Specific IgE <0.35 kU/l (class 0) – for both kinds of mushroom extract.

The study of the Specific IgE-binding protein molecular mass under reducing conditions revealed values of approximately 38 kDa in the Boletus edulis extract.

Conclusion: We present a case of immediate type of allergic reaction to mushrooms (Boletus edulis and Black Trumpet), in which only one 38 kDa IgE-binding protein is found.

It should be pointed out that the patient only manifests symptoms after ingesting raw mushrooms, and both kinds of mushroom are well tolerated when cooked at high temperatures. This suggests that the protein causing the allergic reaction is a thermolabile one.

1499
Meaning of garlic specific IgE finding

Coniglio, G[1]; Mafucci, M[2]; Paggini, M[2]; Migali, E[3]
[1]Specialist Centre, Arezzo, Italy; [2]Dirigente 1° Livello – USL 8, U.O. Laboratorio Analisi, Arezzo, Italy; [3]Direttore U.O. Laboratorio Analisi, USL 8, Arezzo, Italy

Background: Garlic is a much used aroma in the Mediterranean area; allergy to garlic, even though not frequent, must be taken into account, because its symptoms can be severe.

Method: Specific garlic IgE were measured in nine patients with food and respiratory allergy and garlic positive prick-by-prick test. In eight of them, widely polysensitized, it was impossible to single out the component responsible of the symptoms, even after an accurate anamnestic examination. Garlic is often 'hidden' in food preparation and therefore difficult to detect.

Results:

Allergic Year of birth	Sensitive Year of birth	Symptoms to both raw and cooked garlic	Garlic IgEs	Total IgE	Concurrent food allergy	Symptoms to onion	Onion IgEs
MJ M 1995		Diarrhea	11.5	687	profilin oral allergy syndrome	No	neg
CS F 1993		Diarrhea Larynx edema	4.97	594	profilin oral allergy syndrome	No	4.51
PR F 1967		Larynx edema	3.08	268	Anaphlylaxis LTP	Larynx edema	4.82
AP M 1978		Rhynitis	0.51	105	Rhynitis with peas and corn	No	0.49
	LM M 1976		9.92	490	Anaphlylaxis LTP		8.46
	RML F 1955		4.17	115	Asymptomatic		4.17
	JK F 1972		2.03	387	PR-10 oral allergy		2.03
	CL M 1987		1.04	619	profilin oral allergy		1.04
	BA F 1972		0.91	57.8	Anaphlylaxis LTP		0.91

[Garlic IgEs in allergic and sensitive patients]

Among the positive results, it was impossible to establish a cut-off between symptomatic and asymptomatic patients, showing therefore that each patient has a specific threshold.

In three among the symptomatic patients, garlic specific IgE were higher than the others (in patient no. 3 were lower only than peach and apple specific IgE); patient no. 3 had a previous result (dating back to 4 years before, when it was asymptomatic) which showed lower garlic specific IgE (0.96 kU/l).Symptoms reveal that the allergen involved is thermo and gastro resistant.

Conclusion: Higher values of specific IgE in single panels of polisensibilization and a more accurate amamnesis led to suspect allergy to garlic; it was confirmed by repeated 'suspension and reintroduction tests' carried out spontaneously by the patients during the diagnostic phase. Eventually, the removal from the diet determined the disappearance of the connected symptoms.

1500
Anaphylaxis in a child caused by parsley

Caglayan Sozmen, S[1]; Mastrorilli, C[2]; Rizzuti, L[2]; Povesi Dascola, C[2]; Caffarelli, C[2]
[1]Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [2]Parma University Faculty of Medicine, Parma, Italy

Anaphylaxis to parsley independent of cross reactivity has been rarely reported in the literature. Herein, we presented a 6 year old girl who experienced anaphylaxis after ingestion of parsley.The patient was referred with a history of generalized urticaria, hoarse voice and angioedema of face 10 min after eating lunch at school. She had eaten boiled beef meat with sauce containing fresh parsley, lemon, vinegar and olive oil. She has consumed the same sauce several times in the past but never with fresh parsley. She went to emergency department and physical examination revealed edema of hard palate, serous rhinitis, generalized urticaria. Auscultation of the chest showed diffuse reduction in breath sounds and wheezing. Intramuscular adrenaline, intravenous antihistamine and steroid were administered. 6 weeks after the reaction, we performed skin prick test with fresh foods and found 9 × 5 mm positive reaction to parsley. Specific IgE level for parsley was 0.15 kU/l. Oral provocation test was not performed because of the severity of the past reactions. Isolated anaphylaxis to parsley is rarely described in previous literature. Although the 'major food allergens' (peanut, tree nuts, egg, milk, fish, crustacean shellfish) wheat, and soy have been known to cause most of allergic reactions, rare allergens such as parsley should be considered as a trigger.

1500-A
Allium mongolicum Regel induced acute allergic reaction

Wang, X; Shi, H; Kong, R
Beijing Shijitan Hospital, Beijing, China

Here we report on three emergency cases (one man and two women) suffered from anaphylaxis after digesting Allium mongolicum. All three people are China′s Inner Mongolia region, Mongolian. They all gone through stuffy nose, cough, chest tightness, shortness of breath, itchy skin and rash 10–30 min after eating Allium mongolicum. Symptoms alleviated immediately after taking antihistamines, glucocorticoids and oxygen. Unified diagnosis in local hospitals was acute urticaria. No similar symptoms appeared after fasting Allium mongolicum. The patients did allium mongolicum skin prick test using fresh juice in allergy clinic of Beijing shijitan hospital and the result turned out to be strong positive.

Allium mongolicum Regel belongs to Liliaceae family, Allium species. Mongolia leek and Mongolia onion are aliases. As a perennial herbaceous xerophytic plant, it mainly distribute in Inner Mongolia desert, grassland and the sand. Since the flowering time is early August and September, it harvest in late September. It is a kind of vegetables of great nutritional and medicinal value. In this article, all three cases developed definite allergic reactions after eating Allium mongolicum, and no same symptoms appeared after fasting it. Allium

mongolicum skin prick test was positive. Typical medical history and positive skin prick test are enough for diagnosing allium mongolicum induced allergic reaction.

1501
Allergy to cumin: mugwort pollen-related food allergy

Deng, S[1]; Yin, J[1]
[1]Peking Union Medical College Hospital, Beijing, China

Background: Cumin allergy has been reported once. It is unknown whether cumin allergy is caused by direct sensitization or cross-sensitization to pollen allergens.
Method: Two patients allergic to cumin present rhinitis, asthma and urticarial after ingestion of ground cumin.They also have seasonal rhinitis during summer and autumn. Serum total immunoglobulin E (IgE) and specific IgE to pollen were tested using the Phadia CAP System FEIA. Specific IgE to cumin was tested by ELISA. Protein extracts from pollen and cumin were analyzed by sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western blot. Cross-reactivity was evaluated by ELISA and immunoblot-inhibition.
Results: In both patients specific IgE for mugwort was 39.4 and >100 kUA/l, respectively.Immunoblot analysis revealed IgE reactivity to cumin at Mr of approximately 70 kDa.The mugwort pollen-related nature of this allergen in cumin was demonstrated by ELISA and immunoblot inhibition.
Conclusion: Cumin allergy can be added to the list of mugwort pollen-related food allergies.

1505
Small bowel Anisakiasis. The importance of a detailed clinical history in acute abdomen

De las Vecillas Sánchez, L[1]; Martínez Molina, S[1]; Montecchiani, V[1]; Drake Pérez, M[2]; Morchón Miguel, E[1]; Rodríguez Fernández, F[1]
[1]Allergy Service, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [2]Radiology Service, Hospital Universitario Marqués de Valdecilla, Santander, Spain

Background: Anisakis simplex is a parasite which may cause infection and allergic reactions when humans eat raw or undercooked fish. The contact with live larvae through the invasion of gastrointestinal mucosa can develop IgE mediated reactions with allergic features, abdominal symptoms or both. In last case, it is known as Gastroallergic Anisakiasis (GA). Mostly, it involves the stomach but rarely the small bowel. A correct diagnosis approach is a key issue for a successful management.
Method: A 45 year old woman presented left hemi-abdominal pain 72 h after the ingestion of undercooked hake and 48 h after eating raw anchovies. At admission she presented abdominal distension, painful palpation with tenderness to light percussion suggesting peritoneal irritation. Vital signs were normal. Sample blood was taken and image tests were done with a diagnosis of acute abdomen due to nonspecific ileitis and subocclusion intestinal syndrome. Conservative intravenous therapy was tried firstly, in order to avoid unnecessary surgery. Symptoms resolved in 24 h with conservative therapy and she was referred to our Service with suspected gastroallergic anisakiasis (GA).
Results: Complete blood count showed neutrophilic leukocytosis and full chemistry panel were normal on admission. Abdominal echography revealed jejuni and ileal wall thickening. The CT scan demonstrated swelling of the small bowel wall in the hypogastric segment with important lumen reduction and ascitic fluid. Allergy study showed: positive prick test to Anisakis Simplex (5 × 5 mm) with a 48 h reaction; total serum IgE (InmunoCAP) 23.30 kU/l; specific IgE to Anisakis S. 2.59 kUA/l. Other food allergens were negative.
Conclusion: Sometimes, abdominal symptoms may be the first manifestation of GA. When small bowel is affected, the interval between food intake and symptom onset is longer than in gastric cases. A detailed clinical history and imaging are essential for a good diagnosis and prevention of harmful management in a first approach. A conservative attitude with a subsequent allergic study and diet restriction may prevent new and worse episodes.

Poster Session Group III – Green TPS 54

Milk & egg allergy – a problem in children & adults

1506
When and how to end treatment with Omalizumab while introducing cow's milk and egg double oral immunotherapy in severe allergies

Barato, D; Alba, JC
Pediatric Allergy, Hospital de la Ribera, Alzira, Spain

Background: Adjuvant treatment with Omalizumab in oral food immunotherapy has proven its effectiveness in cases of severe food allergies. However it's unknown how long you need to continue treatment with Omalizumab after complete tolerance to the food and the pattern of withdrawal from this. The aim of the study was to evaluate the effectiveness and safety to the withdrawal from Omalizumab after completing cow's milk and egg double oral immunotherapy for a patient with severe allergies.
Methods: A 6 year old girl diagnosed with atopic dermatitis and egg and cow's milk persistent allergy who had anaphylactic clinical and high levels of specific IgE. An allergy study was performed: Skin prick test with comercial extracts, total IgE, cow's milk, egg and proteins specific IgE. She began treatment with Omalizumab (0.016 mg/kg/total IgE) and after 70 days of administration started cow's milk oral immunotherapy and tolerance up to 200 ml per day. After that, she began oral immunotherapy with pausteurized egg white until full tolerance to the egg (30 ml every other day). Then we proceeded to gradually withdrawal from Omalizumab.
Results: Skin prick tests were positive to egg and cow's milk fractions. Total IgE: 1392 kU/l. Specific IgE levels: cow's milk and casein >100 kU/l, alpha-lactoalbumin 23.4 kU/l, beta-lactoglobulin 2.87 kU/l, egg white 50.60 kU/l, yolk 5.05 kU/l, ovomucoid 18.4 kU/l and ovoalbumin 57.30 kU/l. After completing both immunotherapies we continued with Omalizumab for a further 6 months, the first 2 months with a dose of 450 mg per month and then we reduced the dose by 150 mg every 2 months until the patient had been withdrawn from Omalizumab. During this period the patient continued taking maintenance doses of cow's milk and egg white without adverse reactions.
Conclusion: The pattern of gradual withdrawal from Omalizumab after cow's milk and egg double oral immunotherapy has proven a profile of adequate effectiveness and safety.

1506-A
Specific allergy to quail's egg with chicken egg tolerance

Méndez Díaz, YC[1]; García Rodríguez, C[1]; Alfaya Arias, T[1]; Bartolomé Zabala, B[2]; Feo Brito, F[1]; Gómez Torrijos, E[1]
[1]Hospital Ciudad Real, Ciudad Real, Spain; [2]Laboratory for Allergy, Bilbao, Spain

Objective and introduction: Egg allergy is one of the most common causes of food allergy. Allergy to eggs of other species is less frequent and generally described in chicken egg-allergic patients. Our goal is to present an uncommon case of a patient with quail egg allergy with good tolerance to chicken eggs.
Material and Methods: Male patient 21 years old with history of rhinoconjunctivitis and allergic asthma by grass pollen and olive, atopic dermatitis and oral allergy syndrome profilin that after ingestion of boiled quail's egg tolerated previously presented in immediately feel pharyngeal itching and occupation with dyspnea in the upper airways, facial erythema and edema nondeforming without injury the rest of the body, which required emergency assistance. There has not been able to eat these foods tolerates chicken egg.

Skin tests (ST) were performed with commercial chicken egg extract and protein, prick by prick with quail egg (white and yolk, raw and cooked), specific IgE (InmunoCAP) and SDS-Page/Immunoblotting with quail egg extracts.
Results:

- ST (prick by prick): POSITIVE to white raw quail (15 × 11 mm) and cooked (10 × 5 mm), raw yolk quail egg (7 × 6 mm). Negative (Neg) for yolk cooked quail egg.
- ST with chicken egg and proteins (prick commercial extract): Neg. To egg, white, ovalbumin and ovomucoid. ST (Pric by prick) hen white egg (pasteurized): Neg.
- IgE Specific for quail's egg white (15.9) and yolk (16.3). Specific IgE to hen egg (2.4) and yolk (0.35).
- In blotting two IgE binding bands very intensively observed approx. 40 kDa and 31 kDa and two less intense 97 kDa 60 KDa. These bands were identified as ovalbumin and ovomucoid respectively.

Conclusion: We report a case of specific allergy to quail egg, chicken egg tolerance.

Objectify sensitization to ovalbumin and ovomucoid specifically for quail egg.

1507
Two cases of egg allergy in adult patients

Bulut, I; Ozseker, F
Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Immunology and Allergy, Istanbul, Turkey

Background: Food allergy is more common in children and relatively uncommon in adult population.Hereby we evaluated two cases of adults who applied to our clinic with complaint of egg allergy. 1.(A, E) 23 years old woman. She described rashes that occured 2 years ago following intake of antibiotics. Has been recieving asthma treatment in last 2 years.The patien described two episodes of egg allergy, one occuring 2 years ago and the other 1 month proior to applying our clinic. Her symptoms consisted of itching sensation in throat, oral region and ears; swelling in eyelids and lips; dispnea, and respiratory distress. She had applied to emergency service afterwards. 2.(A,D) 26 years old woman. Has been recieving asthma treatment for 14 years now, though not very regulary. She describes that she has not experienced any allergy related to consumption of egg in 22 years, but she began to experience itching in mouth and throat, and rashes over the body lasting less than 24 h, upon consumption off cake, paste and foods containing egg. She even described experiencing violent itching and swelling in her fingers after toucing a boiled egg.She also described swelling in lips, eyelids, tongue and throat; also dispnea that occured after consumption of boiled egg. This had happened 20 days prior to applying our clinic.

Method: We have done prick test with (ALK-Abello-Denmark) containing allergen solution to both of these cases.
Results: Positive reaction against egg yolk and white were detected in both of the cases. Adrenalin oto-injection certificates were issued to both of the patients. They were adviced to avoid consuming products containing egg.
Conclusion: Late onset egg allergy can be seen in adult population, although not very often. We wanted to point out that food allergy should be taken into consideration as a possible etiology in patients with symptoms of urticaria.

1508
Frey syndrome in childhood: a differential diagnosis of food allergy

Blanc, S[1]; Bourrier, T[1]; Pham-Thi, N[2]; Sabouraud-Leclerc, D[3]; Payot, F[4]; Coffinet, L[5,6]; Deschildre, A[7]; Dumond, P[8]; Dutau, G[9]; Donnou, M-D[10]; Ghazouani, J[11]; Gouranton, M[12]; Moreigne, M[13]; Albertini, M[1]; Tran, A[14]; Giovannini-Chami, L[1,15]
[1]Hôpitaux Pédiatriques de Nice CHU-Lenval, Pediatric Pulmonology and Allergology Department, Nice, France; [2]Allergology Department, Institut Pasteur, Paris, France; [3]Pediatric Department, Hôpital Américain, Reims, France; [4]Allergology Department, Pediatric Department, Hospices Civils de Lyon, Bron, France; [5]ENT Department, Centre Hospitalier Universitaire de Nancy, Nancy, France; [6]Université de Lorraine, Nancy, France; [7]Pediatric Pulmonology and Allergology Department, Clinique de Pédiatrie Jeanne de Flandre, CHRU de Lille, Lille, France; [8]Department of Internal Medicine, Clinical Immunology and Allergology, Centre Hospitalier Universitaire de Nancy, Nancy, France; [9]9 rue Maurice-Alet, Toulouse, France; [10]Cabinet de Pneumologie et Allergologie Pédiatrique, Brest, France; [11]Cabinet de Pédiatrie Générale et Allergologie, Ravines des Cabris, France; [12]Cabinet d'Allergologie, Les Abymes, France; [13]Centre Hospitalier Régional La Fontonne, Antibes, France; [14]Emergency Department, Hôpitaux Pédiatriques de Nice CHU-Lenval, Nice, France; [15]Université de Nice Sophia-Antipolis, Nice, France

Introduction: Frey syndrome is a vegetative neuropathy of the auriculotemporal nerve, related, in adults, mainly to traumatic surgical injury, and well known to ENT specialists. In childhood, it is a rare disease, often idiopathic and unknown by pediatricians. The largest pediatric series published to date reported 9 cases. Clinical manifestations often occur in infants at dietary diversification, and correspond to facial flushing in the nerve territory, which is often unilateral, triggered by sweet or acid food. The aim of this retrospective national series was to describe specificities of Frey syndrome in childhood, in order not to confuse with food allergy.
Methods: Recruitment was performed by mailing to members of French Allergology Societies (SFA, ANAFORCAL, SP²A). Diagnostic criteria were based on clinical history, pictures, or provocation test. A detailed questionnaire was sent to referring physicians.
Results: Twenty-seven cases were identified, with a sex ratio of 1.7. Flushing was unilateral in 20 (74%) cases and bilateral in 7 (26%) cases. Instrumentally assisted vaginal delivery was associated with unilateral forms (18/20 vs 1/7; $P < 0.001$). Symptoms were more extensive in unilateral forms, with jugal, pretragal extension ($P < 0.05$) compared to only frequent temporal distribution in bilateral forms. All children experienced flushing, warmth was present only in unilateral forms (10/20; $P < 0.05$), and sudation and pruritus were reported only in 3/27 cases. Median time for appearance after eating was 1 min. and for disappearance, 10 min. Median age at onset (4.5 vs 5.25 months) and diagnosis (6 vs 13 months) was younger in bilateral forms ($P < 0.05$). Allergologic exploration was performed in 12 children, more frequently by an adult allergologist ($P < 0.005$). Elimination diets were prescribed to four children. Diagnosis was performed by a pediatric allergologist in 26 (96%) children and an adult allergologist in 1 (4%). The outcome was complete disappearance in four cases [more frequently in bilateral forms, 3/4 ($P < 0.05$)], regression in 18, and stability in 4.
Conclusion: Frey syndrome in childhood is a rare but benign condition. Symptoms are mild and outcome is regression or complete disappearance in most cases. Uni and bilateral forms may have different physiopathology. Pediatric allergologists are aware of this disease and usually make the diagnosis. There is no need to perform any allergologic investigations, nor to prescribe any treatment in this setting.

1509
An interesting case of adult multiple food allergy with late onset

Bulut, I; Ozseker, F
Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Immunology and Allergy, Istanbul, Turkey

Case: Seventy-four years old female patient (H, L) applied to our immunology clinic with complaint of food allergy. The medical history revealed that in last 3-4 years she has been experiencing episodes of swelling in eyelids, lips and tongue; itching sensation in the mouth and throat, abdominal pain and swelling, vertigo and syncope that occured right after intake of chicken meat. The patient also described having symptoms of abdominal gas and fullness following intake of garlic, tomatoes, carrot and potatoes.
Method: Skin prick tests with extracts of allergens and also another test (ALK-Abello-Denmark) was done. Food panel results were all negative. Among the respiratory allergens, only grass pollen and seed pollen tests were positive.The patient underwent a prick to prick test with boiled chicken meat.A region of hyperemia and induration with a diameter of 11 × 7 mm was seen. The results of prick to prick test done with raw tomatoes, carrot, potatoes and garlic were respectively 9 × 9 mm, 7 × 7 mm, 11 × 11 mm, 13 × 5 mm in diameter and therefore regarded positive. The patient also had positive results for specific Ig E for these mentioned foods.
Results: Skin prick tests and specific Ig E results confirmed the food allergy episodes described by the patient. The patient was issued a certificate for autoinjection of adrenaline. The foods causing allergy were omitted from the diet.
Conclusion: We wanted to point out the probability of food allergy in the population of adult and geriatric population. In our case of multiple food allergy, we wanted to demonstrate importance of food allergy episodes in patient′s past medical history.

1510
Adult-onset cow's milk allergy and bodybuilding: is there a connection?

Sousa, MJ; Ferreira, AR; Moreira Silva, JP
Allergy and Clinical Immunology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, EPE, Vila Nova de Gaia, Portugal

Background: Cow's milk (CM) is one of the main causes of food allergy in the first years of life, but it typically resolves during childhood. Adult onset cow's milk allergy (CMA) is extremely rare and the mechanisms underlying sensitization after the first years of life is unknown.
Aim: To report the case of a previously healthy 24-year-old man referred to our clinic with a 3-month history of abdominal discomfort and nausea during physical exercise at the gym, with progressive worsening to abdominal pain and vomiting. These symptoms were also elicited minutes after the ingestion of CM, without exercise, which he previously tolerated. These complaints were never associated with mucocutaneous, respiratory or cardiovascular manifestations. The symptoms improved without any medication in a few hours. When asked about food ingestion prior to exercise, he reported the ingestion of a protein supplement for muscle building before and during exercise at the gym, for the last 2 years. Lately, while preparing the supplement, he noted rhinoconjunctivitis. This supplement consists of a protein blend of hydrolyzed whey protein isolate and a whey protein concentrate from CM. He

started a 100% vegetable protein supplement, with tolerance. Due to the development of oral allergy symptoms with yogurt and cheese, he began strict avoidance of CM.

Methods: Skin prick tests (SPT) with commercial extracts and skin prick-to-prick tests (SPPT) with the suspect foods, including supplements, were performed. Specific IgE (sIgE; ImmunoCAP Thermofisher®) to CM and CM proteins were determined.

Results: SPT were positive for CM, α-lactalbumin, β-lactoglobulin, casein, cheese, and sheep's milk. SPT to beef was negative. SPPT with CM and the protein supplement mencioned above were positive, and negative with supplement consisting of vegetable proteins. sIgE was 18.20 kU/l for CM, 12.80 kU/l for β-lactoglobulin, 10.50 kU/l for α-lactalbumin, and 0.08 kU/l for casein.

Comments: The *in vivo* and *in vitro* tests results suggest an IgE-mediated CMA. Adult onset CMA has been rarely reported and to our knowledge this is the first case possibly related to bodybuilding supplements. The authors theorize that the presentation of large amounts of altered proteins in the gastrointestinal (GI) tract may favor sensitization and allergy, what may also explain the initial symptoms restricted to the GI tract. With the widespread use of proteins supplements, adult-onset CMA prevalence may increase.

1511
Atypical symptoms of milk allergy in 37-year old patient

Ukleja-Sokolowska, N; Gawronska-Ukleja, E; Zbikowsta-Gotz, M; Bartuzi, Z
Department and Clinic of Allergology, Clinical Immunology and Internal Diseases, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland

Background: Allergy to milk is characteristic for children. Usually symptoms resolve during first years of life. In adults the reason of unwanted reaction after consuming milk products is mainly lactose intolerance.

Bovine serum albumin is the main thermolabile allergen component of beef, responsable for reactions after eating raw meat. It is also responsable for approximately 30% of allergic reactions after fresh milk.

Method: Patient, female, 37-year old, was diagnosed in 2014 in Department and Clinic of Allergology, Clinical Immunology and Internal Diseases because of anxiety, sweating, problems with concentration, episodes of hypotension (50/40 mmHg), anal itching and urticaria as a result of consuming milk and meat products.

During diagnosis we performed skin prick tests with a set of food allergens including milk (Allergopharma). We determinated the level of allergen specific IgE against pork, beef and milk. Open food challenge was performed. We also estimated the level of milk allergen components using Polycheck Milk plus system.

Results: Skin prick tests with a set of food allergens, including milk, were negative. The level of allergen specific IgE against pork, beef and milk was not elevated (<0.35 IU/ml). Open food challenge with 5 ml of milk was positive, with an episode of sweating and rhinorrhea. In Polycheck the level of asIgE against milk, Bos d 4 (alfa-lactalbumin), Bos d 5 (beta-lactoglobulin) and Bos d 8 (casein) was <0.35 kU/l (not elevated), but the level of asIgE against Bos d 6 – bovine serum albumin was elevated (71 kU/l).

Conclusion: Patient was advised to exclude fresh milk and raw beef from the diet. On follow-up visit patient reported that during elimination diet the symptoms did not appear.

Component resolved diagnosis allowed to confirm source of symptoms in patient and indicate a diet specific to her needs.

1512
Diagnostic process *in vivo* and *in vitro* of severe respiratory symptoms in patient after ingestion of soy milk

Barocci, F[1]; Barzaghi, CE[2]; Aliprandi, P[2]; Lodato, A[1]
[1]Immunotrasfusion Center Rho Hospital – Company Hospital G. Salvini Garbagnate Milanese, Rho, Italy; [2]Ambulatory of Allergology and Clinical Immunology Medicine IV Rho Hospital – Company Hospital G. Salvini Garbagnate Milanese, Rho, Italy

Background: A young Peruvian woman was assessed at our clinic during first visit for 4–5 year persistence of breathing disorders and oculus rhinitis, mainly during springtime. In a subsequent checkup she reported OAS after ingestion of raw carrot, apple, walnut, raw fennel, peach, raw celery, almond, raw tomato, hazelnut, peanut. She also reported acute asthma attack after ingestion of soy milk.

Method: She has been submitted to skin prick tests with inhalant allergens and to aspecific bronchial provocation test with metacolina (BPT); then to prick by prick tests with fresh foods and commercial soy extract produced by Lofarma Company. To evaluate deeply and completely polisensitivity to inhalants and foods, native-specific IgE and specific molecular components were dosed with the test system ImmunoCap of Phadia S.r.l. of Thermo Fisher Scientific.

Results: The patient is positive to prick tests for trees, grasses and composite (Ambrosia) and BPT. Regarding fresh foods she shows positive prick tests to banana, carrot, fennel, strawberry, apple, tomato, celery. The native-specific IgE gave positive results for some fresh and dry fruits, therefore, taking into consideration the specific components and cross-reactivity, the molecular components Pru p 3, Ara h 2, Ara h1, Ara h 3, Ara h 9, Cor a 8, Cor a 9, Cor a 14, Gly m 5, Gly m 6 were dosed with negative results. Pru p 1 and Pru p 4 resulted positive, but being markers/proteins allied to plant foods and pollens and being sensitive to cooking and digestion, they are not indicative of risk of severe reaction.

Conclusion: Determination of molecular marking of specific IgE sensitization of soy, storage protein 5 and 6 groups, gave negative results; as a result, the patient would not be at risk of severe reactions with soybeans and derivate products even in case of accidental ingestion. In daily clinical practice it is essential to link anamnesis to the results of history prick tests research of specific IgE for food allergens and their molecular components, in order to highlight the real sensitization and differentiate them from co-identification. In addition, the determination of specific IgE for the molecular components allows you to estimate the potential severity of allergic food reactions in case of a re-exposure of patient to allergen to which is sensitized.

1513
Allergy in products of non enzymatic browning reactions – a case report

Christopoulou, G[1]; Tziotou, M[1]; Psomiadou, M[1]; Tzeli, K[1]; Karantoumanis, D[1]; Kostoudi, S[1]; Zisaki, V[1]; Georgiou, K[1]; Roumpedaki, E[1]; Douladiris, N[1]; Manousakis, E[1]; Xepapadaki, P[1]; Papadopoulos, N[1,2]
[1]Allergy Unit, 2nd Pediatric Clinic, University of Athens, Athens, Greece; [2]Center for Pediatrics and Child Health, Institute of Human Development, University of Manchester, Manchester, United Kingdom

Background: In recent years many confectioners and housewives use condensed sweetened milk for the preparation of caramel. It is an easy and cheap method by which milk is heated in the can for 2–3 h without adding any other ingredients.

Objective: To report the case of allergic reaction in caramel produced from heated condensed sweetened milk in a polysensitized 5-year-old boy.

Methods: We describe a patient with reported clinical symptoms (urticaria) of allergy in caramel produced from 2-h heating of condensed sweetened milk immediately after the consumption. No other ingredients were added in the milk. The history of the child revealed the presence of allergic proctocolitis in milk in the age of 2 months and IgE sensitization in milk (as assessed by sIgE and SPTs). In the age

of 3 years a food challenge was conducted in condensed milk which was negative. Since then, until the reaction in caramel, the child consumed milk (fresh, condensed or condensed sweetened) without any problems. Skin prick testing (SPT) was performed in caramel.

Results: Results of skin prick testing (wheal size >4 mm) in caramel confirmed an IgE-mediated sensitivity to caramel whereas the child tolerates condensed sweetened milk. The boy was instructed to avoid caramel.

Conclusion: Although it is known that heating decreases the allergenicity of milk, the chemical reactions that take part in non enzymatic browning reactions, such as Maillard reaction, of sweetened milk may lead in the production of compounds that cause allergic reactions to some children. Formic acid is one of the main products of the reaction that could be responsible for the reaction. However, it is very difficult to identify the compounds that are implicated in allergies. A kinetic analysis of the Maillard reaction is difficult because it is a complicated reaction with many steps. More research is needed on the field of biochemistry of foods in order to obtain more knowledge on the formation of new compounds, during different reactions, which may act as allergens.

1514
Turbot selective hypersensitivity: report of a case

de Luque Piñana, V[1]; Eguez Hidalgo, MF[2]; Bellido Linares, V[1]; Guardia Martínez, P[1]
[1]Hospital Universitario Virgen Macarena, Sevilla, Spain; [2]Hospital Enrique Garcés, Quito, Ecuador

Background: The turbot is a flat fish that belongs to the Scophthalmidae family. Although allergy to fish usually occurs after ingestion, exposure to fish steam generated by heating seems to trigger symptoms in allergic patients. Likewise, aerosols generated by passive evaporation can cause occupational asthma in workers at food processing plants, such as frozen and smoked fish factories.

Method: A total of 42 year old male, who worked as cook in a restaurant for several years, consulted for, suddenly urticaria, angioedema, dyspnea, pharyngeal bolus sensation and coughing, after handling and inhaling turbot cooking vapors. He needed emergency care following administration of intramuscular corticosteroids and inhaled bronchodilators, symptoms resolve in about 2 h. He had previously tolerated turbot intake as well as other seafood. After this episode the patient avoids exclusively this fish intake, handling and inhalation during cooking. Other fish and seafood are tolerated without problem.

Results: Blood test and complement were normal, specific IgE to codfish, anisakis, and shrimp: negative, serum tryptase normal.

Prick test codfish, squid, hake: negative.

Prick-Prick test with turbot: Positive.

Conclusion: Allergy to several species of fish has been reported in fishermen and cooks. Inhalation of the aerosols was significantly associated with occupational asthma, and the severity of the symptoms was correlated with the distance from the source of the aerosols. In the literature we found a study with three patients, worked at the same fish farm for several years. They experienced symptoms of rhinoconjuntivitis and asthma in work, improved during weekends and holidays. The allergens were parvalbumin in one case and a different allergen in the remaining two patients. We report a patient with turbot selective hypersensitivity, that sensitization was probably by inhalation, therefore we are going to continue the study, to conclude the proteins correspond only to the major fish allergen or a different allergen.