Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

Poster Session 57

Effector cells in inflammation

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Role of the disease status of the donor on sensitivity of cultured mast cells

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Background: Binding of IgE to FcεRI increases the expression of FcεRI on mast cells and basophil granulocytes. Distinct properties (affinity of IgE for allergen, clonality of allergen, fraction of specific IgE of total IgE) of the IgE repertoire determine basophil degranulation on exposure to allergen. We investigated whether disease status (atopy or asthma) of the donor influences the sensitivity of mast cells cultured under identical conditions.
Method: This study included 12 patients with an objectively confirmed asthma diagnosis according to GINA-guidelines and eight healthy subjects. Allergic sensitisation was defined as a positive skin prick test (>3 mm) response to at least 1 of 10 allergens in a standard panel. Ten subjects were atopic, and 10 were non-atopic. We investigated the sensitivity for IgE-mediated activation of peripheral blood derived mast cells. During the last 2 weeks of culture, mast cells were sensitised with IL-4 and 80 kU/l recombinant human IgE containing two IgE clones (7% + 7%) specific for recombinant mite allergen Der p2.
Results: We found no significant difference in the number of mast cells cultured from asthma patients compared to controls. After activation, the maximal CD63 Median Fluorescence Intensity was 20 456 ± 1640 [standard error (SE)] for asthma patients and 22 275 ± 1971 (SE) for controls [not significant (ns)] and the percentage CD63+ mast cells was 54.4% for asthma patients and 48.4% for controls (ns). The sensitivity, $EC50_{Der\ p2}$, (effective allergen concentration inducing 50% of the maximal response) based on the percentage CD63+ mast cells of all mast cell lines cultured from patients with asthma and controls was comparable (0.332 ng/ml ± 1.235 (SE) for asthma patients and 0.232 ng/ml ± 1.211 (SE) for controls (ns). There was no difference in mast cell sensitivity between atopic and non-atopic subjects.
Conclusion: Cultured mast cells from asthma patients and controls respond with similar sensitivity to allergen activation. Degranulation of cultured mast cells appears to depend more on culture conditions (IL-4, IgE) than on donor status (atopy or asthma).

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Leukotriene E4 regulates gene expression in human mast cells

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Background: Leukotriene E_4 (LTE_4), the most stable of the cysteinyl leukotrienes (cysLT), binds poorly to classical type 1 ($CysLT_1$) and 2 ($CysLT_2$) cysLT receptors although in asthmatic individuals it may potently induce bronchial constriction, airway hyperresponsiveness and inflammatory cell influx to the lung. In recombinant models, LTD_4 potently activates calcium mobilisation while LTE_4 induces very weak responses. In contrast, in a human mast cell line, LAD2, LTE_4 induced calcium with similar potency as LTD_4, with EC_{50} 9.3 nM and 4.9 nM for LTE_4 and LTD_4, respectively. Our aim was to analyse responsiveness of human mast cells to cysLTs.
Method and results: LTE_4 was the most potent activator of gene expression in LAD2 cells when measured using Affymetrix microarrays, regulating the expression of more than 70 genes, including immediate early genes, transcription factors, cytokines and membrane receptors. This has been confirmed for a selection of genes at the mRNA and protein level. Although the pattern of responses to cysLTs did not resemble classical $CysLT_1$ or $CysLT_2$ activity, both intracellular calcium signalling and gene expression were significantly inhibited by $CysLT_1$ inhibitor montelukast and not affected by $CysLT_2$ inhibitor HAMI3379.
Conclusion: Our data suggest that leukotriene E4 is a potent activator of human mast cells acting potentially through $CysLT_1$ or an unidentified receptor.

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Immunodeficiency, hypopituitarism and mastocytosis: a puzzling association

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Background: Authors emphasize the role of hormones for T and B cell to generate humoral or cell mediated immune responses. Compelling evidence confirm that B lineage deficiency, in the absence of thyroid hormone, is due to the decreased survival or lower rate of proliferation of committed B cell precursors.
Method: A 39-year-old white man presented to our Department for not pruritic, Darier's sign positive, red-brown macules gradually appeared and distributed over trunk, upper arms and neck. Medical history included a GH-deficiency treated with replacement therapy from 12 to 16 year old. No history of recurrent infections, familiar immunodeficiency or thyroid disease. Physical examination revealed a height of 168 cm and weight of 83 kg. The skin was dry, hair and eyebrows were thinning. Examination of other districts was normal.
Results: Hormones dosage showed hypothyroidism (FT4 0.83 μg/dl, TSH 6.660 μU/ml) while antithyroperoxidase and antithyreoglobulin antibodies were negative. Data confirmed low levels of GH (IGF-1 <25 ng/ml; GH <0.05 ng/ml) showing also testosterone deficiency. Antipituitary antibodies were negative. Moreover we revealed humoral immunodeficiency (IgA 0.441 g/l, IgM 0.317 g/l, IgG 8.940 g/l) with normal values of T and B cell subpopulations. Brain MRI evidenced Chiari type I malformation and reduced volume of the anterior pituitary gland. Posterior pituitary gland and hypothalamus were normal. Bone density scan (DEXA) evidenced a severe osteoporosis (T-score −3.1; Z-score −3.0). No evidence of focal lesions by X-ray of major bones. Echocardiogram exhibited normal volume of heart cavities. Histology of skin biopsy confirmed mast cell accumulation in a perivascular distribution within derma.
Conclusion: We first describe the association of hypopituitarism, immunodeficiency and mastocytosis, a rare disorder characterised

by mast cell proliferation and accumulation within various organs, most commonly the skin. This association supports *in vivo* the functional link between the endocrine and immune systems as shown in many reports where the development and function of the immune system are strightly related to hormonal levels. In this patient hormonal deficiency may have been the cause of immunodeficiency. We stress the importance of immunological screening in patients with hormonal deficiency, even if asymptomatic, since, in some cases, replacement hormonal therapy can correct immunodeficiency.

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Systemic mastocytosis in the emergency department

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Introduction: Systemic mastocytosis is a rather uncommon disease characterised by mast-cell proliferation and massive release of vasoactive mediators such as histamine. Its clinical features generally include erythema, urticaria, hypotension and epatosplenomegaly. Less common clinical manifestation are possible. We report two cases in which a cardiac arrest was the first appearance of the disease.

Case 1: A 72-year-old male previously in good health, suddenly complained of epigastric pain after dinner, rapidly followed by nausea, vomiting and loss of consciousness. When emergency medical team reached, he appeared unconscious, with respiratory activity but pulseless. EKG showed no electrical activity. A laryngeal tube was positioned and epinephrine 2 mg was administered, obtaining a reprise of cardiac activity. The EKG showed a mild ST elevation in inferior leads and signs of anterior subendocardic ischemia, recovered in the following EKGs. Echocardiography, coronary angiography and serum troponins were normal. A laboratory test for tryptase was then performed and showed markedly elevated values (75 μg/ml). Bone-marrow biopsy and fine-needle aspiration showed a pattern of severe mast-cell hyperplasia, with atypical inter- and paratrabecular mast-cell aggregates CD117 and CD25 positive and CD2 and CD34 negative. PCR-RFLP highlighted D816V mutation of the c-kit gene. We therefore made the diagnosis of severe systemic mastocytosis.

Case 2: A 57-year-old male, with no previous history of allergic or cardiac diseases, developed general malaise, flushing and loss of consciousness while was at work. He was given cardiopulmonary resuscitation by colleagues and came to the hospital in coma. EKG showed diffuse ST depression, echocardiography was normal. Tryptase values were significantly higher (200 μg/ml) and kept elevated after 10 days (18.6 μg/ml). Fine needle aspiration and bone marrow biopsy showed mast-cell hyperplasia with mast-cell paratrabecular aggregates CD117 and CD68 positive and rare CD2 positive cells. PCR-RFLP did not show D816V mutation of the c-kit gene.

Conclusions: A relatively uncommon clinical feature like a cardiac arrest may underline a rare disease like systemic mastocytosis, so that diagnosis should be considered in every case of cardiac arrest not otherwise explainable. Serum level of tryptase demonstrates a high specificity in confirming the diagnosis.

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KIT D816V mutation burden does not correlate to mediator related symptoms, anaphylaxis or osteoporosis in indolent systemic mastocytosis

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Background: Patients with indolent systemic mastocytosis (ISM) suffer from mediator related symptoms, anaphylaxis and osteoporosis. A new method for KIT D816V mutation detection allows determination of the level of mutation positive cells.

Objective: To investigate whether the severity of clinical manifestations in adult patients with ISM correlates to the level of KIT D816V positive cells in peripheral blood (PB) or bone marrow (BM) aspirate.

Methods: We included 48 adult ISM-patients (28 female/20 male) from our centre in whom the KIT D816V mutation level in both BM aspirate and PB was available. For each patient the severity of mediator related symptoms (skin, gastrointestinal, musculoskeletal and neuropsychiatric) was graded and episodes of anaphylaxis were evaluated by interview and medical record files. Bone mineral density (BMD) was determined by dual-energy x-ray absorptiometry (DXA).

Results: Median fraction (range) of KIT D816V positive cells was 0.6 (0.01–90)% in BM and 0.3 (0.003–49)% in PB. Skin symptoms was present in 41 (85.4%), gastrointestinal in 33 (68.8%), musculoskeletal in 17 (35.4%) and neuropsychiatric in 15 (31.2%) patients. Seventeen (35.4%) had experienced at least one anaphylactic episode. Fourteen (29.2%) had osteoporosis and additional 18 (37.5%) had osteopenia. No significant differences in KIT D816V mutation level were detected when comparing patients with none/mild symptoms and patients with moderate/severe symptoms, patients with and without anaphylaxis or patients with osteoporosis/osteopenia and normal BMD. Even though some of the included patients exhibited high mutation levels, none had progression into aggressive forms of SM in the observation period.

Conclusion: Fraction of KIT D816V mutation positive cells is a new parameter generally applicable in SM. In the present study we did not detect any significant correlation between the severity of clinical manifestations and the level of KIT D816V mutated cells. Whether this reflects the KIT D816V mutation being carried by cells of non-MC lineage or by non-mature MC-progenitors is presently not clear.

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Idiopathic anaphylaxis as a presenting symptom of clonal mast cell disorders

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Background: Idiopathic anaphylaxis (IA) is a diagnosis of exclusion and remains to be a challenge for allergists. Multiple theories on the pathogenesis of IA have been proposed, although none of them can explain the underlying mechanisms. Clonal mast cell disorders (CMD) and its substantial overlap in the clinical manifestations of idiopathic anaphylaxis have led to the search for an association between these rare disorders. Currently, two forms of CMD have been characterised: systemic mastocytosis (SM) and monoclonal mast cell activation syndrome (MMAS). In this study, we sought to determine the prevalence of CMD among IA patients, and to explore if pathogenesis of IA could be explained by unrecognised CMD.

Method: We identified patients (≥18 year) who were referred to the Allergy clinic between *January 2006 and Dec 2012* due to recurrent or unexplained anaphylaxis. All patients initially underwent a complete allergy work-up; thereby the diagnosis of

IA was confirmed after exclusion of possible elicitors. Baseline tryptase (sBT) levels were measured. Twenty-seven patients, 14 males and 13 females, who either had minimum of three anaphylactic reactions or elevated sBT levels (>11.4 ng/ml) regardless of the number of anaphylactic episodes were recruited and enrolled in this prospective study. None of the patients had signs of urticaria pigmentosa. All 27 patients further underwent a bone marrow biopsy and aspirate to investigate clonal markers of CMD and underlying mast cell hyperreactivity using current WHO-criteria. We evaluated characteristics of the bone marrow mast cells by pathology, flow cytometry and detection of *KIT* D816V mutation.

Results: Thirteen (48%) out of 27 investigated patients (10 males and 3 females) were diagnosed with CMD; 8 with indolent systemic mastocytosis (ISM) and 5 with MMAS. All ISM patients had a sBT levels >11.4 ng/ml (in six patients >20 ng/ml), whereas sBT was elevated only in two MMAS patients (15 and 23 ng/ml). Four of the eight patients with ISM had bone marrow mast cell aggregates. Among 14 non-clonal IA patients, only one had elevated (17 ng/ml) level of sBT. There was a clear male predominance in patients with CMD (77%).

Conclusion: In this study, mechanism of IA could be explained by a hyper-reactive mast cell phenotype in 48% of the IA patients. Thus, our study suggests that clonal mast cell disorders are a substantial differential diagnosis of IA, particularly in male patients with elevated sBT.

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The clinical features and long-term prognosis of Churg-Strauss syndrome

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Background: Churg-Strauss syndrome (CSS) is a rare disease characterised by asthma, eosinophilia, and systemic vasculitis.

Method: We retrospectively analyzed clinical manifestations and long-term outcomes of 53 patients who diagnosed as CSS at Samsung Medical Center from 1995 to 2011. Subjects included 27 men and 26 women with a mean age of 43 (18–80) years. The mean follow-up period was 48 (3–152) months.

Results: Most commonly involved organs were peripheral nervous system (70%), lung (51%), skin (42%), and heart (21%). ANCA was detected in only 5 of 36 (14%) patients. Thirty six patients were treated with corticosteroid plus cyclophosphamide pulses, and 17 patients were treated with corticosteroid alone. Ten patients were lost to follow-up and three patients expired. One patient died of heart failure due to uncontrolled vasculitis, and two died of pancreatic cancer and unknown etiology. Twenty four patients showed sustained remission, of which seven patients could discontinue the medication, and 17 patients were well controlled with low-dose (<5 mg/day) prednisolone.

Conclusion: CSS was highly variable in its presentation, and the prognosis was relatively good if the patients get proper treatment.

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Etiology of hypereosinophilia

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Background: The most frequent cause of eosinophilia worldwide is helminth infections, while that in industrialized nations is atopic diseases, which are often accompanied with mild eosinophilia (<1500/μL). On the other hand, eosinophilia (>1500/μL) is defined as hypereosinophilia, indicating existence of some special causes.

Method: We explored all patients with hypereosinophilia (>1500/μL) who visited our medical center in 2012 and reviewed to categorise their etiologies according to the severity of eosinophilia. Our medical center located in an urban area in Japan has about 1000 outpatients and 500 inpatients a day.

Results: There were 64 patients with hypereosinophilia. The overall most frequent cause was adverse drug effect (22). Presumable responsible drugs include antibiotics (6: ABPC, LVFX, etc.), proton-pump inhibitors (5: omeprazole, lansoplazole, etc.), and anti-epileptics (3: carbamazepine, valproate).

The etiologies of 13 patients exhibiting severe (>5000/μL) hypereosinophilia were drug (6), HES (2), eosinophilic gastroenteritis (2), Churg-Strauss syndrome (1), eosinophilic pneumonia (1), and myeloproliferative disease (1).

Eighteen cases had moderate hypereosinophilia (3000<, ≤5000/μL) due to drug (7), bronchial asthma (2), myeloproliferative disease (2), milk allergy (1), Kimura's disease (1), urticarial (1), PIE syndrome (1), urethral cancer (1), and unknown cause (2).

Thirty three patients were with milder hypereosinophilia (1500<, ≤3000/μL) associated with drug (9), malignancy (5), Gleich syndrome (2), egg allergy (2), bronchial asthma (1), atopic dermatitis (1), myeloproliferative disease (1) and unidentified cause (12). Some adverse drug effects and Gleich syndrome were not diagnosed by the doctors in charge, but by revising process.

Interestingly, 14 cases with unknown etiology include four cases with artificial vessels or stents and three cases with renal failure. And four of the six patients with cancer were urinary tract origin. No parasitic infection was noted.

Conclusion: Adverse drug effect is the most frequent origin of hypereosinophilia regardless of its severity. Antibiotics, proton pump inhibitors, and anti-epileptics account for two-thirds of drug-induced hypereosinophilia. As it is difficult to make simultaneous adequate evaluation of hypereosinophilia in some cases, especially in milder cases, revision, considering entire clinical course, is a useful way to seek the etiologies.

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Montelukast reduces peripheral blood eosinophilia in atopic children

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Background and objectives: The antiinflammatory properties of montelukast were reported in reducing tissue eosinophilia in asthma, nasal polyps, duodenal eosinophilia, eosinophilic esophagitis and gastroenteritis. This is the first report to observe the effect of montelukast on reducing peripheral eosinophilia, particularly in children.

Case 1: A 10½ year boy, relocated to Doha, had been diagnosed to have asymptomatic, unexplained, persistent blood eosinophilia, for 2 years, discovered on CBC study for acute tonsillitis. The mean (±SD) absolute eosinophil count (AEC) was 34 843 ± 375 cells/μl and eosinophilia of 68.61%. He had mild asthma only during first 5 years of life. Otherwise, he was asymptomatic and physical examination was normal. Rest of CBC studies, peripheral blood smears, ESR,CRP, liver

function tests, serum LDH, urinalysis, repeated stool study, serum immunoglobulins, lymphocyte subsets, specific IgE for inhalant allergens, chest X-ray, and abdominal ultrasound all were normal. On 5 mg daily oral montelukast for 12 weeks, AEC gradually decreased and remained low (1160 ± 152 cells/μl) without the medication for 6 months.

Case 2: A 5 year boy was discovered, on screening workup for squint surgery, to have eosinophilia. He was completely asymptomatic. He has horseshoe kidney and had mild virus-induced wheezing of infancy. Physical examination was totally normal. Repeated CBC peripheral eosinophilia (44.3 ± 33.2%) and elevated AEC (23 128 ± 18 486 cells/μl). Rest of workup including hemoglobin, platelets counts, ESR, serum chemistry, liver function tests, urinalysis, repeated stool studies, serum immunoglobulins, an *in vitro* test for panel of inhalant allergens, chest X-ray, and abdominal ultrasound all were normal.

His peripheral eosinophil count gradually reduced, over 12 weeks of 5 mg daily oral montelukast therapy, and remained low (1000 ± 565 cells/μl, 7.9%).

Conclusion: Oral montelukast might be a potential therapeutic agent for primary peripheral eosinophilia. However, larger studies are required to verify this effect.

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A case of idiopathic hypereosinophilic syndrome accompanied by suspicious allergic bronchopulmonary aspergillosis

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Idiopathic hypereosinophilic syndrome (HES) represents a heterogeneous group of disorders with the common features of prolonged eosinophilia (>1500/mm^3) of an undetectable cause and organ system dysfunction by eosinophilic infiltration, predominantly at skin, heart, lung, gastrointestinal tract, and nervous system. It involves gallbladder very often. Allergic bronchopulmonary aspergillosis (ABPA) is an immunologic pulmonary disorder caused by hypersensitivity to Aspergillus fumigates in patients with chronic asthma. Here we report a case of idiopathic hypereosinophilic syndrome presenting with acute cholecystitis in patients with suspicious allergic bronchopulmonary syndrome.

Case: A 64 year-old female came to our hospital with acute right upper quadrant abdominal pain. She also complained of dyspnea and tingling sensation of both hands and feet. She had had chronic asthma with frequent exacerbation for 10 years. An abdominal computed tomography (CT) scan revealed diffuse gallbladder wall thickening and distension which was compatible with acute cholecystitis. There was no evidence of gallbladder stones. Pulmonary function test showed 32% of FEV_1 and 45% of FEV_1/FVC ratio. A chest CT scan revealed bronchiectasis with mucus plug and diffuse bronchial wall thickening. Nerve conduction study showed mononeuritis multiflex which involves right hand and both feet. Initial peripheral blood eosinophils were increased (10 400/mm^3). Total serum IgE was >2000 IU/ml and ECP was 146 ng/ml. Stool examination for parasites and serum IgG antibodies to parasites were all negative. Anti-neutrophil cytoplasmic and cardiolipin antibodies were negative. A bone marrow biopsy showed normal cellularity with increased eosinophils. Fip1-like1 and platelet-derived growth factor receptor alpha gene (FIP1L1-PDGFRA) fusion was not detected. An echocardiogram was normal. IgE antibodies to Aspergillus fumigatus was detected (by CAP system, Uppsala, Sweden). Taken all together, she was diagnosed with IHES manifested as acute cholecystitis and mononeuritis multiplex. She was treated with glucocorticosteroids (1 mg/kg). Her symptoms were improved and PFT was normalised, however, peripheral eosinophil counts were not normalised with the treatment of glucocorticosteroids for 4 weeks. Then, hydroxyurea (20 mg/kg) were added and peripheral eosinophil count was normalised.

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Butterbur extract exerts antiinflammatory effects on primary human nasal epithelial cells *in vitro*

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Background: Nasal epithelial cells represent the first line of defence against respiratory pathogens and allergens. They are thus an integral part of the innate immune system.

Aim of the study: To establish 2D and 3D cultures of human primary nasal epithelial cells and to evaluate the antiinflammatory effect of butterbur extract (Tesalin®), of which mechanisms of action are currently unknown.

Method: Biopsies were obtained from patients undergoing turbinoplastic surgery. Scratch biopsies were obtained from the inferior turbinates of healthy, non-atopic volunteers. Scratch biopsies and Trypsin-digested turbinates were cultured in 24-well plates until 80% confluent and then stimulated with the viral stimulus Poly IC alone or in combination with Tesalin®. Readouts were production of IL-8 and neutrophil chemotaxis. For the 3D model, a collagen/fibroblast layer was created. On day 7, primary human nasal epithelial cells were seeded on top. The model was cultured in fibroblast media and moved to the air-liquid-interface at day 13. Paraffin sections were stained with epithelial specific antibodies and analysed by immunofluorescence microscopy.

Results: 2D cell culture could be established from both turbinates and scratch biopsies. In the 3D model, the epithelial layer showed specific expression of Cytokeratins and Caveolin. Stimuation of nasal epithelial cells with Poly IC lead to increased production of IL-8, which was inhibited by Tesalin®. This effect was paralleled by decreased neutrophil chemotaxis towards supernatants of Poly IC/Tesalin®-treated cells.

Conclusion: We established isolation and culture of primary human nasal epithelial cells from both turbinates and scratch biopsies. Functionality of the cells was shown by inflammatory mediator release upon stimulation with a viral mimic and by chemotaxis of neutrophils. Notably, Tesalin® inhibited both, Poly IC induced IL-8 release and neutrophil chemotaxis.

Poster Session 58

Immune regulation in the upper and lower airways

1382
A report of four cases with IL-12 receptor B1 defeciency

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Background: Mendelian susceptibility to mycobacterial diseases (MSMD) is a rare syndrome characterised by predisposition to infections caused by weakly virulent mycobacteria. Salmonellosis has been reported in almost half of affected patients. Mucocutaneous candidiasis is more common. Interleukin-12 receptor ß1 (IL-12Rß1) deficiency is the most frequent genetic cause of MSMD.
Method: We report four cases with IL-12 receptor B1 defeciency with different clinical symptoms.
Results: Two patients twins. Four month old male patients. Three months after the BCG vaccine came with the complaint of lymphadenopathy. Have persistent yeast infections in the mouth. Axillary lymph node biopsy histology have histiocyte-rich active chronic inflammation and fibrosis. Patients 3 years old and healthy.

10-year-old male patient. Nine years old, bloody diarrhea, weakness, weight loss, and abdominal pain began. Who received treatment with the diagnosis of Salmonella. On physical examination, neck lymphadenopathy, cachectic appearance, and there was a decrease in subcutaneous adipose tissue. LAP biopsy in cervical region, non-necrotizing granulomatous inflammation were reported as a result of pathology. The colon biopsy showed mycobacterium avium intraselülare. In addition, was diagnosed with Crohn′s disease. Eleven-year-old patient with the diagnosis of Crohn′s disease and severe protein energy malnutrition has been lost.

Eleven-year-old male patient. Admitted with acute appendicitis. Persistent fungal infection in the mouth of the patient′s medical history since the age of 5. Appendectomy apandix and lymph node pathology report and granulomatous appendicitis diagnosed with EZN staining bacilli seen. M. Tbc PCR positive. Salmonella O antigen 1/400 positive. Our patient was 12 years old, made a break for 1 month treatment with IFN gamma. Following this, presented with abscess formation extending to the neck under the chin. Drainage of abscess material were sent to the ARB (+). Started antibiotics relieved the patient clinically. Follow-up continues.
Conclusion: As well as various symptoms of patients, severity of disease was also different. Four case too, there was generalised lymphadenopathy. Three patients had persistent fungal infection. A serious problem in our two cases occurred after BCG vaccination, one patient with mild formed at the problem occurred and no problems other of our cases. There were two cases of salmonella infection. A case of autoimmune disease (Crohn′s) was present.

1383
Septic arthritis in a young adult with hyper IgE syndrome: a case report

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Introduction: Hyper-IgE syndrome is a primary immunodeficiency (PID) syndrome which is characterised by elevation of serum IgE, eosinophilia, sinopulmonary infections, chronic eczema and cold skin abscesses. In this report, a case of septic arthritis in a young adult with hyper-IgE syndrome is presented.
Case report: A 20-year-old male patient, he was applied with fever, night sweats, shortness of breath, left axillary, right shoulder and neck pain, swelling and limitation of motion in arms. On physical examination: two different palpabl lesions, one of at the scapular region and the other one at the edge of the left latissimus dorsi muscle were detected. They were fluctuating, hyperemic, painful and at a diameter of 10 × 10 cm in size. Laboratory tests: WBC: 16.200/mm3, erythrocyte sedimentation rate: 92 mm/h. Fluid collections consistent with abscesses were shown at right shoulder and the left axillary region by both ultrasonography and computed tomography. The abscesses were drained and antibiotic therapy was started. S. Aureus was isolated at aspirate cultures. Right shoulder magnetic resonance imaging was consistent with septic arthritis. Immunological analysis of patient revealed low phagocytosis function (73.4% in granulocytes and 61.4% in monocytes), decreased CD4 + T-cell ratio (27.6%), low CD4 + T/CD8 + T ratio (0.68), increased serum IgG (28.6 g/l) and increased total IgE (929.53 IU/ml). This case had 24 points according to Grimbacher et al's hyper IgE syndrome scoring system.
Conclusion: Although, hyper IgE syndrome is one of the PID syndromes which is frequently diagnosed in childhood, it must be considered especially in cases with extensive staphylococcal abscesses in adulthood.

1385
New aspects of the pathogenesis of respiratory diseases in frequently ill children

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Background: Bronchopulmonary pathology remains one of the most urgent problems of pediatrics. Despite multiple research papers on this problem, diseases of the respiratory system, continue to worsen, recur and swich to a chronic form.
Method: The aim of our study was to identify the pathogenic mechanisms respiratory diseases in frequently ill children (FIC). To this end, were examined 340 FIC with respiratory diseases at the age of 6 months to 6 years. In 55 FIC acute viral infections without complications, in 74 FIC was observed acute bronchitis, in 175 FIC-recurrent bronchitis and in 36 FIC was acute pneumonia. In patients were examined in the acute period of the disease and in the period clinical remission of number of CD3-cells, CD4-cells, CD8-cells, CD19-cells, the content of serum immunoglobulins A, M, G,E, the content of cytokines IL-1betta, TNF-alfa, IL-2, IL-6, IL-8, IFN-gamma, the level of substance P, state of hemostasis, microbiocenosis upper respiratory tract and intestinal.

Results: Our results show that in the acute period of the respiratory disease, reduced the level of cellular immunity (mainly, CD3-cells, CD4-cells and the index immunoregulator cells), marked imbalance of humoral immunity reduction of IgA and IgG, increase of IgM and IgE. By the marked in cytokine status increase proinflammatory cytokines IL-1betta, TNF-alfa, IL-6, IL-8, and reducing IL-2 and IFN-qamma. In acute period of the disease is marked as raising the neuropeptide -substance P and blood clotting. The high correlation between the immune system including cytokine status, substance P and hemostatic system. We found that the clinical remission of respiratory diseases in FIC is not accompanied by a normalisation parameters of the immune system, cytokine status, substance P and hemostatic system. High level of proinflammatory cytokines in the period of clinical remission, reflect ongoing inflammation, which is associated with persistence of the infection agent. Of these infectious in our patients revealed chlamydia, mycoplasma, cytomeqalovirus, Staphylococcus aureus, Candida albicans. Our FIC in 67. 6% of cases observed dysbiosis, the severity of which correlated decrease the immune system.

Conclusion: Given all this, it is necessary to carry out adequate therapy of respiratory diseases in FIC.

1387
Lack of immunological response to protein vaccines in a pediatric patient

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Case presentation: We present the case of a 7-year-old girl who was evaluated for suspected Brown syndrome. Her blood tests showed a lack of antibody response to tetanus, pertussis, poliovirus, and measles vaccines, and a borderline response to the diphtheria vaccine. These findings were confirmed after a second course of vaccination. She had no history of recurrent or severe infections. A complete immunological work-up showed non-protective antibody levels for tetanus and rubella, borderline antibody levels for measles and diphtheria, and protective antibody levels for parotitis; on the other hand, she showed IgG antibodies for EBV, CMV, VZV and HSV-1. She also presented low levels of IgM and IgG3, absent T cell proliferation to tetanus toxoid (with normal proliferation to Candida and mitogens), normal distribution of T cell subsets, borderline values of B cells able to switch and switched B cells, and normal *in vitro* Ig production. Interestingly, the mother of the patient, aged 40, presented with similar immunological findings and no history of recurrent or severe infections. We administered a new course of vaccination (tetanus, pertussis, diphtheria and poliovirus) to the girl and then monthly we evaluated both antibody titres and T cell proliferation. One month after vaccination, the patient showed normal antibody responses, and normal T cell proliferation responses; however, these responses gradually decreased and eventually disappeared at 5 months. In conclusion, the child and mother present a low antibody response to protein vaccines, in particular to tetanus toxoid. After an adequate initial antibody and T cell response, no immunological memory was mounted. The mechanisms of such an abnormal immunological response have not been completely clarified yet. Similar conditions have not been reported in humans, while, in murine models, they seem related to deficits in signaling lymphocyte activation molecule-associated proteins. It is interesting that the patient presented with VCA-IgG and EBNA-IgG antibodies, indicative of a previous infection, which actually occurred without any complication. Given the presence of similar findings in the mother, suggestive of a mendelian inheritance, exome sequencing is currently in progress. However, the clinical impact of this condition is still undefined: thus, we may only recommend that the patient undergo tetanus prophylaxis together with a booster vaccine dose, as indicated.

1389
Hyperimmunoglobulin E syndrome with bronchiectasis and splenic tuberculosis

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Background: A syndrome of recurrent staphylococcal infections, severe eczema and sinopulmonary infections was described in 1966 and initially called Job syndrome. This was after termed hyperimmunoglobulin E syndrome (HIES), when an associated increase in serum level of immunoglobulin E (IgE) was described.

Case report: E.L.S., male, 30 year. By the first year of life, he developed eczema, with mild pruritus, being diagnosed and treated as atopic dermatitis. Since then, the patient reports nine episodes of pneumonia, resulting in dilatation of the large airways (bronchiectasis), recurrent skin infections with development of pustules and recurrent herpes zoster. Since 19 years is undergoing treatment with Tenofovir 300 mg for chronic hepatitis B. In 2012 the patient was admitted to Internal Medicine Service of Antonio Pedro University Hospital / Fluminense Federal University to investigate splenic nodules observed in abdominal CT. The phisical examination demonstrated atipical facies, xerodermia with desquamation but without pruritus, absence of lymphadenopathy and no abdominal or thoracic abnormalities. A complete blood count revealed 12 500 cells mm^3 white blood cells, of which 25% were eosinophils. C3 was 137, serum IgG 2169 mg/dl, IgM 216 and IgE was very high at 34 508. Undergoes splenectomy and the histopatological features was granulomatous chronic inflammatory process with extensive areas of caseous necrosis. Liver with micronodular cirrhosis. The patient is still in use of Ethambutol and Ofloxacin, an alternative tuberculosis treatment, with less hepatotoxicity.

Conclusion: HIES is a clinical diagnosis, based on a group of clinical and laboratory findings. This case is compatible with the autossomal recessive form. The main teaching is the attention to the possibility of diagnosis, avoiding sequelae like bronquiectasis. In this patient, the delay until diagnosis was 30 years. There are no descriptions in the literature (PubMed) of splenic tuberculosis in HIES patients, drawing attention to this possibility.

1390
Granulomatous lymphocytic interstitial lung disease in common variable immunodeficiency: a case report

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Background: Common variable immunodeficiency (CVID) encompasses a heterogeneous group of antibody deficiency diseases defined by hypogammaglobulinemia, poor responses to vaccination, and recurrent infections. About a third of these patients show signs of autoimmunity or develop immune-mediated diseases. Among the non-infective complications in CVID the lung may be involved in the course of Sarcoidosis-like syndromes or Granulomatous-lymphocytic interstitial disease (GLILD).

Method: We recently observed a woman with history of recurrent infections of upper and lower airways, which progressed over the years from selective IgA deficiency to full-blown CVID with autoimmune haemolytic anemia, nodular lymphoid hyperplasia of gut and reactive lymph node hyperplasia. However, since 2005 she pre-

sented worsening of respiratory symptoms and lung infiltrates on chest X rays, which were diagnosed as Sarcoidosis and treated with courses of steroids, resulting in transient clinical improvement followed by multiple relapses. In 2012 we evaluated the patient, which underwent to bronchoscopy and lung biopsy, finally demonstrating the presence of Lymphocytic Interstitial Pneumonia and granulomatous lesions.

Results: She has been treated with steroids and started intravenous immunoglobulin (Ig) substitution, then switched to Subcutaneous Ig replacement. After 6 months a clear improvement of symptoms and of infectious episodes was observed, nevertheless chest CT showed the presence of focal areas of ground-glass attenuation, particularly evident in the right middle lobe. Focal areas of consolidation with air bronchogram were evident in the right upper and middle lobe as well as in the left upper lobe. Moreover, some nodules of various sizes, most with irregular margins and some with associated thickening of the adjacent interlobular septa, were also found. By comparing the CT pattern in the scans obtained in 2004, 2011 and 2012 we found that the areas of ground glass attenuation were not modified whereas the number and dimensions of the nodules increased.

Conclusion: Therapy was adjusted adding high-dose intravenous steroids and immunosuppresants. GLILD or Sarcoidosis-like syndromes or granulomatoid disorders could be one of the clinical presentations of CVID patients. Treatment with steroids and IgG replacement are the mainstay of treatment, being effective in most patients. However a close clinical and radiologic surveillance is required for this patients.

1392
Efficacy and safety of intravenous immunoglobulin in patients with common variable immunodeficiency

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Background: Common Variable Immunodeficiency (CVID) is one of the most common symptomatic primary immunodeficiency disorders. Intravenous immunoglobulin replacement therapy (IVIG) has improved the clinical course of CVID by reducing the burden of recurrent infections and complications. The aim of our study was to document the safety and effectiveness of IVIG by reducing the incidence of infections.

Methods: A study evaluating patients with CVID undergoing IVIG in our department, since 2011, was performed. The following items were assessed: current age and at diagnosis, gender, occupation, family history, months on IVIG, number of infections before and after treatment, adverse reactions and complications of the disease.

Results: The study included 10 patients (7♂; mean age 45.40 ± 13.97 years [33–75]). Only one third were employed. Age at diagnosis: 36.50 ± 17.75 [13–71]. None of the patients had family history of primary immunodeficiency. Seven patients were on daily medication for concurrent diseases (diabetes mellitus, hypertension, pulmonary chronic disease, epilepsy). All patients were treated with IVIG at concentrations of 400–500 mg/kg every 4 or 5 weeks administered in an outpatient setting. Median treatment time was 52.50 [5–204] months. 50% of the patients complied regularly.

50% of the patients did not have any adverse reactions. Three reported mild reactions with shivering that required decreased infusion rate. One reported an episode of fever; one had a moderate reaction with wheezing. No severe reactions were reported.

Eight patients had pneumonia with hospitalisation at least twice before diagnosis. Of these, two had more than three episodes. Along with respiratory infections, three reported cutaneous infections and two had gastrointestinal infections.

Since treatment was initiated, four patients had a single respiratory infection requiring antibiotherapy (two requiring hospitalisation). One patient had two hospital admissions: inaugural episode of ascites associated with hepatosplenomegaly and lymphadenopathy; intraperitoneal abscess.

The most frequent complication of the disease was pulmonary chronic disease affecting four patients and four still have no complications.

Conclusion: Our study confirmed that IVIG in patients with CVID has a low rate of adverse reactions and that is a safe procedure. Immunoglobulin therapy reduced bacterial infections and hospitalisations, as described in the literature.

1393
Advertising works for primary immunodeficiency. The clinical center at the Aguascalientes University in Mexico

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Background: As published in the proceedings of the Latin American Society of Immunodeficiencies, there is a variety of factors negatively impact the level of diagnosis and management for Latin American patients with Primary Immunodeficiency Diseases (PID).

Therefore three programmes were initiated to improve the diagnosis and management of PID in Latin America: an educational outreach programme (The L-Project), an immunology fellowship programme, and the establishment of a laboratory network to expand access to testing facilities.

Aguascalientes is a 1.3 million inhabitants state, located 500 km. north of Mexico City lacking of PID clinics or referal services.

Method: As part of the mentioned programs a PID clinic was initiated in the City of Aguascalientes in October 2011 receiving patients from regional hospitals, clinics, generalists and general public referrals as a product of the educational program and public alert in the region. After several media appearances, academic lectures and regional hospital visits to promote PID diagnosis and warning signs, we received referral patients in a University based clinic with history of recurrent infections or the presence of at least one warning sign for PID. Here we describe the results of the program and the clinical manifestations and characteristics of the PIDD patients diagnosed between November 2011 and November 2012 at the clinic.

Results: Twenty-four lectures were given to generalists, specialists and hospital staff with a total of 993 attendants, 12 media appearances were achieved. During the period we have received 151 consultations (First time visit 94, subsequent 57). The patients attending to the center were 94 male (57.6%), 57 female (37.7%) median age of 120 months (1–708, IQR 198). The diagnosis were; PID 15 patients (9.9%) Allergies 72 (47.6%) Other 23 (15.2%) Under investigation 41 (27%). The PID diagnosis were; Antibody deficiencies 4/15 (33%) well defined syndromes 7/15 (47%) innate immunity deficiencies 1/15 (7%) Severe combined immunodeficiency 2/15 (13%). PID patients were eight males (53.3%) and seven females (46.6%) median age 60 months (2–192, IQR 102) with a mean diagnostic delay of 44 months, mean number of infections at diagnosis 6 (1–24). All patients are receiving appropriate treatment.

Conclusion: The frequency of PID among our series is similar to other described in ambulatory practice around 10%. As the program goes on these results are encouraging with at least one PID patient per month.

Poster Session 59

Immunodeficiencies

1396
Single nucleotide polymorphisms of proinflammatory cytokines in allergic rhinitis

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Background: Allergic rhinitis (AR) is a complex polygenic disorder of the upper respiratory airway with an increasing prevalence worldwide. As proinflammatory cytokines, including tumor necrosis factor (TNF), interleukin-1 (IL1) family and interleukin-6 (IL-6) seem to be involved in development of allergic rhinitis, this study was performed to evaluate the associations of single nucleotide polymorphisms (SNPs) of TNF-α, IL-1 family and IL-6 genes with AR.
Method: Ninety eight patients with AR diagnosed according to modified allergic rhinitis criteria in the 'Allergic Rhinitis and its Impact on Asthma' (m-ARIA) document were enrolled in the study and 140 healthy volunteers with no history of AR and with the same ethnicity of the patient were recruited as the control group. Genotyping was done for two TNF-α promoter variants, one variant in promoter region of IL1α, two SNPs in IL1β gene, one in IL1 receptor and IL1RA, and two promoter variants of IL-6 gene, using PCR sequence-specific-primers method.
Results: Patients homozygous for the T allele of *rs16944* in IL1β had an 8.1-fold risk of having AR than those with the C allele. In TNF-α, there were also significant relationships between two SNPs of rs1800629 and rs361525 and having AR. Patients homozygous for the G allele of *rs1800795* in IL-6 had a 3.35 fold risk of having AR than those with the C allele. AA genotype in *rs1800797* of IL6 was associated with increased risk of developing AR. Frequencies of A/G haplotype for TNF-α (rs1800629, *rs361525)* and G/G haplotype for IL6 (rs1800795, *rs1800797*) were significantly higher in the patient group. In some subgroups of patients, there were significant relationships between IgE levels, eosinophil count, eosinophil percentage, nature of sensitivity, persistency and severity of AR and these SNPs.
Conclusion: We found that genetic variants in TNF-α, IL1 gene complex and IL-6 not only were associated with the risk of developing allergic rhinitis, but also affected the course of disease and its severity.

1397
Normal alleles of rs2237060 of RAD50 in Iranian patients with common variable immunodeficiency and IgA deficiency

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Background: Common Variable Immunodeficiency (CVID), the most prevalent symptomatic primary immunodeficiency disease and Selective IgA Deficiency (IGAD), the most common primary antibody deficiency, both comprise heterogeneous groups of disorders which represents two opposite poles of humoral immunodeficiency. Recently, association between rs2237060 in RAD50 and these two disorders have been reported by a Swedish study. Based on this finding, they suggested that a subset of patients with IGAD and CVID are predisposed to hypogammaglubinemia due to variations in RAD50. This study aimed to evaluate such an association in Iranian patients with CVID and IGAD.
Method: Thirty nine patients with CVID, 19 patients with IGAD, and 34 healthy volunteers with the same ethnicity of the patient were enrolled in this study. Genotyping was done in all groups for one intronic SNP in RAD50 (Rs2237060), using Real-Time PCR allelic discrimination TaqMan genotyping assays.
Results: Although the allele frequency for rs2237060 in RAD50 was different between the patients with hypogammaglubinemia and healthy individuals, this difference was not significant. There was not any significant difference in allele frequency of this SNP between healthy controls and both groups of CVID and SIgAD patients when analyzed separately.
Conclusion: In this study, we did not find any association between alleles of this SNP with IGAD or CVID. Despite our negative result, it is important to identify possible association between CVID and IGAD and variations of genes involved in class switch recombination, mismatch repair system and somatic hypermutation.

1400
A case of Wiskott-Aldrich syndrome with a novel WASP gene mutation

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Background: Wiskott-Aldrich syndrome (WAS) is a rare X-linked recessive immunodeficiency disorder characterised by thrombocytopenia and small platelets, eczema, recurrent infections, and an increased risk of autoimmunity and malignancy. Clinical features of the disease are highly varied; therefore, the diagnosis is sometimes difficult. The WASP gene encodes a multidomain protein (WASP) that is expressed predominantly in hematopoietic lineages. The main function of WASP is to couple signals generated at the cell membrane level with the reorganization of the cellular cytoskeleton, ultimately resulting in cell activation and the promotion of cell motility. Approximately 400 unique mutations have been reported in the WASP gene. In this study, we report a boy with classical, and identified a novel WASP gene mutation: a splicing mutation IVS3-2A>G.

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Case: A 4-mount-old boy was admitted because of recurrent infection, bloody diarrhea, and thrombocytopenia. The family history revealed that his maternal cousin had WAS. Physical examination revealed petechiae and eczema. On laboratory examination, the Hb level was 9 gm/dl, and the white blood cell count was 8.6 × 109 l, with absolute lymphocyte count 2.6 × 109 l The platelet count was 74.0 × 109 l. MPV was 7.1 fl. Immunologic studies revealed IgG/A/M 382/ 22/ 55 mg/dl and IgE 6.28. Lymphocyte subset analyses showed CD3 52%, CD19 14%, CD4 39%, CD8: 15%, CD16/56: 23%. Through direct sequencing of genomic DNA of the WASP gene in the patient, we identified a novel mutation of WASP gene (IVS3-2A>G.

Conclusion: To our knowledge, this is the first report describing WAS patients with novel mutation in the WASP.

1401
Hyper IgE syndrome in the differential diagnosis of atopic eczema

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Background: The mechanisms that promote the enhanced susceptibility to cutaneous infections in atopic dermatitis are complex interactions among several factors. They include skin barrier dysfunction, reduced skin lipid content, and abnormalities of the innate immune response. Some of the innate immune defects observed in atopic dermatitis are primary defects, such as epithelial barrier defects and defects in signaling or expression of innate receptors. Here we report seven cases of Hyper IgE syndrome mainly presenting with atopic eczema.

Case report: Seven patients, five born to consanguineous parents, were evaluated and mean age at diagnosis was 5 years. Eczematous dermatitis, mainly on face, scalp and repeated bacterial skin and lung infections were present in all patients. Cutaneous viral infections and chronic candidiasis of the nails were seen in two patients. Facial paralysis was observed in one of the patients. All but one had high serum IgE levels. Hypereosinophilia, and CD4 lymphopenia were observed in all patients. DOCK8 mutations were identified in four patients and under evaluation in three patients. Therapeutic measures included antibacterial and antifungal prophylaxis, immunoglobulin replacement therapy in all patients with interferon alpha therapy in one case who presented with widespread papillomas. All patients were evaluated for hematopoietic stem cell transplantation.

Conclusion: The hyper-IgE syndrome is a rare primary immunodeficiency disorder characterised by high serum levels of IgE, recurrent skin and lung infections and atopic eczema. It is very important for pediatricians to contemplate atopic eczema as a differential diagnosis for hyper-IgE syndrome mainly in patients born to consanguineous parents and suffering from recurrent respiratory infections.

1402
IFN-γ deficiency in adult bronchiectasis: a case report

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Background: Bronchiectasis is an irreversible and abnormal dilatation of one or more bronchi, as a result of destruction of the muscles and elastic connective tissues. Progressive lung damage is due to the disruption of the mucociliary clearance resulting in retention of secretions, which in turn attracts bacterial colonization with chronic inflammation. Currently, the etiology of bronchiectasis remains unknown in a high percentage of patients (26–53%).

Method: A 33-year-old non-atopic, nonsmoker male, was referred to our Department for recurrent pulmonary infections (3–4/year) and progressive lung function deterioration despite aggressive multidrug antimicrobial treatment. He referred dyspnea and impaired physical performance. A perimembranous interventricular septal defect with no significant hemodynamic effects was reported. Physical examination revealed bilateral basal crepitating and crackles.

Results: HRCT revealed cystic spaces in the right hemi-thorax, suggestive of bronchiectasis with collapse of the right lung. Lung function tests revealed a mixed obstructive and restrictive pattern. Arterial blood gases showed respiratory alkalosis. Immunoglobulins dosage and sweat chloride were normal. Negative sputum culture and PPD skin test. Abdominal fat biopsy for amyloid deposits was negative. *In vitro* production of IFN-γ was reduced.

Conclusion: Bronchiectasis may be the result of several processes. Two types of bronchiectasis are known: cystic fibrosis (CF) and non-CF associated. COPD, postinfectious, congenital defects (primary ciliary dyskinesia, Kartagener syndrome), amyloidosis and immunodeficiency may be the cause of non-CF bronchiectasis. In our case, aberrant IFN-γ secretion can be considered the trigger of bronchiectasis. IFN-γ has a critical role in innate and adaptive immunity against viral and intracellular bacterial infections through containment and eradication of intracellular organisms, via macrophage activation. The case we describe provides additional evidence that a diagnosis of IFN-γ deficiency should be taken into account in all patients with idiopathic bronchiectasis.

1403
Rapid push subcutaneous immunoglobulin administration. A safe alternative in case of severe systemic reaction with intravenous therapy

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Background: Common variable immune deficiency (CVID) is considered to be a collection of primary immune deficiency diseases (PIDD) characterised by reduced serum levels of IgG, IgA, and/or IgM, with reduced or absent specific Ab production.

Intravenous immunoglobulin (IVIG) has been the preferred route of therapy but subcutaneous infusion (SCIG) offers fewer systemic adverse events, maintains stable serum IgG levels and can be self-administered at home. Recently *rapid push* SCIG administration without need of infusion pump has been described as valid alternative. We present a patient with CIVD who suffered severe systemic reactions with IVIG and tolerated *rapid push* SCIG administration.

Method: A 41 year old patient, diagnosed in 2012 of CVID because of enteropathy and malabsorption without history of respiratory infections, started in May 2012 IVIG reposition. He presented 10 min after initiating slow perfusion of third infusion general feeling of discomfort, diaphoresis and hypotension. Three weeks later, despite premedication with corticosteroids and antihistamines he suffered similar episode shortly after starting infusion. Patient was referred to our clinic in order to evaluate SCIG. The patient was offered the possibility of subcutaneous infusion with conventional pump or rapid push self-administration which is performed using a syringe and butterfly needle delivered over a short period (10 min aprox.). He tolerated without any incidence 10 ml of IgG (160 mg/ml) per injection site (total 20 ml per day/40 ml per week).

Results: Patient actually tolerates 60 ml per week administered subcutaneously, home based, using several infusion sites per session (2–3 days/week) in abdominal region. IgG levels have increased from

129 mg/dl to 405 mg/dl (40 ml/week). Patient uses two injection sites per session, 10 ml per injection site. Patient did not refer any local or systemic symptoms (e.g., headache, nausea, fever).

Conclusion: SCIG using a *rapid push* technique with no need of pumps has demonstrated to be a safe and well tolerated alternative to IVIG in our patient. *Rapid push* is a simple, flexible, with shorter infusion times and no need of specialised equipment for home based SCIG.

1404
Immune deficiency should not be overlooked in children with neurological deficits

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Introduction: Recurrent infections are common in children with underlying neurologic conditions such as cerebral palsy, mental motor retardation and epilepsy. However, accompanying immune deficiency may be the etiological factor particularly in children with a history of severe and/or complicated infections. Herein, we describe a girl with epilepsy, mental-motor retardation and frequent infections that were further diagnosed with common variable immune deficiency (CVID).

Case report: A 10-year-old girl admitted to outpatient department of our unit after suffering throughout her childhood from recurrent infections. She was frequently diagnosed with otitis, sinusitis, and tonsillitis and was hospitalised several times for pneumonia. Long duration of antibiotic therapy was frequent and she was usually requiring intravenous antibiotics. Although she had been immunised with Varicella vaccine, she had a severe Varicella infection when she was 8 years old. Along with the frequent infections, she had a history of afebrile convulsions. She was still on levetiracetam and risperidon treatment with diagnosis of epilepsy and mental-motor retardation. Frequent infections have been attributed to her mental-motor retardation and have not been previously investigated in terms of immune deficiency. On presentation, she had mild respiratory symptoms. The physical examination revealed crepitant rales on right hemithorax. The chest radiographs showed an ill-defined opacity in the right middle and lower lobes suggesting pneumonia. Chest HRCT showed bronchiectasis of the right lower lobe. The results of the laboratory tests revealed: a leukocyte count, $14.2 \times 10^3/\mu L$; hemoglobin, 13.4 mg/dl; platelets, $284 \times 10^3/\mu l$; c-reactive protein, 5.54 mg/l. Immunological studies showed: IgG, 398 mg/dl (610–1570); IgA, 99 mg/dl (45–236); IgM, 46 mg/dl (52–242). The CD3-, CD4- and CD8-positive T cell counts and percentages showed no specific findings. However, the percentage of CD19-positive B cells in peripheral blood was only 5.5% (normal range 10–31%). She was diagnosed with CVID and was placed on intravenous immunoglobulin treatment 0.5 g/kg every 3 weeks. This caused a remarkable improvement in her condition with a marked decrease in the frequency of infections.

Conclusion: Although underlying neurologic deficits may cause frequent infections, immune deficiency should always be kept in mind particularly in children who encounter infections with unusual severity and complications.

1405
Severe combined immunodeficiency: clinical and immunological features of six patients from a single center within a year

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Background: Severe combined immunodeficiencies (SCID) are the most severe forms of primary immunodeficiencies characterised by the absence or dysfunction of T lymphocytes affecting both cellular and humoral immunity.

Case presentations: Six patients with SCID were registered during the period from January 2012 till January 2013 in Dr. Behcet Uz Children's Hospital. Two children, 50 days and 5.5 months old admitted to our hospital with pulmonary infection and skin rash. They had lymphopenia, hypereosinophilia and decreased IgG, IgM, IgA levels with reduced CD3, CD4, CD8, CD19 and CD16 + 56 positive lymphocytes. Metabolic findings and mutation analyses were consistent with ADA deficiency. The first patient underwent bone marrow transplantation from an HLA identical healthy sister. A matched bone marrow transplant donor could not be found and ADA replacement therapy was initiated for the second patient. But the patient died from pulmonary insufficiency at the second month of ADA enzyme replacement treatment.

Case three, 4 months old girl presented with fever and recurrent skin rash. Her laboratory work revealed hypereosinophilia, low immunoglobulin levels with low CD4 cell count and absence of HLA-DR expression on B cells. Mutation analysis revealed MHC class II deficiency due to mutation in the RFXAP gene. Case four, 37 day old boy presented with generalised dry skin, eczema with cutaneous desquamation. In initial investigation we found lymphopenia, hypereosinophilia, low immunoglobulin levels, T + B-NK+ phenotype. His clinical and immunological findings were compatible with Omenn syndrome. Case five and six, 3 months old boy and 3 months old girl admitted to our hospital with pulmonary infection. They had lymphopenia and low immunoglobulin levels. Flow cytometry indicated T-B-NK + phenotype severe combined immunodeficiency.

Conclusion: Within this report we want to emphasize the importance of screening for severe combined immunodeficiency in children with lymphopenia and hypereosinophilia. In spite of treatment with IVIG replacement therapy, cotrimoxazole and antifungal prophylaxis, the poor outcome of this disease suggests urgent hematopoietic stem cell transplantation as a treatment of choice.

1408
Primary immunodeficiency disorders in an immunoallergology department

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Background: Primary immunodeficiency diseases (PIDDs) are rare disorders resulting from inherited defects of the immune system: humoral immune deficiencies, severe combined immunodeficiencies and phagocytic or complement defects. There are more than 150 different PIDDs currently recognised by the World Health Organization. The aim of our study was to describe the patients with PIDDs followed in our department.

Methods: A study evaluating patients undergoing consultation between January and December 2012 was performed. A database was designed using SPSS®v19.0, where the following items were assessed: age, gender, occupation, referral, family history and primary diagnosis.

Results: Thirty-eight patients were included (55.3% females). Mean age: 41.45 ± 21.28 [1–77] years. 36.8% were employed, 18.4% students and 15.8% unemployed.

28.9% of the patients were referred from the Hematology Department, 23.7% from Pneumology and 18.7% from Primary

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Health Care. The two most frequent reasons for referral were evaluation of patient with recurrent infections and findings of gamma globulins deficiency on routine analytic evaluation. None of the patients had family history of PIDDs.

Selective IgA deficiency was the most frequent disease affecting 34.2% followed by IgG subclass deficiency (18.4%). 13.2% had IgG subclass deficiency with decrease concentration in the total serum IgG. In 26.3%, common variable immunodeficiency (CVID) was the primary diagnosis. One patient had selective IgM deficiency. In those with IgG subclass deficiency, 58.3% presented with deficiency of at least two subclasses (6 of 7 with IgG1 plus IgG3). Three had a single decrease of IgG3; one had selective IgG1 deficiency and one with only IgG4 deficiency.

The majority of the patients under our supervision have occasional respiratory tract infection without any complications. Only one patient with IgG subclasses deficiency presented a history of repeated urinary tract infections that was controlled with prophylactic antibiotherapy and nonspecific immunostimulants. Excluding patients with CVID, no hospitalisations were reported.

Conclusion: Our study confirmed that selective IgA deficiency and CVID are the most common form of PIDDs, as described in the literature. Patients often present with recurrent respiratory tract infections and suspicion of PIDDs must be kept in mind in order to quickly establish the diagnosis.

1409
Aetiological investigation to cystic bronchiectasis in adult patients: case presentation

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Case presentation: Bronchiectasis is a lung disease but it may be the pathological expression of a large variety of disorders. However, a search for the aetiology is underestimated in many cases. We searched the possible underlying diseases in a 43-year-old woman with a long history of sinopulmonary infections who was diagnosed as having bronchiectasis lately. Her family history was positive for recurrent respiratory infections. During the last two decades Streptococcus and Haemophilus influenzae were isolated repeatedly from her sputum. A high-resolution computed tomography scan revealed bilateral diffuse cystic bronchiectasis and a peribronchial wall thickening predominantly in the right-upper and left-lower lobe, and pansinusitis. At diagnosis, underlying disease process including infections, immune deficiency, cystic fibrosis (CS), and allergic bronchopulmonary aspergillosis was searched. Recurrent sweat-chloride tests were resulted borderline. However, no mutations were detected, and diagnose of CF was imprecise. Next, patient was taken into a follow-up and given an individualised therapy. This case summarizes the screening tools when an adult presents with recurrent respiratory infections, and bronchiectasis.

Poster Session 60

Allergy and the nose – a focus on eosinophils

1410
Increased B-cell activation factor expression in nasal polyps is associated with local IgE production, Th2 response and concomitant asthma

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Background: The molecular mechanism underlying local IgE production in polyp tissue and its importance in the inflammatory process have not been fully understood.
Objectives: This study was performed to evaluate B-cell activation factor (BAFF) expression in polyp tissues of CRSwNP patients and to investigate whether elevated BAFF is associated with local IgE production and asthma comorbidity.
Methods: We collected nasal tissue from patients with CRSwNP, patients with CRSsNP and normal controls for investigation. The expression levels of BAFF, CD20 and CD138 were examined using immunohistochemical staining. The mRNA expression of BAFF, CD20, εGLT, AID, GATA3 and CRTH2 were examined using real-time RT-PCR. The protein levels of BAFF, IL-5 and IgE were measured using ELISA assays and the Unicap system, respectively. Moreover, the mRNA expression of εGLT, AID and GATA3 in dispersed NP cells after BAFF stimulation were measured using real-time RT-PCR.
Results: The mRNA expressions of BAFF, CD20, εGLT, AID, GATA3 and CRTH2 were significantly increased in CRSwNP compared with other groups ($P < 0.05$). The concentrations of BAFF, IgE and IL-5 in tissue homogenates were also significantly increased in CRSwNP patients, and the BAFF level in the polyp homogenates was significantly associated with the IgE and IL-5 levels and with concomitant asthma in CRSwNP patients ($P < 0.05$). Recombinant BAFF (100 ng/ml) significantly enhanced the mRNA expression of εGLT, AID and GATA3 through PI3K δ-dependent pathway *in vitro* ($P < 0.05$).
Conclusions: These findings indicate that BAFF expression is significantly increased in CRSwNP patients and that BAFF might act as the key factor linking the upper and lower airways by promoting local IgE production and the Th2 response.

Keywords: BAFF, nasal polyps, chronic rhinosinusitis, asthma, B cell, IgE, IL-5

1411
Differential suppression of SPLUNC1 in eosinophilic and non-eosinophilic nasal polyps: association with tissue eosinophilia and Th2 cytokine production

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Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is generally characterised by tissue eosinophilia and decreased innate immune response. However, whether the alteration of innate immune response was similarly existed in CRSwNP patients with different inflammatory profiles is unknown. This study is to evaluate the expression of the short palate, lung, and nasal epithelium clone 1 (SPLUNC1), an innate immune protein, in the eosinophilic and non-eosinophilic polyp tissues, and to investigate the possible modulation of SPLUNC1 *in vitro*.
Method: Nasal tissue samples were collected from 35 CRSwNP patients and 24 control subjects. CRSwNP patients were divided into eosinophilic and non-eosinophilic subtypes based on immunohistochimical staining of major basic protein (MBP). The number and morphology of glands in nasal tissues was determined by AB/PAS staining. The SPLUNC1 was examined using real-time PCR, immunoblot and immunohistochemical staining. The mRNA levels of IL-1α, IL-4, IL-13, IL-17A, and IFN-γ in polyp tissues were analyzed by real-time RT-PCR. Moreover, the expression of SPLUNC1 in polyp epithelial cells (PECs) after inflammatory cytokines stimulation was measured using real-time RT-PCR and ELISA assays.
Results: We found the expression of SPLUNC1 was significantly reduced in CRSwNP patients compared to the control subjects ($P < 0.05$). When polyp tissues were divided into two subtypes, we found the number of submucosal glands and expression of SPLUNC1 were significantly reduced in the eosinophilic polyp tissues compared to that in the non-eosinophilic polyp tissues ($P < 0.05$). Accordingly, the mRNA levels of IL-4 and IL-13, but not IL-1α, IFN-γ and IL-17A, were significantly increased in the eosinophilic polyp tissues compared to that in the non-eosinophilic polyp tissues ($P < 0.05$). Moreover, after stimulated by recombinant IL-4 and IL-13, SPLUNC1 expression in the dispersed NP cells was significantly inhibited ($P < 0.05$). In contrast, SPLUNC1 expression in PECs was significantly unregulated after stimulated with TLR-2, 3, 4, 5 and 9 ligands ($P < 0.05$).
Conclusion: The differential suppression of SPLUNC1 in eosinophilic and non-eosinophilic nasal polyps suggested a distinct innate immune response and cytokine-dependent modulation in CRSwNP with different inflammatory profiles.

1412
The difference of TNF-α, RANTES, interleukin-5 levels in nasal polyps in adolescents with allergic and non-allergic rhinitis

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Background: Nasal polyposis is a chronic inflammatory disease of the upper airway which develops in the ethmoidal and middle turbinate area, which characterised by a number of inflammatory cells with infiltration of eosinophil, Th2 cells, mast cells, and macrophages. Nasal mucosal immunereactivity may occur in varying degrees in polyps with allergic and non-allergic rhinitis. RANTES is locally produced within the nasal microenvironment of polyps and may be responsible for the eosinophil recruitment. Tumor necrosis factor (TNF) alpha with TH2 cytokines as interleukin-5 may enhance Nasal polyp fibroblast to produce inflammatory mediators. We evaluated the differences of nasal polyps from adolescents with allergic and non-allergic rhinitis for evaluation of RANTES, TNF-α, and IL-5 contents.
Method: We recruited 29 adolescents with allergic ($n = 15$, mean age: 17.4 years old) and non-allergic rhinitis ($n = 14$, mean age: 15.6 years old) undergoing polypectomy. Immunoassays were performed using polyp tissue homogenates to quantify the levels

of RANTES, TNF-α, and IL-5 and sera to assess total IgE, eosinophil cationic protein (ECP) from them.
Results: TNF-α, IL-5, and RANTES levels in atopic polyp was higher detected compared with non-atopic polyp tissue homogenates (IL-5: atopics 181.5 ± 143.6 vs non-atopics 82.7 ± 88.3 ng/100 mg, RANTES: atopics 174.5 ± 63.5 vs non-atopics 60.3 ± 38.5 ng/100 mg, TNF-α: atopics 180.8 ± 121.9 vs non-atopics 64.1 ± 64.5 ng/100 mg), but INF-γ levels in polyp with non-allergic rhinitis was observed to be not significantly higher than in polyps allergic rhinitis(INF-γ: atopics 14.78 ± 8.5 vs non-atopics 9.02 ± 6.5 ng/100 mg).
Conclusion: TNF-α, IL-5, and RANTES play important role in inflammatory recruitment leading to cell activation and directional migration of Th2 specific leukocyte subsets and contribute to endothelial migration for allergic reaction. Therefore they are involved in the pathogenesis of all of rhinitis and polyps with non-allergic rhinitis may undergo polypous degeneration into non-specific inflammation.

1413
The relationship between basophil and eosinophil in eosinophilic chronic sinusitis patients

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Background: The eosinophilic chronic sinusitis (ECS) has been a challenging disorder and it very often relapses after surgical treatment. ECS patients usually have other allergic diseases, such as bronchial asthma, atopic dermatitis and eosinophilic otitis media. According to the recent literature, the number of both basophils and eosinophils is closely related in ECS patients. This time, we investigated whether the number of basophils simultaneously change with that of eosinophils in ECS patients.
Method: The subjects were 18 ECS patients who performed surgery at our department in 2012. The number and percentage of eosinophils and basophils in the peripheral blood were measured before and after the surgery. We also studied RIST and RAST score before surgery.
Results: In order to examine the currency of eosinophils and basophils, we examined seven patients who were harvested blood for more than three times. The number and percentage of eosinophils decreased after surgery in four cases. Among them, the number and percentage of basophils decreased in parallel with these of eosinophils in two cases.
Conclusion: These results suggest that the number of eosinophils and basophils may run side by side, but that does not occur in all cases. The cause for this discrepancy might be explained by the small number and percentage of basophils and complex allergic mechanisms including eosinophils and basophils.

1414
The importance of local eosinophilia in the surgical outcome of chronic rhinosinusitis: a 3-year prospective observational study

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Background: Patients with chronic rhinosinusitis with/without nasal polyps (CRSwNP/CRSsNP) benefit from endoscopic sinus surgery (ESS), with an estimated success rate of 80%. At present, it remains unclear to what extent the presence of eosinophils, eosinophilic mucin (EM) and fungal hyphae (FH) in secretions influence the clinical outcome and recurrence of disease after ESS.
Objective: By delineating CRS groups and subgroups based on the finding of eosinophils, EM and FH, differences in the frequency of recurrent disease after ESS over a longer period of time were investigated.
Method: A prospective mono-centre study including 221 CRS patients who were unresponsive to medical treatment and underwent ESS, was performed. All tissue and sinonasal secretions were microscopically examined for the presence of eosinophils, EM and FH. Patients were followed for 3 years after surgery. Recurrence was defined according to the EPOS clinical control assessment, based on nasal endoscopy, symptoms and the need for systemic treatment.
Results: In total, 96 CRSwNP and 125 CRSsNP patients were included. Tissue eosinophils were found in 78% of CRSwNP patients compared to 42% in CRSsNP. Eosinophilic mucin was observed in 52% of the CRSwNP group vs 20% of the CRSsNP group. Furthermore, secretion analysis revealed FH in 6.8% of CRS. Recurrence in the total group was 22% over 3 years. CRSwNP patients with tissue eosinophilic involvement showed a recurrence rate of 32%. When the airway mucus secretions were positive for EM the recurrence rate was even 51%.
Conclusion: The presence of eosinophils in the tissue or secretions greatly increases the risk of recurrent disease in CRSwNP patients. The finding of tissue eosinophilia and EM in the collected sinonasal airway mucus secretions provides valuable information regarding the clinical outcome and the increased likelihood of CRS recurrence after ESS, whereas the finding of FH does not.

1415
Downregulation of polymeric immunoglobulin receptor in eosinophilic chronic rhinosinusitis

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Background: Immunoglobulin (Ig) A is the predominant Ig in mucosal tissues, endowed with protective functions including neutralisation of pathogens. Its secretion into mucosal secretions is conditioned by the polymeric Ig receptor (pIgR)-mediated transepithelial translocation of dimeric IgA. Expression of pIgR is decreased in COPD, lung cancer and nasopharyngeal carcinoma, while little is known regarding its role in chronic sinonasal pathologies.
Objective: This study aimed to assess pIgR expression in sinonasal mucosa of patients with chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) polyps and in allergic rhinitis (AR), as compared to control subjects.
Method: Nasal fluid and sinonasal biopsies from patients with CRSwNP, CRSsNP and AR, as compared to control subjects were collected. pIgR expression was analyzed by RT-qPCR and by immunohistochemistry. IgA (and IgA subclasses) and secretory component (SC) were assayed in nasal secretions by ELISA. Cellular infiltration and cytokine expression were assessed by (immuno)staining and RT-qPCR, respectively. Data are presented as median and interquartile range.
Results: pIgR expression was decreased, when compared to controls, in the ethmoidal mucosa from patients with CRSwNP (0.27 (0.04–0.82) vs 0.96 (0.41–2.58), pIgR/RPS18 mRNA copy number ratio; $P = 0.01$), and to lower extent with AR (0.37 (0.04–1.26) vs 0.96 (0.41–2.58); $P = 0.04$). This reduction resulted into reduced levels of SC (104.8 (63.7–173.0) ng/ml vs 210 (160.6–286.2) ng/ml; $P = 0.01$), and trends for reduced IgA (mainly IgA2), in nasal secretions from these patients. CRSwNP patients were characterised by increased eosinophils ($P = 0.0009$) and IL-13 expression ($P = 0.004$) in ethmoidal tissue. In addition, pIgR expression significantly correlated with IL-12p35 mRNA ($r = 0.45$, $P < 0.0001$).

Conclusion: Epithelial pIgR expression is decreased in patients with CRSwNP and AR, results in decreased SC (and IgA) in nasal secretions, and could result from the mucosal Th1-Th2 immuno-inflammatory bias in these patients.

1418
Nasal provocation test with aspirin in patients with Samters triad: study of individual provocation thresholds

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Background: The coexistence of chronic rhinosinusitis with nasal polyps (CRSwNP), bronchial asthma and intolerance to non-steroidal antiinflammatory drugs (NSAIDs) is known as Samter's triad. To diagnose NSAIDs intolerance, European guidelines of the EAACI / GA2LEN recommend nasal provocation test with 16 mg of aspirin. The aim of present study was to determine individual thresholds for aspirin provocation in patients with suspected Samter's triad and to correlate this threshold with the severity of disease as per asthma severity, number of paranasal sinus surgeries and nasal polyps score.
Method: Fourteen patients were enrolled in the study, (seven men and seven women; median age 48 years): All patients had CRSwNP, asthma and all have indicated a history of NSAIDs intolerance. The history of NSAID reactions, sinus surgeries and asthma medication was collected. Nasal endoscopies, spirometries and nasal provocations were performed. To capture the individual provocation threshold, nasal provocation tests were measured with increasing doses of aspirin (5, 15 and 25 mg).
Results: The mean provocation dose of aspirin was 16 mg, reflecting the EAACI/GA2LEN guidelines. However, four patients (28.6%) required higher challenge dose of 25 mg. In addition, two patients (14.3%) had non-specific reactions. The severity of disease as per GINA score, number of surgeries and the nasal polyps score has not correlated with the individual aspirin provocation thresholds.
Conclusion: The challenging dose of aspirin recommended by the European guidelines seems not to be sufficient in all cases. The individual aspirin provocation thresholds do not correlate with the severity of disease.

1419
Allergic fungal rhinosinusitis in four adult patients

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Background: Allergic fungal rhinosinusitis (AFRS) is a clinical entity that has gained importance as a cause of a benign and non invasive form of chronic rhinitis. It usually occurs in inmunocompetent patients with nasal polyps. It is a hypersensitivity fungal reaction. Diagnostic criteria should include the presence of allergic mucin in nasal exudate and typical radiological findings.
Method: Four cases of AFRS are described. All patients presented with a history of persistent nasal obstruction, rhinorrea and sinus headaches during several months. Skin prick testing to aeroallergenes and molds (including Aspergillus) were carried out as well as total serum Ig E, specific Ig E and Ig G (CAP-FEIA System) against fungal antigens. An endoscopic sinus surgery was carried out in all patients. Mucoid material was cultured.
Results: Immediate hypersensitivity to Aspergillus was detected by positive skin prick testing (3/4 patients) and increased levels of specific Ig E (4/4 patients). Total serum Ig E levels were elevated in all cases. Allergic mucin was found in nasal discharge in all patients. Fungal culture was positive in nasal exudate of three patients. Aspergillus could be demonstrated in the histopathology of a patient. ACT showed non invasive heterogeneous density in all cases.
Conclusion: AFRS should be considered as a differential diagnosis in patients with chronic refractory sinusitis, particularly in those with nasal polyps and atopic background.

1420
Vitamin D serum levels in allergic rhinitis: a preliminary study

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Background: Recently it has been suggested that, the worldwide increase in allergic diseases such as asthma, allergic rhinitis and food allergy is associated with low serum vitamin D levels. The aim of this study was to measure serum vitamin D levels in patients with allergic rhinitis.
Method: Serum vitamin D (25-hydroxyvitamin D), calcium, phosphorus, alkaline phosphatase and paratyroid hormone levels were assed in 33 patients with allergic rhinitis diagnosed clinically and the results of skin prick tests for aeroallergens. Subjects with serum containing <20 ng/ml vitamin D were deemed deficient.
Results: The mean vitamin D level in the study group was 17.55 ng/ml and 57% of patients had vitamin D deficiency.
Conclusion: The present study showed that the majority of allergic rhinitis patients had vitamin D deficiency. Therefore measuring vitamin D serum levels could be helpful in the routine assessment of patients with allergic rhinitis.

1421
Gene-environment interaction may modify the development of allergic rhinitis in Korean adolescents

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Background: Prevalence of allergic rhinitis (AR) is increasing worldwide including Asia countries. Allergic disease may develop in genetically susceptible subjects when they exposed to specific environment.
Method: A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to investigate the prevalence of AR. Enrolled number of middle school students was 4094 in 2008 and 3295 in 2011. Environmental factors and *IL-13 + 2044G/A* polymorphism were analyzed to investigate the risk factors for the development of current AR (ever have been diagnosed as AR with AR symptoms in the past 12 months).
Results: Prevalence of current AR was increasing 14.0% in 2008 and 14.4% in 2011. After controlling for potential confounders, age, maternal education level, parental history of AR, antibiotic therapy during infancy, presence of older or younger siblings and pet ownership during pregnancy or infancy had an effect on current AR. Adolescents with both parental history of AR and antibiotic therapy during infancy showed higher risk to develop current AR than those without parental history and antibiotic therapy (aOR 2.80,

95% CI 2.18–3.59). Additionally, current AR was presented higher in subjects with *IL-13 + 2044 GA + AA* who were treated with antibiotics during infancy than those with *IL-13 GG* without antibiotic therapy (aOR 1.91, 95% CI 1.02–3.58, $P = 0.043$).

Conclusion: The prevalence of current AR in middle school students was recently increasing in Seoul, Korea. Older age, high maternal education level, parental history of AR, presence of younger sibling and antibiotic therapy during infancy were the risk factors for current AR, but presence of older sibling had protective effect on it. In addition, adolescents who had been treated with antibiotics during infancy may develop current AR in genetically susceptible subjects.

1422
Immunological features in children with vernal keratoconjunctivitis

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Background: Vernal Keratoconjunctivitis (VKC) is a rare (<1:10 000 in Europe) chronic, bilateral, seasonally exacerbed inflammation of the ocular surface involving tarsal and/or bulbar conjunctiva. VKC especially affects male children and young boys and it tends to regress in puberty.

The diagnosis is based on the common conjuncitval symptoms (itching, photophobia and tearing) and on the characteristic signs (giant papillae, conjunctival hyperaemia and Horner-Trantas dots on the limbal conjunctiva). Moreover, photophobia is a constant feature of the VKC.

Aim: To define a clinical, anamnestic and immunological profile of patients with VKC evaluating also the presence of biomarker autoantibodies.

Methods: The study was performed at the Immunology and Allergology service of the Pediatric Department, Policlinico Umberto I Hospital, Rome. We enrolled 28 children (18:M) aged 4–14 years with diagnosis of VKC made by an ophthalmologist. To each patient, we asked the family history of allergic and immunological diseases. Among the immunological disorders, we evaluated mainly the presence of Hashimoto's thyroiditis, type I diabetes, psoriasis, rheumatoid arthritis and Systemic Lupus Erythematosus (SLE).

All patients with a diagnosis of VKC underwent to a serological evaluation with the dosage of ANA autoantibodies.

Results: 17 patients (60.7%) patients reported a family history of allergic diseases. About the immunological disorders, one patient presented type 1 diabetes and 14 patients (53%) reported a positive family history for autoimmune diseases: 6 (21%) for Hashimoto's thyroiditis, 4 (14%) for type I diabetes, 3 (10%) for psoriasis and one for Systemic Lupus Erythematosus. 10 (35.7%) patients were ANA positive and they tended to present an higher severity of VKC. The association between ANA positivity and the family history of immune disorders was not demonstrated.

Conclusions: These findings encourage us to consider the VKC as a multifactorial disease that can not be explained only by an allergic mechanism.

Moreover, among the patients with VKC, it is important to recognise those subgroups with certain anamnestic, clinical and serum characteristics in order to find out an appropriate therapeutic management and a careful follow-up.

Poster Session 61

Severe drug allergy

1423
Cardio-respiratory arrest Ig E mediated by Iomeprol (radiological contrast)

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Background: Hypersensitivity reactions to Iodinated Contrast Media (ICM) may be Ig E mediated. Cardio-respiratory arrest by ICM has been rarely reported.
Method: A 71-years-old patient was referred to us from Pulmonology department for study of allergy to ICM. Personal history of ex-smoker, high blood pressure, hyperuricemia, COPD, Sleep Apnea Syndrome treated with CPAP. No atopy history. Habitual treatment: Olmesartan/amlodipino 40/5 mg 1-0-0, atorvastatin 80 mg 0-0-1, salmeterol/fluticasone 50/500 ucg 1-0-1, tiotropium bromide 0-1-0, aspirin 100 mg 0-1-0. He felt warmth in forearm with subsequent extension with intense burning sensation, fading, malaise, pallor, vomiting, flushing, sweating immediately after administration of Iomeprol 120 cc i.v. during a CT examination for pulmonary nodules in study. He had cardiopulmonary arrest, requiring CPR maneuvers, admission to intensive care unit, with tracheal intubation for 48 h, administration of inotropics in continue perfursion, corticosteroids and antibiotics i.v. He had been previously submitted to various CT examinations with ICM, five times in 2 years without any reaction
Results: Allergological study: Skin tests: prick test to latex: negative. ICM: Iomeprol [1/10] prick: highly positive, Iohexol [1/10] Intradermal test (IDT): positive. Iobitridol, Iodinaxol prick and IDT were negative; Amidotrizoato prick: negative. Total serum IgE: 140 KU/l, Triptase at baseline: 3.23 mcg/l, specific IgE: Anisakis: 0, 74 KU/l. The basophil activation test (BAT by Baso Flow Ex®) was negative to: Iobitridol, Iodinaxol and Amidotrizoato. However, it had a highly positive result to Iomeprol (>90% of activated basophils, cut-off values for drugs ≥5%) and positive to Iohexol (9%).
Conclusion: We present a case of Anaphylactic Shock (anaphylaxis grade IV) induced by ICM 'Iomeprol' with prick test and BAT positive. Cross-reactivity to Iohexol has been detected by IDT and BAT. It happens to be a good correlation between skin tests and BAT. Repeated exposure to ICM seems to be a predisposing factor to ICM allergy.

1424
Severe immediate hypersensitivity to diclofenac with systemic reaction to intradermal testing: a case report

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Background: Drug hypersensitivity reactions to non-steroidal antiinflammatory drugs (NSAIDs) are frequent and can be distinguished to several subtypes, among which the single NSAID-induced urticaria-angioedema/anaphylaxis. The diagnostic approach for this reaction type includes skin testing with the culprit drug and oral challenges (OC) to NSAIDs with different chemical structure. We present a case of near fatal anaphylaxis to diclofenac who experienced additionally systemic reaction during skin testing with the culprit drug.
Method: A 62-year-old male with no medical history received p.o. 100 mg of diclofenac, due to low back pain. Three minutes later he developed a generalised flushing with intense itching and burning sensation, followed in 5 min by lightheadedness, loss of consciousness and fecal incontinence. His relatives performed basic cardiac resuscitation; hence he regained consciousness in 5 min. He was able to reach the Emergency Dpt. 90 min later, presenting only with generalised mild erythema. He was treated with i.v. corticosteroids and antihistamines and a serum sample for tryptase was immediately obtained. The patient reported uneventful recent intake of mefenamic acid and ibuprofen, while 3 years ago after diclofenac intake he experienced urticarial lesions lasting 1 h. Thirty days after the anaphylactic episode, skin prick tests(SPTs) to 1/1000, 1/100 1/10-fold dilution of diclofenac 25 mg/ml, as well as undiluted, were performed in 20 min intervals, followed by intradermal tests(IDs) of 1/10000, 1/1000, 1/100(twice) and 1/10-fold dilutions. An OC to acetylsalicylic acid up to 500 mg was also carried out.
Results: Tryptase concentration at the episode was 64.6 μg/ml (basal 6.6 μg/ml). All SPTs and IDs were negative. Surprisingly enough, 20 min after the second 1/100 ID, the patient experienced a mild pruritus in the palms, which retreated in a few minutes. However 20 min after the 1/10 ID test a generalised flushing, highly pruritic, appeared accompanied by increased heart rate(110/min). The reaction subsided upon treatment within 30 min. Two weeks later, the OC to aspirin was negative. The patient obtained written instructions for strict avoidance of diclofenac and acetic acid derivatives.
Conclusion: NSAIDs hypersensitivity has several distinct clinical patterns that reflect different mechanisms. Skin testing, if applicable, should be performed cautiously due to the possibility of systemic reaction.

1426
A girl with frequent idiopathic anaphylaxis

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Background: Anaphylaxis is an immediate life threatening reaction that usually initiates within a few minutes after exposure to the trigger factor. The occurrence of anaphylaxis without any identifiable precipitating factor is described as idiopathic anaphylaxis which frequently affects adult females. Idiopathic anaphylaxis tends to be recurrent and the occurrence of two or more episodes in the previous 2 months or at least six episodes in the preceding year is defined as frequent idiopathic anaphylaxis. Here we describe a case of frequent idiopathic anaphylaxis attacks.
Case presentation: A 17-year-old female, referred to our center with recurrent attacks of anaphylaxis without any identifiable trigger that initiated about 4–5 years ago. She had recently experienced more frequent episodes, up to three attacks daily (about 17 episodes during the previous 2 weeks). She had a history of recurrent acute urticaria, eczema and allergic rhinitis.

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She was the 2nd child of non-related parents with a family history of allergic rhinitis and chronic urticaria. She was a well-nourished and well-developed girl and there wasn't any significant physical abnormal finding except for mild eczematous lesions on the extensor surface of her extremities. The most important laboratory finding was increased level of her serum tryptase (26.5 μg per liter with reference range: up to 10.8 μg per liter).

She had admitted repeatedly and had received multiple short courses of ineffective treatment regimens until her last admission, afterward she has been on systemic and inhaled corticosteroids, antihistamine, leukotriene receptor antagonist as well as Epipen and salbutamol spray for emergency conditions by the diagnosis of frequent idiopathic anaphylaxis which controlled her attacks successfully.

Conclusion: Physicians should know and recognise this condition because it essentially requires special considerations including corticosteroid therapy in addition to appropriate emergency measures.

1427
Anaphylaxis to gonadorelin acetate in a girl with central precocious puberty

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Background: Gonadorelin acetate has been widely used in Europe for diagnosis of central precocious puberty. Although anaphylactic reactions to Gonadotropin releasing hormone analogues that have been used for treatment such as triptorelin acetate and leuprolide acetate have been previously reported; life-threatening reactions to gonadorelin acetate is extremely rare. Herein, we describe the first case -to the best of our knowledge- who encountered severe anaphylaxis after intravenous gonadorelin acetate administration.

Case report: An 8-year-old girl who was diagnosed with central precocious puberty was receiving triptorelin acetate uneventfully for 7 months. In order to evaluate the efficacy of the treatment, LHRH test with gonadorelin acetate was planned. Within 3 min after intravenous administration of gonadorelin acetate, she lost her consciousness whereas tonic seizures started in her hands and feet. She developed generalised hives along with edema in her tongue, lips and eyelids. Cyanosis was also present and she had hypotension (60/30 mmHg). Based on the diagnosis of anaphylactic shock by gonadorelin acetate infusion, she was immediately treated with epinephrine, high-flow oxygen, diphenhydramine and fluids. Her vital signs including blood pressure and pulse rate recovered within 30 min. Although the patient recovered successfully in 6 h, she was hospitalised for monitoring of her vital signs and discharged without any further events. Skin test with gonadorelin acetate was planned; however it could not be performed due to unwillingness of her parents.

Conclusion: Gonadotropin releasing hormone analogues, particularly gonadorelin acetate is generally regarded as safe drugs. However, life threatening anaphylactic reactions can be encountered. Severe systemic reactions during the procedure should be anticipated and administration of these drugs should be performed in a setting that is equipped to deal with anaphylactic reactions.

1428
Acute coronary syndrome without ST elevation induced by ibuprofen anaphylaxis

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Background: We report the case of a patient who developed acute coronary syndrome without ST elevation under treatment with ibuprofen by pain secondary to left ankle sprain. This is non-steroidal antiinflammatory drug (NSAIDs) on a daily basis, making this class of drugs one of the most commonly used in the world. This has been seen as a reaction very unlikely. There are few cases described in the literature related to myocardial ischemia and nonsteridal antiinflammatory.

Method: A 72-years-old man, immediately after taking tablet oral ibuprofen 600 mg, presented the following symptoms: lightheaded, pale skin, cold sweats, loss of consciousness, malaise, hypotension (70/40), decrease in oxygen saturation (92%), angioedema of lips, conjunctival injection, itching and generalised maculopapular rash with rapid onset. He goes to the emergency room where the patient was treated with Antihitamines and intravenous steroids improving his symptoms. So the patient was assessed by coronary care service of cardiology after suffering a syncope; finding elevated Troponin.

Result: Troponin level was 11.57 ng/ml (enzyme indicative of myocardial damage). EKG: no evidence of myocardial ischemia or ST elevation. Echocardiogram: normal ejection fraction. Stress echocardiography: negative for myocardial ischemia. Total IgE: 611 IU/ml. Serum tryptase levels obtained 60 min later measured 148 mcg/l and 48 h later 7.24 mcg/l (this is one of the main markers of anaphylaxis). Skin prick test with Ibuprofen was negative. Controlled oral exposure test whit Celecoxib (200 mg) and Paracetamol (500 mg) were negative, tolerated therapeutic doses.

Conclusion: As it is known, Ibuprofen is a common cause of allergic reactions drug. In our knowledge, few cardiac manifestations have been described in the medical literature. We report the case of a patient in which we observed predominantly cardiac involvement as a result of anaphylactic reaction caused by ibuprofen. Therefore, the serious allergic reactions may be the cause of acute coronary syndrome. Elevated serum tryptase levels were crucial to the diagnosis, to conclude that the reaction observed in the patient was caused mainly by taking ibuprofen.

1429
Kounis Syndrome in a patient after administration of influenza vaccine

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Background: Kounis Syndrome (KS) is defined as an acute coronary syndrome associated with hypersensitivity. Also known as allergic angina syndrome because of chest pain and allergic reactions accompanied by clinical and laboratory finding of angina pectoris caused by inflammatory mediators released during the allergic insult. Several allergens have been reported to trigger KS as drugs, foods, hymenoptera venom, latex and contrast media. We report the case of a patient who developed acute coronary syndrome, according to analytical parameters, electrocardiographic abnormalities and coronary angiography, in the context of an anaphylactic episode after administration of influenza vaccine.

Method: A 69-years-old man, with a history of ischemic heart disease, presented 15 min after administration of influenza vaccine: general malaise, weakness predominantly in both arms, chest tightness, warmth and suffocation. The patient went to the emergency room where he was treated with sublingual nitroglycerin 0.4 mg presenting improvement in short time. So the patient was assessed by coronary care service of cardiology for analytical parameters, electrocardiographic and coronary angiography.

Result: Troponin T level was 43 ng/l (enzyme indicative of myocardial damage).

The electrocardiogram revealed ischemic changes (ST depression in leads V4-V6). The echocardiogram showed apical akinesia, inferior hypokinesia and left ventricular dysfunction (evidence of myocardial ischemia). Coronary angiography showed circumflex artery occlusion, atheromatous coronary, inferior hypokinesia and left ventricular dysfunction. Total IgE level obtained a week later measured 64.30 IU/ml. Serum tryptase levels were not determined. Skin prick test with influenza vaccine, egg, egg white and yolk were negative.
Conclusion: We report a patient with clinical support Kounis Syndrome after administration of influenza vaccine. He has history of ischemic heart disease, reason why we have classified it as KS type II. Serious allergic reactions may be the cause of acute coronary syndrome in patients with healthy or altered coronary arteries and no cardiovascular risk factors. In our knowledge, there aren't cases reported in the medical literature of Kounis Syndrome induced by administration of influenza vaccine.

1430
Anaphylaxis to gadobutrol in a patient with low grade astrocytoma

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Background: Gadobutrol is a paramagnetic macrocyclic contrast agent considered to be safe for magnetic resonance imaging (MRI). We report a patient diagnosed with a low grade astrocytoma who presented with an anaphylactic reaction 10 min after the intravenous administration of Gadobutrol in a routine brain MRI.
Method: A 57-year old woman with low grade astrocytoma presented with palms and soles pruritus, disseminated hives, breathlessness, dizziness, loss of consciousness and hypotension (100/50 mmHg), 10 min after intravenous administration of Gadobutrol. Skin testing with gadolinium-based contrast (Gadobutrol, Gadoterate meglumine, and Gadopentetic acid) was carried out. Histamine and isotonic saline were used as positive and negative controls respectively. Skin tests with Gadobutrol were performed in five control subjects.
Results: Prick and intradermal skin testing elicited positive results to Gadobutrol, and negative to Gadoterate meglumine and Gadopentetic acid. Skin testing with Gadobutrol in five control subjects was negative. The patient was advised to avoid the administration of Gadobutrol. Pretreatment with steroids and antihistamines for future administrations of gadolinium-based contrast agents (Gadoterate meglumine and Gadopentetic acid) was recommended.
Conclusion: A case of IgE-mediated anaphylaxis to Gadobutrol in a patient with low grade astrocytoma is reported. Skin cross-reactivity was not found between gadolinium-based contrasts tested. As she will require future administrations of Gadolinium-based agents, a premedication protocol is recommended.

1431
Peri-operative anaphylaxis – a challenge…

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Background: Severe adverse reactions during anesthesia are rare but represent an important problem for anesthesiologists and allergologists.
Method: The authors present three case reports of peri-operative anaphylaxis.
Results:
Case 1: Male, 52 years old, submitted to epidural anesthesia due to Urologic surgery. Five minutes after the administration of midazolam, the patient had hypotension, respiratory distress and generalised urticarial. The anesthetic protocol also included i.v. acetaminophen and lidocaine at the lumbar area. Due to the severity of the reaction it was decided to start the investigation with laboratory tests. Basophils Activation Test was positive for local anesthetics and negative for acetaminophen. Skin prick tests excluded latex and iodopovidone allergy. Intradermal tests (IT) with midazolam were negative and oral provocation test with acetaminophen was also negative. Diagnosis of allergy to local anesthetics was presumed. The patient was then submitted to general anesthesia without any adverse reaction.
Case 2: Female, 60 years old, who had respiratory arrest and urticaria during general anesthesia protocol. Symptoms started 15 min after the administration of rocuronium. Propofol and midazolam had already been administrated. IT were positive for all muscle relaxants (except atracurium) and negative for midazolam and propofol. Skin prick tests for latex, iodopovidone and eggwhite were also negative. The patient was submitted to surgery with atracurium as an alternative muscle relaxant with no complications.
Case 3: Female, 37 years old, who had hypotension, respiratory distress and generalised urticaria during epidural anesthesia for Cesarean section. Besides the anesthetic drugs, cefixime was also administrated. Skin prick tests were positive for latex. IT for anesthetic drugs and oral provocation with cefixime were negative. Diagnosis of latex allergy was confirmed by positive latex specific IgE.
Conclusion: Most anaphylactic reactions during anesthetic induction are allergic and therefore further exposures to the same drug may induce severe reactions. Diagnosis is not always easy and similar clinical cases can be caused by different drugs. With these three case reports we emphasize that a thorough allergic workup is crucial for the identification of the culprit drug and to find safer alternatives.

1434
The combination of an angiotensin converting enzyme inhibitor and a beta-blocker aggravates passive systemic anaphylaxis in mice

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Background: The beta-blocker metoprolol and the angiotensin converting enzyme ACE-inhibitor ramipril are frequently used for the treatment of cardiovascular diseases. These drugs have been reported to augment anaphylactic responses in sensitive individuals, but the mechanisms behind this effect remain to be determined.
Method: We established a mouse model which mimics the long term treatment in cardiovascular therapy. To this end, Balb/c mice were pre-treated with ramipril and metoprolol (either alone or in combination) for 14 days and passive systemic anaphylaxis (PSA) was induced. Core body temperature was measured up to 70 min. Levels of mast cell (MC) mediators were determined by ELISA. Additionally, we used the model of passive cutaneous anaphylaxis (PCA). *In vitro*, murine bone marrow-derived cultured mast cells were incubated with the drugs, sensitised with IgE and treated with (or without) anti-IgE before histamine release was assessed.
Results: Pre-treatment of the mice with either ramipril or metoprolol alone showed only slight enhancing effects on hypothermia. However the combination clearly potentiated the symptoms of PSA. These effects were confirmed in the passive cutaneous model. In line with the exacerbated hypothermia, elevated amounts of LTC_4 and PGD_2 as well as increased levels of the pre-formed mediators histamine and serotonin were detected in mouse sera upon combined treatment with the respective drugs. Consistent with these findings histamine release of MCs pre-treated with metoprolol *in vitro* was likewise enhanced.

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Conclusion: The combination of ramipril and metoprolol potentiates PSA and PCA. The enhancing effects seem to be mediated, at least in part, by a direct increase in mast cell reactivity. Our model can be used to study cofactors of anaphylaxis and their underlying mechanisms.

1435
Anaphylactic shock cases growth among the population of big industrial city

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Background: The aim of the research is to investigate the prevalence of anaphylactic shock in industrial city (Kazan, Russia, more 1 million population) within the period of 2000–2011. We've analysed the medical records of patients with acute allergic reactions, treated in the allergology department of the local hospital.
Method: There have been hospitalised 493 patients 14–80 years old (274 women and 219 men) with diagnosis 'Anaphylactic shock'. The prevalence of the anaphilactic shock has increased from 3.1 per 100 000 of population in 2000 up to 4.3 per 100 000 in 2011.
Results: Among the etiological reasons of the anaphylactic shock there are 291 cases of drug allergy (60%), 133 cases – hymenoptera sting (27%), 34 cases of food allergy (7%), 31 cases (6%) are included into the group, named 'other'.

Anaphylactic shock caused by drugs takes the third place in the structure of acute allergic reaction of same genesis after the acute urticaria and angioedema, and acute dermatitis. The leading reasons of anaphylactic shock caused by drug allergy are antibiotics – 13.1% of cases (42% of which are beta-lactam), nonsteroid antiinflammatory drugs – 10.7%, and local anaesthetics – 8%, in 7.3% of cases – polypharmacy. In almost half of those cases (42%) anaphylactic shock has devepoled after taking of medicines of the same group. Among the reasons of anaphylactic shock, caused by the Hymenoptera stings, 69 cases were induced by wasp sting (52%), 33 cases of bee sting (25%), six cases – hornet sting (5%) and three patients – bumblebee (2%), in five cases (4%) the type of the insect was not defined. In 17 cases (13%) we had a multiple wasp and bee sting (13%).
Conclusion: Our results show the growth of anaphylactic shock cases among the population of big industrial city. The main causes of anaphylactic shock are the drugs and the hymenoptera sting.

1436
Immunologic mechanism of selective anaphylaxis to aceclofenac

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Background: The pathogenic mechanism of cyclooxygenase(COX)-1 inhibition in NSAIDs hypersensitivity results in multiple cross-reactive intolerance to aspirin and NSAIDs. However, selective reaction to single NSAID resembling type I hypersensitivity has been sporadically reported. Aceclofenac and diclofenac are widely used NSAID derivative of phenylacetic acid. Selective hypersensitivity reaction to aceclofenac has been rarely reported, and there is no report about cross-reactivity between aceclofenac and diclofenac. This study was performed to investigate pathogenic mechanism of selective anaphylactic reaction to aceclofenac, and to evaluate cross-reactivity between aceclofenac and diclofenac.
Case presentation: Three female patients with aceclofenac-induced anaphylaxis were enrolled. All three patients had definite history of anaphylactic shock to aceclofenac, and two patients also had episode of anaphylaxis to diclofenac. However, all were tolerable to aspirin or other NSAIDs. Skin test with aceclofenac, diclofenac, aspirin and other NSAIDs were performed. One patient showed positive response to aceclofenac and diclofenac both in prick and intradermal tests. Another patient showed positive intradermal response to aceclofenac and diclofenac, but the other patient showed negative skin reactivity to all test drugs. Oral provocation test with aspirin and other NSAIDs showed no specific response in all patients, even though the challenge tests with aceclofenac or diclofenac could not be performed because of the risk. To detect serum-specific IgE, we prepared aceclofenac- and diclofenac-human serum albumin (HSA) conjugates respectively. ELISA result showed high level of specific IgE to aceclofenac- and diclofenac-HSA conjugates in sera from two patients with positive skin response to the drug. ELISA inhibition tests showed significant inhibitions of specific IgE responses with additions of aceclofenac- and diclofenac-HSA conjugates in dose-dependent manners in these two sera.
Conclusion: In conclusion, we demonstrated the presence of specific IgE to aceclofenac- and diclofenac-HSA conjugates in two patients with selective hypersensitivity to these drugs. We also showed immunologic cross-reactivity between aceclofenac and diclofenac. These results suggest specific IgE-mediated mechanism of phenylacetic acid-induced anaphylaxis by clinical history, skin tests and specific IgE measurement.

Poster Session 62

Classical and emerging drug allergy

1438
Spontaneously reported adverse drug reactions in a tertiary university hospital during 2012

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Background: Adverse drug reactions (ADRs) frequently occur in hospital setting and affect negatively patient outcomes. The number of self-reported ADRs has been rapidly increased in Korea. This study was conducted to investigate the clinical characteristics of ADRs in a single university hospital, and to evaluate the features of ADRs to anti-asthma or anti-allergic drugs in patients with allergic diseases.
Method: ADRs reported to hospital Pharmacovigilance Center were collected from Jan 2012 to Dec 2012. Assessment was performed for causality and severity. Clinical information was also collected from electronic medical records.
Results: The total number of ADRs through spontaneous reporting system was 2673. Among them, 1693(63.3%) were reported from female, and 35.4% were reported from patient aged 60 and over. ADRs were reported by doctors (36.5%), nurses (39.7%), and hospital pharmacists (23.8%). Central nervous system (CNS) agents and anti-infective agents (AIA) were the drug class most commonly involved, and NSAIDs and cephalosporin antibiotics were the most frequently offending subclass. The most frequently reported system-organ class was GI system disorders (33.9%), and skin and appendages disorders (22.1%) were the next. Serious adverse events (SAE) were developed in 109 cases (4.1%), severe cutaneous adverse reaction (SCAR) such as DRESS syndrome and Stevens-Johnson syndrome were noted in 17 cases. About 6.9% of total ADRs were severe in severity. Compared to ADRs reported from doctor or pharmacists, severity of ADR reported from nurses was more mild form ($P < 0.01$). Eighty-five ADRs (3.2%) were developed against anti-asthmatic or anti-allergic drugs. Most of them were mild (71.8%) and moderate (24.7%) in severity. Anti-histamines (29 of 85) were the most commonly involved drugs in these classes. ADRs to inhaled steroids with/without LABA (9) and LTRA (4) were also reported.
Conclusion: Nurses report relatively mild ADRs, however, doctors and pharmacists may have tendency to report more severe cases of ADRS. Anti-infectives and NSAIDs can elicit ADRs most frequently. Although the severity is usually mild or moderate, ADRs to anti-asthmatics or anti-allergic drugs are not uncommon in patients with allergic diseases in university hospital setting.

1439
Immediate and nonimmediate allergic reactions to betalactam antibiotics in childhood

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Background: Hypersensitivity reactions to betalactam antibiotics are common during childhood. Studies have shown that 12–60% of children with suspected allergy were actually allergic to betalactams. The aim of this study is to determine the rate and risk factors for betalactam allergy in children with history of immediate and nonimmediate hypersensitivity reactions.
Method: We performed a prospective study of 105 children [6.25 (3.62–9.41) years] who had 128 hypersensitivity reactions to betalactams. After filling ENDA questionnaire, all cases underwent prick and intradermal skin testing with major and minor determinant mixture, penicillin G, ampicillin, amoxicillin and clavulanic acid followed by the culprit drug. In patients with a history of nonimmediate reaction and negative skin tests, patch tests and intradermal tests with late readings were performed with the culprit drug. Drug provocation test was performed in case of negative interventional tests.
Results: Thirty-four children (32.4%) had 39 immediate and 71 children (67.6%) had 89 nonimmediate reactions in the history. The most frequently incriminated drugs were amoxicillin-clavulanic acid (47.7%), penicilin (14.8%), cephalosporins (22%), sulbactam ampicillin (7%), amoxicillin (5.5%), ampicillin (2.3%), meropenem (0.8%). Eight children with an immediate reaction (23.5%) and 13 children with a nonimmediate reaction (18.3%) were diagnosed as betalactam allergic. The diagnosis of drug allergy was determined by skin tests ($n = 6$), provocation test ($n = 1$) and doctor diagnosed anaphylaxis in our hospital ($n = 1$) in immediate reactions whereas by skin tests ($n = 3$), patch tests ($n = 2$) and provocation tests ($n = 9$) in nonimmediate reactions. Respiratory system involvement during the drug reaction was found to increase the risk for diagnosis of betalactam allergy in immediate reactions in children (OR:6.9, 95% CI:1.3–37.5, $P = 0.024$).

Corticosteroid use for the treatment of acute drug reaction was associated with higher risk for diagnosis of nonimmediate betalactam allergy (OR:4.3, 95% CI:1.2–15.7, $P = 0.025$).
Conclusion: Diagnosis of drug allergy is also common in children with a history of nonimmediate reactions to betalactams. In the majority of cases, the drug allergy was confirmed by skin tests in immediate reactions whereas by drug provocation in nonimmediate reactions. A detailed history of drug reaction including the treatments given for the reaction itself is important for an appropriate diagnostic work up.

1440
Prevalence of abacavir-associated hypersensitivity syndrome and HLA-B*5701 allele in a Portuguese HIV population

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Background: Abacavir is an antiretroviral drug used as first line treatment for HIV infection. Of treated patients, 5–8% develop an *abacavir-associated hypersensitivity syndrome* (ABC-HS) in the first 6 weeks, which can be life-threatening. ABC-HS has been strongly associated with the presence of the HLA-B*5701 allele. Screening for this allele is recommended for all patients prior to beginning therapy with abacavir since it virtually eliminates all immunologically confirmed ABC-HS.

Aim: To determine the prevalence of HLA-B*5701 in the adult HIV population followed in our hospital and to characterise suspected ABC-HS.
Methods: Clinical data on patients under abacavir treatment since January 2006 was analyzed to search for symptoms of ABC-HS. HLA-B*5701 screening was performed by real time PCR in all patients since January 2008 and those with positive HLA-B*5701 began HIV treatment with an alternative drug. Reactions of suspected ABC-HS were characterised. HLA-B*5701 and patch tests (1% and 10% abacavir in petrolatum) with readings at 48 h were performed in those without previous testing. Direct costs of ABC-HS were also analyzed.
Results: Of 573 patients screened in the 5 year period, 35 (6.1%) were HLA-B*5701 positive. After HLA-B*5701 screening implementation, no suspected ABC-HS were observed. During 2006 and 2007, 186 patients began treatment with abacavir: data was unavailable in 23; 7 (4.3%) patients stopped abacavir for suspected ABC-HS (median age 45 years, five male). The median time for reaction onset was 7 days (0–13 days) after starting abacavir; reactions were characterised by rash ($n = 2$), fever and malaise ($n = 2$), rash, fever and myalgia ($n = 1$), liver enzymes elevation ($n = 1$) and subjective sensation of dyspnea and throat swelling ($n = 1$). Two patients were treated with oral corticosteroids; none required hospitalisation. Patch tests and HLA-B*5701 results are currently available in two patients: one patient with pruritic rash in the trunk had positive HLA-B*5701; both had negative patch tests.
Conclusions: The prevalence of HLA-B*5701 was of 6.1% and the rate of reactions prior to screening was of 4.3%, in accordance to the described for the European population. Most suspected ABC-HS reactions were either rash or fever and none required hospitalisation. No ABC-HS occurred from January 2008, when HLA-B*5701 screening was implemented.

1441
Severe cutaneous adverse drug reactions: clinical patterns and follow-up

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Background: Severe Cutaneous Adverse Reactions to Drugs (SCARs) are rare, but life-threatening conditions. Case definition for SCARs can help in its early diagnosis and management. There are limited data about the follow-up of these cases. Our aim was to analyze series of cases of SCARs based on the clinical and demographic data and on clinical follow-up.
Method: A cohort study was developed including all patients with history of SCARs in the last 10 years. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Acute Generalised Exanthematous Pustulosis (AGEP), Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) were considered SCARs. The evaluation was based on standardised scoring systems using an adapted ENDA (*European Network of Drug Allergy*) questionnaire, medical records and on the clinical follow-up in our Allergy Clinic.
Results: Thirty-seven cases were validated as probable or definitive SCARs, 15 DRESS, 15 SJS, 4 TEN and 3 AGEP. Nineteen males (51%) and the mean age was 32.5. Mucosal involvement was found in 16 patients (43%), 25% in DRESS. Fever was present in 87% and lymphadenopathy in 41%. Of all 34 subjects (92%) who presented internal organs involvement, predominantly liver (59%), kidney (26%), spleen (15%) and lung (15%). Forty-one percent had commitment of a single internal organ, 47% of SJS and TEN cases had this involvement. Thirty-three percent of patients with renal involvement required dialysis. Eosinophilia was documented in 24% and atypical lymphocytes in 13.5%. Thirty-five percent were related with antibiotics, 32% with antiepileptics, 19% with non-steroidal anti-inflammatory drugs, 8% with sulfonamides and 2.7% with allopurinol. Five fatalities (13.5%) occurred, all for sepsis, 60% in TEN. During the follow-up, 35% cases developed skin/mucosa sequelaes, 5.4% autoimmune diseases, 5.4% biliary cholestasis and 5.4% presented different drug allergies to non-related medications.
Conclusion: This series confirmed the clinical variability of SCARDS, highlighting skin, fever and internal organs involvement. Antibiotics were the main culprit pharmacological group. There was severe internal organ involvement and most of fatalities were related to sepsis in TEN. The clinical outcomes verified after the acute phase of these reactions, supports the need of a long-lasting clinical follow-up of these patients.

1442
Suspected allergy to betalactam antibiotic: the value of diagnostic evaluation

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Background: To evaluate patients referred to the Allergy Department for suspected betalactam antibiotic allergy. To assess the number of patients with confirmed allergy, drugs involved in reactions and the usefulness of the diagnostic tests.
Method: Prospective study in patients who had experienced a reaction suspected to be due to betalactam allergy. Diagnosis was based on ENDA protocol (positive clinical history, specific IgE, cutaneous and/or challenge test). One year after the study, in 40 patients we carried out a telephone survey to find out the usefulness of the diagnostic study based in the final report given to the patient.
Results: We studied 154 patients (103 female) with age 44.48 ± 16.13 years old (16–78 years). Suspected drugs were: amoxicillin (32%), amoxicillin/clavulanic acid (31%), penicillin (30%), ampicillin (3%), cefuroxime (3%) and betalactams (1%). 76% of the patients reported cutaneous manifestations, 3% anaphylactic shock, 7% gastrointestinal involvement and the other, non-specific symptoms. Clinical history was not suggestive in 42% of the patients. 117 patients had a negative challenge test with the suspected drug. Betalactam allergy was diagnosed in 37 patients (24%). 57% of these had suffered anaphylaxis. Two of 29 patients showed positive serum specific IgE antibodies, 18 of 33, positive cutaneous tests and 4 of 4 had a positive challenge test with the suspicious drug. In 14 patients (11 of them with negative cutaneous tests), diagnosis was made by highly positive clinical history. In 2 of 5 patients with negative serum specific IgE antibodies, cutaneous tests were positive. Challenge test with alternative drug was carried out in 26 patients (70%) and in one of them (4%) was positive. The results of telephone survey showed that 14 patients had took and tolerated the recommended drug and in 26 patients the drug was not administered: 18 patients because it was not necessary, 6 patients due to fear and 2 patients still considered themselves allergic despite their negative diagnosis.
Conclusion: Only 24% of the patients were diagnosed with allergy to any betalactam antibiotic. Cutaneous tests and, especially, specific IgE show low sensitivity. Most of the patients tolerated an alternative betalactam. One of five patients surveyed did not accept the diagnosis. A greater implication of the family Doctor in interviewing the patients is needed to determine the necessity of referring them to the Allergy unit.

1443
A survey on non-steroidal antiinflammatory drug-induced hypersensitivity reactions in Latin America

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Background: The prevalence of hypersensitivity reactions induced by non-steroidal anti-inflammatory drugs (NSAIDs) is unknown, and the present study focuses on predisposing factors, clinical pictures, and allergological work up.
Methods: A descriptive cross sectional study using a modified ENDA questionnaire was implemented in 19 allergology units from 11 different Latin American countries; reporting patients assisted for NSAIDs hypersensitivity reactions evaluated in a first visit to a specialist, during the last year. Severity was graded as mild, moderate and severe.
Results: Of 564 patients evaluated because of hypersensitivity drug reactions, 302 (53%) presented NSAIDs related reactions. Fifty-six percent had an atopic background. In the group with certain and probable causal relationship with NSAIDs (252 patients), Urticaria-angioedema (85%), was the most prevalent clinical presentation. Maculopapular exanthema was present in 5% of the cases. Immediate reactions (<1 h after taking the drug) were present in 55% of the patients, while only 10% occurred after 24 h. Thirteen percent had a history of previous reactions with drugs of the same group. Seventeen percent of the reactions were severe. Drug provocation tests (DPT) were performed in 123 patients (44%), being positive in 41 (three non immediate reactions).
Conclusions: NSAIDs were the most frequent inducer of reactions in our population. A significant factor that may account for such high rate of reactions is the easy access to NSAIDs, as they are Over-the-counter (OTC) medications in most countries. Almost 2/3 of the reactions were immediate, and 17% were severe emphasizing the need for raising awareness among the population and health authorities in Latin America about the potential dangers of self medication.

1444
Differences between self-reported drug hypersensitivity reactions in Lithuanian adults and children

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Background: Drug hypersensitivity reactions (DHRs) are the adverse effects of drugs that, when taken at doses generally tolerated by normal subjects, clinically resemble allergy. The aim of our study was to assess the prevalence of self-reported DHRs in adults and in children and to analyse the risk factors in both groups.
Method: Cross-sectional survey of a population from Vilnius and Kaunas regions of Lithuania was made. 35 questions about drug allergy symptoms and also about food and pollen allergy, family history were examined. 5370 patients included in the study. 3222 of them were children (1628 females, median age 8.25 [3–14] years), and 2148 were adults (1247 females, median age 48 [28–63] years) recruited from both adults and children general practices.
Results: 7.9% of children and 13.8% of adults declared DHRs for at least one drug ($P < 0.001$). Female were predominant in adults with DHRs (17.5% vs 8.7%, $P < 0.001$), but there was no statistical difference for gender in the children. 69.8% of children and 59.5% of adults had skin symptoms like redness, rashes, itch, oedema and these were the most common clinical symptoms in both groups ($P = 0.012$). Anaphylaxis rate was similar in both groups (about 10%). All other symptoms were significantly more frequent in adults: ocular symptoms were detected in 3.1% of children and 9.5% of adults, nasal symptoms in 1.6% of children and 7.4% of adults, respiratory symptoms in 2% of children and 13.5% of adults, gastrointestinal symptoms in 5.1% of children and 13.2% of adults. In our population the frequency of immediate type DHRs was 60.1% in adults and 25.7% in children ($P < 0.001$). 4.4% of children and 7.2% of adults had antibiotic induced DHRs and it was the most implicated group of drugs ($P < 0.001$). Food and pollen allergy was declared more frequent in the DHRs group. Statistically significant risk factors for DHRs were age (OR = 1.017 in favour of adults, 95% CI 1.013–1.021), female sex (OR = 1.439, 95% CI 1.187–1.744), concomitant food (OR = 1.92, 95% CI 1.505–2.448) and pollen allergy (OR = 2.0, 95% CI 1.573–2.544) and family history of DHRs (OR = 6.007, 95% CI 4.756–7.587).
Conclusion: Self-reported drug hypersensitivity reactions were more frequent in adult females. The skin reactions were dominant in both groups. The risk factors were age, female sex, food allergy, pollen allergy and family history of drug hypersensitivity reactions.

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Associations of food sensitisation and multiple hypersensitivity to non-steroidal antiinflammatory drugs

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Background: An increased prevalence of atopy has been observed in patients with cross-intolerance to non-steroidal antiinflammatory drugs (NSAIDs). This association has been observed between inhalant allergens (mainly house dust mites) and several clinical manifestations of cross-intolerance to NSAIDs (acute urticaria/angioedema). Whether an association exists with food allergens has not been assessed. The aim of this study was to investigate sensitisation to food allergens in patients diagnosed as acute urticaria/angioedema induced by cross-intolerance to NSAIDs (AUA).
Methods: Patients with confirmed history of AUA (≥3 episodes with at least two different NSAIDs or positive drug provocation test), selective responders to NSAIDs (SR) and subjects who tolerated NSAIDs were included. Skin prick tests were performed with a battery of 31 common food allergens that included animal and vegetable allergens. Specific IgE was determined in serum by ImmunoCAP, considering positive a value higher than 0.35 IU/ml.
Results: A total of 80 patients with confirmed history of AUA, 30 SR and 152 controls were studied. The 62.5% were females with a mean age 42.54 ± 14.76 years. Positive skin tests and specific IgE in serum were detected in 3

(3.75%) patients AUA and in 7 (4.6%) controls ($P > 0.05$). None of SR had positive tests. No differences were found in the allergens tested in both AUA and control groups.

Conclusions: Food allergy sensitisation does not seems to be increases in subjects with AUA in spite that these patients are more sensitised to inhalants. Further studies are needed to confirm this finding.

1447
Diagnostic evaluation of the patients with drug hypersensitivity reactions

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Background: Allergic reactions to drugs comprise a major public health problem associated with substantial mortality and morbidity. Recent studies confirmed that drug allergy frequency is overestimated by both parents and physicians. The aim of this study is to find out the frequency and the risk factors for drug allergy in children with a history of allergic drug reaction admitting to a tertiary allergy clinic in Turkey.

Method: The children with a history of allergic reaction to any drug admitted to our department within last year were involved. Epidermal, intradermal and/or patch tests and provocation tests according to EAACI-ENDA recommendations. The demographic features, presence of atopic or another chronic disease, concomitant drug use, atopy status and familial atopic status of the patient together with the clinical features of suspected drug reaction were recorded.

Results: The children ($n = 237$) [7.3(3.9–10.2) years, 96 male] who had a total of 366 allergic reactions attributed to any drug were included. The diagnostic work up was complete in 169 (71.3%) patients with 266 reactions. Suspected reaction history was with one drug in 103 (60.9%) patients, two drugs in 45 (26.6%) patients, three drugs in 17 (10.1%) patients, four and five drugs in two patients. The most frequent suspected reactions were due to antibiotics (59.4%), non-steroidal antiinflamatory drugs (19.1%), chemotherapeutics (3.2%) and local anesthetics (3%). The diagnosis of drug allergy was made in 51 (30.1%) patients, proven by provocation tests ($n = 23$), skin prick or intradermal tests ($n = 12$), patch test ($n = 2$) and doctor diagnosed anaphylaxis in our hospital ($n = 14$). The frequency of atopy, food sensitisation, chronic disease and concomitant chronic drug use were higher in drug allergic patients compared to nonallergic ones ($P = 0.002$, 0.021, 0.031, 0.003, respectively). Angioedema[(OR: 2.8, 95% CI:1.5–5.2, $P = 0.002$)], vomiting[(OR:8.1, 95% CI:1.4–45.2, $P = 0.018$) and coughing in the reaction history increased the risk for actual drug allergy in multivariate regression analysis.

Conclusion: One third of the patients who were tested for suspected drug allergy were diagnosed as drug allergic in a tertiary allergy clinic in Turkey. Higher frequency of atopy and food sensitisation in patients with drug allergy might point a tendency of atopic individuals to hypersensitivity to drugs. Angioedema, vomitting and coughing in history were associated with actual drug allergy after diagnostic work up.

1448
Clinical characteristics of adverse reaction to iodinated contrast media

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Background: Adverse reactions to iodinated contrast agents (MCI) are uncommon since the appearance of nonionic low-osmolality contrast media. The aim of study was to describe the clinical characteristics of adverse reactions to MCI referred to an Allergy Service in 2012.

Method: Retrospective study of all patients referred to an outpatient clinic reporting a history of adverse reaction to MCI ($n = 82$). Variables such as age, gender, atopy, type of MCI used, radiological imaging, severity and clinical characteristics of reactions (based on Contrast Media Manual of the American College of Radiology, 2012) and results of skin tests (prick test, intradermal and / or patch) were analyzed.

Results: Eighty two patients reporting a history of adverse reaction to MCI were referred to our outpatient clinic. The reactions were more frequent in women (54.8%); median age was 59 (range: 21–85 years), and 20% had atopy. Iohexol was administered for computed tomography (78%) and Iodixanol for coronariography (11%) and urography (11%). The total number of reactions was: 18 to Iodixanol (12 immediate and six delayed) and 64 to Iohexol (35 immediate and 29 delayed). The reactions were: mild (70%), moderate (15%) and severe (15%). Clinical symptoms were: cutaneous 60% (rash, urticaria, angioedema and/or pruritus), nonspecific 24% (nausea, vomiting, dizziness and hot flushes) and systemic 14% (anaphylaxis, dyspnea, chest pain and loss of consciousness) of cases. One subject with anaphylaxis had positive skin testing (prick and intradermal test) to Iohexol (1.6%). Another patient suffered from exanthematous pustulosis caused by Iodixanol and confirmed by histopathology skin biopsy.

Conclusion: Adverse reactions were more frequent to Iohexol and the severity of reactions was associated mainly to Iodixanol. IgE mediated reactions were uncommon.

1449
Non-inmediate exanthematics reactions to non-steroideal antiinflammatory drugs: 3 years study

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Background: NSAIDs are the most important group of drug involved in hypersensitivity drug reactions. This can be IgE dependent (immediate), T cell-mediated (non-immediate) or cross-intolerant. The prevalence of delayed-type reactions to NSAIDs is not well known. The objetive was to study the non-immediate exanthematics reactions to NSAIDs.

Method: A retrospective and descriptive study was performed in the Allergy Unit from Gregorio Marañón Hospital (Madrid, Spain) from January 2010 to December 2012. Clinical records were analyzed from all patients with suspected hypersensitivity reactions to NSAIDs

Results: We studied 2451 adults patients to referred our Service with a suspected drug allergy reactions, 688 (28.07%) to NSAIDs, confirming 434 (63.08%) of which were immediate 225 (51.84%), cross-intolerant 138 (31.87%) and non-immediate 71 (16.35%) of which (78.8% female and 21.2% male). Exanthema occurred in 45 patients (63.38%), Urticaria-angiodema 18 (25.35%), and SCARs 8 (11.26%): Vasculitis 4, Steven-Jonhson syndrome 2, DRESS 1 and Multiform Exudative Erythema 1. In all patients challenges were carried out in order to confirm tolerance to other NSAIDs. The reactions were caused by metamizol in 29 (40.84%), followed by ibuprofen 20 (28.16%), diclofenac 6 (8.45%), paracetamol 5 (7.04%), etoricoxib 3 (4.22%), dexketoprofen 3 (4.22%), naproxen 3 (4.22%), AAS 1(1.40%) and piroxicam 1 (1.40%). The diagnostic test realised were positive in 17 patients (23, 94%), skin test positive in 12 (16.90%), nine intradermal reaction (all to metamizol) and three in patch test (one metamizol, one etoricoxib and one paracetamol). In five patients the oral challenge test was positive.

Conclusion: Exanthematics reactions are the most frequent non-immediate adverse reactions to NSAIDs, the severe reactions are rare. Pyrazolones are the most frequent NSAIDs implicated. The sensitivity of skin test is low; therefore clinical history and tolerance confirmation to other NSAIDs can be needed to achieve the diagnosis.

1450
Urticaria as a presenting symptom in patients with history of hypersensitivity to non-steroidal antiinflammatory drugs: can hypersensitivity predict future development of chronic urticaria?

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Background: Non-steroidal antiinflammatory drugs (NSAIDs) represent one of the most frequent causes of drug-induced urticaria/angioedema worldwide. Almost 30% of patients with chronic urticaria (CU) develop hives after ingestion of NSAIDs.
Method: In the first part – retrospective analysis we reviewed data of all patients that were tested for NSAID hypersensitivity and had positive history of NSAID intolerance from 1.1.2007 to 31.12.2010 at our clinic (medical data from medical database BIRPIS). Among those we focused on a group of patients who had urticaria as a leading symptom of hypersensitivity reaction to NSAID. We also conducted a follow up part of the study in which we interviewed patients after a 5 year period, to establish if during this period they had had any symptoms of chronic urticaria.
Results: In a 4-year period we tested 569 patients (387 women – 68%, 182 men – 32%) with positive history of hypersensitivity to NSAIDs. Among all tested subjects 324 patients (56.9%) had a history of urticaria as a leading symptom of reaction. Among these, 98 patients (30.2%; 62 women and 36 men) had a history suggesting existing chronic urticaria (but none with previously confirmed diagnosis of CU) prior or soon after the reaction (but before testing) to single or multiple NSAIDs. The most frequently reported drug that caused urticaria was naproxen, followed by ASA paracetamol. We tested all of these patients with one or more NSAIDs. Eighty-six patients (78.8%) had negative tests and only 12 positive. In patients that had negative tests the most frequently used drug was paracetmaol and least used drug were pyrazolones. The drug that most frequently provoked hypersensitivity reaction was ASA.

All patients, with urticaria as a presenting symptom of NSAID hypersensitivity, tested during this period are now enrolled in a follow up study. We contacted all patients ($N = 89$) that were tested 5 years ago. We were able to interview 69 patients (77.5%). The final number of patients with no history of spontaneous urticaria prior to NSAID reaction/testing and recently reported spontaneous hives was 14 (20.3%).
Conclusion: We found important discordance between history and test results; in our group only 12.2% patients have had positive tests. In a follow up only one fifth of patients (20.3%) with no previous history of spontaneous urticaria have developed spontaneous episodes of urticaria.

1451
Compliance of NSAIDs patients to drug related instruction: a phone survey

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Background: Great effort has been made to clarify and classify hypersensitivity reactions caused by NSAIDs; however few data exist on compliance with drug avoidance and the use of alternative medications. The goal of this study is to evaluate the adherence of patients to written instructions regarding management of their NSAIDs hypersensitivity. Additionally, the incidence of urticaria in this population was appraised.
Method: Seventy-eight patients (♀ 59, mean age 48 years, range 19–84) were included in study analysis. The compliance was evaluated by phone interview using a standard questionnaire with specific parameters: time interval from last consultation (mean interval 25 months, range 3 month–5 years), necessity to receive NSAID, NSAID intake and specific agent used, reason of intake-accidental or intentional- and occurrence of chronic spontaneous urticaria).
Results: Fifty five out of 78 pts (70.5%) avoided all NSAIDs or have been using only paracetamol; 29/55, were instructed to use alternative NSAIDs; 12/29 were advised to use COX-2 inhibitors, 8/29 were allowed to take all NSAIDs, 7/29 had to avoid the specific culprit drug and 2/29 oxicame derivatives. Twenty six out of 55 did not complete the diagnostic procedures due to risk-benefit considerations or denial to consent and were given stricter avoidance instructions. Although several reported paracetamol to be insufficient for pain relief, they still refrained from using other medication, due to NSAID pharmacophobia. No reaction was reported following inadvertent or intentional exposure to the culprit drugs. Additionally, 3 out of 78 reported symptoms of chronic spontaneous urticaria during this period.
Conclusion: In their majority, the patients in our population disregarded the written instructions and -spurred by a fear of reaction- refrained from using allowed medication. Effective patient-doctor communication is of cardinal importance in an effort to improve adherence and therefore, the patients' quality of life. Accordingly, a simple but concise explanation of the reasoning behind said instructions will go a long way into improving the patients compliance to them.

1452
Ceftriaxone induced non-serious adverse drug reaction in 11-year-old male patient

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Background: This report was received from a nurse via Medicines and Medical Devices Agency of Serbia on 2012-December-05. Medicines and Medical Devices Agency of Serbia assigned the following number to the case: 515-00-04539-2012-2.
Method: Case report.
Results: A 11-year-old male patient receoved Azaran (INN: ceftriaxone) [(MAH: Hemofarm A.D.) 1000 IU daily intramuscular from 2012-Nov-20 to 2012-Nov-20 for infection (high C-reactive protein, high leukocytes)].

On 2012-May-12 he developed itching eyes, itching mouth, itching skin, without hives. The patient complained that it was very hot.

The outcome of the event was reported to be recovered.

The patient′s medical history included the same reaction to the sting axis.

Concomitant medication was not reported.
Conclusion: This case was classified as non-serious.

1453
Formulation and evaluation of Tramadol hydrochloride transdermal patches for pain management

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Background: Tramadol is a potent analgesic offering many advantages over conventional opioids and non-steroidal antiinflammatory

drugs. Transdermal drug delivery systems are topically administered medicaments in form of patches that deliver the drug for systemic effects at a predetermined controlled rate.

Method: In this work, Tramadol was formulated in different polymeric transdermal patches, using hydroxyl propyle methyl cellulose,eudragite E po and sodium alginate all formulae were evaluated for their physicochemical properties, In-vitro release profile and the drug permeation patches through the skin was tested and as whole released amount of drug from the device couldn't permeate the skin barrier different types penetration enhancers were added to selected formulae H1 which showed highest release and excellent physical properties. Finally the pharmacological efficiency of the best transdermal patch was evaluated on female wister rats using hot-plate test.

Results: HPMC films attained excellent tensile strength and good flexability. H1 has the highest tensile strength (5.03 ± 0.39 N/mm^2) and very satisfactory flexibility and elasticity. The formula which contains lecithin in a concentration of 20% w/w showed the highest permeation extent of a cumulative amount permeated at 24 h and thus it was selected for further pharmacodynamic evaluation on living rats, which showed a gradual increase in the analgesic effect till reaching its peak followed by a period of maintenance effect till 36 h the effect then began to decline.

Conclusion: This would be advantageous as it prevents drug plasma peaks responsible for more severe adverse effect like drug abuse and providing controlled pain relief.

Poster Session 63

Drug allergy: diagnosis and pathomechanisms

1454
Biselective non-steroidal antiinflammatory-drug-induced-reaction: Case report

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Background: Non-steroidal antiinflammatory drug (NSAID) are a major cause of adverse reactions. When they occur, it is usually the result of an intolerance to NSAIDs (reaction with cross-reactivity between different chemical groups-constituting 70% of cases) or an hypersensitivity to NSAIDs (selective reaction to one NSAID with tolerance to others, 30% of cases). We present a case of a patient with hypersensitivity to two different potent inhibitors of COX-1 administered parenterally.
Method: A 65 year old man with history of nephrolithiasis and renal colics, experienced, on two separate occasions, generalised urticaria. The first episode occurred after diclofenac and dypirone intramuscular (im) administration and the second after dexketoprofen im administration. Wheals lasted 3 days and required corticosteroid and antihistamine treatment. He currently tolerates ibuprofen and paracetamol.

Skin tests were performed with diclofenac (Prick: 25 mg/ml; Intradermal: 1 mg/ml–2.5 mg/ml) and dypirone (Prick: 1:10 and 1:100 intradermal with metamizol 400 mg/ml).

A single-blind, placebo-controlled oral challenge (SBPCOC) and parenteral challenge (PC) was carried out after obtaining written consent with:

1 Diclofenac: day 1 (25, 50 mg every 60 min, 120 min of observation); Day 2 (75 mg im, 180 min of observation).
2 Dypirone: day 1 (doses of 10, 50, 125 and 250 mg every 30 min, and observation of 120 min); Day 2 (575 mg single dose); Day 3 (2 g im, 180 min of observation)
3 Dexketoprofen: day 1(12.5, 12.5 and 25 mg every 60 min, 120 min of observation); Day 2 (50 mg im, 180 min of observation).

Results: Skin tests with diclofenac and dypirone were negative. SBPCOC and PC to diclofenac were negative SBPCOC to dypirone (day 1 and 2) were negative. PC to dypirone (day 3) was positive (pruritic papular rash 8 h after administration). Reaction resolved in 3 days with steroids and antihistamine treatment. SBPCOC to dexketoprofen (day 1) was negative. PC to dexketoprofen (day 2) was positive, presenting a non-itchy rash on forearms 4 h after administration.
Conclusion: We have demonstrated a selective reactivity of two non-structurally related NSAIDs (pyrazolones and propionic derivate) with tolerance to other groups belonging to this family of drugs.

1455
Allergy to insulin: a case report

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Background: Since human insulin and its analogues have been introduced, insulin allergy is rare, reported in only 0.1–2% of all patients treated with insulin. As a high-molecular-weight protein, insulin induces mainly type I hypersensitivity reactions, which can range from local erythema to anaphylaxis and death.
Method: The authors describe a case of a 32-year-old caucasian female, with thrombophilia, chronically treated with enoxaparin, that developed *Diabetes mellitus* during pregnancy and needed to start treatment with insulin at 22 weeks of gestation. She initiated Humalog™ (insuline lispro) in the morning and Insulatard™ (insuline isophane) at night. After 4 weeks of treatment, she noted the onset of a pruritic and erythematous papule (2 cm diameter), arising within 2–3 h at the site of subcutaneous administration of both types of insulin. The papule lasted for 24 h and disappeared without a skin mark. Splitting of the dose, changing the needles and the injection sites were not successful in resolving the reaction. Glycemic levels were controlled and the patient used both insulins until delivery at 38 weeks. *Diabetes* disappeared after pregancy. In this moment she was referred to our Immunoallergy Department.
Results: Skin tests were performed with several different types of human insulin and insulin analogues, including Humalog™ and Insulatard™. Prick tests to insulins and latex were negative. Intradermal tests were positive to Insulatard™, Humalog Mix™, Insuman Basal™, Noxomix 30™ and Humulin M3™ (all protamine-containing insulins); were doubtful for Humalog™, Novorapid™ and Mixtard 30™; negative to Actrapid™. Specific IgE to: human, bovine and porcine insulins were positive, negative to latex and protamine. Patch tests with these insulins were negative. These results establish the diagnosis of a IgE-mediated hypersensitivity to human insulin and insulin analogues lispro and aspart. A potential hypersensitivity against excipients was excluded only to protamine because other allergic documented excipients are not available in our hospital to be tested, as metacresol and zinc.
Conclusion: This case corroborates the allergenic potential of insulin analogues. Also shows the difficulty in the management of insulin allergy due to the inability to test all the components of the commercial preparations. Many times ongoing treatment with insulin is essential and these patients should involve a multidisciplinary team.

1456
Allergy to bendamustine

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Background: Bendamustine is an antineoplastic agent, used as monotherapy or in combination with other agents to treat chronic lymphocytic leukemia (CLL) and B-cell non-Hodgkin lymphoma. There are just a few reported cases of adverse reaction to bendamustine, none of them with an allergological study.
Method: A 61-year old woman, diagnosed with CLL. She began treatment with bendamustine, which was adequately tolerated in its first cycle. Three weeks later, she received the second cycle of bendamustine. Eight hours after it she had throat discomfort and later on she presented pruritus,

hives, generalised erythema and facial swelling. She was treated with 60 mg of intramuscular metilprednisolone at the emergency room and she was prescribed a daily intake of oral antihistamines and oral corticosteroids for 4 days. The symptoms disappeared within the first 24 h, without residual skin lesions.

Results: We performed skin-prick and intradermal testing with immediate and delayed lectures (24 h and 72 h). Skin-prick tests were done at 1 mg/ml concentration and intradermal tests at 0.001, 0.01, 0.1 and 1 mg/ml concentration.

Our patient had negative skin-prick tests and a negative immediate lecture of the intradermal tests. The 24 h lectures of the intradermal tests were negative at 0.001 and 0.01, but positive at 0.1 and 1 mg/ml, which were negative 72 h later.

Two control subjects, suffering from CLL and being treated with bendamustine, had negative skin-prick tests and intradermal testing.

Conclusion: We report the first case of hypersensitivity to bendamustine with a positive result in the allergological study carried out. This study demonstrates a delayed cutaneous hypersensitivity to bendamustine.

1457
Fixed drug eruption due to clarithromycin with good tolerance to azithromycin

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Background: Macrolides are antibiotics safes and usefules for both upper respiratory tract and skin infections. Adverse reactions, and specially fixed drug eruption (FDE), to this group of antibiotics are very rares.

Method:

Case report: A 14 – year-old woman, was treated for respiratory infection, with clarithromycin. Four hours after ingestion of the first tablet she developed erythematoviolaceous and pruritic macules on the thorax, abdomen and arms with local residual hyperpigmentation, requiring urgent attendance. Three months later, she experienced another similar reaction, at the same localisation, after a new intake of clarithromycin 200 mg. The patient's symptoms cleared in 1 week with corticosteroids treatment. She had previously tolerated this antibiotic. Later she has tolerated azithromycin. Six months later, after the mother of patient had given written informed consent, an allergy study was carried out. Epicutaneous patch tests were performed on the upper back and on previously involved skin using different macrolides antibiotics. The drugs were prepared by the Pharmacy's Department of our hospital:

1 clarithromycin and erythromycin at 10% concentration in dimethylsulfoxide,
2 roxythromycin and midecamycin at 10% concentration in petrolatum. We used petrolatum and dimethylsulfoxide as negative controls.

Results: Positive results to clarithromycin (3+) and, erythromycin (2+) on affected skin, were noted at 96 h. Patch tests were positives (1+) on unaffected skin to clarithromycin and erythromycin. A negative result was obtained for roxythromycin and midecamycin. Controlled oral challenge with another macrolides, with negative or positive result in patch tests, was not carried out, because the mother of patient denied the consent.

Conclusion: We report a rare case of clarithromycin-induced fixed drug eruption. Patch test on affected skin has proved useful for etiologic diagnosis in our case. The results of patch test suggest a cross-sensitisation pattern between clarithromycin and erythromycin, which has not been confirmed by oral challenge test. Good tolerance to azithromycin be explained by their different molecular structure.

1458
Hypersensitivity to nabumetone. Reactivity with naproxen

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Background: Nabumetone is a non-steroidal antiinflammatory drug (NSAID) which active metabolite is structurally similar to naproxen. This active metabolite inhibits the cyclooxygenase enzyme and preferentially blocks COX-2 activity so it is a safe alternative in patients with intolerance to NSAIDs. Hypersensitivity selective reactions to nabumetone are uncommon.

Method: We present three cases of urticaria-angioedema after the intake of nabumetone. Patient 1: A 42-year-old woman, with no known allergies, had been treated with nabumetone for artrosis; 90 min later developed pruritus and angioedema in her lips and urticarial in abdomen, brest and legs.

Patient 2: A 35-year-old developed 6 h after the intake of 1 g de nabumetone, pruritus and erithema in face, neck and thorax with lips-angioedema.

Patient 3: A 67-year-old woman presents a generalised urticaria 6 h after the treatment of 1 g of nabumetone.

After the patients gave written consents we performed a single-blind oral challenge test (OCT) with nabumetone (250, 500 and 1000 mg) at gradually increasing doses at 1-h intervals.

To investigate the cross-reaction patterns with other NSAIDs we performed an OCT with aspirin (1000 mg) and considering the similar structure between naproxen and nabumetone also with naproxen (125, 250 and 500 mg).

Results: The OCT with nabumetone was positive in the three cases. All patients tolerates aspirin. Patient 1 and 2 tolerates naproxen. OCT with naproxen was positive in patient 3.

Conclusion: The clinical manifestations, the reproductibility of the symptons with the re-exposure to nabumetone suggests an immunological mechanism. The similarity of the chemical structure to naproxen and the active metabolite of nabumetone could be the reason for cross- reactivity between both but in our cases two patients tolerates naproxen. We think this serie is too short to extrapolate the results to other possible cases of hypersensitivity to nabumetone. We decide avoid both drugs (naproxen and nabumetone) in the three patients for its safety.

1460
Acute generalised exanthematous pustulosis caused by amoxicillin and clavulanic acid: a case report

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Background: Acute generalised exanthematous pustulosis (AGEP) is a rare cutaneous reaction characterised by fever and a generalised pustular skin eruption that occurs mostly after exposure to drugs, and less commonly, viral infections or heavy metals such as mercury. It is a self-limited disorder that resolves within 1–2 weeks. We report a case of AGEP after the intake of amoxicillin-clavulanic acid and we underline the importance of patch tests for the confirmation of the causative drug.

Method: A 37-year-old female patient was admitted to the hospital complaining for fever (up to 40°C) and papular pruritic skin rash affecting the trunk and limbs which had appeared 12 h prior to admis-

sion. The patient was under treatment with amoxicillin-clavulanic acid due to periodontitis. The patient's clinical assessment revealed numerous erythematous, non-follicular pustules (<5 mm in diameter), painfull lymphadenopathy and tachycardia. Physical examination was otherwise normal. Laboratory investigations showed mild leukocytosis (WBC: 11 800/mm^3). Serologic screening for Epstein- Barr virus, cytomegalovirus, hepatitis B virus, parvovirus and mycoplasma was negative. Bacterial culture of the pustule and blood revealed no growth of microorganisms and mercury serum levels were below toxic levels. A skin biopsy was consistent with AGEP. After the admission to the hospital treatment with oral methylprednisolone 0.5 mg/kg/day and cetirizine were initiated. On the second day of admission, she became afebrile and pustular lesions started to resolve. Oral methylprednisolone was discontinued with gradual tapering.

Results: Two months later, she was examined to allergy outpatient clinic and performed patch tests to b-lactam antibiotics. We conducted tests to cefuroxime, penicillin, amoxicillin, ampicillin and amoxicillin-clavulanic acid diluted at 10% in petrolatum and negative control (petrolatum). The results were strongly positive for ampicillin, amoxicillin and amoxicillin-clavulanic acid, weakly positive for penicillin and negative for cefuroxime and control. One month later the patient underwent provocation test to cefuroxime which was negative and written instructions were given about which antibiotics should be avoided.

Conclusion: AGEP is a result of delayed-type IV hypersensitivity reaction mainly in drugs. Patch tests are a very useful and safe diagnostic tool in determing the culprit drug and making an accurate diagnosis for the patient.

1461
Selective sensitisation to penicillin V with tolerance to other betalactams

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Background: Penicillin G and V have the same betalactam ring, and penicillin V is obtained from the substitution of the phenyl acetic acid of benzylpenicillin by the phenoxy methyl side chain.

Method: Our patient was a 34-year-old man who experienced generalised urticaria after ingestion of phenoxymethylpenicillin. Skin prick tests and intradermal tests with a battery of betalactams including phenoxymethylpenicillin were tested. Specific IgE against penicillin V, penicillin G, amoxicillin and ampicillin was determinated. A single blind oral challenge was performed with phenoxymethylpenicillin, amoxicillin, cefuroxime and ceftazidime.

Results: The results of skin prick and intradermal tests with all betalactams tested were negative. Specific IgE with betalactams was <0.10 UI/ml. The results of a single blind oral challenge with phenoxymethylpenicillin was positive: 40 min after receiving 125 mg of phenoxymethylpenicillin, the patient presented generalised pruritus with hives on his back and chest. The patient tolerated an oral administration of amoxicillin, cefuroxime and ceftazidime.

Conclusion: We report a case of sensitisation to phenoxymethylpenicillin with negative results in the allergy workup. Diagnosis was based on a positive single-blind oral challenge result. The patient tolerated other betalactams.

1462
Selective allergy to cephalosporins: case series

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Background: Betalactam antibiotics are a frequent cause of drug allergy. The incidence of cross-reactivity reactions between cephalosporins and other betalactams is controversial.

Method: Patient 1: 54 years old female. Suffered anaphylaxis during the infusion of the first dosis of ceftriaxone.

Patient 2: 41 years old female. Had urticaria after the first dose of ceftriaxone.

Patient 3: 92 years old female. Presented with urticaria hours after the third dose of cefixime.

Patient 4: 39 years old male. Minutes after the administration of cefazoline in the perioperative setting, had an anaphylactic shock.

Patient 5: 16 years old female. Presented with an exanthema 2 days after an 8 days treatment with cefaclor.

Allergy study: Patients were tested with skin tests (ID), specific IgE (sIgE) (ImmunoCAP, Phadia, Sweden) and controlled challenge tests (CCT) were made based on the results of the previous tests.

Results: Patients 1–4 had negative ID with PPL, MDM, penicillin G and amoxicillin. Also sIgE was negative to penicilloyl G, penicilloyl V and amoxicillin.

Patient 1: positive ID with ceftriaxone, negative with meropenem. Negative sIgE to cefaclor. Negative CCT with amoxicillin and meropenem. Diagnosed of anaphylaxis by ceftriaxone.

Patient 2: Positive CCT with ceftriaxone, and negative with amoxicillin and cefuroxime. Diagnosed of urticaria caused by ceftriaxone.

Patient 3: negative ID to cefixime. Negative sIgE to cefaclor. Negative CCT with amoxicillin, penicillin V, cefditoren. No CCT were done due to co-morbidity. Diagnosed of allergy to cephalosporines.

Patient 4: positive ID with cefazoline, negative with meropenem, cefuroxime. Negative sIgE to cefaclor. Negative CCT with penicillin V, amoxicillin, cefuroxime, ceftriaxone. Diagnosed of anaphylaxis by cefazoline.

Patient 5: negative ID with PPL, MDM, penicillin G, cefuroxime, ceftriaxone and cefazoline. Positive sIgE to cefaclor, negative sIgE to penicilloyl G, penicilloyl V. Negative CCT with ceftriaxone and cefuroxime. Diagnosed of exanthema by cefaclor.

Conclusion: We present five cases of selective allergy to cephalosporins. Allergy to cephalosporins must be often caused by the side-chains, instead of the beta-lactam ring. In these patients, other beta-lactams must be tested in order to prevent complications in the future, derived from limitations in therapeutic options.

1463
Finger-nail onycholysis, leukonychia and acrocyanosis observed in a patient treated with valproic acid

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The authors would like to present a case of a 30-year old female patient with the symptoms of acrocyanosis together with nail changes (leukonychia, onycholysis), who has been treated with valproic acid for 3 years. Acrocyanosis is a painless condition, characterised by symmetrical discoloration of various shades of blue colour, involvimg hands, feet and face, often associated with hyperhidrosis of hands and feet and exacerbated by cold. Due to multifactorial aetiology of the phenomenon, this case may be considered as a diagnostic challenge. Valproic acid has been described as a causative factor of various skin and nail conditions, also onycholysis. On the other hand, nail abnormalities have been observed in patients with acrosyndromes (for example erythromelalgia). Capillaroscopy together with photoplethysmography revealed numerous abnormalities. The

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patient remains under the observation and monitoring of any possible signs and symptoms of connective tissue diseases.

1464
Anaphylactic reactions to ranitidine: report of two cases

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Background: Ranitidine, an H2-receptor antagonist, is among the most commonly prescribed medications for gastric-acid related disorders. Despite its wide use, anaphylactic reactions to ranitidine are seldom reported. We report two cases of anaphylactic reactions induced by ranitidine.

The first patient (case A), a 64 years old woman, received ranitidine and hydrocortisone intravenously in A&E department for a maculopapular rash attributed to amoxicillin treatment. She immediately developed anaphylaxis with hypotension, bradycardia, facial erythema and angioedema. Adrenaline was administered intravenously and the patient fully recovered in <2 h. The second patient (case B), a 67 years old woman, had taken intramuscularly ranitidine, metoclopramide and diazepam for epigastric pain. She reported immediate onset of burning sensation in oral cavity, headache, rhinorrhea, sneezing and cough while facial erythema flared up within minutes. She was treated with hydrocortisone intravenously and her symptoms subsided fully within 60 min.

Method: Cutaneous sensitivity to H2-receptor antagonists was evaluated by skin-prick(SPT) and intradermal testing (ID); 1:1000, 1:100, 1:10 and 1:1 preparations of commercially available ranitidine (25 mg/ml), cimetidine (100 mg/ml) and famotidine (20 mg/ml) were used. Accordingly, single-blinded oral challenges (OC) with alternative -negative in skin testing-agent were carried out.

Results: IDs were positive to ranitidine and cimetidine in both subjects. In ranitidine, the 0.025 mg/ml was the minimum concentration that provoked a reaction in both patients, while in cimetidine case A reacted on 10 mg/ml and case B on 1 mg/ml. In all positive tests there was a clear crescendo type of reaction that confirms their non- irritative nature. On the contrary, all performed tests to famotidine were negative. OC with famotidine were negative in both patients.

Conclusion: The clinical features, as well as the positive skin tests to ranitidine, suggest that both patients had developed IgE hypersensitivity to ranitidine. Surprisingly enough, cross-reactivity among ranitidine and cimetidine, but not famotidine, was demonstrated in both cases. In literature, only few reports of cross-reactivity among H2-receptor antagonists exist so far. To our knowledge, this is the first report of exclusive cross-reactivity between these two commonly prescribed H2-antagonists.

1465
Delayed type hypersensitivity reactions due to second line antituberculosis drugs

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Background: Non-immediate type hypersensitivity reactions due to antituberculosis drugs are rare but can be life threatening. Diagnostic evaluation is important, because of the multiple drug combination necessity and the restricted number of drugs.

Cases: Three multi drug resistant tuberculosis (MDR-TB) patients with delayed type drug hypersensitivity reactions, their and control subjects' patch test results will be presented. Allergic reactions were presented as dermatitis in two patients, toxic epidermal necrolisis (TEN) in one patient. Improvement was acquired for skin lesions after appropriate treatment. Then, patch tests were performed. 1/1 and 1/10 concentrations were applied to the dermatitis patients. In TEN patient, thiacetazone was removed from the treatment. Intra-group variation was made for the drugs which have alternatives. Then, patch tests with the decided drugs were performed with 1/100, 1/10 and 1/1 concentrations on separate days. Sixteen control subjects were also tested with the same concentrations of the drugs. Patch test results were positive for cycloserine (CYC) and amikacin (AMK) in the first and for CYC in the second dermatitis patient. Positivity were seen at 1/10 and 1/1 concentrations in these patients. In 8 of 16 control subjects CYC patch tests were positive only at 1/1 concentrations. TEN patient had no positivity in patch tests but as a result of the obligation, drugs were re-challenged cautiously with gradually increasing doses. In all of the patients, culprit drugs were stopped, a new regimen composed and drugs were given with gradually increasing doses on 2 days. TEN patient developed a generalised erythema after 45 min of first day's full dose of PAS. Reaction improved immediately after steroid and antihistamine applications. No reactions occurred with other drugs. All patients completed the therapy and cured from MDR-TB.

Conclusion: Drug patch tests guided successful therapies in a life treating disease. However they have limited efficacy in TEN. v

1466
Drug fever by bendamustine

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Background: Although bendamustine was first synthesised in 1963, scarce adverse reactions have been described so far.

Method: A 63-year old man, diagnosed with B-cell chronic lymphocytic leukemia (B-CLL) refractory to rituximab. He received treatment with bendamustine, for the first time, during three cycles. In each of the first two, he had generalised tremor and fever of 39°C, 3 h after the infusion was completed. The symptoms disappeared after treatment with acetaminophen 650 mg. About 3 h after the third cycle of bendamustine he began with generalised tremor, generalised erythema, dizziness and fever of 39°C. The symptoms were not resolved with acetaminophen as in previous reactions. At the emergency room, a blood pressure of 87/48 mmHg was verified, as well as a paroxistical auricular fibrillation and a mild renal failure. This episode ceased with acetaminophen 1 grame and an adequate hydration. The symptoms disappeared within the first 24 h, without residual skin lesions.

Results: We performed skin-prick and intradermal testing with immediate and delayed lecture. Skin-prick tests were done at 1 mg/ml concentration and intradermal tests at 0.001; 0.01; 0.1 and 1 mg/ml concentration.

The results for the skin-prick and intradermal tests, both immediate and delayed lecture, were negative. The later 24 and 72 h lectures of the intradermal tests were also negative for all the concentrations.

Two control subjects, suffering from B-CLL and being treated with bendamustine, had negative skin-prick tests and intradermal testing.

Conclusion: We report the first case of drug fever by bendamustine. The study carried out has not demonstrated a type I or IV hypersensitivity to bendamustine.

1467
Acute tongue ulcer

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Background: A single ulcer of the tongue includes different etiologic factors. Clinical differential diagnosis contains primarily traumatic ulceration, malignancies, eosinophilic granuloma, primary syphilis, tuberculosis or other unusual infections.
Case report: A 31-year-old man presented with a 5-days history of painful tongue ulcer. He was transferred to our outpatient clinic with the presumed diagnosis of a sexually transmitted disease. The patient had a history of unprotected, mutual oral sex with a prostitute about 4 weeks ago. Two weeks later the general practitioner had prescribed clarithromycin because of an incipient tonsillitis. But patient′s sore throat had deteriorated and additionally an ulcer of his tongue had developed within the next days.

Our clinical examination revealed a single ulcer, 2 cm in diameter to 4 cm in length, on the lateral border of his tongue as well as red, slight swollen tonsils. Mandibular lymph nodes were not enlarged and examination of entire skin including genitalia showed no pathological findings. Laboratory tests revealed negative results for syphilis, gonorrhoea, chlamydia trachomatis, herpes simplex and human immunodeficiency virus.

Based on the clinical picture, the clinical course of the condition and the medication history we suspected a fixed drug eruption (FDE) to clarithromycin. Therefore this drug was withdrawn.
Result: After withdrawal of clarithromycin the tongue ulcer healed without specific therapy in 14 days.
Conclusion: The diagnosis of FDE is usually made on the basis of the patient's clinical symptoms and medication history. In our patient the development of tongue ulcer and aggravation during drug therapy as well as the rapid healing after withdrawal of clarithromycin confirm the diagnosis FDE. An oral drug provocation test, the gold standard in diagnosis of FDE, was refused by the patient. The case history of tonsillitis and tongue ulcer after mutual oral sex with a prostitute was misleading in this case.

After exclusion of primary syphilis, FDE is an important clinical differential diagnosis of acute tongue ulcer. Clarithromycin must also be taken into account as a possible cause of FDE.

1469
An interesting case: clarithromycin-related anaphylaxis that developed during drug provocation test

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Background: Drug allergy is an important problem. Penicillin group antibiotics are frequent reasons of such reactions, although other antibiotics can occasionally cause such reactions too. We hereby present a case of anaphylaxis that developed during oral drug provocation. The drug was macrolide, which is a rare cause of such a reaction.
Case: 39 years-old woman applied to our clinic due to a drug allergy reaction. Past medical history revealed an anaphylactic reaction that happened 15 years ago due to intake of penadur-LA flacon (benzathine penicilline-G). Also, a dry itching and urticaria that happaned twice 3 years ago after intake of Largopen (amoxicilline) and Augmentine (amoxicilline -clavulanic acid) was also reported. To offer the patient a safe antibiotic, we planned a prick test and oral provocation tes with clarithromycine. The result was negative. Following this, oral provocation with a placebo drug was done. There was no reaction. When ¼ clarithromycine was given, a dry itching was observed after 20 min. With inspection, there was only a hyperemia on the places scratched by the patient. Then the patient was given another dose of placebo. There was no reaction. After this, another ¼ of clarithromycine was given to the patient. A generalised dry itching was observed 15 min later. Then, restlessnes, a sense of fullness in the throat, difficulty of swallowing and a sense of heaviness in the head were added to the complaints. At the beginning, TA was 140/90 mmHg. So an IV Avil amp 1 × 1 and prednol 40 mg 1 × 1 IV were administered. Oropharynx was observed as hyperemic and edematous, being prominent in uvula and soft palate. In follow-up, TA fell down to 80/60 mmHg. The sense of fullness in the throat had increased. Then, adrenalin 03 ml SC was injected and anaphylaxis protocol was applied. The patient's status became stabilised afterwards.
Conclusion: Dry itching can be an important indicator of anaphylaxis. This should alert us for allergic reactions and the oral provocation should be discontinued promptly. We should take into account the probability that clarithromycine, too, can cause anaphylaxis.

1470
Urticaria vasculitis induced by over the counter diet pills

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Background: Urticaria vasculitis (UV) is known to be associated with drugs. UV lesion are different from common urticaria. Extracutaneous manifestations could be present. Histological diagnosis include nuclear debris or fibrin deposits, with or without extravasated red blood cells. Increased weight-loss pills are available, even on line. Some of them reports dangerous effect and we know that this pills aren't subject to rigorous standards quality control.
Method: A 35 year old woman with history of intermittent rhinitis presented with a 5 days history of urticaria, fever, headaches, myalgia and arthralgia. The hives appeared in all body. They were principal painful with burning sensation. The lesions lasted >24 h. Angio oedema in hand fingers, ankle and feet was no pitting. Severe headaches and myalgia affected her daily work and fever reaches as high a 39.5°C. Our patient was taking over the counter diet pills 18 days ago and six previous days consulted by deshidratation and violaceous hives in palms, after that she suspend the pills. On physical examination revealed wheals in trunk, extremities and abdomen with muscular pain and a urticaria severity score of six. Rest of the examination was unremarkable. Complement components and antinuclear antibodies aren′t detected.

A skin biopsy from one lesion showed leukocytoclastic vasculitis. After confirm diagnosis of Vasculitis Urticaria the patient was prescribed with oral corticosteroid and antihistamines with rash remission. Due to persistence of headaches, fever and myalgia, it was added hydroxychloroquine for the treatment with remission of all the symptoms 1 month later.
Results: Urticaria vasculitis.
Conclusion: A lot of weight loss pill are available over the counter and online. Most haven't been proved effective and some may contain dangerous substances that can cause life-threatening effect. UV have been reported in association with drugs but to what we know this is the first report to UV with use of diet pills.

Several ingredients in diet pills had been reported of producing urticaria, but no one to induce vasculitis. We believe that the diagnosis of diet pills induced UV was based on the temporal relationship between intake pills and wheals lesion, systemic manifestation, histologically proven vasculitis and finally by reversal of the clinical

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signs after discontinuation of the therapy. For the other hand we have patients with urticaria who were using the same diet pills.

1471
Simvastatin induced toxicoderma

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Background: Statins are widely used for the treatment of hypercholesterolemia and prevention of cardiovascular events. They may be associated with rashes, including Stevens-Johnson syndrome, toxic epidermolytic necrosis, porphyria cutanea tarda. We describe a case of skin reaction with systemic symptoms secondary to taking simvastatin.

Method: A 43-year-old male patient with a history of hypertension, dyslipidemia, hyperuricemia, obesity. In treatment with simvastatin, olmesartan/amlodipine and allopurinol for 2 years. He came to the emergency room for intense itching on palms, soles and genitals with generalised erythema and an unusual sensation in his throat. He was prescribed antihistamines and parenteral corticosteroids, supplemented by amoxicillin/clavulanate 24 h later due to persistent pharyngeal discomfort without clinical improvement. Despite this, his symptoms worsened and required hospitalisation. He reported no problems with foods or another drugs.

Results: Total serum IgE: 876 Ku/l. Serum tryptase: 5.8 mcg/l.

Anisakis IgE: 8.96 Ku/l.

Skin lesion biopsy: lymphocytic vasculitis with presence of eosinophil, consistent with drug-induced toxicoderma.

Basophil activation test by flow cytometry: positive results to simvastatin and atorvastatin.

Skin prick and intradermal tests: Inmediate erythema response (10 mm) for simvastatin and negative for atorvastatin.

Controlled Challenge tests with: olmesartan, amlodipine, allopurinol and amoxicillin/clavulanate: negative.

Conclusion: A case of drug-induced toxicoderma in relation to simvastatin diagnosed primarily by basophil activation test.

Simvastatin and atorvastatin have previously been implicated in skin symptoms so they must be prescribed with caution.

1472
Local pustulosis induced by amoxycillin

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Background: Pustular eruption induced by drugs is an unusual disease ocurring at any age. Antibiotics have been reported as etiological agents, although betalactams have infrequently been involved. The clinical course shows a rapid onset with erythema followed by dozens to hundreds of sterile, non-follicular pinhead-sized pustules.

Method: A 24 years old male who attended to Hospital Central de la Defensa. He develops a pruritic exanthematous pustular eruption in face, lips and upper chest twice during oral amoxycillin treatment. The eruption began with erythema at least 5 h after the administration and increased during the next 12 h when pustules appeared. Duration of pustules was 7 days and later desquamation 8 days, time for resolution took 15 days.

Allergologic study: immediate and delayed prick and intradermal test with benzyl penicilloyl PPL, minor determinant mixture MDM, benzyl penicillin and amoxycillin. Patch test for amoxycillin, oral provocation and culture of material from pustules were performed.

Results: Prick test with PPL, MDM, benzyl penicillin and amoxycillin were negative in immediate and delayed lecture.

Intradermal test with PPL, MDM, benzyl penicillin and amoxycillin were negative in immediate and delayed lecture.

After 72 h amoxycillin patch test was negative.

Oral challenge with amoxycillin was positive and pustules appeared in face, lips and upper chest in the previous locations.

Culture of pustular material was negative no viruses, bacterial or fungi were found.

Conclusion: We report a case of local pustulosis induced by antibiotic betalactam, amoxycillin, confirmed by drug provocation test. We could not find any pathogenic mechanism for this accelerated allergic reaction to amoxycillin.

Poster Session 64

Advances in the understanding of the genetic variants relevant to asthma pathology

1475
Association between *TAAR6* polymorphisms and airway responsiveness to inhaled corticosteroids in asthmatics

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Background: Genetic polymorphisms may be responsible for the wide variation in responses to inhaled corticosteroids in asthmatics. The goal of this study was to evaluate the association between polymorphisms in Trace amine associated receptor 6 (TAAR6), which encodes a putative G protein-coupled receptor for trace amines inducing bronchoconstriction, and airway responsiveness to inhaled corticosteroids in asthmatics.
Method: The change in FEV_1 (ΔFEV_1) induced by 4 weeks of inhaled treatment with fluticasone propionate (1000 μg daily) was measured in 246 asthmatics. Fifteen single-nucleotide polymorphisms (SNPs) of *TAAR6* were genotyped using a TaqMan assay. The association analysis between ΔFEV_1% and *TAAR6* polymorphisms was performed using a linear regression model controlling for age, gender, smoking status, presence of atopy, and basal FEV_1 as covariates. Statistical analyses were performed using SAS v9.1 (SAS Institute, Cary, NC).
Results: Among the 15 SNPs and three haplotypes of *TAAR6*, *rs7772821* (T>G) on the 3′UTR appeared to affect ΔFEV_1. The association analysis revealed a significant association between the *TAAR6* rs7772821 T>G SNP and the inhaled corticosteroid-induced ΔFEV_1% ($P_{corr} = 0.00005$ in codominant model, $P_{corr} = 0.001$ in dominant model, $P_{corr} = 0.0004$ in recessive model). The ΔFEV_1% value of the rs7772821 T>G minor homozygotes (60.77%) was higher than the values of those harboring the rs7772821 T/G or T/T genotype (21.32% and 31.60%, respectively).
Conclusion: The *TAAR6* rs7772821 minor allele may be an important genetic factor for a good response of the airway to treatment with inhaled corticosteroids in asthmatics.

1476
Association between TLR3 polymorphism and IgG subclass deficiency in adult asthma

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Background: Respiratory viral infection is a major exacerbating factor for adult asthma. Asthmatic patients with IgG subclass deficiency suffer from frequent asthma exacerbation TLR3 binds with RNA virus and involves in antiviral defenses. We hypothesised that genetic polymorphisms of TLR3 may be associated with viral exacerbation in adult asthma
Method: 663 patients with adult asthma and 321 normal healthy controls (NC) were enrolled in a Korean cohort. Two genetic polymorphisms of TLR3 at -299698G>T (promoter) and 293391G>A (coding exon) were genotyped. IgG, M and A level were measured by immunoturbid method and IgG subclass level was determined by a single radial immunodiffusion method. All the asthma related clinical parameters were compared according to the genotype.
Results: No significant differences were noted in the genotype and haplotype frequencies of two genetic polymorphisms. Significant associations were found between -299698 G>T polymorphism and IgG1 deficiency and/or IgG3 deficiency; The patients with T allele at TLR3 -299698 G>T had significantly lower level IgG1 and/or IgG3 ($P = 0.046$, $P = 0.033$). Moreover, among the patients with IgG subclass deficiency, the patients with T allele at TLR3-299698 G>T had significantly higher prevalence of chronic rhinosinusitis and higher level of total eosinophil count. No significant associations were found with other asthma related parameters.
Conclusion: These findings suggest that the promoter polymorphism at TLR3 -299698G>T was associated with IgG subclass deficiency, which may increase viral induced exacerbation in adult asthma.

1477
Genome-wide association studies of asthma and atopic dermatitis in the Japanese population

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Background: Allergic diseases are common inflammatory diseases caused by the interaction of genetic and environmental factors. A large number of genetic studies have been conducted to determine the genetic components of allergic diseases and to discover the cellular pathways underlying them.
Method: We conducted genome-wide association studies (GWASs) of asthma and atopic dermatitis in the Japanese population.
Results: We identified a total of five susceptibility loci of adult asthma: the major histocompatibility complex (MHC) on 6p21, *TSLP-WDR36* on 5q22, an *USP38-GAB1* locus on 4q31, a locus on 10p14 and a gene-rich region on 12q13. We observed the most significant association with adult asthma at rs404860 in the MHC region, which is close to rs2070600, a SNP previously reported for association with FEV1/FVC in GWAS for lung function. We also identified eight new susceptibility loci of atopic dermatitis with genome-wide significance: *IL1RL1-IL18R1-IL18RAP*, the MHC region, *OR10A3-NLRP10, GLB1, CCDC80, CARD11, ZNF365* and *CYP24A1-PFDN4*. We also replicated the associations of the *FLG, C11orf30, TMEM232-SLC25A46, TNFRSF6B-ZGPAT, OVOL1, ACTL9* and *KIF3A-IL13* loci that were previously reported in GWAS of European and Chinese individuals and a meta-analysis of GWAS for atopic dermatitis.
Conclusion: Candidate genes in the susceptibility loci suggest roles for epithelial barrier functions, innate-adaptive immunity, IL-1 family signaling, regulatory T cells

and the vitamin D pathway in the pathogenesis of allergic diseases. Interestingly, the *IL1RL1*, *HLA*, *IL13* and *C11orf30* regions are overlapping susceptibility loci among atopic dermatitis and asthma. Although a more complete collection of associated genes and pathways is needed, biologic insights revealed by GWASs improve our understanding of the pathophysiology of human allergic diseases. Further cross-disciplinary studies combining genetics, proteomics, bioinformatics, immunology, epidemiology, and clinical allergology are necessary for translation of research into clinical practice. It is anticipated that the cross-disciplinary studies will help to protect humans from developing allergic diseases and provide molecular targets for therapeutic intervention.

1478
Associations between asthma traits and vitamin D pathway genes in Hong Kong Chinese children

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Background: In recent years, epidemiological studies suggested that vitamin D pathway plays an important role in mediating asthma and allergy. After dietary intake or cutaneous production, vitamin D is metabolized to its major circulating stable form 25(OH)D by *CYP27A1* in liver or *CYP2R1* in microsome and further to 1α, 25 $(OH)_2D$. This active vitamin D is transported to blood vessel and then nuclei by the group-specific components vitamin D binging protein (GC:VDBP) and binds to vitamin D receptor (*VDR*). This study investigated the genetic associations between asthma phenotypes and single-nucleotide polymorphisms (SNPs) of vitamin D pathway genes.
Methods: Twenty SNPs from the above four genes were genotyped in 914 asthma and 1231 non-allergic controls, who were all southern Chinese in ethnicity.
Results: Two previous association studies which were carried out in northern China reported two common GC functional SNPs, rs4588 and rs7041, and one *VDR* SNP rs7975232 to be associated with asthma. Only rs7041 was found associated with asthma under recessive model ($P = 0.049$). A novel SNP rs645163 in *CYP27A1* has association under additive ($P = 0.018$) and dominant ($P = 0.022$) models. None of these remained significant after Bonferroni correction. A GC haplotype rs2282679-rs4588-rs7041 showed different frequencies between asthma and control. The wild-type ACT is more common among asthmatics (0.436) than controls (0.395) ($P = 0.007$) whereas ACG is protective against asthma (0.289 vs 0.327; $P = 0.008$). Forced expiratory volume in 1 s (FEV_1) was associated with rs7935792 in *CYP2R1* under recessive model among 458 asthmatics, adjusted for age, sex and inhaled steroid usage as covariates. Subjects homozygous for minor alleles had significantly higher FEV_1 ($108.2 \pm 26.8\%$) than those with wild-type alleles ($91.7 \pm 17.3\%$) and the heterozygote ($90.9 \pm 18.2\%$) ($P = 0.002$). The same haplotype under recessive model was also associated with forced vital capacity (FVC) ($P = 0.014$), although such did not satisfy Bonferroni correction. Significant associations were also found between FEV_1/FVC and three other *CYP2R1* SNPs.
Conclusions: This study detects an association between a novel SNP in *CYP27A1* and lung function but not asthma diagnosis in Chinese children. We suggest to measure serum vitamin D levels in order to better understand the relationship between asthma and vitamin D.
Funding: Direct Grant for Research and Research Committee Group Research Scheme (3110087), CUHK

1481
Association of ADAM33 gene polymorphisms with asthma in Turkish children

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Background: A disintegrin and metalloprotease domain 33 (ADAM33) is the first asthma-susceptible gene discovered by positional cloning. The objective of this study was to determine the association between ADAM33 polymorphisms and asthma in Turkish children population with asthma.
Method: Four single nucleotide polymorphisms (SNPs) previously reported to be related with asthma were genotyped in 98 cases and 100 controls. The genotyping procedure consisted of polymerase chain reaction (PCR) amplification and SNP detection of the 12433 T/C (T1), 12462 C/T (T2), 12540 C/T (T + 1) and 12601 T/G (T + 2) variants of ADAM33 gene.
Results: No significant differences were observed for T1, T2, T + 1 and T + 2 polymorphisms between asthmatic patients and controls. There was also no difference between atopic and non atopic asthma group by means of ADAM33 polymorphisms.
Conclusion: Our data revealed that there is no association of these four SNPs of ADAM33 gene with asthma in Turkish children population.

1483
Association analysis of glucocorticoid receptor and corticotropin-releasing hormone receptor 1 gene polymorphisms with asthma in the Volga-Ural region of Russia

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Background: Glucocorticosteroids (GCs) are currently the most effective antiinflammatory medications for the treatment of asthma. Studies have demonstrated their efficacy in reducing asthma symptoms, controlling airway inflammation and improving quality of life. GCs exert their therapeutic effects by binding and forming a complex with the intracellular GC receptor. This complex is activated and translocates into the nucleus to directly alter transcription of genes involved in inflammation. The aim of the study was to investigate the association of gene polymorphisms with the susceptibility to asthma and determine whether variants in the genes of glucocorticoid receptor *[GR (rs41423247)]* and corticotropin-releasing hormone receptor 1 *(CRHR1 (rs242939, rs1876828)* are associated with clinical response to inhaled corticosteroids treatment.
Method: A total of 1137 unrelated participants of Russian, Tatar and Bashkir ethnic groups were recruited, including 702 patients with asthma and 435 non-atopic individuals from the Volga-Ural region of Russia. Data were analyzed using the chi-square test.
Results: SNP *rs41423247* in the *GR* gene have been found to be associated with severe asthma in Tatar ethnic group. The higher frequency of allele *rs41423247*G* was revealed in the patients compared with controls ($P = 0.02$; OR = 1.29; 95% CI 1.10–3.34). We found significant association of *rs1876828*C/T* genotype and *rs1876828*T* allele in the *CRHR1* gene with decrease FEV1 (forced expiratory volume in 1 s) and VC (*vital capacity*) in patients. The frequencies of genotype

*rs1876828*C/T* and allele *rs1876828*T* were increased in asthmatics with FEV1 <60% predicted ($P = 0.002$; OR = 2.14; 95% CI 1.31–3.50 and $P = 0.03$; OR = 1.63; 95% CI 1.04–2.54, accordingly) and in patients with VC <60% predicted ($P = 0.002$; OR = 2.31; 95% CI 1.24–3.98 and $P = 0.008$; OR = 1.90; 95% CI 1.18–3.08, accordingly) compared to controls. Allele *rs1876828*T* in *CRHR1* gene was associated with asthma in Russian ethnic group ($P = 0.03$; OR = 1.68; 95% CI 1.04–2.73). The frequencies of genotype *rs1876828*C/T* and allele *rs1876828*T* were increased in Tatar patients with severe asthma compared to controls ($P = 0.01$; OR = 3.05; 95% CI 1.24–7.50 and $P = 0.04$; OR = 2.34; 95% CI 1.03–5.29, accordingly).

Conclusion: These results suggest an important role for polymorphisms of GR and CRHR1 genes in the development of asthma in the Volga-Ural region of Russia.

Supported by the Russian Foundation for Basic Research, RFBR №11-04-97063.

1484
Retinoic acid activates *PTGDR* gene in A549 lung carcinoma cell line

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Background: Asthma is an inflammatory disorder of the airways, caused by the interaction of multiple genes and environmental factors. T cells and IgE-mediated responses are key factors in the development of allergic asthma. It was reported that RA could regulate the IgE production in inflamatory processes. All-trans-retinoic acid (at-RA) transactivates downstream target genes by binding to retinoic acid receptors (RARs, RXRs). RARs bind to retinoic acid response elements (RAREs) recruiting a protein complex to activate transcription. The prostanoid D receptor gene (*PTGDR*) is a G-protein-coupled receptor ubiquitously expressed that binds PGD2. It has been identified as an asthma-susceptibility gene. The objective of this work was to investigate the possible role of RA as regulator of the *PTGDR* gene transcription.

Method: MatInspector and TESS software were used for an initial *in silico* analysis of *PTGDR* promoter region. A construction of pGL3-PTGDR bearing 700 pb of PTGDR promoter region was transfected into the A549 cell line. Luciferase assays were performed using the Dual Luciferase Reporter System. Firefly luciferase measurements were normalised to Renilla luciferase measurements as a control for transfection efficiency. Cells were treated with at-RA. Real-time PCR was used to measure gene expression and Luciferase assays to analyze the promoter activity of *PTGDR*. A retinoid responsive *CYP26A1* gene, was used as positive control.

Results: Bioinformatic analysis identified RARE elements in the *PTGDR* promoter region. The expression of *PTGDR* and *RARs* in response to RA was firstly analyzed in A549 cells pretreated cells. After at-RA treatment, elevated levels of *CYP26A1* and *RAR* isoform β were detected. This increase was maintained until 48 h after at-RA treatment. The A549 cell line transiently transfected with pGL3-PTGDR bearing 700 pb of PTGDR promoter region and treated with at-RA showed an increase in the PTGDR expression of 1.5 fold.

Conclusion: The findings presented in this study suggest that *PTGDR* would be regulated by RA via RARs. As *PTGDR* is an important gene in allergic asthma these results open an interesting new insight about the mechanisms that regulate Retinoic Acid control over this inflammatory process. Further studies are underway to identify the mechanisms by which activation occurs in allergic reactions.

1485
Interleukin-1 receptor antagonist and interleukin-1 beta polymorphisms in patients with asthma in Venezuela

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Background: Asthma is a common chronic respiratory disease characterised by airway constriction and hyperreactivity, chronic eosinophilic inflammation and mucus hypersecretion, caused from the complex interaction between several genes and environmental factors. A variety of cytokines, as family of interleukin-1 (IL-1), are involved in the development of different illness. Each of the genes of the IL-1 locus on chromosome 2 is polymorphic: Interleukin 1 alpha (IL-1A), Interleukin 1 beta (IL-1B) and receptor antagonist for Interleukin 1 (IL-1RN). The functional expressions of some gene polymorphisms have been correlated with a wide range of chronic inflammatory conditions, including allergic asthma. This study was performed in order to analyze the genetic profile of IL-1B and IL-1RN cytokines in Venezuelan population.

Method: IL-1RN (intron 2) 86 pb pentaallelic Variable Number Tandem Repeats (VNTR) and IL-1B +3953 C>T (exon 5) polymorphisms were genotyped by Polymerase Chain Reaction (PCR) and Restriction Fragment Length Polymorphism (RFLP) techniques respectively in 100 asthmatics and 100 non-allergic controls with the same ethnicity. Serum total IgE level was measured by enzyme immunoassay. The strength of association between this pair of genes in patients and controls was estimated by the odds ratio (OR) after performing Fisher's exact test. Haplotypes frequencies and linkage disequilibrium were estimated using the Expectation Maximisation algorithm (ELM) implemented in the SNPalyze software package.

Results: IL-1B +3953 C/C ($P = 0.009$; OR = 0.27), and IL-1RN I/I ($P = 0.007$; OR = 0.48) genotypes in the patients group were significantly lower than controls. The frequency of IL-1B C/IL-1RN I haplotype was higher in controls in comparison with asthmatics ($P = 0.000413$).

Conclusion: Based on these results, we conclude that there was an association with the IL-1B + 3953 C>T and IL-1RN intron 2 VNTR genes polymorphisms with presence of asthma in Venezuelan population. These genetics polymorphisms could be protective for development of chronic inflammation and progression of respiratory allergic disease.

1486
Frequency of IL-10 -592 C/A single nucleotide polymorphism in asthmatic children

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Background: Interleukin-10 (IL-10) is one of the main regulatory cytokines, which have a role in regulation of humoral immune responses and is produced by Th2 lymphocytes, monocytes, and epithelial cells. IL-10, formerly recognised and cloned as a cytokine synthesis inhibitory factor, has a major downregulatory effect on the inflammatory process and is therefore considered an intrinsic regulatory protein. Polymorphism of IL-10 within coding and promoter regions could affect the expression and secretion of this cytokine.

Bronchial asthma, one of the most frequent respiratory diseases in children, represents a heterogonous disease with respect to its immunopathology, genotype, and clinical phenotypes. The single nucleotide polymorphism situated at position -592 (a C-to-A substitution) in the promoter region of IL-10 gene was investigated in this study.

Method: In our study we analyzed 497 individuals (12.71 ± 0.36 years). Gene polymorphism was genotyped in asthmatic children and healthy children with the use of polymerase chain reaction-restriction fragment length polymorphism method (digestion by RsaI).

Results: Frequency of A allele was higher in asthmatic children compared to healthy individuals (OR = 1.849; 95 CI = 1.37–2.50; $\chi = 16.06$; $P < 0.0001$). The AA genotype of interleukin 10 was more frequent among the patients (10.5%) than in healthy children (4.9%) (OR = 2.28; 95 CI = 1.12–4.69; $\chi = 5.47$; $P = 0.01$).

Conclusion: IL-10 has potent immunoregulatory and antiinflammatory activity. The variant A allele of interleukin 10 at the -592 locus was associated with decreased IL-10 expression in the *in vitro* experiment. IL-10 deficiency could therefore play an important role in pathogenesis of bronchial asthma in children.

1487
-31C/T polymorphism of the interleukin 1β gene in children with bronchial asthma

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Background: Polymorphisms in interleukin 1 gene play a role in inflammatory diseases through the possible modulation of cytokine levels. Interleukin 1β (IL1B) is a key pro-inflammatory cytokine that has been associated with chronic inflammation. IL1B is a crucial cytokine produced and secreted by many cell types after activation by biological or chemical agents. There are inter-individual differences in IL1B expression which may be due to single nucleotide polymorphisms in the regulatory regions of the gene. In our study we investigated the -31 T/C polymorphism in the regulation of the *IL1B* gene in asthmatic children and healthy subjects.

Method: We analysed 497 subjects (12.71 ± 0.36 years). Genotyping of healthy and affected individuals with bronchial athma was realised using PCR-restriction fragment length polymorphism technique. Restriction enzyme AluI was used to digest the PCR fragment of the *IL1B* gene.

Results: The *IL1B* TT genotype at position -31 was significantly higher in the patient group with bronchial asthma (45.6% in patients vs 7.6% in healthy children, $P < 0.0001$). The allele frequency of T allele was also significantly higher in asthmatic children (62.8% in patients vs 28.5% in healthy children, $P < 0.0001$).

Conclusion: The -31T/C polymorphism of interleukin 1β is located in the core promoter (a TATA box) and may affect the binding of transcription factors and thereby promoter activity. The C allele disrupts this box and reduces binding and induction; hence suggesting that the T allele may be proinflammatory because of enhanced binding of transcription factors. In consequence, the presence of T allele is associated with increase in the production of interleukin 1β and may be responsible for promotion and persistence of chronic inflammation in children with bronchial asthma.

1488
Polymorphisms in 17q12-21 region interact with pet exposure in relation to asthma presence and asthma severity

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Background: Polymorphisms in 17q12-21 region are associated with asthma across different populations, but possible gene-environment interactions have rarely been investigated. We sought to investigate the possible interaction between genes in this region and pet (cat and dog) ownership amongst Croatian schoolchildren.

Method: In a case-control study, we recruited 423 children with asthma and 414 controls aged 5–18 years. Fifty-one haplotype tagging SNPs in 17q12-21 were genotyped, including polymorphisms in six genes (*GSDMA, GSDMB, ORMDL3, IKZF3, ZPBP2* and *TOP2*). Data on pet ownership was collected using a validated questionnaire. Amongst asthmatic children, information on hospital admission due to severe asthma exacerbations was extracted from hospital notes. All asthma cases underwent spirometry.

Results: There were significant interactions between 2 *GSDMA* SNPs (rs921651 and rs8077456) and current pet ownership in relation to asthma presence. For one of these SNPs (rs921651), there was also an interaction with pet ownership during the first year of life, in that A allele homozygotes had significantly lower risk for asthma if they kept pet in home, with no effect of early-life pet ownership among G allele carriers. Amongst children with asthma, three SNPs in *ORMDL3* (rs3744246, rs4795403, rs4795404) significantly interacted with current pet ownership in relation to asthma severity (hospital admissions with asthma exacerbation). For example, carriers of the T allele of rs4795403 were at significantly higher risk of hospital admission with acute asthma exacerbation if they currently had a pet, with no effect of current pet ownership amongst C allele homozygotes. Amongst patients with asthma, we observed one significant interaction in relation to lung function (FEV_1% predicted), in that T allele carriers in *IKZF3* SNP rs9635726 had significantly better lung function if exposed to pets in early life, with no effect of pet ownership among C allele homozygotes.

Conclusion: Polymorphisms in 17q12-21 region interact with pet exposure in relation to both asthma presence and asthma severity.

1489
Sphingosine-1-phosphate – a novel mediator of airway remodelling and airway hyper-responsiveness

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Background: Sphingosine-1-phosphate (S1P), a bioactive lipid and ligand for five G protein coupled receptors (S1P1-S1P5), is a key regulator of cell trafficking, cell differentiation and immune responses. Increased concentrations of S1P have been detected in airways of asthmatic subjects and S1P has been shown to stimulate proliferation and constriction of human airway smooth muscle (HASM) cells.

The aim of this study was to investigate the effect of S1P on signalling and regulation of gene expression in HASM to elucidate its role in the pathophysiology of asthma in humans.

Method: HASM cells have been grown from bronchial biopsies of healthy individuals. Affymetrix Human Exon 1.0 ST arrays and real-time PCR have been used to determine gene expression. Intracellular signalling in response to S1P was measured using MAP kinase phosphorylation, intracellular calcium and cAMP assays.

Results: A range of selective agonists/antagonists has been verified in recombinant S1P receptor overexpression models

and used together with knock down experiments to define receptor specific responses in HASM cells. Microarray data showed that S1P potently activated gene expression in HASM cells, regulating the expression of more than 100 genes, including transcription factors, cytokines and membrane receptors and several genes known to be involved in regulation of airway remodelling and airway hyperresponsiveness. This has been confirmed for a selection of genes at the mRNA and protein level. S1P induced changes in intracellular calcium and Erk phosphorylation were required for gene regulation. Three of the five known S1P receptors are expressed in HASM cells at mRNA level: S1P1, S1P2, and S1P3. S1P induced intracellular calcium flux in a concentration-dependent manner, with $EC50 = 4 \times 10^{-9}$ M, mediated solely through S1P3 leading to induction of gene expression in HASM cells.

Conclusion: This study shows that S1P is an important activator of HASM cells and might play a key role in inducing major features of asthma such as airway remodelling and airway hyperresponsiveness.

1491
The effect of the montelukast sodium of *CysLT1R, CysLT2R* mRNA on peripheral blood mononuclear cells

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Background: Leukotrienes (LTs) are products of 5-lipoxygenase (5-LO) pathway. They are known as potent mediators of inflammation in upper and lower airways. Leukotrienes consist of two groups: LTB_4 and cysteinyl-LTs (LTC_4, LTD_4, LTE_4). The cells produce leukotrienes are nowadays well known, in this group we classify macrophages, basophils, eosinophils, dendritic cells, neutrophils and mast cells. Big number of this mediators is produced during inflammatory response. All leukotrienes have receptors that function as a G-protein-coupled receptors. Montelukast sodium is a drug for asthamitcs which is a leukotriene receptor antagonist. It inhibited IL-8 expression in U937 cells and decreased expression of urokinase plasminogen activator receptor. Montelukast also reduced secretion of metalloproteinase-9 in human eosinophils.

Aim: In this research was checked if montelukast sodium influence on the level of *CysLT1R*, *CysLT2R* mRNA.

Method: Peripheral blood mononuclear cells (PBMC), from healthy volunteers and mild asthmatics, were isolated using Histopaque ®-1077 and were grown at 5% CO2 in RPMI 1640 medium supplemented with 10% FBS and 4, 2 or 1 μM of Montelukast Sodium. After 10 min incubation total RNA was obtained using RNeasy Mini Kit and were transcibed by High Capacity RNA-to-cDNA Kit. Real-time PCR analysis was performed to check *CysLT1R*, *CysLT2R* and *GAPDH* mRNA expression on Applied Biosystems 7900HT Fast Real-Time PCR System. During reaction was used TaqMan Universal PCR Master Mix and primer set, which are commercialy available (Applied Biosystems). To analyse results was used *t*-Student test.

Results: Expression of all receptors was higher in asthmatics than in healthy volunteers. There are statistical significance in expression of *CysLT1R* for 4, 2 and 1 μM of Montelukast Sodium. There is not statistical significance in expression of *CysLT2R* in healthy and asthmatics.

Conclusion: The results are based on Real-time PCR. Asthmatics have higher level of *CysLT1R* and *CysLT2R* mRNA because of inflammatory response. Incubation with montelukast sodium during 10 min is not decreased expression of these receptor to healthy volunteers level.

Funded by Polish National Science Centre, grant nr N N402 599340

Poster Session 65

Understanding the epidemiology of asthma through the eyes of the child

1492
Investigation of children asthma prevalence in Beijing urban area

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Background: Children asthma incidence seems increasing with the change of living style in China, especially in cities, but no data available on the prevalence of children asthma in Beijing since 2000.
Method: Multi-stage stratified random cluster sampling was used to recruit children aged 0–14 years from urban area of Beijing. The unified questionnaires for the third national epidemiological survey of children's asthma were distributed to parents from representative schools, kindergartens and communities. Screening-positive children were diagnosed according to on-site interrogation, physical examination, previous medical records and supporting test results. All data were required double entry by epi-info 3.5.3 software and processed by SPSS v19.0.
Results: 14 085 questionnaires were distributed to parents, 13513 (95.9%) were completed. Totally 497 children were diagnosed with asthma (451 cases were diagnosed as typical asthma and 46 cases as cough variant asthma), and 33 children could not be made a definite diagnosis. Among the 497 children, 40.6% (202 cases) had not been diagnosed with asthma before. The overall prevalence of asthma among children aged 0–14 years old in Beijing urban area was 3.68%, and the prevalence of typical asthma and cough variant asthma was 3.34% and 0.34% respectively. The prevalence of asthma was twice as great in boys (4.80%) as in girls (2.40%). The prevalence of pre-schoolers was 5.05%, which was significantly higher than that of school-age children (3.97%) and infants (0.74%). 38.2% of the asthma children had onset during infant and toddler period. 69.4% of the 497 children still have associated symptoms in the last 2 years, the current 2-year prevalence of asthma was 2.55%. Among the 295 children had ever been diagnosed as asthma, only 46.4% had used inhaled steroids. And the usage of antibiotics reached 82%, regardless of the previous diagnosis of asthma.
Conclusion: The prevalence of asthma among children aged 0–14 years old in Beijing urban area was 3.68%. There's significant difference of asthma prevalence between children with different gender and different ages. A considerable number of children were not diagnosed in time. Treatment and management of asthma also needs to be further improved.

1493
Plasminogen activator inhibitor-1 and angiotensin converting enzyme gene polymorphisms in Turkish asthmatic children

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Background: Polymorphisms of plasminogen activator inhibitor-1 (PAI-1) and angiotensin-converting enzyme (ACE) genes have been implicated in susceptibility to asthma. In this study, we aimed to investigate whether there was any association between childhood asthma and polymorphisms of the PAI-1 and ACE genes.
Method: Two hundred and three Turkish children aged 5–15 years, including 102 asthmatic patients and 101 healthy control subjects were included in this study. Asthma group was divided into two groups as follows: Group I: Asthmatic children with positive family history for atopy (n = 53), Group II: Asthmatic children without any family history for atopy (n = 49). One hundred and 28 atopic family members were also included in the study. The insertion/deletion (I/D) polymorphism of the ACE and PAI-1 4G/5G gene polymorphisms were carried out by polymerase chain reaction.
Results: The prevalence of the PAI-1 4G allele was significantly greater in asthmatic children compared to control group ($P < 0.05$, OR: 1.64% 95 CI: 1.11–2.43) but there was not any significant relation between ACE I/D genotypes and childhood asthma. No significant difference was detected between Group I and II in terms of these ACE and PAI-1 genotypes and allele frequencies. No significant relationship was found between both gene polymorphisms and total serum IgE and skin prick test results.
Conclusion: It has been established that PAI-1 4G allele may be a genetic risk factor childhood asthma but ACE gene I/D polymorphisms do not play a role in development of asthma in the sample of Turkish children.

1494
Identifying children with persistent troublesome wheeze in childhood

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Background: Previous studies suggest the presence of different childhood wheeze phenotypes based on statistical modeling of parentally-reported wheezing.
Objective: To investigate whether joint modeling of observations from both medical records and parental reports helps to more accurately define wheezing disorders during childhood, and better characterises severity.
Method: In a population-based birth cohort (n = 1184), we analyzed data from two sources (parentally-reported current wheeze at four follow-ups and physician-confirmed wheeze from medical records in each year from birth to age 8) to determine classes of children who differ in wheeze trajectories. We tested validity of these classes by examining their relations with objective outcomes (lung function, airway hyper-reactivity, atopy), asthma medication and severe exacerbations.
Results: Longitudinal latent-class modeling identified a five-class model that best

described the data. We assigned classes as: No wheezing (NW, 53.3%); Transient-early wheeze (TEW, 13.7%); Late-onset wheeze (LOW, 16.7%); Persistent-controlled wheeze (PCW, 13.1%); Persistent-troublesome wheeze (PTW, 3.2%). Longitudinal trajectories of atopy and lung function differed significantly between classes. PTW had diminished lung function and more hyper-reactive airways compared to all other classes. We observed striking differences in exacerbations, hospitalisations and unscheduled visits, all of which were higher in PTW compared to other classes (e.g. risk of exacerbation was much higher in PTW compared to PCW [OR 3.58, 95% CI 1.27–10.09], LOW [15.92, 5.61–45.15 and TEW [12.24, 4.28–35.03]). Amongst children with a history of wheeze in the first 3 years, those with PTW were significantly more likely to have diminished lung function (sR_{aw} >1.6 kPa/s; OR = 6.48 [1.87–22.46], $P = 0.003$), eczema (OR = 4.04 [1.79–9.10], $P = 0.001$), Skin Prick Test Mean Wheal Diameter (SPT MWD – sum of all allergens) ≥10 mm (OR = 8.14 [3.22–20.62], $P < 0.001$) and had ≥3 exacerbations by age 3 years (OR = 12.38 [4.35–35.21], $P < 0.001$). Children who had three of these features (exacerbations, eczema, SPT MWD ≥10 mm and/or sR_{aw} >1.6 kPA) were at markedly higher risk to be in PTW class compared other wheezers (OR = 39.74 [8.84–178.65], $P < 0.001$).

Conclusion: We identified a novel group of children with persistent troublesome wheezing, who have markedly different outcomes compared to persistent wheezers with controlled disease.

1495
Physical activity and inactivity in relation to asthma among 16 year olds in a Swedish birth cohort study

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Background: The time adolescents spend in front of screens (TV, computers etc) increases. Time spent watching TV is often used as a marker of physical inactivity in epidemiological studies and has been associated with asthma in some studies. In addition, physical activity has been associated with both increased and decreased risks of asthma in previous studies. In this study we have examined the association between physical inactivity (e.g. watching TV, playing video/computer games or read) and moderate and/or vigorous physical activity and asthma among adolescents.
Method: In the ongoing 16-year old follow up in the birth cohort BAMSE, questionnaires were sent out to the adolescents and their parents. The adolescents were asked about how many hours the last 12 months they watched TV, played computer/video games or read per day and how many hours they did physical activities during a typical week. Parents were asked about symptoms of asthma. Asthma was defined as at least two of the following three criteria; symptoms of wheeze in the last 12 months, ever doctors diagnosis of asthma, or been using asthma medicine occasionally or regularly the last 12 months.
Results: In the total study population ($n = 2293$), 13% of the adolescents had asthma. Of the adolescents, 35% spent more than 4 h per day watching TV, playing computer/video games or reading (classified as inactive), 53% did vigorous physical activities 3 h or more per week and 29% did moderate or vigorous physical activities 7 h or more per week. Among the inactive adolescents, the proportion with asthma were slightly higher compared to the not inactive, but the difference was not statistically significant (14% vs 12%, $P = 0.139$). Among the physically active adolescents, the proportion with asthma was slightly higher among the physically active compared to the less active, but statistically significant only for the adolescents being moderate or vigorous physically active 7 h or more per week (15% vs 12%, $P = 0.009$).
Conclusion: High levels of physical activity were more common among adolescents with asthma compared to the ones with no asthma. Despite this, adolescents with asthma also tended to have higher levels of physical inactivity.

1497
Assessments of asthma control in the BAMSE birth cohort up to 12 years

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Background: The study objective was to evaluate burden of asthma symptoms and features of impaired asthma control in schoolchildren.
Method: The population-based birth cohort BAMSE was used to assess 3015 children, from birth to 12 years of age. Repeated parental questionnaires collected data on environmental exposures, lifestyle factors, asthma symptoms and treatments. Asthma was classified as controlled, partly controlled or uncontrolled according to modified GINA classification.
Results: Among children with asthma, 84% of 323 were classified as partly controlled or uncontrolled at age 8, and 53% of 329 at age 12, ($P < 0.001$). Characteristics of symptoms in these children varied significantly between 8 and 12 years, with more activity limitation (66% vs 48%, $P < 0.001$) and wheeze ≥4 times in last year (52% vs 38%, $P = 0.002$) at age 12, but less nocturnal symptoms (36% vs 82%, $P < 0.001$) and acute healthcare utilisation (15% vs 34%, $P < 0.001$) at 12 years.
Conclusion: In conclusion, the proportion of asthmatic children with impaired asthma control was high among schoolchildren. Parental reports with age-related differences in children's asthma control was seen, underlining the importance of using validated measures of asthma control in paediatric health care, with a focus on children's own perception.

1499
Wheezing phenotypes and lung function in pre-school children

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Background: Wheezing in infants and young children is a common problem. There are a few studies supporting the usefulness of pulmonary function tests in pre-school children with wheezing, or in distinguishing between episodic and multiple-trigger wheezing. In the individual patient, however, determination of lung function can help in the discrimination of common wheezing disorders from other conditions.
Objective: To determine the relationship between wheezing phenotypes and lung function in pre-school children.
Method: 47 children, aged 4–6 years, with lower respiratory tract symptoms underwent physical examination, investigation of a chest radiography and lung function tests. According to the ERS Task Force definition, multiple-trigger wheezing was defined as wheezing that shows discrete exacerbation, but also symptoms occur between episodes. Episodic (viral) wheezing was defined as wheeze in discrete episodes, with the child being well between episodes.

Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), and peak expiratory flow (PEF) levels were measured in three groups: healthy children (12 patients, mean age 5.22 years), patients with multiple-trigger wheezing (22 patients, mean age 5.28 years) and patients with episodic (viral) wheezing (25 patients, main age 5.26 years).

Results: Multiple-trigger wheezers were associated with the significant reduction of FVC, FEV(1) and PEF to compare with viral (episodic) wheezers and healthy controls. We found no association between lung function and viral (episodic) wheezing: pulmonary functions (FVC, FEV1 and PEF) in episodic (viral) wheezers were not significantly differ to compare with healthy subjects.

Conclusion: Our findings show that: (1) wheezing experience in pre-school children may be associated with lung function deficit, and (2) multiple-trigger wheezing wheezing is associated with reduced pulmonary function in pre-school children.

1500
Clinical characteristics of asthmatic children in an outclinic population: gender differences

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Background: We aimed at assessing possible gender differences in personal and environmental characteristics of an asthmatic children outpatient population.

Method: We reviewed personal histories of asthmatic children who underwent medical visits at our outpatient clinic from September 2011. Medical history was taken in a standardised way and data fed into personal computer. Out of 250 asthma patients, so far data on 66 were fed into the computer and analyzed. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS 19 release.

Results: 38 (57.6%) males and 28 (42.4%) females were analyzed, aged 9.7 ± 3.2 in males and 8.9 ± 2.8 years in females. Gestational age was 39.04 ± 1.76 in males and 38.11 ± 2.70 weeks in females ($P < .09$); birthweight was 3354 ± 503.35 in males and 3045 ± 780.07 g in females ($P < 0.05$). Exposure to maternal smoke in pregnancy was 21.1% in males and 3.6% in females ($P < 0.04$); Exposure to current maternal smoke was 28.9% in males and 7.1% in females ($P < 0.03$); Exposure to third-hand smoke was 42.1% in males and 25% in females ($P < 0.15$); Conjunctivitis was reported by 34.2% in males and 39.3% in females ($P < 0.06$); Sleep Disorders was reported by 47.4% in males and 25% in females ($P < 0.01$); Food Allergy was reported by 42.1% in males and 10.7% in females ($P < 0.04$); Gastroesophageal reflux was reported by 21.1% in males and 7.14% in females ($P < 0.12$).

Conclusion: By these preliminary analyses, pre-adolescent male children show higher exposure to passive smoking and higher frequencies of comorbidities than females. Multivariate analyses to assess the relative risks will be performed on the whole population.

1501
Correlation between young adults with asthma and obesity

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Background: Obesity is regarded as a potential risk factor for asthma. The purpose of this study was; first, to compare the Body Mass Index (BMI), FEV1/FVC ratio, low-density lipoprotein (LDL) and fat percentage between asthmatic young adults and normal control subjects; secondly, to determine the correlation between BMI, LDL and FEV1/FVC ratio in young adult with asthma.

Method: Ten randomly selected both asthmatics and normal control young adult (age between 18 and 24) subjects were recruited for this case-control study. Total body fat percentage, BMI and spirometric value were measured before and after using the inhaler. LDL from each subject was measured from 3 ml blood serum using the biochemistry analyzer.

Results: Mann-Whitney test exhibit a highly significant difference between asthma and normal in BMI ($P = 0.0016$), FEV1/FVC ratio ($P = 0.00$), LDL ($P = 0.008$) and fat percentage ($P = 0.003$) with $P < 0.05$. Correlation analysis using Sperman shows a moderate positive correlation between BMI and FEV1/FVC ratio (0.4, $P = 0.153$). Whereas, there was a low negative correlation between LDL and FEV1/FVC ratio (−0.17, $P = 0.65$) in young adult with asthma.

Conclusion: In conclusion, further study is needed to explore the positive correlation between BMI and FEV1/FVC ratio in young adult asthma.

1502
Prevalence of obesity in children with allergic asthma of recent admission to the service of Allergy and Clinical Immunology UMAE of La Raza

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Background: The association of prevalence of obesity and asthma has increased significantly, this phenomenon seems multifactorial. Obesity is considered a risk factor for asthma. It has been positive association between obesity and allergic asthma. In our country there is no conclusive data.

Material and methods: The study was conducted in patients 4–14 years of age of recently admitted to our service the diagnosis of allergic asthma. A History and Physical, examination and a BMI calculation were performed as well as the determination of the severity of the asthma.

Results: We included 244 patients diagnosed with childhood allergic asthma, Fifty two patients (21.31% $N = 244$ OR 3.6) showed some degree of childhood obesity (above the 85 percentile), 15.1% were male and 6% were female ($N = 244$). Morbid obesity was found in 40 patients (16.3%, $N = 244$ OR 0.20).

Conclusion: Our study found increased prevalence of obesity in children with asthma, with a predominance in gender, and showed a high association between the severity of asthma and increased BMI.

1503
Prevalence of allergies among children in the district of Gjirokastra, Albania

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Background: Allergies are increasing among Albanian children. For now, studies about their prevalence are exclusively focused in Tirana, the capital of Albania. This study intends to check the prevalence in Gjirokastër, one of the southern districts of Albania.

Method: This is a cross-sectional survey where participated all the children of the third and fourth level of the elementary schools of the Gjirokastër town in 2010. 313 children with a mean age of 9.34 ± 1.16 years old, 139 (44.4%) males, received a questionnaire that was filled up

by their parents. The questionnaire included ISAAC questions on ever wheezing, current wheezing, allergic diseases and allergic reactions. The data were analysed with PASW Statistics 18.

Results: 23.72% (74) had experienced at least once wheezing during their life, but only 5.81% (18) had experienced wheezing last year. 2.59% (8) answered positively to the asthma ever question, and 23.72% (74) to the allergic rhinitis ever. 18.53% respond positively to the question 'Have you ever had any severe and sudden allergic reaction?', 6.71% (21) blamed antibiotics (mostly beta-lactamides), 5.11% insect stings and 4.15% (13) different foods.

Conclusion: These were the first data on the epidemiology of asthma and allergy out the capital of Albania. Furthermore it can be seemed clearly a higher prevalence of wheezing, asthma and allergic rhinitis compared to the ISAAC findings on Tirana. Other studies could be able to identify the factors that impact these differences.

1505
Association of BMI, biomarkers, exercise and airway hyper-responsiveness among treatment-naïve asthmatic children

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Background: In previous epidemiology, obesity was one of risk factors for asthma, but the effect of obesity on airway hyperresponsiveness, exercise and inflammation biomarkers were still not clear. It is worth to investigate the relationship between obesity and airway inflammation and hyperresposiveness in treatment naïve asthma children.

Method: A total 148 newly diagnosed asthma children without using any anti-asthmatic mediation were enrolled. These children received spirometry, exhaled NO (FeNO), exercise challenge, and methacholine challenge test. Their urine samples were also collected to evaluate Leukotrient E_4 (LTE_4) levels. According to their Body Mass Index (BMI), age, gender and official standard published by Department of Health, children were divided in three groups into underweight, normal and overweight. One hundred and 10 children completed all surveys, and Chi- square and Kruskal-Wallis test were used for analysis.

Results: In 110 asthma children (age from 6 to 13 years), 15 (13.6%) of them were below weight, 70 (63.6%) were normal and 25 (22.7%) were overweight. It was 66.7% of underweight children presented with airway hyperresonsiveness and was the case of 52% in overweight children. It was significant that asthmatic children with low BMI presented with airway hyperresponsiveness than the other group ($P < 0.01$). The FEV1 value was also lower in underweight group ($P = 0.025$). The FeNO or corrected urine LTE_4 level had no significant difference in three groups ($P = 0.83$, $P = 0.341$ respectively), and not in LTE_4/FeNO ratio, either ($P = 0.631$). Although eight overweight children presented with positive exercise challenge test, the BMI value was not associated with exercise challenge ($X^2 = 4.34$, $P = 0.23$).

Conclusion: Treatment-naïve asthmatic children with low BMI presented with airway hyperresponsiveness, which is not related to inflammation markers such as FeNO or urine LTE4.

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Poster Session 66

The epidemiology of adult asthma and factors related to severe asthma

1506
IgE sensitisation to food allergens is independently associated with exhaled nitric oxide and blood eosinophils in asthmatics – results from the MIDAS study

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Background: We have recently reported an independent association of IgE sensitisation to food allergens with increased airways inflammation, assessed by the fraction of exhaled nitric oxide (FeNO), in a previous population-based study (Patelis et al JACI 2012). Similar studies have not been performed in a population of asthma subjects.
Aim: To examine the importance of IgE sensitisation to food- and aeroallergens in relation to markers of local and systemic inflammation in asthma.
Method: Within the frame of an industry-academy collaboration on minimally-invasive diagnostics (MIDAS), FeNO, blood eosinophil count (B-Eos) and IgE sensitisation to food- and aeroallergens were determined in 408 subjects with asthma, aged 10–34 years.
Results: In univariate analyses, FeNO levels were 58% higher in mould-sensitised compared to non-sensitised asthmatics ($P < 0.001$), 89% higher in furry animal-sensitised asthmatics ($P < 0.001$) and 58% higher in food-sensitised asthmatics ($P < 0.001$) than in the asthmatics not sensitised to the corresponding group of allergen. Similarly, B-Eos levels were 50% higher in mould-sensitised asthmatics ($P < 0.001$), 100% higher in furry animal-sensitised asthmatics ($P < 0.001$) and 200% higher in food-sensitised asthmatics ($P < 0.001$).

FeNO was independently related with IgE sensitisation to mould ($P = 0.012$), furry animals ($P < 0.001$) and food ($P = 0.004$), respectively, and B-Eos was independently related with IgE sensitisation to mould ($P = 0.001$), furry animals ($P < 0.001$) and food ($P < 0.001$)(Table 1) as well.

*Adjusted for the variables in the table and age, sex, height, smoking history, use of inhaled corticosteroids and antileukotrienes.
Conclusion: Independent effects of IgE sensitisation to furry animal, mould and food allergens were found on both local and systemic markers of inflammation in asthma. These novel findings indicate that both food- and aeroallergen sensitisation must be mapped to be able to fully understand the signalling of exhaled nitric oxide and blood eosinophil count. The clinical importance of these results warrants further research.

Table 1. FeNO and Beos in relation to sensitisation

Type of IgE sensitisation	Number subjects sensitised	FeNO relative increase (95% CI)*	B-Eos relative increase (95% CI)*
Mite	117	−3.5 (−19, 14)	11 (−8.3, 34)
Mold	75	24 (3.0, 50)	45 (8, 79)
Pollen	281	−6.6 (−22, 12)	−10 (−27, 12)
Furry animal	268	67 (38, 102)	48 (20, 83)
Food	148	31 (10, 55)	43 (18, 74)

1507
Influence of obesity and nasal polyps on severe asthma

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Background: Asthma is often associated with various comorbidities that can influence its control, phenotype and response to treatment. Aim of this study is to evaluate the influence of two common comorbidities (obesity and nasal polyps, NP) on pulmonary function, inflammation, asthma control and quality of life in patients with severe asthma (SA).
Method: We studied 64 patients with SA. All patients underwent spirometry and methacholine test. Asthma control was evaluated according to GINA guidelines and also by ACT questionnaire, ACQ questionnaire and PEF diary. Sputum eosinophils percentage and exhaled nitric oxide (eNO) were measured as markers of airway inflammation. Furthermore, all patients underwent ENT visit to evaluate the presence of pathology of the upper airways (in particular NP).
Results: The percentage of patients with uncontrolled asthma (according GINA guidelines) was high (46.9%): 21 patients (32.8%) were obese (BMI³30) and 55 patients (85.9%) had some upper airways diseases, 23 of them (35.9%) had NP. Obese asthmatics had a similar functional data than non-obese, but worse asthma control and quality of life index, as well as a trend to have lower sputum eosinophilia (Table), with no-difference in asthma treatment. Asthmatics with NP showed similar asthma control and quality of life index than asthmatics without NP, but worse spirometry and higher sputum eosinophilia (Table). Asthmatics with NP had the same level of therapy than others, but a higher use of intranasal corticosteroids (95.7% vs 65.9%, $P = 0.005$). In a multivariate analysis taking into account age, sex, FEV1 (% of predicted), obesity, NP and sputum eosinophilia, only the obesity predicted the lack of asthma control (OR: 5.6, CI: 1.4–22.8, $P = 0.01$).
Conclusion: In patients with severe asthma, NP is associated with increased eosinophilic airway inflammation and with worse lung function, but it has less impact on asthma control and quality of life than obesity.

Table 1. Comparison between asthmatics divided according to the presence of obesity or nasal polyposis.

	Obese ($N = 21$)	Non obese ($N = 43$)	P	Nasal Polyps ($N = 23$)	No Nasal Polyps ($N = 41$)	P
FEV1 (% pred)	76.4 ± 23.2	77.8 ± 14.6	n.s.	71.1 ± 16.7	81.0 ± 17.3	<0.05
FeNO (ppb)	23 (5.2–68.5)	28.3 (3.5–86)	n.s.	35.5 (8.6–72.5)	21.5 (3.5–86)	n.s.
Sputum Eos (%)	6.6 (0–71.2)	17.6 (0–95.6)	0.07	29.8 (0.4–95.6)	8.5 (0–84.1)	<0.05
Sp Eo > 2%	64.7%	78.9%	n.s.	90.5%	64.7%	<0.05
ACT score	16 (7–25)	21 (10–25)	<0.05	21 (10–24)	20 (7–25)	n.s.
AQLQ score	4.5 (3.0–6.2)	5.1 (2.7–6.79	<0.05	4.6 (2.7–6.6)	4.9 (3.0–6.7)	n.s.
Poorly controlled (according GINA)	15 (71.4%)	15 (34.9%)	<0.05	9 (39.1%)	21 (51.2%)	n.s.

1509
Correlation between the adiponectin concentration with oxidative stress parameters in obese adolescents with and without asthma

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Background: Through the National Health Survey (ENSANUT 2006) we know that one of every four teenagers are overweight or obese and that 9–12% of them have asthma. The association between obesity and asthma has been already studied, demonstrating the presence of low-grade chronic inflammation and increased oxidative stress as well as an imbalance of adipokines, decreased adiponectin and increased leptin.
Method: Cross-sectional study that included adolescents 11–16 years, both gender, obese and eutrophic classified based on their body mass index (BMI) as eutrophic (BMI PC 5–84) and obese (BMI PC >95) with and without asthma (mild intermittent asthma, GINA 2006). After the signature of assent and consent underwent medical history, anthropometry parameters, spirometry and blood samples for triglycerids, cholesterol, HDL-cholesterol, LDL-cholesterol, glucose, insulin, adiponectin, leptin and oxidative stress parameters (malondialdehyde, glutathione peroxidase and paraoxanasa-1).
Results: We recruited 260 patients with a mean age of 12.23 (1.72 + DE) classified into four groups: eutrophic nonasthmatic (ENA) 89 (34.2%), b) eutrophic asthmatic (EA) 71 (27.3%) of these 56.20% where male and 43.7% female; c) nonasthmatic obese (NAO) 56 (21.5%) and obese asthmatic (OA) 44 (16.9%) of these 58% where male and 42% female. The correlation between the ratio of weight, BMI and anthropometric and metabolic parameters obtained, specifically triglycerides, HDL-cholesterol and VLDL-cholesterol were statistically significant when comparing ENA and EA vs NAO and OA ($P < 0.05$ ANOVA). Regarding adipokines, we only found a statistically significant difference when comparing leptin among the four groups, as the analysis of the values obtained in oxidative stress tests were not considered statistically significant ($P = 0.05$ ANOVA).
Conclusion: We found no correlation between adiponectin with oxidative stress parameters. The leptin concentration in OA was inversely proportional to the malonaldehyde. All obese studied had hypertriglyceridemia, low HDL-cholesterol, and leptin increased compared with normal weight adolescents.

1510
A birth cohort study in the southeast part of Turkey evaluating wheezing phenotypes

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Background: The purpose of this study is to identify the frequency of wheezing cases and the associated risk factors in infants during first year of life in Adana.
Method: Physical examination records within the first day after birth as well as the family demographics and history information through surveys were collected for all infants born in 2010. Physical examinations of all infants were made during their visits after 3rd, 6th and 12th months. Information on nutrition levels, infection history and changes in home conditions were also recorded in each of these visits. Moreover, skin test was applied on all infants after 6 and 12 months, in which blood samples were taken to measure food specific IgE concentrations. In order to clarify the etiology in infants with recurrent wheeze, complete blood count was taken, peripheric blood smear examination was made to check eosinophil and serum immunoglobulin levels, sweat test was conducted and when necessary thorax CT scan was analyzed. Wheezing phenotype was determined based on European Respiratory Society's report
Results: A total of 1377 infants were included in the study. Within the follow-up period of 1 year, wheezing was observed in 16% ($n = 220$) of cases. Among these cases, 94% ($n = 206$) were viral induced (episodic), 6% ($n = 14$) were multiple trigger wheezing and 17% ($n = 37$) were recurrent. We observed that the risk of wheezing and viral induced wheezing is higher in patients with a history of lower and upper respiratory tract infections. Recurrent wheezing was found to be more prevalent among infants living in large households. A statistically significant relationship ($P < 0.05$) was observed between multiple trigger wheezing and variables such as the period of breastfeeding, presence of atopy history in the family, maternal smooking, birth season and presence of atopic dermatitis. Term birth, pet breeding, and having birth in summer and winter seasons were among the protective factors that reduce the risk of wheezing.
Conclusion: Our study is significant for being the first study in Turkey on prevalence of wheezing in this age group. Monitoring of the infants included in this study is still continuing. For early treatment and prognosis, it is important to clarify the etiology of patients that suffer from wheezing in early.

1511
Prevalence of doctor diagnosed asthma and its association with quality of lifestyle and smoking habits among adult population in Barrackpore area in West Bengal, India

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Background: Bronchial asthma is common disease and important cause of morbidity among both children and adults. It is estimated that the number of people with asthma will grow by more than 100 million by 2025 (WHO 2007). In India, the prevalence of asthma is found to be about 2.4% in adult over 15 years of age using the International Union Against Tuberculosis and Lung Disease (IUATLD) questionnaire. It is also a global concern on the change in asthma epidemiology and clinical spectrum. Quality of lifestyle and active tobacco smoking has got important effects on asthma. A cross-sectional study was conducted among adults in an urban population of Barrackpore, in west Bengal, India.
Method: A cross-sectional study was conducted in 6 of the 24 wards in 2011, chosen randomly for the longitudinal Population Health study established in 1999. Approximately 500 households per ward were selected by systematic random sampling. A book of questionnaires was prepared, based on standard guideline.
Result: Data from 9061 respondents (4287 male, 4774 female) were analyzed after excluding children below 18 years age. Asthma was diagnosed in 3.1% and 2.9% of the male and female respectively. Present smoking was reported 37.77% of males and 0.82% of females. Smoking, cough, breathlessness, phlegm, wheezing and tightness in chest were common symptoms, being present in 15.6%, 26.8%, 75%, 16.7%, 38% and 30.4% in the asthmatic subjects respectively. Asthma is strongly associated with the age. 3.05% prevalence of bronchial asthma noted in the adults in this study cohort.
Conclusion: The result provides information on prevalence of respiratory symptoms and asthma of the study cohort, also relationship of asthma and various symptoms with several risk factors and their significance. More than 46% male are tobacco smokers. The study confirms the existence of direct relationship of smoking with bronchial asthma and related symptoms. Awareness intervention regarding the hazards of tobacco smoking is expected to result measurable reduction of the community prevalence of bronchial asthma.

1512
Clinical relevance of inhalant and food allergens sensitisation in a cross-sectional epidemiological study of atopic diseases

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Background: Skin prick testing(SPT) is the standard for diagnosing atopy. A positive skin prick reaction does not always correlate with clinical symptoms. It is well known that a positive SPT reveals rather a specific IgE presence, than an atopic disease itself. When combined, clinical manifestation and SPT are a powerful instrument for defining allergic diseases. The objective of the present study is to assess clinical relevance of environmental and food allergens with regard to patient history in a cross-sectional community sample.
Method: Patients, 225 men and women, age 4–81 years, consulting the outpatient clinic of a major private hospital in Sofia, because of a suspected IgE-mediated allergic disease were included. All participants completed a written questionnaire to define asthma and rhinitis prevalence and frequency of their symptoms. Patients underwent SPT with 18 commercial inhalant and food allergen extracts using individual lancets(Alyostal Prick, 100IR-IC/mL Stallerpoint, Stallergenes, France; Cow milk prick 1000 BU/ml Bul Bio-NCIPD, Bulgaria). All test and reading procedures were in line with published practice guidelines. The clinical relevance of each of the positively tested allergens was assessed for each allergen separately and subdivided into three distinct categories (no clinical relevance, relevant, unknown relevance). This assessment was done by an allergologist according to patient history about type and season of symptoms. Relevant is an allergen sensitisation, causal to reported symptoms. No relevance was stated if an allergen sensitisation did not elicit any symptoms upon exposure. Unknown is a SPT sensitisation for which neither presence nor absence of symptoms is reported on exposure or more than one sensitisation could have been responsible for the symptoms reported.
Results: Among 225 patients 142(60.2%) were sensitised to at least one allergen, Proportion of relevant tests is the highest in Salicaceae 80%, followed by that in Tree mix 77.8%, Der p 72.2%, Der fr 62.9%, four cereals 69.2%, 12 grasses 69%, Cockroach 54.8%, Betulaceae 52.4% Fagaceae 48%, Penicillium mix 61.9%, Aspergillius mix 45.5%, Whalnut 32.3%, Peanut 29.4%, Milk 22.2%, Egg whole 21.1%, Soy 21.1%, Apple 20.8%.
Conclusions: Our study demonstrates high rates of clinically relevant sensitisations to inhalant and food allergen, in line with the data for Europe. The percentage of clinically relevant sensitisations differ significantly depending on the allergen.

1513
Evolution of bronchial asthma in young adults

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Background: Aim of the study was to investigate the evolution of bronchial asthma (BA) from childhood to young adulthood.
Method: 193 persons (117 man and 76 women), age 16–34, with childhood-onset BA, were investigated. Diagnosis of BA and detection of BA severity were made according to GINA guidelines (FEV1, PEF variability, daytime and nighttime symptoms, therapy). Retrospective analysis of childhood BA severity was based on anamnesis and data from medical archives.
Results: Mild BA in childhood (88 cases) still mild in 88.7% of young adult patients, 11.3% had moderate and severe BA. In cases of moderate childhood BA (69 patients), severity of the disease did not changed in 49.2% of young adults, severe BA was revealed in 8.6% cases (six persons). From 36 patients with severe childhood asthma 73% had severe BA in young adulthood. This data allows determine two variants of natural course of childhood BA: stable and variable. Stable variant, that was characterised unchanged asthma severity from childhood to young adulthood, was revealed in 128 cases (66.4%). Variable type of evolution, that was characterised unstable severity of the disease, was exposed in 65 patients (33.6%).
Conclusion: Retrospective analysis of the natural course of childhood BA in young adults shows, that stable variant of asthma evolution was prevalent (66.4%). In 21.2% of adult patients (41 persons) childhood BA got less severe, in 12.4% (24 cases) severity of the disease was increased.

1514
Allergic diseases in patients exposed to the Madrid enviroment

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Background: In the Allergy Service patients from different parts of the world are attended. These patients greatly differ with respect to the environmental conditions to which each have been exposed throughout their life. To study the environmental influence of the Madrid area, the allergy profile of patients who were born and live most of their lives in this city was characterised.
Method: A retrospective, descriptive, study of patients aged more than 15 years born in Madrid, first seen in the Allergy clinic of H.G.U Gregrorio Marañón in 2008 or 2009. Age, sex, final diagnosis and main allergens causing pathology were analized. Of the 4048 new patients seen at the clinic, 2102 (51.24%) were born in Madrid, of these, a random sample of 258 patients were selected for the study.
Results: Patients had a mean age of 39.2 years, (SD 17.46), 64.3% were women. 220 (85.3%) patients completed the study. Final diagnosis was rhinoconjunctivitis and/or asthma in 116 (52.7%), food allergy in 32 (14.5%), urticaria and/or angioedema in 22 (10%), anaphylaxis in 10 (4.5%), drug allergy in 48 (21.8%), sensitisation to Anisakis simplex in 20 (9.1%), and other diagnoses in 14 (6.3%). Allergy disease was discarded in 33 patients (15%). Rinoconjuntivitis and/or asthma were allergic in 88.8%. The most common allergens involved were: pollen (73.01%), mainly grass (67.46%), trees (46.8%) and weeds (46.8%). 43.7% were sensitised to pets, 23.8% to mites, and 9.5% to molds. Only the 10.3% were mono-sensitised. The most common drug involved in allergy were NSAIDs 43.7%, followed by beta-lactam antibiotics 25% and other antibiotics 16.7%. Patients had taken from 1 week to 55 years (median 3 years) from the onset of symptoms, to consult the allergist. At 55.4% of these underwent subsequent monitoring visits to the allergy clinic.
Conclusion: The main pathology studied in our Allergy clinic is allergic rhinoconjunctivitis and/or bronchial asthma, In these, the most important allergen is pollen, mainly grass, but with a high rate of polysensitisation. Allergy to pets is also a very prevalent allergen.

NSAIDs are the drugs most commonly studied in the Allergy Service, reflecting its important use in this area, and Anisakis simplex highly allergy is still prevalent in Madrid.

1515
Smoking and male gender, but not atopy are associated with fixed airway obstruction in severe asthmatics in Singapore

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Background: A subset of asthma patients with severe disease have fixed airways obstruction, as characterised by a lack of complete reversibility after bronchodilators. We aimed to elucidate the factors associated with varying degrees of fixed airways obstruction in a cohort of patients with severe asthma.
Method: We screened our database of 205 patients with severe asthma who presented to the Respiratory or Asthma Clinics at Singapore General Hospital between January 2011 and June 2012. Severe asthma was defined according to the World Health Organization classification of 'treatment-resistant severe asthma' (Bousquet et al., 2010), that is, patients who require a combination of high-dose inhaled corticosteroids and long-acting beta agonists. 135 patients with treatment-resistant severe asthma who presented to our asthma clinic were divided into three groups according to postbronchodilator forced expiratory volume in one second (FEV1): no fixed obstruction (FEV1 $\geq$ 80% predicted, $n = 83$), moderate fixed obstruction (50 $\leq$ FEV1 < 80% predicted, $n = 41$) and severe fixed obstruction (FEV1 < 50% predicted, $n = 11$). We compared clinical and demographic parameters between groups.
Results: Patients with severe fixed obstruction were significantly more likely to be male and current or ex-smokers than the other groups. Overall, there was a significant negative correlation between postbronchodilator FEV1 with pack-year smoking history, and a significant positive correlation between postbronchodilator FEV1 with prebronchodilator FEV1/FVC and prebronchodilator FVC. Additionally, the severe fixed obstruction group had significantly lower prevalence of allergic rhinitis. Multiple linear regression revealed that male sex, pack-year smoking history, prebronchodilator FEV1/FVC and prebronchodilator FVC were independent factors for fixed airways obstruction.
Conclusion: Smoking is associated with fixed airways obstruction in severe asthma and manifests as air trapping. Our findings underscore the importance of smoking cessation in asthma patients to mitigate the development of irreversible airways obstruction.

1517
The Isle of Wight birth cohort – seeking the 3rd generation

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Background: From January 1989 to February 1990 a birth cohort ($n = 1456$) was recruited on the Isle of Wight, UK, to prospectively study the natural history of asthma and allergies. Information was collected at birth on the family history of their parents (1st generation). The cohort (2nd generation) has undergone follow-up at 1, 2, 4, 10 and 18 years of age, with follow up rate between 83 and 90%, and has been extensively phenotyped. The cohort is now producing children of their own, giving a unique opportunity to study a 3rd generation. We wish to identify, antenatally, all babies born to the birth cohort and follow them for the first year of life to investigate transgenerational epigenetic mechanisms and its relevance to the development of asthma and allergy.
Methods: For recruitment of the 3rd generation, the cohort was sent patient information sheets and a letter asking them to make contact if they were expecting or planning to have a baby. The Isle of Wight has one hospital where the research nurses identify the women from the clinic lists. Pregnant women are given scans at 12 and 20 weeks giving the opportunity to identify cohort women. Once consented, pregnant women provide blood samples at 12 and 28 weeks and cord blood and placenta samples are collected at birth. They also complete questionnaires and undergo skin prick and lung function testing. Wherever possible the non-cohort parent is invited to participate. After birth, follow-up is at 3, 6 and 12 months. Questionnaires are completed, samples of house dust, babies' stools, saliva and nasal secretions collected.
Results: An average of 90 pregnancies/month are screened, and approximately four are eligible for the 3rd Generation study. To date, 117 have been identified, five refused participation, three dropped out and the remaining 109 are currently in the study. Identifying male members of the cohort who are fathers is difficult. A high percentage of pregnancies early in the study were unplanned, with the mothers often living in less than ideal situations. Despite this, we are achieving good compliance by tailoring our approach to individual circumstances.
Conclusion: This highlights the importance/problems of keeping track of young adults (with changing addresses and contact numbers); recruiting and keeping them

in the follow on study with their children as the participants. When recruiting for this study, it has been necessary to be flexible, taking in to account individual circumstances.

1518
Childhood family adversity seems not to be associated with serum vitamine D levels in a low income Caribbean Colombian asthmatic patients: preliminary results

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Background: It is increasingly recognised that Childhood adversities (CA) may be important determinants for asthma and poor health behavior. Vitamin-D is associated with differences in the factor sociodemographics and asthma, but little is known about vitamin-D and mental health in the pediatric population. The objective of this study was to investigate the associations between CA as a risk factors for allergy asthma in Colombian patients
Method: This was an observational, descriptive study that used a convenience sample of asthmatic children from a previous cohort of low-income families. Samples from 55 children were evaluated for asthma-severity, levels of serum-Vitamin D, and total-IgE. The occurrence of CA was assessed using a semi-structured survey. The items were analyzed descriptively using SPSS-19.
Results: Mean age was -8.8 years (SD = 2.2). Serum-level of Vitamin-D in women was 62.02 ng/ml. Men -66.78-ng/ml. There were no significant differences between men and women in total IgE levels (mean 243.9 and 218.9-IU/ml respectively). Interpersonal-relationships were significantly different by levels of Vitamin D ($P = 0.0001$). On the other hand, there were no differences when relationships were compared against serum-total-IgE-levels and asthma severity ($P = 0.987$ and $P = 0.986$).The same was demonstrated when socio-economical status was compared against levels of Vitamin D, total-IgE, or asthma severity ($P = 0.857$, $P = 0.384$ and $P = 0.397$, respectively). Additionally, divorce or separation of the parents was not significantly different when compared against Vitamin D levels, total-IgE levels, or asthma-severity ($P = 0.652$, $P = 0.959$ and $P = 0.369$, respectively).
Conclusion: These preliminary results showed that the CA studied were not associated with asthma severity, level of Vitamin D, or with total-IgE levels. The exception to these findings is the association between levels of Vitamin D and relationships. More data is needed in order to prove the importance of CA as a risk-factor for asthma.

1519
Dietary patterns and asthma prevalence – evidence from a National Health Survey

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Background: We previously reported that Mediterranean diet, a recognised healthy dietary pattern, has a protective role in asthma control.
Aim: To explore the association between dietary patterns and asthma prevalence in a nationally representative population.
Methods: A representative sample from the IV Portuguese National Health Survey was analyzed. Following asthma definitions were used: ever asthma (ever medical doctor asthma diagnosis), current asthma (asthma within previous 12 months), current persistent asthma (asthma drugs within previous 12 months), current severe asthma (emergency because of asthma within previous 12 months), and incident asthma (diagnosis within previous 12 months). Dietary patterns (DP) were identified by Latent Trait Models (LTM), using MPlus v5.2., based on dietary intake food items at meals and snacks. Age, gender, BMI, education, family income, proxy reporting information and smoking were analyzed as confounders. Unconditional logistic regression models were performed to analyze whether DP were associated with asthma prevalence.
Results: Final analysis included 32644 adults (≥20 years-old), 53% female. Prevalence of ever asthma was 5.3%, current asthma 3.5%, current persistent asthma 3.0%, current severe asthma 1.4%, and incident asthma 0.2%. Five factors or dietary patterns (DP) were identified by LTM ($r \geq 0.35$): DP1 (positively correlated with milk, yogurt/cheese and fruit, and negatively with alcoholic beverages at snacks); DP2 (positively correlated with vegetable soup, bread and pulses at meals); DP3 (positively correlated with pastry, chocolate and sweet desserts, candies, salty snacks, chips, fruit juices, soft drinks and alcoholic beverages at snacks); DP4 (positively correlated with fish, vegetables and fruit at meals); and DP5 (positively correlated with bread, pastry, chocolate and sweet desserts at meals and snacks). DP3 was associated with ever asthma prevalence (OR = 1.13; 95% CI = 1.03–1.24) and current severe asthma (OR = 1.23; 95% CI = 1.03–1.48), while DP4 was negatively associated with current (OR = 0.84; 95% CI = 0.73–0.98), and current persistent asthma (OR = 0.84; 95% CI = 0.72;0.98), after adjustment.
Conclusion: Our results suggest a protective association between essential components of Mediterranean dietary pattern, such as 'fish, vegetables and fruit', and a detrimental association between 'high energy density/low micronutrient density foods' dietary pattern and asthma, supporting rational for diet intervention studies.

1520
Rhinitis and chronic rhinosinusitis with and without nasal polyps in adult asthma. Frequency distribution in relation with asthma severity (the IRIS-ASMA study)

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Background: Many studies have documented the high association between upper (rhinitis, rhinosinusitis) and lower (asthma, COPD, bronchiectasis) airway diseases. However, the prevalence and severity of rhinitis and/or chronic rhinosinusitis related to asthma severity has not been deeply studied. The aim of the IRIS-ASMA study was to assess the frequencies of nasal and sinusal diseases in a cohort of asthmatic patients, stratified by severity.
Methods: Asthmatic patients ($N = 492$), mean age 45(15) year, female 70.5%, were recruited according to GINA asthma severity classification (intermittent 17.3%; persistent 82.7% [mild 24.6%, moderate 31.4%, severe 26.7%]) in a prospective study carried out in 2010–2011 by pneumonologists and ENT specialists of 23 centers from Spain (19) and Latin America (4). Allergic (AR) and non-allergic (NAR) rhinitis and chronic rhinosinusitis with (CRSwNP) and without (CRSsNP) nasal polyps were evaluated according to ARIA and EP^{3}OS definitions and classificated by using nasal symptoms, skin prick test, nasal endoscopy, and sinus CT scan.
Results: The frequencies of nasal and sinusal diseases among asthmatic patients were:

no sinonasal disease 14.2%, rhinitis 49.6% (AR: 37.0%; NAR: 12.6%), and chronic rhinosinusitis 36.2% (CRSwNP: 19.5%; CRSsNP: 16.7%). Most AR (78%) and NAR (84%) comorbidities were present in intermittent and mild to moderate persistent asthmatics. CRSsNP was similarly frequent in all asthma severity levels (from 20% to 29%) while CRSwNP was mostly associated to severe asthma (48%, $P < 0.001$). In addition, chronic rhinosinusitis was more frequent in non-atopic (CRSsNP 46.2%; CRSwNP 57.1%) than in atopic (CRSsNP 30.2%; CRSwNP 45.8%) severe asthma patients.

Conclusions:

1 Most asthmatic patients (85.8%) have concomitant rhinitis or chronic rhinosinusitis.
2 Intermittent and mild to moderate persistent asthma are associated with allergic and non-allergic rhinitis.
3 Severe persistent asthma is significantly associated with chronic rhinosinusitis with nasal polyps, specially in non-atopic patients.

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Poster Session 67

Clinical studies in allergen-specific immunotherapy II

1521
Food allergy due to sensitisation to nickel containing foods: hyposensitisation is feasible and efficacious

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Background: Non IgE food allergy due to sensitisation to nickel containing foods can cause, in patients with allergic contact dermatitis to nickel, systemic manifestations correlated to the ingestion of nickel in foods such as cutaneous symptoms, gastrointestinal symptoms and other systemic clinical signs; these symptoms are referred as 'Systemic nickel allergy syndrome' (SNAS). A clinical suspicion of SNAS is confirmed by an improvement of the symptoms after a low nickel diet.
Method: In the period between June 2006 and December 2012, 250 (240 f- 10 m; mean age, 31 ± 26 + 13.04 years; range, 18–64 years) because of a clinical suspicion of SNAS, underwent a nickel patch-test according to the International Contact Dermatitis Research Group Guidelines. Therefore, after confirming cutaneous sensitisation to nickel, a low nickel diet was prescribed with foods which are generally tolerated by patients with SNAS while foods which usually cause exacerbation of SNAS had to be avoided. The low nickel diet caused clinical improvement of symptoms correlated to SNAS in 221 patients, who underwent an oral nickel provocation test in our allergy outpatient Unit. The test was positive in 198 patients (189 f and 9 m) and negative in 13 (12 f – 1 m). Nickel Oral Hyposensitising Treatment (NOHT) was started in 189 patients, following an up-dosing schedule from 0.1 to 500 ng. The maintenance treatment consisted in the administration of 500 ng capsules three times a week. Visual analogue score (VAS) was assessed at each visit.
Results: NOHT overall improved patient's quality of life, reducing drug consumption, inducing recovery from symptoms and tolerance to nickel containing foods.
Conclusion: SNAS being an allergic disease due to nickel contained in foods and requiring the need for a special diet should be taken into account by health professionals and dieticians when evaluating food related problems in order to reach a correct diagnosis and treatment with NOHT which induces tolerance to nickel containing foods. The above reported experience is in 'real life' but similar inclusion and treatment criteria were used in a recent multicenter double-blind placebo controlled study which also showed the efficacy of nickel oral hyposensitising treatment.

1522
Pollen-specific rush immunotherapy: clinical efficacy and effects on histamine release from basophils

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Background: Pollen immunotherapy is an effective treatment for seasonal allergic rhinitis. Specific immunotherapy with standardised extracts can induce systemic reactions, possibly increased by a rush immunotherapy (RIT).
Objective: The study was performed to investigate the efficacy of RIT with standardised Japanese cedar pollen extracts and to elucidate the mechanisms of immunotherapy.
Methods: This open study included 22 allergic patients treated with RIT and 24 allergic patients treated with normal immunotherapy. One or 2 days after the RIT, intradermal skin testing was performed. Cry j1 was injected intradermally into the skin.

Subjects underwent repeated testing of early- and late-phase skin response to intradermal allergen

We purified basophils from pollen allergic subjects treated with RIT. We then challenged the cells with an optimal dose of Cry j1 (10 g/ml) for 30 min and measured the resulting histamine release.
Results: RIT was safe and effective in reducing symptom scores. The symptom score was significantly decreased, compared with medication group or normal immunotherapy group.

Persent histamine release was decreased in the RIT group. RIT inhibits human basophil degranuration. Before starting RIT, all patients indicated positive skin reaction when injected subcutaneously with Cry j1, while 2 days after the RIT, all patients indicated negative skin reaction. RIT treatment suppressed skin test reactivity.
Conclusions: Our study indicates that RIT with standardised Cry j1 extracts is clinically effective and safe. RIT was able to block Cry j1-induced acute systemic allergic reactivity, degranulation of skin mast cells.

1523
Effectiveness of subcutaneous high-dose modified house dust mites extract in daily practice

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Background: Efficacy subcutaneous high-dose modified allergens of house dust mites is well established by randomised clinical trials. However, information from different geographic areas patients, treated with this product in the allergist's daily practice are rare. This study aimed to evaluate the efficacy perceived by patients treated with these subcutaneous high dose modified allergens 6 months after the start of treatment.
Method: From September to December 2011, 47 office-based allergist included 435 patients with allergic rhinitis and/or bronchial asthma in the study. Data were collected via structured questionnaries.

Patients assessed their conditions on visual analogue scale from 0 (worst condition) to 100 (best condition). A clinical relevant improvement was defined to be an improvement by at least 20 points compare the results of their self-assessment before starting the treatment and at the time of evaluation.
Results: 231 (50%) of the 435 patients were female. 420 patients were diagnosed of allergic rhinitis and 236 of bronchial asthma. The mean age was 24.6 (SD 13) years old and 30% of the population were pediatric patients with a mean age of 10.9 (SD 3) years old.

39.8% of preparations were 100% dermatophagoides pteronyssinus and 60.2% dermatophagoides mixture 50/50.

The overall score of the patients improved by 33.8 points (42.6–76.4 points; $P < 0.001$) being this improvement of between 30 and 50 points on 50.5% of the total population (220 patients) and was clinically significant (>20 improvement points) in 295 patients (67.8%).

six patients interrupted treatment by bad-tolerance (1.37% of population) without medical advice. The treatment was well tolerated by the 429 remaining patients (98.63%).

Conclusion: Subcutaneous immunotherapy with high-dose modified allergens of house dust mites is effective and well tolerated in allergist's daily practice.

The patients's conditions improved remarkably being this effect objectified in the first 6 months after the start of treatment.

1524
Allergic disease 10 years later – the role of specific immunotherapy

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Background: Eczema, rhinitis, and asthma are diseases of high prevalence in developed countries. Their natural history is still not completely understood. Allergen specific immunotherapy (SIT) is the only treatment able to modify the disease by targeting the underlying immunologic mechanisms. There is some evidence that SIT reduces the risk of asthma in children with allergic rhinitis and diminishes the risk of new sensitisations in monosensitised children.

Purpose: Characterise the allergic disease in adulthood in a group of adolescent followed in hospital outpatient clinic in 2002 and evaluate the impact of SIT in disease control.

Material and methods: Adolescents followed in our hospital outpatient clinic in the year 2002. Data were obtained in 2002 by consulting the clinical process and in 2012 by telephone inquiry. Control of Allergic Rhinitis and Asthma Test (CARAT10) was applied to evaluate asthma and rhinitis control. A confidence level of 0.05 was considered.

Results: 103 adolescents were followed in 2002. Thirty six patients had asthma and rhinitis, 18 asthma and 12 rhinitis. Forty are monosensitised and dust mites were the most important allergens. SIT was performed in 56 (80%) patients: 31/36 with asthma and rhinitis, 14/18 with asthma and 11/12 with rhinitis.

In 2012 only 70 (68%) responded to the inquiry. Approximately 47% were male. Asthma and rhinitis exist in 54 adults and only three maintain asthma alone. Progression to asthma occurred merely in three adolescents with rhinitis. All of them completed SIT.

When asked, 63% of patients reported themselves to be '*much better*'. According CARAT10 80% of patients had controlled disease. No significant differences were found in disease control in adulthood between patients who performed SIT and those who didn't.

Conclusion: Over the past few decades, the natural progression of asthma from childhood to adulthood has been the subject of several longitudinal studies.

In our study, progression of rhinitis to asthma occurred in only three (19%) patients but 15 (83%) adolescents with asthma in 2002 also became adults with rhinitis. Ten (25%) adolescents monosensitised became polisensitised 10 years later.

No comparison was possible between patients who received SIT and those who didn't due to the small sample.

In our study, the capacity of SIT to modify the natural course of the respiratory allergic diseases was demonstrated in rhinitis group but not in asthma group.

1525
Therapeutic compliance in subcutaneous immunotherapy

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Background/purpose/introduction: Therapeutic compliance is the degree of adhesion shown by the patient to a prescribed treatment.

Objective: To design and evaluate a pursuit strategy during a year in order to improve the adhesion to a chronic treatment of subcutaneous immunotherapy (SCIT).

Methods: Subjects were recruited from the Department of Allergy at Hospital Central de la Defensa' Gómez Ulla' in Madrid, Spain. Among the 25 participants, there were 19 females and 6 males, average of age 30.4 years (with ages ranging from 12 to 48). SCIT depot of pollens of olive tree and/ or grass. All subjects were diagnosed with allergic rhino conjunctivitis on the basis of their history and positive skin test results.

First starting and maintenance dose is given to every patient and it is performed an inspection at the end of the treatment. A Satisfaction Quality of life Questionnaire (SQLQ) with treatment scale 0–5, is given to each patient.

Results: Twenty-five patients were enrolled in the present study, 13 were treated with perennial SCIT and 12 with preseasonal ITSC. The administration of the seven starting doses and the corresponding maintenance doses recommended by the guidelines, are stated in each patient.

No one dropped out within a year after the initiation. No severe adverse events were observed during the treatment period. A weekly call is received in the time of accomplishment of the study. Average SQLQ 4.36+- 0.57; Median (intercuartil rank): 4.0 (3.0–5.0).

Conclusion: SCIT points to be a major form of allergen-specific immunotherapy in the treatment of IgE-mediated allergy has become a widely accepted routine treatment for allergy. High satisfaction between the patients with the treatment. The information provided with the present study may lead to better appreciation of the potential of SCIT and may foster the design of a large-scale, multicenter studies for its appraisal.

1526
Profile of patients treated with high-dose hypoallergenic pollen subcutaneous immunotherapy in the daily practice in Germany

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Background: Pollen allergy is the most prevelant IgE-mediated allergy type with 86% of allergic patients in Germany reporting pollen-related allergic symptoms (Böcking C et al., Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2012). SIT is the only causal treatment option for IgE-mediated allergies, but nevertheless, <20% of the allergic patients in Germany receive SIT (Chivato T et al., JACI 2012). In Germany, subcutaneous immunotherapy (SCIT) is most often used (75% of therapies acc. to IMS NPA (German market) November 2012). Up to date more than 1 million people received SCIT with high-dose hypoallergenic pollen preparations from Allergopharma. But what is the profile of a typical patient in daily practice?

Method: Demographic data of patients included in two post-marketing surveillance studies with high-dose hypoallergenic pollen preparations were evaluated. Data included sex, age, sensitisation profile, severity and duration of symptoms, medication use, and patients' rating of their condition on a 10-point visual analogue

scale (VAS) during the preceding pollen season.

Results: Data of 4981 patients were evaluated (55% female, 45% male). Patients were aged 4–79, with a median of 30. More than half of the patients were sensitised to only one allergen group. Most patients were sensitised to grass pollen (68%), followed by tree pollen (61%) and weeds (21%). 96% of patients suffered from allergic rhinitis, 84% from conjunctivitis and 32% from asthma. The median duration of disease ranged from 3 (asthma) to 4 years (rhinitis, conjunctivitis). About one half of the patients rated their rhinitis and conjunctivitis symptoms as of moderate severity. Intake of anti-symptomatic medication was as follows: 81% of patients took antihistamines, 41% corticosteroids, 19% beta-2-agonists and 31% mast-cell stabilisers. Patients rated their condition during the preceding pollen season between 1 (very good) and 10 (very bad) points with a median of seven on the VAS. 84% of patients reported six points and worse.

Conclusion: The typical patient receiving high-dose hypoallergenic pollen SCIT in the daily practice in Germany is around 30 years old, sensitised to only one allergen group, suffers since 4 years from allergic rhinitis and conjunctivitis, needs antihistamines and rates his condition with 7/10 points of a visual rating scale.

1527
Cluster immunotherapy can be safely initiated extra and intra-seasonally for grass pollen allergic patients

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Background: Subcutaneous specific immunotherapy (SCIT) as a causal treatment is usually started outside of the pollen season. For this presentation patients' data were retrospectively analysed to assess the compliance of grass pollen allergic patients as well as the safety of SCIT with highly polymerized extracts of grass pollen initiated before, after and during the grass pollen season (May, June, July).

Method: 84 grass pollen allergic patients (18–63 years; 39 female; 45 male) were included for retrospective analysis. The patients were treated with a highly polymerized allergen extract from grass pollen (CLUSTOID; 10 000 TU/ml) according to the cluster schedule starting with two injections on the first treatment day (0.2 ml + 0.5 ml; interval 15 min) and following maintenance injections of 0.5 ml every 4 weeks. The compliance has been assessed on a five-point rating scale from very bad to very good and any documented reactions to the injections were graded as local or systemic side effect according to EAACI position paper (1993), described by Pfaar et al. (Eur Arch Otorhinolaryngol 2009).

Results: Overall, the compliance was identified as 'very good' for 57.1%, as 'good' for 40.5% and as 'satisfactory' for 2.4% of the patients. After 94.7% of all injections ($n = 409$) no reactions have been noted. Local reactions were documented after 5.1% of all injections: 1.9% at intra-seasonally initiation, 3.2% for initiation outside of the pollen season. 4.9% of all injections were of grade 0 and 0.2% of grade 1 (outside the pollen season). One injection (0.2%) resulted in a systemic grade 1-reaction (extra-seasonally). No severe side effects were observed.

Conclusion: The initiation of cluster treatment with a highly polymerized allergen extract of grass pollen outside but also during the pollen season has been shown to be a safe treatment for grass pollen allergic patients and displayed a good compliance.

1528
No exposure to allergens and proteins into the bloodstream during sublingual immunotherapy

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Background: Since the tongue is highly vascularized, there is a theoretical risk of passage into the bloodstream of proteins contained in allergen extracts, especially allergens, during sublingual immunotherapy (SLIT). In the present study, we evaluated such a risk by using western blotting and mass spectrometry approaches.

Method: Mice and/or dogs were administered sublingually with a ragweed pollen extract or the recombinant major birch pollen allergen, rBet v 1. Blood was collected at different timepoints and the presence of ragweed pollen allergens and proteins was monitored by western blotting using polyclonal antibodies raised against, respectively, ragweed Amb a 1 and ragweed pollen proteins. Mass spectrometry (MS) was used to detect rBet v 1 specific peptides within blood samples.

Results: As a control, Amb a 1 and proteins from a ragweed pollen extract administered intravenously to mice and dogs were detected in blood until 1 h after administration. In contrast, sera from mice and dogs collected from 0 to 1 h did not exhibit any reactivity in western blot revealed with polyclonal antibodies to Amb a 1 or to ragweed pollen proteins. Sera from dogs administered sublingually with rBet v 1 did not exhibit either any rBet v 1 specific peptide.

Conclusion: No passage into the bloodstream of proteins, especially of allergens, was observed during sublingual administration in mice and dogs of an allergen extract or a recombinant allergen. This illustrates why SLIT is associated with a very limited risk of systemic adverse events that would be due to a massive activation by intact allergens of inflammatory cells such as basophils. This further documents the superior safety profile of SLIT, when compared to SCIT.

1529
Sublingual immunotherapy for house dust mites and predictive parameters for treatment response

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Background: To evaluate the pre- and post-1-year clinical and immunologic effects of sublingual immunotherapy (SLIT) and to assess predictive parameters on response to SLIT in patients with allergic rhinitis (AR) to house-dust mites (HDM; Dermatophagoides pteronyssinus and Dermatophagoides farinae) in Korea.

Method: Between November 2009 and January 2011, 69 patients suffering from AR symptoms and sensitised to HDM on skin prick tests were enrolled in this study and started once-daily SLIT without escalation therapy. Each patient was followed with diary card of symptom and rescue medication use. Pre- & post-1 year total IgE, immune specific IgE, immune specific IgG4, eosinophil counts, eosinophil cationic protein (ECP) were evaluated using ImmunoCAP. Effective and less effective response group were classified depending on whether they had a reduction of symptom up to 30% compared to their baseline.

Results: All of the allergic symptoms were significantly improved with reduced rescue medication score ($P < 0.001$). There were significant decrements in peripheral blood eosinophil counts, ECP after 1-year SLIT ($P < 0.001$). Specific IgE and IgG4 for HDM increased after 1 year. Effective response group had a tendency to have lower immune specific IgE/IgG4 level for Dermatophagoides farinae after 1-year SLIT than less effective response group ($P = 0.028$).

Conclusion: SLIT improved the symptoms and medication scores in AR patients sensitised to HDM and modified laboratory parameters, such as total and specific IgE

and IgG4 for HDM, eosinophil counts and ECP after 1 year. A low specific IgE/IgG4 for Dermatophagoides farinae after 1-year SLIT may be a useful parameter to predict the effectiveness of long-term SLIT.

1530
Efficiency of sublingual immunotherapy on quality of life and satisfaction of patients with moderate/severe allergic rhinitis: real – life study

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Background: Allergen specific immunotherapy has option not only to change the natural course of allergic rhinitis, but to improve the quality of life. Satisfaction of treatment is of great importance for the compliance. The aim of this prospective study is to evaluate the efficiency of sublingual immunotherapy (SLIT) on quality of life (QOL) and satisfaction in patients with moderate/severe allergic rhinitis, sensitised to pollens.
Method: In this real life study 37 patients (men – 22; mean age – 21.8) with moderate/severe allergic rhinitis, sensitised to pollens were included. QOL at baseline and after one season of SLIT was established by Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ®). The patients' satisfaction was evaluated by using visual analog scale (VAS).
Results: The mean values of all the QOL items improved significantly ($P < 0.01$) with the following reductions: activities – 3.65 to 1.61; sleep – 1.97 to 0.80; general problems – 1.61 to 0.80; practical problems – 3.39 to 1.26; nasal symptoms – 3.58 to 1.45; eye symptoms – 3.45 to 1.29; emotions –2.43 to 1.02. The patients' satisfaction was increased significantly ($P < 0.01$) – 36.9 mm to 73.2 mm.
Conclusion: Our study demonstrates significant improvement in quality of life and great satisfaction after one season of sublingual immunotherapy of moderate/severe allergic rhinitis in patients, sensitised to pollens.

1532
How late can a perlingual pre-co seasonal immunotherapy against grass pollen rhinitis be started? It's never too late

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Background: Among the several regimens of immunotherapy (IT), those pre-co seasonal seem to obtain more and more consent, even for the major demonstrated compliance. Nevertheless it is not clear yet, how long it is possible to delay the beginning of the pre seasonal phase to obtain anyway effectiveness against the allergic grass pollen rhinitis. The perlingual immunotherapy (PLIT) is a recent alternative to the most known sublingual IT. In this study, we observed if, starting the PLIT late, you get also a significant reduction of symptoms in grass pollen rhinitis.
Methods: It has been administered PLIT against grass pollen with a pre-co seasonal regimen to 25 children (16 males and 9 females) between 5 and 18 years old with grass pollen rhinitis, 4 of them with grass pollen asthma. The PLIT starts from March/April. The clinical symptoms (0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms) and rescue therapy were recorded in a daily diary. It has been created a single effectiveness parameter (SEP) inclusive of the severity of the symptoms as well as of the rescue therapy. At the end of each year was made a meeting with patients and parents together to estimate the outcome of PLIT. Our observation was conducted for two consecutive pollen seasons
Results: All the children have completed the study. Both the single score of general symptoms, nasal symptoms, pulmonary symptoms, rescue therapy and the SEP, related to total symptoms and the rescue therapy, have demonstrated a significant reduction of 41% ($P < 0.01$) compared to the one obtained in the previous year of the treatment's beginning.
Conclusions: This study, confirming a good compliance to PLIT, refers to a significant effective reduction of symptoms even though the IT started late compared to the recommended pre-co seasonal regimens.

1533
Efficacy and safety of subcutaneous immunotherapy with pollen allergen extracts in asthma and allergic rhinoconjunctivitis

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Background: The Previsora Allergy Service, Camagüey has studied sensitisation to the following allergens: Ambrosía psilostachya, Amaranthus leucocarpus, Helianthus annuus, Rumex acetosella, Lolium perenne, Cupressus lindley, and Cocos nucifera. Forty percent of individuals with rhinitis and / or asthma were sensitised to these allergens.
Objective: Specify the efficacy and safety of monotherapy in patients with asthma and allergic rhinitis sensitised to pollen allergens.
Methods: There were 210 patients whose Prick Test was positive to pollens; monotherapy was indicated in those who expressed the largest wheal diameter in the skin test. Immunotherapy (IT) was begun by the fourth decimal dilution of 10 000 protein nitrogen units (10 PNU / cc). A weekly dosage increment regimen was initiated. Efficacy and safety were actively monitored for 15 months. Efficacy variables included reducing the frequency and severity of symptoms, drug consumption behavior, and the quality of life questionnaires (RQLQ and AQLQ). Safety was assessed by local allergic reactions (rash, itching, and wheals), systemic allergic reactions were classified by grades (I, II, III, and IV).
Results: There were nine patients who initiated then left IT. The reduction in frequency and severity of the crisis was 41% compared to baseline. The use of medications was reduced by 64%. The quality of life was increased by 3 points in asthma and 2 points in allergic rhinoconjunctivitis. There were 16 (7.6%) local allergic reactions and 5 (2.3%) grade I systemic allergic reactions.
Conclusion: Subcutaneous monotherapy with pollens was effective and safe in patients with asthma and allergic rhinoconjunctivitis in the province of Camagüey.

1534
Safety and effectiveness of sublingual immunotherapy in the non-interventional study LINGUA

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Background: Non-interventionalstudies (NIS) provide information regarding real-world safety and effectiveness that cannot be retrieved from clinical studies due to predefined selection of the patient population.

Method: The NIS LINGUA (TOL SL plus®, Laboratorios LETI, Spain) with a native allergen extract for specific sublingual immunotherapy was conducted at 103 office-based allergologists in Germany which included 323 patients. Of 295 patients valid for analysis, 288 patients (97.6%) were diagnosed with allergic disease of the immediate type. The most common sensitivities were grasses (83.1%), trees (81.4%) and mites (80.3%). About 162 patients (54.9%) had prior treatments of allergic diseases.

Results: For all effectiveness parameters regarding symptoms (concerning nose, eyes and lung), the percentage of patients who had no symptoms increased clearly from initial to final visit, whereas the percentage of patients with moderate or severe symptoms decreased. In all medication groups the frequency of medication use was reduced. The effectiveness was assessed as 'very good' (60.7%) or 'good' (27.3%) by the majority of physicians. Similarly, the majority of patients assessed the effectiveness as 'very good' (557%) or 'good' (29.3%).

During this study, a total of 130 adverse events (AEs) were documented in 66 of 295 patients (22.37%). A non-serious adverse drug reaction (nsADR) was documented in 58 patients. For 1 patient, 1 event (muscle tightness) met the criteria for a serious adverse drug reaction (SADR); causality has not been established and the outcome is unknown. No other serious adverse events (SAE) were observed in this study. No patients died during this study. The vast majority of patients had no local intolerability in form of oral burning (86.4%) and oral swelling (88.6%). The tolerability was assessed as 'very good' by most physicians (77.1%) and patients (71.1%).

Conclusion: Sublingual immunotherapy with TOL SL plus® is well-tolerated and effective in daily clinical routine.

1535
Polyallergic patients treated in daily medical practice – results from a 2-year sublingual allergen immunotherapy study

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Background: Patients with respiratory allergies are often polyallergic. Clinical trials have shown that these patients can effectively and safely be treated with SIT, however data from routine practice SIT treatments are still scarce.

We documented the tolerability and the impact of birch pollen SLIT (Stallergenes, France) on symptoms and use of symptomatic medication in a large population of birch pollen allergic patients with rhinoconjunctivitis (RC).

Method: This non-interventional, open, prospective, non-controlled, multicenter study across Germany was conducted over two consecutive birch pollen seasons between fall 2010 and 2012. About 716 patients (409 female, 300 male, 7 unknown; mean age: 38 ± 16 years) participated in the study. Thirty-seven percent of the patients were monoallergic with allergic symptoms only to birch (and/or alder/hazel) pollen, while 63% ($n = 448$) were polyallergic: The majority of polyallergic patients had a concomitant grass/cereal pollen allergy (70%), 38% suffered from a house dust mite allergy and 27% were allergic to animal dander. Patients were treated according to the SmPC of the product.

Allergic symptoms were analyzed as combined scores of severity [scale: 0 (none) – 3 (severe)] and frequency [scale: 0 (none) – 4 (very often)]. In the combined RC score, the severity of rhinitis and conjunctivitis were pooled. Different subgroups were analyzed.

Results: For monoallergic patients, the RC score was reduced by 52% (from a mean value of 3.25 in the birch pollen season prior to the study to 1.85 in the 1st study year and 1.57 in the 2nd study year). The polyallergic patients were more symptomatic at study start, but similar score reductions were observed: the RC score decreased by 53% from 4.05 to 2.56 (year 1) to 1.90 (year 2). The rate of patients without symptomatic medication intake increased from 23% to 40% (year 1) to 55% (year 2) (monoall. pat.) and from 17% to 41% to 50% (polyall. pat.) respectively. All scores improved significantly ($P < 0.001$).

In both subgroups of patients, treatment was well tolerated. Five percent of the monoallergic patients experienced adverse events (AE) during the 2 study years vs 14% of the polyallergic.

Conclusion: Used in daily medical practice, an AIT with birch pollen extract over two consecutive birch pollen seasons reduced allergic symptoms and symptomatic medication intake in mono- and polyallergic patients. Polyallergic patients benefited as much from AIT as monoallergic patients.

1536
Use of a computer system in the follow up of allergic pediatric patients during allergen immunotherapy

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Background: Allergen specific immunotherapy (AIT) is the only treatment able to act on the causes and not merely on the symptoms of allergy. AIT may be administered mainly in two forms, subcutaneous (SCIT) and sublingual (SLIT). Several trials have highlighted the efficacy and safety of both forms in allergic rhinitis and asthma.

Method: There are many clinical, diagnostic and therapeutic data that must be monitored in patients during AIT therapy; for this purpose, we created a database that allows to input the patients' clinical, laboratory and personal data, and to easily manage a large number of data. The database has been realised through Microsoft Access.

Results: A numeric ID is assigned to each patient, and for each patient there are different cards corresponding to the number of blood samples done. Each card is composed of the following slots: blood samples data, diagnosis, clinical data (rhinitis, conjunctivitis, asthma, hives, itch, dermatitis), drugs, skin prick tests, IgE, IgG and IgG4 levels, basophil activation tests. Clinical data are expressed by a value between 0 and 3, corresponding to the severity of symptoms: absent, slight, moderate, severe. Spirometric data are also collected in asthmatic patients: FEV1%, FVC% and FEF %. Therapy is constituted by a list of the most commonly used drugs, each of these expressed by a numerical score between 0 and 5, in relation to the frequency of use: never, rarely, often, almost daily, continuously at the lowest dose, continuously at the highest dose. IgE slot consists of specific entries, varying according to the different respiratory allergens to which AIT is directed. At last, also IgG and IgG4 values and basophil activation test slots entries are specific according to the different allergens.

Conclusion: This database allows a close monitoring of a large number of data. It is possible to quickly evaluate the patient clinical evolution, to study possible symptoms improvements, as well as the decrease in the use of drugs and of rescue drugs. It also allows monitoring the evolution in IgG and IgG4 levels, whose performance during AIT has not been completely understood yet.

1537
Comparison of effect of subcutaneous immunotherapy with single or multiple allergens given in the same time

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Background: Specific immunotherapy is widespread used in treatment of allergic disease. Route of application of allergen is crucial for therapeutic efficacy. Subcutaneous route (SCIT) is well documented for success, and other routes improved their efficacy. The other very important challenge is use of only one or multiples allergens in same preparation. Here we analyzed single or multiple allergen use in same time, but separated injected in treatment of SCIT immunotherapy.
Method: Patient treated with SCIT at least two years was included in the study. Total and specific IgE was measured using enzimimmunoessay (ELISA). IgE were measured before SCIT and after one of treatment, Data were analyzed with Mann Whitney test of multiple correlation. Statistical analysis was performed with statistical package Statistica for Windows.
Results: We analyzed 32 patients, 19 female and 13 male. Among all 17 were asthmatics, 6 with allergic rhinitis and 9 with eczema. Mean age was 33.29 years (SD 19). Mean total IgE concentration before SCIT was 648 IU/ml (SD 1287), and after one year mean total IgE was 512 IU/(ml (SD 884). Decrease of total IgE level was statistical significant at level $P < 0.05$. Specific IgE were measured for ragweed, tress, grass, home dust and fungi. Ten patients were treated with only one allergen, 12 with two, and 4 with three or four allergen. For all patients specific IgE was measured. No differences of results were noted if one or more allergen were given for SCIT. Improvement of clinical outcome according to used questionnaire was the same in any group.
Conclusion: Clinical outcome of SCIT was the same in patients with only one allergen or more allergen, if they were injected separately.

1538
Efficacy and safety of sublingual immunotherapy in Korean children

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Background: Sublingual immunotherapy is currently accepted as a suitable alternative to subcutaneous immunotherapy because of its easy and painless administration and improved safety. Many clinical trials have demonstrated that sublingual immunotherapy is an effective and safe treatment for pollen or mite allergic rhinitis. However, there have been very few studies overall on children with allergic rhinitis who are sensitised to house-dust mites in Asia. The purpose of the present study was to investigate the efficacy and safety of sublingual immunotherapy in children with allergic rhinitis to house-dust mites.
Methods: A total of 112 patients under the age of 15 who had allergic rhinitis to Dermatophagoides pteronyssinus and Dermatophagoides farinae were included. All patients were treated with sublingual immunotherapy (Staloral®). Symptom scores and quality of life were evaluated by questionnaires until one year after sublingual immunotherapy. The medication score was assessed monthly using a diary medication card and serologic tests were evaluated before and 6 and 12 months after treatment. Adverse effects and compliance were also investigated.
Results: All nasal and non-nasal symptoms and quality of life were significantly improved after treatment. The total medication score was decreased significantly after sublingual immunotherapy. There was no significant change in serologic tests. Some minor adverse effects were reported, however there were no systemic reactions. The drop-out rate was 21%.
Conclusions: Sublingual immunotherapy is a valuable therapy for the treatment of allergic rhinitis in Asian children sensitised to house-dust mites.

1539
Subcutaneus vs sublingual immunotherapy

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Background: Subcutaneus (SCIT) and sublingual (SLIT) immunotherapy are the two most prescribed ruotes for administering allergen specific immunotherapy (ASI). They were shown to be effective in control of symptoms and in reducing rescue medication use in patients with allergic disease, but their effectiviness has to be balanced against side-effects. In recent years, SLIT has been increasingly prescribed, instead of SCIT, because of improved safety and easy administration. To assess which route is the most effective in the treatment of patients with seasonal allergic rhinitis to grass pollen.
Method: An indirect meta-analysis-based comparison between SCIT and SLIT was performed. Treatment efficacy was determined as the standardised mean difference (SMD) in symptom and medication scores obtained with active treatment, SCIT or SLIT, compared to placebo. Studies were included if they were duoble-blind randomised controlled trials (RCTs) comparing SCIT or SLIT to placebo. Thirty-six RCTs (3014 patients, 2768 controls) were analyzed.
Results: The overall effecy size of SCIT for symptom score (SMD, −0.92; 95%CI, −1.26 to 0.58) was significantly higher than SLIT, both administered via drops (SMD, −0.25; 95%CI, −0.45 to −0.05) and tablets (SMD, −0.40; 95% CI, −0.54 to −0.27). Similar resuls were reported for medication score (SCIT: SMD, −0.58; 95% CI, −0.86 to −0.30. SLIT drops: SMD, −0.37; 95% CI −0.74 to −0.00 SLIT tablets SMD, −0.30; 95% CI, −0.44 to −0.16).
Conclusion: Our results provide indirect but solid evidence that SCIT is more effective than SLIT in cotrolling symptoms and reducing the use of anti-allergic medications in seasonal allergic rhinoconjuntivitis to grass pollen.

Poster Session 68

Clinical studies in allergen-specific immunotherapy III

1540
Grass allergen immunotherapy tablets vs symptomatic treatment for allergic rhinoconjunctivitis – a health economic evaluation

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Background: Previous health economic analyses for specific immunotherapy (SIT) have been based on short term clinical data or retrospective database searches. The purpose of this analysis is to assess the cost-effectiveness of the grass allergy immunotherapy tablet (AIT), GRAZAX® (*Phleum pratense* 75 000 SQ-T / 2800 BAU, ALK, Denmark) GRAZAX® compared to symptomatic treatment, using primarily evidence based data from a large long-term clinical trial. In that study, sustained effect in post-treatment years was demonstrated.
Method: A health economic evaluation was performed based on a Markov model with a 10-year time horizon. A Danish societal view was adopted. The outcome was identified as quality-adjusted life-years (QALYs). Information on resource consumption and the outcome was retrieved from trial data and the published peer-reviewed literature. Sensitivity analyses were performed to identify parameters of critical importance for the result.
Results: The incremental cost-utility ratio amounted to € 21 271.01 per QALY for GRAZAX® compared to symptomatic treatment. The cost-utility ratio is therefore below the commonly accepted willingness-to-pay threshold of £ 20 000 (€ 25 000), stated by the UK's National Institute for Health and Clinical and Excellence. The sensitivity analysis identified the critical parameters to be the applied time horizon, inclusion of indirect costs, and risk of developing asthma.
Conclusion: This health economic evaluation demonstrates that GRAZAX® in combination with symptomatic medication provides a cost-effective treatment option within a commonly accepted willingness-to-pay threshold.

1541
Effects of treatment with sublingual and subcutaneous grass pollen specific immunotherapy preparations on IgG_4 antibody level

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Background: Specific immunotherapy (SIT) is characterised by a time and dose dependent induction of serum IgG antibodies. Recent findings suggest that IgG-associated inhibitory activity like IgE blocking activity or IgE facilitated allergen binding are correlated to the clinical success of treatment. We compared the IgG_4 levels during the first and second years of treatment in patients desensitised with three different high-dose preparations: a sublingual unmodified allergen, a subcutaneous allergoid, and a subcutaneous recombinant grass pollen allergen preparation.
Method: Prospectively planned analyses of serum IgG_4 levels were performed using the Allergopharma ELISA in three double-blind, placebo controlled clinical trials. For randomisation patients (18–60 years) had to have a history of hay fever, positive skin prick and conjunctival challenge test results, serum IgE to grass pollen allergens (EAST class $\geq$2), and relevant symptoms during the baseline grass pollen season (BL). Serum specific IgG_4 levels were determined before and after 1& 2 treatment years.
Results: Whilst for sublingual immunotherapy moderate increases in mean IgG_4 levels from [μg/l]: 64 (BL) to 418 after 1 year and 1971 after 2 years were found, substantial increases of IgG_4 levels occurred in subcutaneous immunotherapy using allergoid: [μg/l] 942 (BL), 61765 (year 1), 73433 (year 2) and recombinant phleum preparation [μg/l]: 539 (BL), 48631 (year 1), 352942 (year 2). There were no relevant changes of serum IgG_4 levels in the placebo groups.
Conclusion: The induction of the serum specific IgG_4 antibody response appears to depend on the route, dose, and immunogenic properties of specific immunotherapy preparations. Although immune reactive activity to a certain extent for the high-dose sublingual preparation was observed, both SCIT preparations were more effective.

1543
Efficacy of 300IR 5-grass pollen extract sublingual tablet assessed by daily combined score: results of three double-blind placebo-controlled natural field studies in children/adolescents and adults

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Background: Efficacy of 300IR 5-grass pollen extract sublingual tablet has been demonstrated in short-term and long-term studies. Here we report the results of three single-season, natural field studies using the daily Combined Score (CS), a measure which equally weights symptom scores and rescue medication use. The use of this score is consistent with the World Allergy Organization's recommendation that a combined symptom and rescue medication score, especially one with equivalent importance of the two components, be utilised as the primary outcome measure of clinical trials with allergen specific immunotherapy for respiratory allergy.
Method: In three short-term studies (2 in adults, 1 in children and adolescents), participants with grass pollen associated-allergic rhinoconjunctivitis (ARC) were randomised to placebo or 300IR 5-grass pollen extract sublingual tablet starting 4 months (4M) prior to the pollen season and continuing for its duration. Participants scored each of their 6 rhinoconjunctivitis symptoms on a 0–3 scale [rhinoconjunctivitis total symptom score (RTSS, scale 0–18)] and reported rescue medication use (RMS, scale 0–3). The daily CS [(RTSS/6 + RMS)/2] was evaluated using a repeated measures ANCOVA model.
Results: In the two adult studies, 284 (placebo = 148; 300IR 4M = 136) and 436 (placebo = 228; 300IR 4M = 210) participants comprised the full analysis sets (FAS). In the pediatric study, 266 children

and adolescents (placebo = 135; 300IR 4M = 131) were in the FAS. Significant differences in daily CS between the 300IR 4M group and placebo were shown in each of the studies ($P \leq 0.0005$). Over the pollen period, the daily CS least-squares (LS) mean differences between the 300IR 4M and placebo groups were −0.13 [95% CI (−0.19; −0.06)], and −0.21 [95% CI (−0.30; −0.11)] in the adult studies, respectively and −0.19 [95% CI (−0.29; −0.08)] in the pediatric study, corresponding to relative differences of −28.2%, −29.6%, and −30.1%, respectively.

Conclusion: In analyses using the state of the art measure, daily Combined Score, the efficacy of 5-grass pollen extract sublingual tablet administered according to a 4-month pre-seasonal and co-seasonal regimen was observed in patients with grass pollen-induced allergic rhinoconjunctivitis.

1544

Clinical efficacy of 300IR 5-grass pollen extract sublingual tablet by sensitisation status: pooled data analysis from four natural field clinical studies

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Background: The efficacy of the 300IR dose of 5-grass pollen extract sublingual tablet administered according to a 4-month pre-seasonal and co-seasonal regimen has been consistently demonstrated in 4 DBPC natural field studies of patients with grass pollen-associated allergic rhinoconjunctivitis. Here, we present results of a pooled efficacy analysis by sensitisation status (mono-sensitised vs poly-sensitised).

Method: Adults, adolescents, and children (>5 years of age) underwent skin prick testing to a panel of seasonal and perennial aeroallergens prior to randomisation. Sensitisation status was derived from these results. Those with a positive test to 5-grass pollen alone were considered mono-sensitised and those with a positive test to 5-grass pollen and at least one other allergen were deemed poly-sensitised. Participants self-scored each of their rhinoconjunctivitis symptoms (sneezing, rhinorrhoea, nasal pruritus, nasal congestion, ocular pruritus, watery eyes) on a 0–3 scale (from absent to severe) for a rhinoconjunctivitis total symptom score (RTSS) of 0–18. They also recorded their daily use of rescue medication (RMS, scale 0–3, according to the type of medication used). The daily Combined Score (daily CS, scale 0–3), which equally weights symptom and rescue medication scores [daily CS = (RTSS/6 + RMS)/2] was analysed using a linear mixed model with repeated measures for the single or first pollen period of the four studies.

Results: Of 1381 participants, 490 (35.5%) were mono-sensitised (placebo = 252, 300IR 4M = 238) and 891 (64.5%) were poly-sensitised (placebo = 464, 300IR 4M = 427). Significant differences in daily CS between the 300IR 4M group and the placebo group were observed in both mono- and poly-sensitised subsets of patients ($P < 0.0001$). The daily CS relative LS mean difference vs placebo was −24.8% [95% CI (−36.0%; −13.6%)] in mono-sensitised patients and −29.8% [95% CI (−39.3%; −20.4%)] in poly-sensitised patients.

Conclusion: Treatment with 300IR 5-grass pollen extract sublingual tablet was similarly effective in mono-sensitised and poly-sensitised patients.

1545

Sublingual carbamylated monomeric allergoid for patients with respiratory allergy due to parietaria: follow-up in real life of a double blind placebo controlled study

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Background: Respiratory allergy due to *parietaria* pollen is particularly relevant in Mediterranean areas. A one year multicenter double blind placebo controlled randomised study was conducted in 2009–2010 to document the safety and efficacy of a vaccine with carbamylated monomeric allergoid of *parietaria* for sublingual administration in two different treatment regimens (coseasonal and precoseasonal).

Method: Patients who concluded the previous study were openly followed-up for an additional season to assess their destiny in real life conditions. The eight centers involved were asked to directly contact patients and to fill-in a data form investigating whether they continued (with a standard pre-coseasonal regimen) or discontinued the treatment, how they judged retrospectively their allergic condition by means of visual analogue scale (VAS score 0–100) during 2009–2011. Averages VAS changes were calculated on the basis of immunotherapy continuation (shift to active treatment) or discontinuation in 2011 and with stratification depending on the kind of initial treatment.

Results: At the end of 2011 *parietaria* peak pollen season, data on 90 out of 151 patients (60%) were available from 7 centers. From 2009 to 2010 in all the three arms a VAS improvement was evident (placebo +9; coseasonal +27; precoseasonal +28), but higher for the active treatments, not substantially different between them. From 2010 to 2011 the VAS further improved only in patients actively treated (+17), including those previously treated with placebo. Conversely patients who discontinued, in 2011 maintained the same VAS levels reached at the end of the study, excluding those who had received placebo that deteriorated. Stratified on the basis of the initial treatment, in 2011 patients previously randomised to placebo improved (+23) only if they shifted to active treatment, patients randomised to coseasonal or precoseasonal further improved (+8 and + 9, respectively) only if proceeded, or maintained the level of 2010 if interrupted.

Conclusion: The clinical benefit for patients allergic to *parietaria* provided by carbamylated monomeric allergoid after one course of treatment remains unchanged regardless of the coseasonal or precoseasonal regimen. Patients' condition further improved when the treatment was continued for a subsequent year.

1546

Monosentitization may still be regarded as the unique indication for sublingual immunotherapy?

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Background: Monosensitised children are still considered as ideal candidates for SLIT and they are included in the most part of the studies to assess its beneficial effects. In this regard its use in polysensitised patients is still a matter of debate, even though polysensitisation is reported as the most prevalent condition among allergic children.

Method: We selected 70 children, 43 boys (61.4%), aged between 6 and 14 years (mean age 10 years) with a clinical history of allergic asthma and/or rhinitis nasal. Sensitisations were assessed by skin prick test, S-IgE and by the demonstration of a clear relationship between allergens exposure and symptoms. Within the 70 children group, 29 (41.4%) underwent SLIT for house dust mite (HDM) and 41 (58.6%) for Grass mix. During the 3 years of treatment, clinical symptoms were evaluated by

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a Nasal and Bronchial Symptom score: a score of 1 was assigned to mild symptoms, 2 to moderate and 3 to severe. Drug consumption was assessed by a Medication Score (MS): a score of 1 was assigned to the use of CST and BLD, 2 to ANTILT, and 0 if no medication was needed.

Results: At the baseline 41 children (58.6%) were polysensitised to both HDM and to Grass mix while 29 children were monosensitised: 16 to HDM (22.9%), 13 to Grass Mix (18.6%). At T0, among monosensitised children, 6 (20.7%) were affected by rhinitis, 7 (24.1%) by asthma and 16 by rhinitis and asthma. Concerning polysensitised patients: 14 (34.1%) had rhinitis, 3 (7.3%) asthma and 24 (58.5%) asthma and rhinitis. In all 70 patients receiving SLIT, a significant clinical improvement was observed since the first year of treatment, irrespective of the allergen, in both monoallergen and polyallergen sensitised group. The reduction of asthma, rhinitis and medication scores over time did not show any statistically significant difference among monosensitised and polysensitised patients. ($F = 0.24$, $P > 0.05$; $F = 1.436$, $P > 0.05$; $F = 0.57$, $P > 0.05$).

Conclusion: SLIT is effective in determining a decrease of the severity of asthma and rhinitis symptoms, assessed by a reduction of Symptoms Scores after three years of treatment. An improvement in clinical outcome was observed in both monosensitised and polysensitised patients, demonstrating that polysensitisation might not rappresent a counter-indication for prescribing sublingual immunotherapy.

1547
Cow's milk tolerance and casein specific IgG4 in the CM anaphylaxis children with treatment of specific oral tolerance induction or elimination diets

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Background: During one year specific oral tolerance induction (SOTI) in 29 cow's milk (CM) allergic children, 73% of non-anaphylaxis group and 30% of anaphylaxis group were completely tolerated in the previous study. We followed up for 2 years in the CM anaphylaxis children with SOTI and non-SOTI, and compared to milk tolerance levels and casein specific IgG4 in two groups.

Method: Twenty nine (mean age of 5.6 years, Male/Female; 18/11) enrolled to SOTI and 16 children (mean age of 5.4 years, Male/Female; 6/10) received CM-removal guidance with documented IgE-mediated milk allergy history and underwent physician-supervised oral food challenges. According to the study protocol, SOTI were starting with an equivalent of 1/5–1/10 of threshold (CM levels failed blind challenge) with 3.3% fresh pasteurised CM in hospital and underwent a home daily ingestion increased by 1.2–1.5 times in hospital setting followed-up for 2 years. CM, Casein specific IgE and casein specific IgG4 were measured by ImmunoCAP (Phadia).

Results: All case without anaphylaxis tolerated to 200 ml for 1–2 years SOTI with mild side effects. In anaphylaxis group, 50% of cases completely tolerated to 200 ml and 50% tolerated 40–100 ml but five cases had severe anaphylaxis needed adrenalin injection at hospital at first year SOTI. One case with anaphylaxis before and during SOTI had completely tolerated by SOTI but developed to FDEIAn to CM at 1 year after SOTI. Nobody of elimination group had tolerance to the small amount CM after 2 years elimination. Casein sIgE decreased significantly in SOTI and not in non-SOTI group. Casein sIgG4 significantly increased in SOTI group and no changed at very low levels in non-SOTI group. Casein sIgG4 were positive correlation with tolerance levels of CM.

Conclusion: SOTI reduce sensitivity of CM in children with immediate CM allergy and it seems to increase CM-food intakes every day, although careful and continuous medical supervision requires during and after SOTI. Measurement of Casein specific IgG4 is useful to evaluation for CM-tolerance in IgE-mediated CM allergy children.

1548
Is there an international consensus on clinical contraindications in allergen immunotherapy?

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Background: Despite the research progress that has been made in the field of Allergen Immunotherapy (AIT) over the last decades, there is still a lack on evidence-based medicine regarding clinical contraindications to AIT. Guidelines and manual practices published from various National and International Allergy Societies and Academies throughout the world are mainly based on experts' opinions.

Method: Within the framework of EAACI, a Task Force (TF) has been organized to review all published National and International guidelines on clinical contraindications to AIT for respiratory and venom allergy. A research has been conducted using online medical search engines, 'exploring' official web sites of registered National and International Academies and/or Societies in Allergy and with personal communication via e-mail with each of them.

Results: We identified 20 published clinical guidelines on AIT; 10 from European Countries, 4 from non-European Countries and six from International Allergy Societies. Some national allergy societies in their websites are citing and reproducing other guidelines, usually originated from International Societies/Academies. In some countries clinical contraindications to AIT are totally missing, whereas there are countries sharing more than one different ones. Similar clinical contraindications have been reported by most of the published guidelines; however, a high heterogeneity in the level of clinical relevance has been identified. TF members also contributed to translate papers published in their national official journals when guidelines were not published in English. Not all contacted webmasters have replied.

Conclusion: We identified a major heterogeneity regarding clinical contraindications to AIT, enforcing the need for this TF. Most national guidelines focus in subcutaneous AIT for respiratory allergy. We are aiming to achieve a harmonized EAACI position paper on clinical contraindications to AIT for respiratory and venom allergy.

1549
Patient journey in house dust mite respiratory allergic disease

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Background: Patients suffering from HDM respiratory allergic disease may experience a considerable time span from onset of symptoms until an appropriate intervention. The purpose of this pilot survey was to investigate the time to diagnosis at either a General Practitioner (GP) or Specialist Physician (SP) and the time to treatment for patients with HDM respiratory allergic disease.

Method: A qualitative pilot study comprising open ended questions was conducted among 24 SPs as individual interviews to

uncover personal motivation in a session expecting to last 60 min. Responses reflected practice of the SPs being interviewed and the time estimates reflect the experience of patients in the care of the interviewed SPs. The SPs had been practicing between 3 and 29 years and spent more than 60% in direct patient care including treatment choice and initiation for HDM respiratory allergic disease. The survey was conducted in Germany and France and the results are presented as a descriptive summary as no statistical analyses was performed.

Results: The average time from onset of symptoms until the patient presented to a GP was 2–3 years (range: 0–30 years). Common reasons for delay were patients' self-medication and hope that symptoms will resolve. The average time from presentation to the GP until referral to SP was 1–2 years (range: 2 weeks–10 years). The most common reasons were lack of GPs' awareness about HDM respiratory allergic disease and treatment options available at the specialist level. After referral to a specialist, the average time to specific diagnosis was 2 months (range: 0–1 year) and 1–2 weeks (range: 0–3 months) in France and Germany, respectively. Reasons for the delay were the SPs' need to assess diagnosis, disease severity, and optimise symptomatic treatment. After diagnosis and treatment optimisation, for those patients who were still uncontrolled, the average time to allergen immunotherapy was 2 months–1 year (range: 0–2 years).

Conclusion: The time from onset of symptoms to diagnosis and appropriate treatment in patients suffering from HDM respiratory allergic disease was found to be up to 5 years suggesting a risk of having poor disease control for years. This qualitative pilot study uncovers a knowledge gap with patients and with GPs' about HDM respiratory allergic disease and stresses the need for improving patient information and raising awareness among physicians about HDM respiratory allergic disease and its treatment options.

1550
Barriers for initiation of allergen immunotherapy treatment in house dust mite respiratory allergic disease

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Background: ARIA guidelines recommend IT to be considered in allergic patients with poor control despite symptomatic treatment (64% of allergic patients in specialist care). We report findings from a pilot survey conducted to investigate attitudes towards initiating IT among specialist physicians (SPs) and patients with HDM respiratory allergic disease.

Method: A qualitative pilot study comprising open ended questions was conducted among 24 adult patients. They were selected if diagnosed within the past two years based on the ARIA criteria for moderate to severe HDM induced allergic rhinitis ± concomitant allergic asthma. The study was conducted in France and Germany by interviewing in each country six patients who had been prescribed IT previously and six patients who had not. Interviews took place separately in the groups to facilitate sharing disease experience. Outcomes from the patient interviews were complemented with 24 individual SP interviews with a separate qualitative open ended questionnaire to uncover personal attitudes. SPs had been practicing between 3 and 29 years and spent more than 60% in patient care including treatment choice and initiation for HDM respiratory allergic disease. Results are presented as a descriptive summary.

Results: Barriers among SPs: The most frequently mentioned reasons were 'inconvenience or incompliance' (i.e. patients reject IT due to inconvenience, or SPs or patients suspect that incompliance will be an issue) ($n = 27$), 'polysensitisation or comorbidities' ($n = 16$), and 'lack of knowledge of IT or concerns of side effects' ($n = 12$). SPs had a misperception of not being able to use IT in combination with symptomatic medication ($n = 10$), did not consider the condition to be severe enough for IT ($n = 10$), and admitted to be unaware that respiratory allergic disease may progress if left untreated ($n = 10$).

Barriers among patients: Primary mentioned reasons were lack of knowledge of how IT works or concerns about potential side effects ($n = 11$). Some patients neglected their disease or were unaware that respiratory allergic disease may progress if left untreated ($n = 6$). Some had a negative perception of IT due to word of mouth/internet ($n = 5$).

Conclusion: The primary barrier for initiation of allergen immunotherapy appears to be a fundamental lack of knowledge. This qualitative survey implies a need for patient information and physician education about HDM respiratory allergic disease and allergen immunotherapy as a treatment option.

1551
Full symptom control in patients with allergic rhinoconjunctivitis caused by grass pollen – results of a 2-year sublingual allergen immunotherapy study

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Background: The aim of this non-interventional study was to document the impact of the routine sublingual immunotherapy and the tolerability with 5-grass pollen tablets (Stallergenes, France) on the symptom severity and the use of symptomatic medication in patients with grass pollen-induced allergic rhinoconjunctivitis over 2 years of treatment. This paper focuses on the subgroup of all patients who completed the entire observation period of the study and describes those patients achieving full symptom control.

Method: This prospective, open, non-controlled, multicenter trial included 1482 patients was conducted from September 2010 to October 2012 in Germany. About 652 of these patients completed the entire study period and built the subgroup of patients used for this analysis of the results after two years. The patients rated the severity of rhinitis and conjunctivitis as a combined rhinoconjunctivitis-score (0–6 scale). We defined a subgroup of patients who were fully controlled after the second year of treatment, i.e. patients with a rhinitis- and conjunctivitis-score of lesser degree of severity (max. mild).

Results: According to this definition 82% ($n = 534$) of all patients who completed the entire study period were fully controlled after two years of medication use.

The rhinoconjunctivitis-score decreased in these patients from a mean value of 4.10 to 1.77 during the first year and to 1.05 during the second year of treatment. The asthma-score decreased in fully controlled patients with asthma from a mean value of 3.42 to 1.31 during the first year and to 0.81 during the second year of treatment.

During the grass pollen season preceding AIT treatment, 82% of the fully controlled patients had used symptomatic medication. This rate dropped to 45% during the first season and to 35% during the second season under SLIT therapy.

Treatment was well tolerated in fully controlled patients with an incidence of adverse events of 8.4% during the 2 years of treatment.

Conclusion: Adherence plays an important role in the management of patients with allergic rhinitis treated with AIT. Our results show that those patients being most

adherent to therapy benefit most in terms of symptom control. A remarkably high number of the adherent patients (82%) treated with 5-grass-pollen tablets achieved a very good symptom control after two years of treatment.

1553
Allergen specific immunotherapy and asthma control and future risk

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Background: Allergen specific immunotherapy (SIT) beneficial effect on asthma is controversial.
Method: We enrolled in a longitudinal 5 year study 35 children aged 5–11 years old (mean age 8.2 ± 2.48), 33 children aged 12–16 years old (mean age 13.06 ± 1.23) and 56 adults (mean age 33 ± 10.5) with allergic asthma. SIT was administered SC for a period of minimum 3 years and the subjects were observed for an additional year after SIT. Asthma control was defined according to GINA criteria and treatment was reduced or increased in a step-wise manner accordingly. Lung function (LF) and exhaled NO (FeNO) were measured at SIT start and then every 3 months until the end of the observation period. Future risk was evaluated as rate of asthma exacerbations in the year before SIT compared to the year following 3 years of SIT, as unfavorable LF trend defined as persistent airway obstruction or decline compared to SIT start and as persistent high FeNO (>50 ppb) at all measurements. Statistics by *t*-test.
Results: All subjects completed the 5 year observation period. In all age groups asthma control was achieved in the majority of subjects with a decrease by >50% of asthma controller medication compared to SIT start or no medication needed and there was a significant decrease in the rate of mild, moderate and severe asthma exacerbations in all age groups (Table 1). LF improved significantly in 54.3% cases in the age group 5–11 years, in 48.5% cases in 12–16 years age group and in 39.3% cases in the adults group. Persistent high FeNO was observed in 8.6% children 5–11 years old, in none 12–16 years old and in 19.6% adults.
Conclusion: Both in children and in adults with asthma SIT has a beneficial effect on asthma control allowing to decrease or even stop controller medication. SIT is associated with a significant decrease in the exacerbation rate and with an improvement in lung function in all age groups.

1554
Comparison of three modalities of mucosal administration of carbamylated monomeric allergoid tablets to treat respiratory allergy due to house-dust mites in a real-life setting for three years

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Background: Carbamylated allergoids (monoids) are chemically modified allergens resistant to proteolytic activity of gastroenteric enzymes. Pharmacokinetics studies revealed they exert sublingual tolerogenic mechanisms and some systemic effects after swallowing. Different modalities of mucosal administration were compared to explore the contribution of sublingual and oral absorption.
Method: Adults with respiratory mite-allergy, in addition to daily cetirizine randomly received monoid (1000 UA twice/week) for 3 years with three intake modalities: sublingual/spit (SSP), oral or sublingual/swallow (SSW). A control group received cetirizine alone. Upper (UAS) and lower (LAS) airways symptoms, on-demand nasal steroids (NS) and salbutamol (B2) were registered with 6-month diary card in winter. Nasal eosinophils (EOS) were compared season by season, bronchial reactivity (MCH), lung function (FEV), and skin sensitisations at the beginning and after 3 years.
Results: Eighty patients concluded the study. A significant improvement was observed in all outcomes with all modalities in respect to controls. Notably SSW was superior to both oral and SSP in reducing UAS, LAS, NCS, EOS, and improving FEV. Oral was equivalent to SSW in reducing the use of B2; oral was also equivalent to SSP in reducing UAS, LAS, B2, FEV, MCH and superior on NCS and EOS. The MCH threshold increase determined by SPP was inferior to SSW but not to oral. Only SSW appeared protective upon the onset of new sensitisations.
Conclusion: Monoid for 3 years provides additional relief to mite-allergic patients treated with antihistamine. Both sublingual and oral absorption contribute in making sublingual/swallow the most advantageous administration modality.

1555
Effect of two different doses of monomeric carbamylated allergoid on nasal reactivity to house dust mite

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Background: Carbamylated allergoids showed benefit on allergic rhinitis over a wide range of doses, because the threshold for efficacy is easily reached through the enhanced bioavailability of the extract

Table 1. SIT and asthma control and future risk

			Children 5–11 years *n* = 35	Children 12–16 years *n* = 33	Adults *n* = 56
Asthma control	No controller medication		4 (11.4%)	8 (24.2%)	10 (17.9%)
	<50% controller compared to SIT start		21 (60%)	20 (60.6%)	25 (44.6%)
	No benefit		10 (28.6%)*	5 (15.2%)*	21 (37.5%)*
Asthma exacerbations rate/year (mean ± SD)	Mild	Pre SIT	3.11 ± 1.09	3 ± 1.11	1.98 ± 1.19
		Post SIT	1.29 ± 0.79*	0.97 ± 0.96*	0.46 ± 0.66*
	Moderate	Pre SIT	1.6 ± 1.12	1.57 ± 1.43	0.71 ± 1.12
		Post SIT	0.46 ± 0.56*	0.4 ± 0.62*	0.16 ± 1.12*
	Severe	pre SIT	0.57 ± 0.86	0.63 ± 0.81	0.15 ± 0.44
		post SIT	0.06 ± 0.23*	0*	0*

consequent to the selective chemical modification. We compared the effect of two different doses on nasal reactivity.
Method: This study involved patients with clinically relevant sensitisation to house dust mites and positive response to nasal provocation challenge (NPT). Carbamylated allergoid (1000 or 2000 AU daily) was delivered for 12-weeks during the lowest level of mites exposition. Primary outcome: change of the threshold of allergen concentration for a positive NPT before and after the treatment. Secondary outcomes: change in the mean percentage fall of peak nasal inspiratory flow (PNIF) during NPT, efficacy and tolerability rated by investigators, patients' satisfaction and frequency of adverse events.
Results: Thirty-four patients were enrolled. Fifteen in group 1 and 14 in group 2 concluded the study. After 12 weeks of treatment all patients in group 1 and all but one in group 2 showed an increase in the threshold dose provoking a positive TPN and those with no symptoms occurrence with the highest dose delivered were 80% in group 1 and 78.6% in group 2 ($P = 0.92$). From first to second NPT the mean percentage fall of PNIF was reduced of 11.63 (SE 4.92; $P < 0.05$) in group 1 and 12.23 (SE 9.26; $P = 0.21$) in group 2 ($P = 0.95$), with no difference between the final mean percentage falls ($P = 0.65$). In the two groups efficacy rated by physician was distinct in 53% and 54%, tolerability was very good in 83% and 77%; patients very satisfied were 62% and 51%. No serious AEs occurred during this study; the frequency of events, all mild, was similar in the two groups.
Conclusion: Twelve weeks of carbamylated sublingual allergoid delivered at 1000 AU or 2000 AU once daily are equally safe and shows comparable effect in increasing the threshold of allergen concentration for a positive nasal provocation test.

1556
The long-term health related quality of life consequences of asthma for children with allergic rhinitis

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Background: To assess the long-term burden of asthma in children with allergic rhinitis/conjunctivitis.
Method: We reviewed the literature on incidence of asthma in patients with allergy. Furthermore, we estimated long-term outcomes associated with allergic rhinitis/conjunctivitis in children using a Markov health state model. The model was populated using data from a long-term prospective follow-up, where asthma status was recorded up to 10 years in patients recieving only symptomatic treatment for allergy and asthma symptoms. The model was used to explore the impact of key drivers of long-term patient outcomes. Burden to patients was measured as the difference between net present value of QALY and life-years.
Results: Allergic rhinitis/conjunctivitis in childhood is associated with a risk of developing asthma. The asthma risk is highest at younger age and decreases as the child reaches adolescence and adult age. Furthermore, allergic rhinitis is a risk factor for childhood allergic asthma to persist into middle age. The model analysis showed that in per one hundred 10-year old patients with hay fever, but no previous asthma:

1. Sixty-one patients will develop asthma over a 10 years horizon
2. In total 70 QALYs are lost over a 10 year time horizon of which 40% is attributable to allergic asthma
3. Additional 17 respectively 39 QALYs are lost when analyzing on a 15 respectively 20 year time horizon also assuming no additional cases occur after year 10.

Conclusion: Childhood allergic rhinitis is a risk factor for developing allergic asthma in childhood/ preadolescence. Allergic asthma in turn has a pro-found effect on the long-term burden of allergic rhinitis/ conjunctivitis. Literature suggests that childhood asthma may impact quality of life also when the patient reaches middle age. This suggests a large potential for specific immunotherapy with disease modifying properties to reduce the burden of allergy and allergic asthma.

1558
Patients' adherence to begin immunotherapy treatment

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Background: Spain is now in a very important economic crisis, with a high percentage of population unemployed. Our city has got unemployed levels near to 35% of total active population. In this situation our aim was to determine the adherence to an immunotherapy treatment in our patients, and to describe them.
Method: Patients referring respiratory symptoms that came to our Allergy Department with immunotherapy criteria (according to position papers published) from June to December 2012 were included. After a clinical report focusing in their respiratory symptoms, skin prick test with the most frequent aeroallergens in our city (House Dust Mites (HDM), molds, pollens and epithelia dander) and total and specific IgE to positive cutaneous test, we proposed immunotherapy treatment, and signed an informed consent. We registered the adherence and why they didn't buy it.
Results: Fifty-five patients (25 males and 30 females; mean age 29.85 years) were included. All patients referred allergic rhinitis and 28 (50.90%) asthma. Twenty-five (4.45%) began the treatment (12 (48%) asthmatic patients), being 17 (68%) sensitised to HDM and 8 (32%) to pollens. All patients were working (or their parents if they were students). On the other hand (30 patients (54.55%)), 16 (53.33%) were asthmatics, being 19 (63.33%) to HDM, and 11 (36.67%) to pollens. Four patients (13.33%) were unemployed and 9 (30%) were students with their parents working. Asking about the no adherence, all of them preferred a medical treatment because it was cheaper.
Conclusions:

1. Although a high percentage of patients are working and they have clinical symptoms that recommend immunotherapy treatment, the adherence isn't very high.
2. Patients prefer a medical treatment, which could be more expensive per year than an immunotherapy treatment.
3. Being a student isn't a safety factor to begin immunotherapy.

1559
Three year follow up after rush oral immunotherapy for cow's milk-induced anaphylaxis

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Background: The purpose of this study is to clarify the efficacy of cow's milk (CM)-OIT's prolonged course to induce the desensitisation and tolerance for CM-induced anaphylactic children.
Method: Hundred-nine CM anaphylactic subjects, who were confirmed by double-blind, placebo-controlled food challenges (DBPCFC), underwent rush oral immunotherapy (ROIT). After ROIT, they had slowly built up to 200 ml/day CM at home (slow OIT). The subjects, who had taken maintenance doses without any symptoms at least for 3 months, underwent food

challenge (FC) after 2 weeks' CM complete avoidance to confirm tolerance acquisition (Final FC). We analyzed the clinical course of OIT (rate of tolerance, number (rates) of adverse reactions, laboratory data) in these subjects.

Results: Currently, 81 subjects had received OIT for 1 year, 57 subjects were already more than 2 years' follow up. We further analyzed the data from 18 subjects (median age 8.8 years old) who had received OIT for 3 years or more. In prior to ROIT, median threshold to induce earliest reaction was 2.1 ml, to induce anaphylaxis was 50 ml CM and median milk specific IgE was 27.6 Ua/ml. After 3 years or more, five subjects (28%) dropped out the protocol due to difficulty in taking milk or CM products, two subjects (11%) couldn't reach to 200 ml/day and 11 subjects (61%) could achieve desensitisation. Ten subjects could undergo the final FC. Two subjects (11%) were confirmed achieving tolerance acquisition by the final FC within 1 year, 4 subjects (22%) at 2 years later, and 7 subjects (39%) at 3 years later. Milk specific IgE (Ua/ml) decreased with years (Prior to OIT; 27.6, 1 year later; 15.1, 2 year later; 10.7, 3 year later; 8.6, respectively). Adverse reaction rates tended to decrease through the course of slow OIT. However some subjects, who had achieved this temporary tolerance acquisition, infrequently had reactions due to exercise after taking CM or infection.

Conclusion: CM-OIT for CM-anaphylaxis seemed to be effective to reduce the risk of accidental adverse reactions with increasing the rate of desensitisation and tolerance during prolonged therapy. However acquisition of tolerance by CM-OIT seems to be differ from that by natural outgrow.

1560
Measurement of fractional exhaled nitric oxide as a new tool for patient's adherence to sublingual immunotherapy

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Background: Sublingual immunotherapy (SLIT) is clinically effective, but, as any other long term treatment, faces the problem of adherence. The perception of treatment efficacy represents the main factor influencing patient's adherence. The availability of an objective 'marker', able to help the patient follow his own improvement should represent a step forward in adherence optimisation.

Measurement of fractional exhaled nitric oxide (FeNO) is a non-invasive exam which has been validated for asthma management. The exam results in a clear numeric parameter which correlates with airway inflammation and increases the patient's and physician's perception of the disease state. The aim of our pilot study was to evaluate if repeated FeNO measurements could increase SLIT therapy adherence.

Method: We included 44 patients (23 males and 21 females, mean age: 25.5 ± 12.9 years) with allergic rhinitis, who started SLIT therapy for house dust mites (HDM). We divided patients in 2 groups: patients performing at least 2 FeNO measurements during the 3 years of therapy (with FeNO) vs patients who had never measured FeNO or had only once (without FeNO). To evaluate adherence to therapy, we considered treatment renewal rate (number of vials) as a parameter, considering that patients cannot comply SLIT therapy if they have not obtained the prescribed drug.

Results: No patient reached the number of vaccine vials needed to complete SLIT treatment as indicated in the summary of product characteristics. However the group with FeNO had a significant higher renewal rate compared to the group without FeNO. In the first year the group with FeNO reordered a mean number of vials as 6.9 ± 2.2 vs 3.8 ± 1.3 for group without FeNO ($P < 0.001$). Considering the following years the group with FeNO reordered a number of vials as 8.2 ± 6.3 vs 0.1 ± 0.6 for group without FeNO ($P < 0.001$).

Conclusion: Adherence remains a problem for AIT and new methods for increasing patient′s adherence to therapy have to be assessed. We found a correlation between FeNO measurement and adherence to SLIT therapy in terms of product reorders. These findings suggest that monitoring the disease with a clear numeric parameter, as FeNO, may help patients to understand their disease state and motivate their continuation of immunotherapy.

Poster Session 69

Mechanisms in food allergy

1561
Frequent sensitisation to *Candida albicans* and profilins in adult eosinophilic esophagitis

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Background: Eosinophilic esophagitis (EoE) is often associated with atopic airway and skin diseases. More than 80% of EoE patients are sensitised to aero- and/or food allergens. Immunoglobulin (Ig)E-mediated immune responses to microbes were reported to deteriorate atopic diseases. The aim of this study was to obtain a comprehensive overview about the sensitisation profile of EoE patients.
Method: Specific IgE in sera of 35 patients with active EoE were analyzed to Candida albicans as well as to a panel of recombinant and purified natural allergen components using a microarray.
Results: IgE sensitisation to Candida albicans was found in 43% of EoE patients. More than 80% of EoE patients were sensitised to aeroallergens and 22% to food-specific allergen components. Sixty nine% of the patients exhibited specific IgE to cross-reactive allergens. Among them, profilins were identified as most frequent IgE cross-reactive allergen components. Interestingly, dysphagia the main symptom of adult EoE patients, following rice and/or bread ingestion was associated with sensitisation to cross-reactive allergens such as profilins, pathogenesis-related 10 and lipid transfer proteins whereas intolerance of meat rarely correlated with sensitisation to animal food allergens.
Conclusion: Candida albicans and cross-reactive plant allergen components in particular profilins were identified as frequent sensitisers in adult EoE patients. Specific elimination therapies are suggested to reveal their actual role in the pathogenesis of EoE.

1562
Detectable peanut allergens in house dust – a risk factor for developing sensitisation to peanut?

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Background: It could be shown that household peanut consumption is a risk factor for the development of peanut allergy. Thereby cutaneous exposure to food allergens may be an important way of sensitisation. As house dust is a potent allergen vehicle and as it is easily distributed in all domestic areas, we aimed to investigate whether peanut allergens are detectable in house dust and whether the peanut level correlates with the household peanut consumption.
Method: 21 households were included in the study. All participants completed a questionnaire regarding dietary habits concerning peanuts and cleaning habits. Dust samples were collected in the habitual eating area and from bed sheets, using a special vacuum cleaner device. Peanut protein was extracted and peanut allergen levels were measured with a commercially available ELISA (range of quantification: 2.5–20 ppm). Eight selected households with low peanut-allergen baseline levels were asked to consume roasted peanut snacks in their habitual eating areas. Forty-eight hours later, dust samples were collected. Spearman's rank correlation coefficient was calculated to evaluate the relation between peanut levels and peanut consumption. Wilcoxon rank test was used to compare peanut levels before and after peanut consumption.
Results: In 17 of 21 households peanut was detectable in the habitual eating areas and in 20 households on bed sheets. Comparing the frequency of peanut consumption to peanut levels in house dust, we found a moderate correlation of peanut consumption and peanut levels in the habitual eating areas ($r = 0.595$, $P < 0.01$) but not on the bed sheets. In 8 households with low peanut levels at baseline (range 1.4–14 μg/g) we could measure significantly increased peanut levels after peanut consumption, in the habitual eating areas (range 6.4–59.5 μg/g) as well as on the bed sheets (range 4.4–57.8 μg/g).
Conclusion: In summary, peanut allergens were detectable in the house dust, not only in areas where peanuts are habitually eaten but also in the bed where peanut is usually not consumed, indicating a spreading of food allergens within the household. As infants spend most of the time in bed, peanut containing house dust on bed sheets could be considered as important risk factor for environmental sensitisation. Nevertheless further research is required in order to proof whether peanut allergen in house dust can cause sensitisation via cutaneous contact or inhalation.

1563
Polyunsaturated Omega-3 fatty acids restore reduced social interaction and dopaminergic activity in the prefrontal cortex of cow's milk allergic mice

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Background: The dopaminergic system in the prefrontal cortex (PFC) is known to modulate attentional skills, perception and social behavior. Decreased levels of dopamine (DA) in the PFC are implicated to be involved in various psychiatric diseases. Furthermore, disturbed levels of polyunsaturated fatty acids (PUFA) in blood have been observed in these disorders and literature suggests a potential beneficial role for dietary intervention with PUFA as well. In this study, we investigated the effect of n-3 PUFA on altered social behavior of cow's milk allergic (CMA) mice and corresponding DA levels in the PFC.
Method: Male C3H/HeOuJ mice were orally sensitised with whey protein and cholera toxin (CT) or CT alone, once a week for 5 weeks and subsequently orally challenged with whey protein once. Starting two weeks before first sensitisation, mice were kept on an omega-3 PUFA diet or control diet. The morning after challenge, a social behaviour test was performed, mice were sacrificed and brains were collected. PFC was isolated and dopamine levels were determined by using HPLC.

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Results: Cow's milk allergy in mice caused reduced social interaction and a dietary intervention with n-3 PUFA significantly improved social behavior in allergic mice. Furthermore, dopamine and metabolite levels in the prefrontal cortex were significantly reduced in cow's milk allergic mice. When allergic mice were fed an n-3 PUFA diet, both dopamine and metabolite levels were restored to those found in non-allergic mice.

Conclusion: n-3 PUFA possibly exerts its beneficial effect on behavior via modulating the dopaminergic system in the prefrontal cortex and might offer a dietary intervention in some psychiatric disorders.

This study is part of the Utrecht University 'Focus en Massa' program and is financially supported by Danone Research-Centre for Specialised Nutrition.

1565
Tuna oil high in docosahexaenoic acid is most effective in the prevention of allergic sensitisation and symptoms induced by food allergens in mice

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Background: Recently we have demonstrated that dietary supplementation with tuna oil rich in docosahexaenoic acid (DHA) largely prevents allergic sensitisation in a mouse model for cow's milk allergy (CMA). Aim was to assess whether high eicosapentaenoic acid (EPA) vs high DHA fish oil differ in allergy prevention early in life in food allergy.

Method: Mice were fed a control (soy oil), EPA (EPA rich fish oil) or DHA (tuna oil) diet before and during oral sensitisation with whey protein or peanut extract. Acute allergic skin response, serum immunoglobulins and T-cell proliferation and subsets were determined. In addition, peanut or whey hyperimmune serum high in IgE was passively transferred to naïve recipient mice fed the different diets. These mice were challenged intradermally in the ear with the respective antigens.

Results: The acute allergic skin response was reduced in DHA fed peanut allergic (PA) mice as compared to control or EPA diet fed mice. In CMA mice both EPA and DHA reduced the acute allergic skin response, however whey-specific immunoglobulins were suppressed most pronounced in DHA mice. The DHA diet also reduced T-cell proliferation in spleen of PA mice, and cytokine secretion showed the same tendency. The percentage of activated Th2 cells was reduced in mesenteric lymph nodes of CMA mice fed DHA as compared to controls. In addition, DHA but not EPA did enhance regulatory T-cells in the small intestine of PA mice. Furthermore, fish oil fed naïve recipients passively sensitised using hyperimmune serum had diminished allergic symptoms upon allergen challenge. For whey this response was significantly lower in DHA fed mice compared to EPA, indicating that suppression of the effector response is most effective by DHA.

Conclusion: Fish oil largely prevents allergic sensitisation in a mouse model for CMA and reduces allergic symptoms caused by peanut extract. Tuna oil high in DHA is more effective than fish oil rich in EPA in the prevention of allergic sensitisation and symptoms in food allergic mice.

1566
Kinetic of *in vitro* response to β-lactoglobulin in children allergic and tolerant to cow's milk protein

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Background: Cow's milk protein allergy (CMPA) affects 2–6% of children. About 80–90% of children allergic to cow's milk protein (CMP) outgrow their allergy within their fifth year of age. The profile of the immune responses to the main CMP in the different clinical condition has not been completely elucidated. In this report we describe two children (P1 and P2) with CMPA in whom we performed a long clinical and immunological follow up. P1, with a history of bronchospasm and atopic dermatitis after introduction of cow′s milk and CMP positive diagnostic tests (T1), after elimination diet, developed first a selective tolerance to milk derivatives (T2) and then complete tolerance to CMP (T3). P2, with a history of angioedema and urticaria after introduction of milk formula (T1) and anaphylaxis after accidental assumption of cow milk (T2), still does not tolerate CMP (T3).

Method: At the three different time points (T1, T2 and T3), PBMC of patients were collected and stimulated with an extract of β-lactoglobulin (BLG), and in parallel, with 22 peptides of BLG (20 aminoacid long, overlapping of 10). T cell proliferation to BLG and peptides was measured by overnight [^{3}H]Thymidine incorporation. Cytokines (IL-4, IL-5, IL-9, IL-10, IL-13, IFN-γ, TNF-α and IL-17), were measured by Bioplex, in PBMC's culture supernatants, after 7 days of stimulation.

Results: In P1, BLG-specific T cell proliferative response revealed a gradual decrease, from T1 to T3, in parallel with clinical tolerance acquisition. In both patients we detected a selective response to the peptides 9–12 of BLG, indicating that this region contains a common BLG epitope. In P1, the proliferation to the peptides 9–12 showed a trend similar to that of BLG. In P2, on the contrary, T cell proliferation persisted elevated, as well as the response to the peptides 9–12. Furthermore, in P1, IL-10 and TNF-α declined gradually, whereas, in P2, IL-10 was unchanged and TNF-α increased markedly over time. IL-4 was not detectable at any time in both patients, whereas IL-5, undetectable in P1, increased over time in P2. IL-9, IL-13 and IL-17 levels decreased with similar trend in both patients. Interestingly, IFN-γ decreased in P1, but not in P2.

Conclusion: The study of immunological characteristics of children with CMPA and who outgrow CMPA is important to understand the mechanism that mediate tolerance acquisition and might provide crucial information to design a more effective immunotherapy.

1567
Wheat-dependent exercise-induced anaphylaxis – a review of eight cases

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Background: There is marked heterogeneity in wheat allergy prevalence within Asia. Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a specific form of wheat allergy caused by the combination of wheat ingestion and physical exercise and has been reported in other parts of the Asia. WDEIA has yet to be reported in Singapore hence this study aims to characterise the common clinical, epi-cutaneous and laboratory manifestations of this distinct disease entity seen here.

Method: This was a retrospective descriptive study of all WDEIA who presented to a tertiary Singaporean Hospital between over a 2-year period from 2010 to 2012.

Results: Eight patients aged 9 to 41 years old were characterised. Five were males and the majority (5) was of Chinese ethnicity. An atopic history was found in five individuals. The symptoms of anaphylaxis

included cutaneous manifestations such as urticaria ($n = 8$), angioedema ($n = 6$), respiratory symptoms of dyspnea and wheezing ($n = 4$), and hypotension ($n = 5$). The symptoms occurred between 5 min to 2 h after consumption of wheat-based products and various forms of exercise [running ($n = 4$), walking ($n = 3$) and swimming ($n = 1$)]. The WDEIA was recurrent in six patients. The skin prick tests were positive to wheat in five patients and omega 5-gliadin test to wheat was positive in 2.

Conclusion: With the emergence of wheat allergy in East Asian countries, WDEIA has become an important condition for physicians and Singapore is no exception. Under-recognition combined with life threatening symptoms warrants better public awareness measures. In addition further studies are necessary to identify possible unique genetic and environmental exposures that could in part explain the interregional differences of WDEIA.

1568
Subjects sensitised to sunflower seed (*Helianthus annuus*) are tolerant in a high proportion of cases

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Background: Although not detailed studies have been carried out in allergy to sunflower seed (*Helianthus annuus*), this is an important cause of food allergy and/or sensitisation in many populations. The aim was to study a large group of sensitised subjects to sunflower.

Method: We performed a search in the data base belonging to the Spanish network for the study of adverse reactions to drug and allergens (RIRAAF). All those with skin prick test positive were considered hypersensitive and they were included in the study. Four major groups were subclassified as detailed below. Specific IgE to sunflower and ELISA inhibition studies to sunflower, Lipid transfer proteins, LTPs (Pru p3 and Ara h9), Thaumatin-like proteins, TLPs (Act d 2) and 2S albumins (Ara h6) were carried out

Results: A total of $n = 200$ cases was included with skin prick positive. From these 7% had anaphylaxis, 7.6% urticaria, 4% oral allergy syndrome and 82% tolerant. The analysis of the specific IgE response did not show any statistical differences between the groups in the number of positives. Direct ELISA and inhibition studies showed that LTPs, TLPs, 2S albumins were relevant allergens in all groups although no differences in the recognition pattern were observed.

Conclusion: In hypersensitivity reactions to *Helianthus annuus* a significant proportion of cases are tolerant, although anaphylaxis or other entities may be induced by sunflower allergens. Those belonging to different families were recognised in the sera of all the groups. Studies are in progress to identify the primary and the secondary sensitisation to the different sunflower allergens in order to better understanding these observations.

1570
Drug reaction to lipid transfer protein by excipient?

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Background: Sometimes drug reactions are caused by the excipients. Peanut allergy is increasing in our society. In some drugs, the peanut oil is used as an excipient.

Method: Twenty six years old woman was referred to own service by drug reaction. She suffers of polycystic ovary and started treatment with progesterone (peanut oil excipient). In the second administration, she immediately presented hand, foot and oropharyngeal pruritus, tongue edema, generalise urticaria and respiratory distress. She went to the hospital and was treated with corticosteroids and antihistamines. She, previously had tolerated peanuts and nuts. and referred an oral allergy syndrome with pineapple and melon. Four months later she had a similar reaction with apple.

Results: Prick test: Peanut 5 mm. Hazelnut 5 mm. Apple skin 5 mm. Pinapple 5 mm. Walnut 5 mm. Sunflower 5 mm. D. Pteronyssynus 10 mm. D. farinae 8 mm. E. maynei 8 mm. Ig E: 40.50 IU/ml. Triptase: 239 μg/l. IMMUNOCAP specific IgE: Peanut 1.26 kU/l. Hazelnut 2.56 kU/l. Almond 0.73 kU/l. Pomace 3.56 kU/l. Prup p3 4.26 kU/l. IMMUNOCAP-ISAC: Fel d1 0,9 ISU-E. Der f1 1,9 ISU-E. Der f2 11 ISU-E. Der p1 2 ISU-E. Der p2 ISU-E. Lep d2 0,5 ISU-E. Jug r3 3.6 ISU-E. Pru p3 5 ISU-E. Art v3 4 ISU-E. Progesterone provocation test without excipient: Negative with good tolerance.

Conclusion: The patient was diagnosed of LTP allergy. In our case, LTP may act as an excipient to hidden drug allergy. Metabolized vegetable oils, such as peanut oil can serve as adjuvants, increasing the immune response to antigens. Whipping or emulsifying peanut butter to prevent the oil from separating from the peanut solids bring more of the water soluble protein into direct contact with the oil, potentially increasing the immunogenicity of peanut proteins ingested in this manner. Highly refined peanut oil is usually tolerated by people with peanut allergy. However, processing variations exist and sources may not be easily traced, so avoidance of even refined peanut oils must be advisable.

1571
The effect of maternal folic acid intake during pregnancy on incidence of child food allergy

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Background: Food allergy is the most common in infants and young children. In Japan, intake of folic acid during pregnancy is recommended to prevent neural tube defects. Supplementary intake of folic acid during pregnancy has recently become increasingly common; thus, we have evaluated the effect of folic acid intake on the prevalence of food allergy in infants and young children.

Method: A survey was conducted at the same location from July to October 2011 and from May to August 2012.

Results: The average age of 2688 children was 18.6 ± 0.9 months. Only the existence of a child′s food allergy was distinguished based on a doctor′s diagnosis. The breakdown of those who developed allergies was 10.0% with food allergy, 8.3% with atopy, 5.9% with eczema, 4.1% with asthma. In addition, 41.5% of the pregnant mothers had taken folic acid supplements. Atopy occurred in 7.6% of children in the group where the mothers took folic acid supplements (FA+ group) compared with 9.0% in the group where the mothers did not take folic acid supplements (FA− group). There was a downward trend in the FA+ group, but the difference was not significant ($P = 0.064$). Furthermore, asthma developed in 3.7% of children in the FA+ group compared with 4.5% in the FA− group, which indicates that the effect of folic acid supplements was small. On the other hand, eczema occurred in 7.8% of children in the FA+ group compared with 4.6% in the FA− group [odds ratio, 1.754 (95% confidence interval, 1.273–2.415)], which indicated that the percentage of allergic children increased based on folic acid intake. Food allergy occurred in 11.9% of children in the FA+ group

compared with 8.6% in the FA− group (odds ratio, 1.447). This suggests that children tend to have food allergy when their mothers take folic acid supplements during pregnancy. In particular, in mothers without an allergy, taking folic acid supplements increased food allergy onset in children without atopy [odds ratio, 1.991 (95% confidence interval, 1.233–3.215)].
Conclusion: A mother's intake of folic acid supplements during pregnancy affects the prevalence of allergies in their children.

1573
New food allergies in a European non-Mediterranean region: is *Cannabis sativa* to blame?

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Background: Allergy to fruit and vegetables exhibit geographic variation regarding the severity of symptoms and depending on the sensitisation profile of the patient. These sensitisation profiles and routes remain incompletely understood. Cannabis is a very popular drug and derived from *Cannabis sativa* a plant containing lipid transfer proteins (LTP) also known as important allergens in plant and fruit allergies. In this study we sought elucidate on a potential connection between *Cannabis sativa* allergy (CSA) and plant food allergies
Method: Case-control study involving 21 patients consulting for plant food allergies. Twelve patients were cannabis allergic and nine had a pollen or latex allergy without cannabis allergy. Testing for cannabis IgE implied measurement of sIgE, skin testing and basophil activation tests. Allergen component analysis was performed with a microarray technique
Results: Plant food allergy in patients with documented cannabis allergy had more severe reactions than patients without cannabis allergy and frequently implied fruits and vegetables that are not observed in a (birch) pollen-related food syndrome. All, except one of the patients with cannabis allergy were sensitised to non-specific lipid transfer proteins
Conclusion: Our data suggest that illicit cannabis abuse can result in cannabis allergy with sensitisation to non-specific lipid transfer proteins. This sensitisation might result in various plant-food allergies. Additional collaborative studies in different geographical areas are needed to further elucidate on this hypothesis.

1577
Food allergy – Indian scenerio

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Background: Claims of marked increases in the prevalence of food allergy (FA) and celiac disease (CD) are common in the US and EU and increasingly in India where little is known about food allergy. Studies suggest increasing trends, but often lack rigorous definition of symptoms and tests. Reliance on Skin Prick Tests (SPT) or specific IgE alone, without corroborating clinical histories may be misleading. Once diagnosed, patients with FA or CD must avoid eliciting foods, which requires accurate information of food ingredients.
Method: A prospective study in the Dept. of Pediatrics, SMS Medical College, Jaipur was carried out in hospitalised as well as out patients. Diagnosis of Food Allergy and Celiac Disease was made on the basis of history, clinical examination and laboratory investigations. Information has also been gathered from Nationally accredited laboratories conducting food allergy testing and national surveys.
Results: Any food can be allergenic, Patterns of common allergens differ across regions and culturs, dairy, eggs, peanuts, tree nuts such as walnuts, almonds and cashews, fish, shellfish, soya, wheat, seasame top the list, Incidence of allergies to milk, eggs and wheat less frequent then in the West, Dals (Pulses) such as chickpeas more common allergy to rice has been reported, Food Allergy evenly distributed More in urban and semi urban areas as compared to rural areas, Changing food pattern moving away from Traditional Dal, Rice, Vegetables to Fast Food, Ice cream, Chocolates. increased Houses have Carpets & Pet.
Conclusion: Food allergy on the rise, Need for establishing a national registry, Urgent need to educate medical personnel, Social & Psychological cost to the patient and the family needs focus. Food labeling generally improper, Scientific support on preventing food allergy & making food safe required, Quality control of marketed foods need to be monitored. It seems appropriate to encourage development of valid testing systems and gather reliable information to aid the food industry and government regulators develop methods to help the food industry protect FA and CD patients from unintended exposure.

1578
Sensitising capacity and allergenicity of enzymatically cross-linked sodium caseinate in comparison to sodium caseinate in a mouse model for cow's milk allergy

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Background: A new transglutaminase cross-linked caseinate (Excellion EM7 High Viscosity) was designed for the use in dairy products to increase the viscosity of food matrices. The difference in structure of the cross-linked caseinate compared to sodium caseinate might have implications for the risk of developing cow's milk allergy. The sensitising capacity and the allergenicity (the potency to induce an allergic effector response) of cross-linked sodium caseinate in comparison to sodium caseinate was investigated using a mouse model for cow's milk allergy.
Method: Mice were orally sensitised with a blunt needle on day 0, 7, 14, 21 and 28 with either 20 mg cross-linked caseinate or caseinate homogenised in saline mixed with 10 μg cholera toxin as an adjuvant. Non-sensitised mice received cholera toxin in PBS only. One week after the last oral sensitisation anaphylactic shock reactions, change in body temperature, and acute allergic skin responses were determined as clinical related symptoms for cow's milk allergy after an intradermal challenge with cross-linked caseinate or caseinate. Allergen-specific IgE and mMCP-1, as a reflection of intestinal mast cell degranulation, were measured in serum 30 min after an oral challenge to caseinate or cross-linked caseinate.
Results: In contrast to mice sensitised to caseinate, sensitisation of mice with cross-linked caseinate did not result in any anaphylactic shock symptoms, a drop in body temperature or release of serum mMCP-1. A tendency towards decreased casein-specific IgE levels was observed in mice sensitised to cross-linked caseinate. The allergenicity (capacity to induce an allergic effector response in caseinate-sensitised animals) upon challenge with cross-linked caseinate was not significantly different from the caseinate.
Conclusion: These results indicate that in already caseinate-sensitised mice, cross-linked caseinate did not provoke more pronounced allergenic reactions compared to sodium caseinate. On top of that, a reduced sensitisation to caseinate was

observed in mice sensitised to cross-linked caseinate. Cross-linked caseinate might therefore be an interesting new dietary concept for humans at risk for food allergy although more mechanistic studies and clinical trials are needed for validation.

1579
Serum IgA and IgG antibodies to wheat gliadin and milk β-lactoglobulin in early infancy predict atopic sensitisation at school age

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Background: The introduction of food and bacterial antigens to the immune system is mainly conducted via the gut. Serum IgA and IgG antibodies against wheat gliadin and cow's milk β-lactoglobulin are indirect markers of gut permeability and inflammation. Living on a farm has been shown to decrease allergies in children. Our aim was to study whether living in a farming environment affected the gut permeability, IgE sensitisation, and allergic diseases in European children.

Method: The birth cohort study PASTURE was conducted in Finland, France, Germany, Austria and Switzerland. At age 1, we measured serum immunoglobulin A (IgA) and immunoglobulin G (IgG) against wheat gliadin and cow's milk β-lactoglobulin (n = 643) using ELISA method. Specific immunoglobulin E (sIgE) against 19 common allergens was tested with the Allergy Screen Test Panel for Atopy (Mediwiss Analytic, Moers, Germany) at age 6. Cut-off for sensitisation was a specific serum IgE level at 0.7 kU/l. Data on environmental factors and allergic diseases were collected by questionnaires from pregnancy up to age 6. Multivariate logistic regression models were used for analysis. P-values below 0.05 were regarded as statistically significant.

Results: The levels of serum IgA and IgG against milk β-lactoglobulin varied between countries ($P < 0.001$), as did the levels of IgA and IgG against wheat gliadin ($P = 0.014$ and $P < 0.001$, respectively). Children with sensitisation to any of the measured allergens at age 6 showed elevated levels of IgA and IgG against milk β-lactoglobulin ($P < 0.001$), and elevated levels of IgA and IgG against wheat gliadin ($P = 0.013$ and $P = 0.002$, respectively) at age 1. The children who were sensitised to inhaled allergens had elevated IgA and IgG against milk β-lactoglobulin ($P = 0.009$ and $P = 0.015$, respectively). There was no significant difference between children of farmers and non-farmers or asthmatics and non-asthmatics, although, children who had asthma at age six tended to have elevated IgA against gliadin at age 1 ($P = 0.065$).

Conclusion: Increased production of antibodies to wheat gliadin and cow's milk β-lactoglobulin at age 1 was associated with sensitisation at age 6. We suggest that enhanced antibody response to food antigens at early age reflects aberrancies of mucosal tolerance, e.g. increased gut permeability or inflammation, which is later seen as sensitisation to allergens.

Poster Session 70

Diagnosis of food allergy III

1580
Poultry meat allergy: description of a new allergen

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Background: Poultry meat allergy is an unusual pathology. Most cases are associated with hypersensitivity to egg or with another allergen like parvalbumins. The aim of this study was to describe a case of poultry allergy and to identify the allergens for a correct diagnosis.
Case report: A 38-year-old male, with no medical history, was studied. In the last 10 years, he referred dyspnea, labial angioedema, hives, itching and dysphagia after consuming well done poultry meat (chicken and turkey).
Method: Skin prick tests to commercial meat extracts (chicken and ostrich) and hen's egg proteins were performed. Specific serum IgE against commercial poultry and egg proteins extracts was determined by CAP system Pharmacia. Specific serum IgE against extracts from raw and boiled meats (turkey, chicken, ostrich, duck and quail) was determined by EAST. Poultry allergens were studied by SDS-PAGE, IgE Immunobloting, 2D-Immunoblotting and Mass Spectrometry.
Results: Skin prick tests to commercial meat extracts were positive. Skin prick tests to egg proteins were negative. Specific IgE to raw and boiled meats were positive. SDS-PAGE and Immunobloting with meat extracts showed some common prominent IgE-binding protein bands at 28 kD, 20 kD and 14 kD. The 2D Immunoblotting revealed three spots at 20–25 kD. Actin was identified by Mass Spectrometry as the responsible allergen.
Conclusion: We present a case of poultry meat allergy due to a new heat-resistant allergen (Actin). To our knowledge, this is a protein which has not been previously described as an allergen.

1581
Allergy to milk cream not due to habitual milk's proteins

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Background: Food allergy is highly prevalent in our environment, especially among atopic patients. We report the case of a patient with suspected allergy to milk cream

The use of proteins within the lipid fraction were used to confirm the diagnosis of specific hypersensitivity to milk cream.
Methods: Patient referred to our department for an episode of itching and swelling after eating olives, hamburger and a sandwich with meat and milk cream. Two months later did react to margarine. Skin prick test with a commercial food battery and prick by prick with milk cream were performed. We also analyzed patient sera for Total and specific IgE to different allergenic sources such as latex, Anisakis, milk, egg white, peach, nut and peanut, different seafood, mustard and wheat.

The proteins of hydrosoluble and liposoluble fraction from milk cream were transferred to PVDF membranes for subsequent Western blot assays
Results: Patient didn't demonstrated specific IgE to allergen sources tested neither did she react to prick tests because of dermographism however she did have positive prick by prick to milk cream.

The serum of the patient was analyzed with proteins from hydrosoluble and liposoluble fraction extracts from milk cream. The serum recognised a protein of 60 kDa in liposoluble fraction leading us to suspect that protein were responsible of the clinical symptoms
Conclusions: We describe a case of sensitivity to milk cream not due to habitual milk's proteins. A protein of 60 kDa from liposoluble fraction of milk cream was recognised by patient's serum. It could be used for diagnostic purposes and the patients with negative results to standard extracts in prick tests can be diagnosed using the liposoluble protein fraction in prick tests.

1582
Allergen profile of beer components

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Background: Beer is one of the world's most widely consumed alcoholic beverages. There are very few described cases of hypersensitivity reactions to beer. Among the ingredients of beer we can find: malt, which is mainly made from germinated barley seeds, aromatic hops that give beer its bitter flavor, and yeasts (Schacaromices) that cause the fermentation.
Method: We report two patients: one of them with hives (1) and another with anaphylaxis (2) after drinking beer.

Skin tests with inhalers, flours, and storage mites were performed, together with a prick-prick test with beer, specific Ig E blood test to beer components and microarrays. Immunoblotting with malt extracts, hop and yeast (Saccharomyces cerevisae) was used as well.
Results: Skin tests with grass and olive pollen were positive in both patients. The first patient had also positive results in skin tests with wheat flour, barley and specific IgE with malt and other cereals. The second patient had negative results in specific IgE. Prick-prick test with beer was negative for both.

Blotting results show that the first patient recognises strong bands of 30–60 kDa in the three extracts and another band of 20–25 kD in the yeast extract. The second patient recognises a more intense band of 50 kDa in the yeast extract and a weaker band in malt and barley extracts, as well as bands of 22–25 kDa in yeast.
Conclusion: We report two patients allergic to beer with specific IgE to proteins bands in malt, barley, and specially yeast extracts that seem to correspond to enolises of saccharomyces. Both patients present a band around 20–25 kD as well, that only appears in the yeast extract and that we have not found in other described cases.

Cross-reactivity should be taken into account given that yeast extract is widely used in other types of processed food.

1583
Camel milk allergy: an allergy that needs to be considered in some patients

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Background: Cow's milk is one of commonest food allergens in children. However, camel's milk allergy is almost unheard of. We wish to report these two cases to increase awareness on the existence of this type of food allergy.
Case 1: A 3 ½ year old boy presented history of acute swelling of both lips while taking 'home-made food' at dinner at age of 2 years. He was managed at the Pediatric Emergency Center (PEC) and his lip swelling cleared 1 h after injections of adrenaline and Diphenhydramine. At age of 3 years, he had acute generalised urticaria, dyspnea, and wheezing 10 min after camel milk ingestion. He tolerates other dairy products quite well. Family history is positive for asthma. His lab work up revealed AEC count at 600 cells/μl, serum IgE 254 ku/l, and food-specific IgE [RIDA3™] was negative. Skin prick test was markedly positive to camel's milk.
Case 2: A 4 ½ year old girl developed acute urticaria and facial angioedema immediately after ingestion of camel milk at home at age of 4 years. Her father is a camel breeder. She received treatment of anaphylaxis at PEC Al-Sadd (oxygen, B2-adrenergic inhalations, adrenaline, steroids, IVF, Diphenhydramine). She is known to have atopic dermatitis and confirmed eosinophilic esophagitis and colitis. Her AEC count was 378 cells/μl, serum IgE 349 ku/l, and food-specific IgE [RIDA3™] was negative. Skin prick test was markedly positive to camel's milk.
Conclusions: Camel's milk allergy is rare but still an existing food allergy. It should be considered in unexplained allergic reaction in patients living in areas where camel milk is consumed.

1584
Allergy to Pangasius fish species not due to parvalbumin

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Background: Fish allergy is usually due to sensitisation to parvalbumin which leads to cross reactivity among different species however allergy to one fish family as well as monosensitivity to one fish species with tolerance to others has been described, be it due to recognition of species or family specific parvalbumin or due to proteins of different molecular weights to that of parvalbumin. Pangasius is becoming ever more popular due to its economic price and boneless flesh, recently becoming the fastest growing fish product in the U.S market.Monosensitivity to Pangasius has been described in the past involving low molecular weight proteins. We hope to describe a new profile of three patients seen in our outpatients Department with monosensitivity to Pangasius due to a protein of a different weight to that described previously.
Methods: Skin prick test with raw and cooked Pangasius and cod were done in each patient and in a control. We analyzed patient sera for specific IgE to fish species, shellfish, tropomyosin and parvalbumin. The proteins of allergenic extracts were transferred to PVDF membranes for subsequent Western blot assays. The recognition of proteins with similar molecular weights in extracts of different allergenic sources led to a more thorough study of their characteristics by Western blot inhibition and peptide fingerprinting.
Results: None of the patients demonstrated specific IgE to parvalbumin neither did they react to prick tests with cod however 2 of the patients did have positive prick tests to Pangasius extracts. Western Blot: Sera did not recognise proteins of weights similar to that of parvalbumin however they did recognise a protein of approximately 37–43 kDa in Pangasius as well as in some fish and shellfish extracts leading us to suspect that the protein responsible could be Aldolase A (40 kDa), aldehyde phosphate dehydrogenas (41 kDa) or glyceraldehyde-3-phosphsate dehydrogenase (36 kDa).Western blot inhibition: IgE fixation was inhibited by lobster, prawn and octopus extracts. Peptide fingerprinting revealed a protein with a nominal mass of 43065 and a sequence of AFKDEDTQAMPFR consistent with the crystal structure of uncleaved ovalbumin.
Conclusion: We describe a series of cases of monosensitivity to Pangasius fish species due to a protein other than parvalbumin consistent with uncleaved ovalbumin not described previously.

1585
Allergy to the lipid fraction of sunflower seeds

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Objective: We report the case of a patient with suspected allergy to sunflower seeds which shows that the measurement of proteins that form part of the lipid fraction of foodstuffs may confirm the diagnosis of specific hypersensitivity to these foodstuffs.
Materials and methods: A 42-year-old man with indolent systemic mastocytosis presented anaphylactic shock after eating 2–3 sunflower seeds. Administration of two doses of self-injectable epinephrine and ICU admission was required. Tryptase was 200 μg/l 2 h after the onset of the reaction.

The patient had a history of severe anaphylactic reactions after wasp (vespula) sting, the ingestion of chamomile, honey and peanuts and after administration of metamizol. In all cases, the diagnosis was confirmed by allergy study. The patient also reported mild intermittent rhinitis with sensitisation to mugwort (Artemisia) pollen.

Skin tests (prick test and patch-prick) to foodstuffs (chamomile, honey, sunflower seeds, sunflower oil, peanuts and lipid transfer protein) and inhalants (sunflower, mugwort) were made. Baseline tryptase (in non-anaphylactic phase) total serum IgE and specific IgE to sunflower seeds were measured. Western blot with extracts of European honey bee (Apis), vespula, mugwort, ragweed (Ambrosia), sunflower (Helianthus) and the soluble and water-soluble fractions of sunflower seeds and peanuts were carried out.
Results: Skin tests were positive for chamomile, honey, peanut and inhalants but negative for sunflower seeds, sunflower oil and lipid transfer protein (Pru p 3). Baseline tryptase (in non-anaphylactic phase) was 44 μg/l. Total serum IgE was 27 IU/ml. IgE to sunflower seeds was negative.

The patient's serum recognised a number of proteins present in the hydrosoluble extract of Apis, Artemisia, Ambrosia, Helianthus and the extract of the liposoluble fraction of peanuts and sunflower seeds.
Conclusions: The recognition of proteins derived from the liposoluble fractions of foodstuffs such as sunflower seeds, in the case reported here, demonstrates its diagnostic utility in avoiding the risk of false negatives with current commercial extracts. In mastocytosis and recurrent anaphylactic reactions due to suspected agents, IgE-mediated hypersensitivity should be ruled out.

1586
Allergy to bird and mammalian meat

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Background: Allergy to meat in adulthood is not frequent. Patients allergic to veal meat have shown cross reactivity to meats of other mammals however not to bird meat

Method: Clinical case: A 59 year old male employed in a chicken poultry factory with a background history of hypertension, smoking, hypercholesterolemia, mild renal failure, chronic alcoholism and liver disease, was sent to our Department to study episodes of periorbital, cheek and lip swelling 15 min after eating cold cuts (smoked pork, smoked loin and sausage) and semicooked pork, veal and chicken.

He tolerates well-cooked chicken and veal, boiled pork and hen's eggs as well as pepper, garlic, onion and other marinating products.

Results: *In vivo* tests: Skin prick tests to a battery of meat extracts (ostrich, horse, pig, rabbit, lamb, chicken and veal) were positive to lamb and chicken. The rest of meats were negative including seroalbumin.

Skin prick tests with batteries of spices, mites, fungi, dog and cat dander, bird feathers and egg proteins were negative.

Prick -prick tests with raw pork, loin and smoked pork were positive.

In vitro tests: Specific IgE (ImmunoCAP) to pork, lamb, chicken, and veal were negative.

Total IgE was 274 KU/l SDS PAGE demostrated bands of 25 and 75 kDa and immunoblotting (DIATER lab.) identified IgE fixation to proteins of 37 and 50 kDa in raw and semicooked extracts of veal, pig and chicken meat. We later on was identified the protein to be Aldolase A Fructose bisfosfate using proteinomic fingerprinting and MS/MS analysis.

Conclusion: We present a case of allergy to meat of two mammals (pig and cow) and to bird meat (chicken). We isolated a thermolabile protein of 39 kDa consistent Aldolase A and C Fructose bisfosfate and not seroalbumin, in veal, pig and chicken meat in raw and semicooked extracts not described in previous studies to date.

1588
Wheat gastrointestinal hypersensitivity: a case report

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Background: The spectrum of wheat hypersensitivity is extremely wide and making a clear diagnosis can be very challenging.

Method: A 28-year-old woman was admitted to our hospital for suspected wheat allergy. Two years before, she had started complaining of eructation, abdominal bloating, severe abdominal pain and diarrhoea few minutes after eating wheat-made products. For this reason she had started a wheat-free diet with relief. Gastroscopy and serological antibody screening for celiac disease were negative, HLA-DQ2 was positive. Skin Prick Test (SPT) and prick by prick with cereals, gliadin, alpha-amylase were negative, as well as for other foods allergens. Total IgE level was 28 UI/ml; specific IgE for gluten and other wheat-related allergens were <0.10 kU/l. Challenge-test with an alimentary product made of 3 g of wheat flour and salt was performed: few minutes after ingestion, the patient presented gastroesophageal spasms with continuous eructation and severe abdominal. The physical examination revealed an acute abdomen with hyperperistalsis. Metilprednisolone and scopolamine were administrated intravenously, with a partial remission, but 2 h later the patient was still symptomatic and was readmitted to our Emergency Department; scopolamine 20 mg and metilprednisolone 20 mg were administrated with relief but complete resolution was achieved only after one week. Gastroscopy, performed 2 weeks after wheat-challenge, was negative. Basophil activation test (BAT) performed before the challenge was weakly positive for alpha-amylase and negative for gliadin (CD63 = 5.5%, stimulation index (SI) = 2.4, CD63 = 2.0, SI = 0.9, respectively). BAT repeated 2 weeks after the challenge remained unchanged for alpha-amylase (CD63 = 5.0%, SI = 2.4) and was increased for gliadin (CD63 = 8.3%, SI = 4.0). BAT for all the other cereals tested resulted negative both before and after the challenge.

Results: After the positivity of the challenge-test, the absolute remission of symptoms with the wheat-free diet and the positivity of the BAT for gliadin and for alpha-amylase, we concluded for acute hypersensitivity to gliadin and alpha-amylase, characterised by gastrointestinal motility disorders.

Conclusion: We believe that, in some cases, particularly when total IgE are very low, BAT associated with challenge test might be a useful tool to better characterise 'Gluten hypersensitivity' syndrome.

1589
Anaphylaxis due to crayfish (*Procambarus clarkii*) ingestion

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Background: The crayfish (*Procambarus clarkii)*, also known as red crawfish or American crawfish is a decapod crustacean belonging to the family Cambaridae, largely distributed throughout the world. Despite its wide consumption there are very few documented cases of allergic reaction after ingestion. We report a case of anaphylaxis after intake of *Procambarus clarkii*.

Method: A 22-year-old woman presented 13 years ago an episode of cutaneous erythema with pruritus, dyspnea, dysphagia and diarrhea immediately after the ingestion of *Procambarus clarkii*. She needed emergency assistance and was treated with methylprednisolone i.m. improving within 1–2 h. After the reaction, she has avoided eating crawfish, but she has tolerated other crustaceans and molluscs. The patient's medical history was relevant for atopic dermatitis and asthma with sensitisation to grass and *Platanus* pollens and house dust mites.

Results: Skin prick tests with inhalant allergens proved positive for grass and *Platanus* pollens and house dust mites, and were negative with commercial food extracts, latex, Anisakis, cockroach, profilin and peach LTP (Pru p 3). Prick-prick with cooked crayfish was positive and negative with raw crayfish. Total IgE was elevated (1416 IU/ml) and specific IgE to crayfish (*Astacus astacus*) and shrimp (CAP, Phadia) proved negative. Immunoblotting was carried out with extracts of raw and cooked shrimp (only meat) and crayfish (meat and shell). The patient's serum recognised several bands, especially intense in cooked crayfish (meat and shell), between 30 and 45 kDa, and other less intense about 74, 15 and 20 kDa. The same bands, weaker, also appeared in the raw crayfish meat. In cooked shrimp, bands about 74, 48 and 6 kDa were identified. None of the bands seem to correspond to tropomyosin.

Conclusion: We report a case of anaphylaxis due to hypersensitivity to *Procambarus clarkii* with good tolerance to other crustacean, an event rarely reported. Skin tests and immunoblotting support our diagnosis. Our immunoblotting identified different proteins than those reported in other cases.

1591
An interesting case of asthma compllicated by food allergy that renders the disease difficult to control

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Case presentation: Twenty five years old woman N.T applied to our clinic with

rhinitis and complaints suggestive of asthma. The skin prick test result was erythema (E): 14 × 12 mm, wheal (W): 11 × 12 mm, dog epithel was E: 5 × 5 mm, cat epithel was W: 5 × 5 mm. The diagnosis was allergic rhinitis and allergic asthma. Allergic rhinitis treatment was started. Also, budesonid-formeterol 160/4.5 μg 2 × 1 regimen was started for asthma. Clinical follow-up revealed frequent night symptoms and frequent need for beta-2 agonist use. The patient was applying to emergency service with an asthma attack at least once a week. Although all possible medications capable of controlling the disease had been given in combination, these symptoms were not under control. Upon further questioning the patient with regard to dietary habits it was revealed that she was under a strict diet because of her overweight and therefore had a regular intake of a bisuict that contains rye bran and oat. Then, another skin prick test was done with flour panel. Rye flour was measured as 5 × 5 mm which indicated rye allergy. She was adviced to avoid foods that contain rye. Her symptoms improved dramatically thereafter. She didn't apply to emergency services anymore. It was thought that the ineffectivity of the drug therapy resulted from rye flour allergy, which also caused respiratory anaphylaxis attacks.

Conclusion: In the case of uncontrolled asthma, the possibility of food allergy and food related respiratory anaphylaxis should be considered.

1592
An adult-onset egg allergy

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Background: The development of egg allergy in the late adulthood is rare. In most of the cases manifestation of the clinical symptoms begins in childhood or early adulthood. Adult-onset egg allergy usually develops either as an occupational disease inflicting workers in bakery and confectionery industries or a bird-egg syndrome caused by cross-reactivity in patients suffering from bird feather sensitivity. Herein we present an adult-onset primary egg allergy appeared differently from the previously reported cases. A 50-year-old housewife presented with a history of uvula oedema, itching of the throat and mouth, urticaria and dyspnea necessitating epinephrine, antihistaminic and steroid administration following ingestion of baked egg 12 years ago. These symptoms recurred by eating well-cooked egg containing foods such as pastry. She had no symptoms after cessation of ingesting egg and egg-containing foods.

Method: A skin prick test (SPT) with a wide panel of food allergens and common aeroallargens (Allergopharma, Hamburg, Germany) was performed. The serum specific IgE to egg white and yolk was measured by using CAP system (Pharmacia, Uppsala, Sweden).

Results: The SPT was found to be positive with egg yolk, egg white and whole (5, 9 and 9 mm, respectively). Serum specific IgE to egg white and yolk was positive at 1.22 kU/l (+2) and 0.44 kU/l (+1), respectively.

Conclusion: The present case is unique in that she developed adult-onset egg allergy presenting with anaphylaxis and neither had a history of occupational exposure nor had a sensitivity to animal epithelium.

1593
A withe nightmare

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Background: Allergic reactions to milk are the second cause of food allergy, affecting 1–3% of population. For patients and their relatives, it is a very important problem. Initiatives like *Stop Anaphylaxis* to be developed in EAACI-WAO Congress, Milan 2013, may help in cases like the one we are presenting.

Method: A 36 months old patient, female, treated in Hospital Central de la Defensa (HCD), living with her parents and sister. She attended a daycare center with 1000 children. Isolated dining facilities for allergic children were available. Period: July-December 2012.

Results: The patient was diagnosed of milk allergy at 4 months age, showing urticaria after her first feeding bottle. Her five years older sister, currently tolerant, also had milk allergy. In July 2012, she suffers of an asthma crisis after eating a candy, which the house caretaker had given her. She starts daycare center on 25 October 2012. An allergic children's dinning room worker gave her a croquette and the patient immediately showed erythema, urticaria, vomit and dyspnea. The worker took the child to HCD emergency service, where epinephrine was administered and she stayed under surveillance for 24 h. On December 2012, an egg allergic child gave her some purée at the daycare center dining room, provoking urticaria, dyspnea and loss of consciousness. She is aided by the daycare doctor, who is unable to provide the required epinephrine dose using an autoinjector after several attempts. The doctor called an ambulance and the child was brought to HCD emergency service, where she was treated with epinephrine and recovered within 48 h. The daycare center informed the child's parents that she could not use the center dining room, as they could not prevent the patient to have similar problems in the future. HCD provided the parents with an urgent treatment, including drugs prescription. They were also informed about the therapeutic alternatives, including desensitisation or omalizumab, and also about the Spanish Food Allergy Children Parents' Association. Control and monitoring visits every two months were scheduled. The daycare doctor was contacted to inform her about anaphylaxis treatment with epinephrine, the use of GALAXIA (Spanish Guide for Anaphylaxis Management) and the Stop Anaphylaxis initiative.

Conclusion: This case shows the serious health, social, economic and educational problems behind some anaphylaxis diagnoses. In the patient's parents words, 'a nightmare'.

1594
Quail egg allergy

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Background: Hen's eggs are one of the major causes of food allergies especially in childhood. Increasing egg consumption of other birds species such as quail, goose, duck or partridge has facilitated the development of sensitisation to proteins of these eggs

Method: A 41 year-old-woman with antecedents of rhinoconjuctivitis and asthma due to pollens and danders, was referred for presenting oropharyngeal itching, lips swelling, facial and uvula edema and dysphagia immediately after eating cooked quail egg. These symptoms were successfully treated in the emergency room. At a later time, she tolerated hen's egg without problem. She did not present a history of current or past exposure to birds.

Skin prick tests with commercial common inhaled allergens, egg yolk and white, ovomucoid and ovoalbumin (ALK-Abelló S.A.Madrid. Spain), chicken meat and feathers were performed; prick by prick were also carried out with white and yolk

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raw and cooked egg from partridge and quail; total IgE, specific IgE for hen′s egg and IgE-immunoblot to eggs from chicken, quail, partridge, goose and duck were also carried out.

Results: Prick tests were positive with pollens, mites, cat and dog dander and LTP and were negative with chicken egg proteins, chicken meat and feathers. Prick-prick were positive with raw white and yolk egg from quail and partridge.

Immunoblotting showed two IgE-binding bands, one of 45 and other of 75 kD, less intense, in the extract from quail and partridge ′s egg white. These bands seem to correspond to ovoalbumin and ovotransferrin respectively.

No similar bands were observed in the chicken, duck or goose eggs extracts.

Conclusion: We present a patient with an IgE-mediated allergy to egg white from quail that cross-reacts with egg white from partridge. Ovoalbumin seems to be the responsible protein.

In our case there is no cross-reactivity with other galliforme species as hen nor anseriformes as duck and goose.

1595
Anaphylactic reaction from food in a health care worker with latex allergy

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Background: Different studies demonstrate an increased prevalence of latex sensitisation in health care workers, ranging 9% to 12%.*Latex allergic reactions can range from mild skin rashes to severe and life-threatening anaphylactic shock*. Latex gloves are associated with three types of adverse reactions: irritant contact dermatitis, immediate-type, and allergic contact dermatitis. Latex has cross reactions with different foods and consuming them may cause allergic reactions to the persons allergic to latex.

Method: We present a 25-year-old patient, working as a nurse for the last 3 years. Few minutes after consuming banana, at her home, she had difficulty in breathing, cough, hypotension, generalised itching and urticaria. She was shifted to emergency room, and received subcutaneus adrenaline, prednisolone, antihistamine and oxygen. She was discharged of the hospital two days later. At her workplace, she mostly used latex gloves. A first skin manifestation occurred 2 years before and was described as contact dermatitis which disappeared 1 week after local therapy with corticosteroids, but she never performed allergy tests. Nearby the same time, she began to have sneezing, runny nose, itchy and watery eyes, at spring time. After she performed allergy tests she resulted: allergic to banana in prick by prick and had positive IgE for banana, negative skin prick test to aeroallergens and positive prick by prick test for latex.

Discussion: It is reported that more than 50% of latex-sensitised people had specific IgE antibodies to proteins for some kind of fruits and vegetables. About 1/3 of the patients, experience immediate-type reactions when they ingest foods such as avocado, banana, chestnut, kiwi and potato. Populations at risk for developing latex allergies are: patients with spina bifida and congenital genitourinary abnormalities, health care workers, atopic patients. In case of an allergic reaction it is the possibility that the reaction may vary from urticaria to anaphylactic reactions In our case the patient developed anaphylaxis after eating banana.

Conclusion: Latex-fruit syndrome is a cross-reaction that may seriously risk patient life; in this case it is needed to inform the patients about the possible risks for cross- reaction between latex and food. It is needed a very careful medical history, skin prick testes with latex and with different fruits vegetables and specific IgE measurement for latex and foods cross reacting with latex.

1596
Atopy and the risk for food, drug and latex allergy

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Background: Generally atopy is defined as a genetic disposition to develop allergic diseases such as allergic rhinitis, asthma, or atopic dermatitis. It is also known as an increased capacity to produce IgE response to common environmental antigens. This study intends to measure the relative risk of atopic individuals to develop allergy to food, drug and latex.

Method: In a cross-sectional study, 639 nurses (from 662 that were asked for) at the UHC 'Mother Theresa' in Tirana, accepted to fill up a questionnaire where questions about personal atopy, food, drug and latex allergy were included. About 589 were females and they have a mean age 43.28 (+10.71) years. We considered atopic every person that has at least any of the atopic diseases (allergic rhinitis, asthma, or atopic dermatitis). The chi-square test and the RR with a 95% CI were calculated for each case. MS Excel 2007 and PASW Statistics 18 were used to analyze the data.

Results: 20.81% (133) of nurses reported to have had at least one of the atopic diseases. No differences in prevalence of atopy were observed between two sexes. The RR for the atopic individuals to develop allergies to foods resulted 4.44 (95% CI = 2.42 to 8.16, $P < 0.05$) while the RR for this category to develop allergic symptoms to latex were 5.08 (95% CI = 3.17 to 8.13, $P < 0.05$). Atopic individuals had a RR of 1.45 to develop allergic symptoms to different drugs (95% CI = 0.94 to 2.23, $P < 0.05$) compared to non-atopic ones.

Conclusion: The presence of atopic diseases such as asthma, allergic rhinitis and atopic dermatitis bears a significant increased risk of developing allergies to foods latex, and drugs.

1597
Food allergy in children aged 6–8 years in Warsaw

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Background: Food allergy is common problem. Epidemiological data are very poor because of diagnostic difficulties. According to ECAP study (www.ecap.pl) about 7% of Polish population suffer from food allergy. Simple screening is expected in premedical diagnosis.

Method: The questionnaire study was conducted 2012 in the primary schools of Warsaw. The sample was randomised. About 1801 full questionnaires were collected and verified. The response rate was 53.5%. Questionnaire consisted of 58 questions in four sections: basic information, diet and nutrition, health status and information about the guardian.

Results: The prevalence of food allergy in children at early school age (6–8 yrs) based on declarations of their parents was 36.9% (95% CI 34.7–39.2%). In 12.2% of children with food allergy doctor diagnosed

disease in the first month of life. In 79.6% of cases food allergy was confirmed by a physician. In 48.4% between 2nd and 12th months of age. Among the children with declared food allergy 56.5% of cases are allergic to dairy products, 27.4% to cocoa and chocolate, 21.7% fruit and 18.2% nuts.

There is a relationship between the prevalence of mother's food allergy and the child′s – OR = 3.81 (95% CI 2.73–5.32). The relationship was also observed between father food allergy and child's – OR = 3.36 (95% CI 2.3–4.91).

Conclusion: A third of parents in the study declared the presence of food allergy of their child. Child′s gender was not a significant factor.

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Management of food allergy II

1599
Specific oral tolerance induction in children with cow's milk allergy – 6 years of experience

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Background: Cow's milk allergy (CMA) is the leading alimentary allergy in children. The primary strategy currently used in CMA management is the dietary elimination. However, desensitisation or tolerance induction seems to be promising as an alternative treatment in children who have not built up tolerance spontaneously. The aim of our study was to evaluate all children with CMA who started the Specific Oral Tolerance Induction (SOTI) protocol.
Method: Retrospective study from 2006 to 2012 based on clinical records' review. Children with CMA and age more or equal than 2 years and positive oral provocation tests were submitted to a semi-rush SOTI protocol. Demographic and clinical data were analyzed. Free diet was considered when tolerance achieved was 200 ml of milk or one yogurt/day.
Results: Twenty-seven clinical records were reviewed, 20 (74.1%) were male, with mean age at the beginning of protocol 6.6 years (SD $\pm$ 4.2) and median duration 21 weeks (1–156). Twenty-one (77.8%) achieved the end of protocol, 15 (71.4%) of them are in free diet and 6 (28.6%) are in restrictive diet, tolerating from 2 to 50 ml of milk. Six (22.2%) didn't achieve the end of protocol (2 were lost to follow-up, 1 re-started the protocol and in 3 the protocol is in progress). Initial specific IgE for cow's milk was <class 3 in 4 (14.8%) cases and ≥class 3 in 18 (66.6%) and at the end of protocol <class 3 in 1 (4.8%) and ≥class 3 11 (52.4%). There were no differences in age at the beginning ($P = 0.243$) and duration of protocol ($P = 0.051$) in free diet group vs restrictive diet. Sixteen (59.3%) children had adverse reactions, 13 (81.3%) presented respiratory symptoms. Most of them had mild adverse reactions, treated in hospital.
Conclusion: SOTI led to a reduction of risk of severe allergic reactions with no episodes of anaphylaxis in real life and an improvement of quality of life.

1600
Three-months elimination diet in eosinophilic esophagitis pediatric patients: allergic and nutritional aspects

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Background: The use of dietary treatment in eosinophilic esophagitis (EoE) in children was promoted in updated consensus recommendations. In this study we evaluated anthropomorphic and biological parameters in EoE children before and after elimination diet.
Method: 87 consecutive patients with EoE (>15 eosinophils/hpf in esophageal biopsies) were retrospectively analyzed. All children followed the so-called modified six-food elimination diet (SFED), excluding 6 main offending foods retrieved together with those eliciting positive SPT and APT, supplemented with a nutritional support by an amino acid formula. Patients followed the next treatment sequence: endoscopy/ clinical/biological assessment, 3 months elimination diet and second endoscopy/ clinical/ biological assessment.
Results: Forty nine patients were included in analysis. At enrolment, BMI was significantly lower in females than in males ($P < 0.05$), and total circulating IgG and IgM levels were higher in females ($P < 0.05$). At the end of the study recovered patients had at enrolment a BMI significantly higher than those showing only partial or no recovery ($P < 0.05$). Elimination diet led to complete recovery (no symptoms & <5 eosinophils/hpf) in 53% cases. Following the elimination diet, BMI remained lower in females than in males. Also, blood eosinophils counts ($P < 0.0001$), IgG (p0.003) and IgM levels (p0.05) showed a significant decrease as well as IgE titers against CMP ($P < 0.02$) and egg ($P < 0.02$), with a tendency for decrease for fish (p 0.09) and wheat (p 0.09).
Conclusion: Female/male differences are recognised in EoE: lower BMI, higher risk for malnutrition and more active biological parameters. The elimination diet leads to maintenance of nutritional status, decreased immune activity, identical female/male differences.

1601
Food allergens in atopic dermatitis – are they really important?

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Background: The pathogenesis of atopic dermatitis is complex. The role of food allergens as the potential contributing factors both in initiating and maintenance of chronic inflammatory skin disorder is still discussed. The aim of the study was the estimation of the role of food allergens in atopic dermatitis and the effect of elimination diet on the course of the disease. Method

Thirty-two subjects (18 women, 14 men, mean age 34.87 $\pm$ 6.21 years) with the diagnosis of atopic dermatitis were asked to answer a questionnaire. Each of them underwent skin prick tests with 20 food allergens. Allergen-specific IgE serum levels against food allergens were assessed (Quantiscan, Immunogenetics). The skin state was assessed with the use of SCORAD scale twice: before and after the four weeks lasting elimination diet.
Results: The most numerous group of patients, 25% ($n = 8$) of patients indicated milk as the main food factor worsening the course of atopic dermatitis. The majority of positive skin prick tests were caused by chammomile ($n = 6$; 18.8%). Twelve subjects showed elevated specific IgE serum concentrations against potato allergens (37.5%), while 11 subjects (34.4%) were positive to cow milk proteins. Significant improvement of the skin condition to the extent that enabled shift to lower class of severity was observed in 60% ($n = 6$) of patients in the severe group, and in 18.9% ($n = 2$) of patients in the moderate group. None in the mild group observed a positive influence of diet on the skin.
Conclusion: Food hypersensitivity contributes to atopic dermatitis pathogenesis. The elimination diet provides benefit in the treatment of moderate/severe form of the disease.

1602
Sensitisation/allergy to peanut

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Background: Food allergy occurs in 6–8% of the children and 3–4% of the adults. Allergic reactions to peanuts are particularly severe, with frequent anaphylactic reactions. Peanut allergy usually begins in childhood and often persists throughout life. The aim of our study was to evaluate the peanut sensitisation/allergy evolution for a 6-year period in a group of patients previously studied.
Method: A study was conducted in order to find the prevalence of peanut sensitisation and allergy in a population followed in the Immunoallergology Department of Dona Estefânia Hospital. Skin prick tests (SPT) and a questionnaire about the ingestion of peanut were carried out in 2006 and 2012 to evaluate the peanut sensitisation/ allergy. We included all of the 1415 patients who performed SPT to aeroallergens during the year of 2006 in our department. We reassess in 2012 the sensitised patients.
Results: In 2006, the prevalence of sensitisation found was 2.8% (40 patients with positive peanut SPT), of whom 5 had symptoms with peanut ingestion, matching an allergy prevalence of 0.4%. Of the 40 patients, 19 were re-evaluated in 2012 (3 allergic and 16 with asymptomatic sensitisation in 2006). The three patients allergic kept peanut eviction with no reported accidental ingestion or symptoms since 2006. The SPT remained positive. Of the 16 patients with asymptomatic sensitisation, 12 maintained positive peanut SPT and four had negative peanut SPT. Of these 12 patients with SPT positive (asymptomatic in 2006), two reported symptoms after peanut ingestion (eczema and angioedema/ tightness of the oropharynx), corresponding to new allergies. Two patients, who in 2006 had positive SPT but ate peanuts without reacting, did peanut avoidance on their own initiative.
Conclusion: The small sample size is a limitation of this study, but some patients with asymptomatic sensitisation to peanuts seem to develop symptoms in the future. It is important to understand if there are differences in the sensitisation profile of these groups in order to predict the evolution. Similarly, it is important to consider which indication should we give to sensitised patients without symptoms – avoidance for all, because of the risk of developing symptoms, or only in certain cases?

1603
A pilot study assessing adequacy of epinephrine autoinjector needle length to deliver epinephrine intramuscularly in adult patients with food and venom allergy

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Background: Epinephrine delivered by an autoinjector in the anterolateral aspect of the thigh is the standard of care in the emergency self-treatment of anaphylaxis. The route of administration affects its rate of absorption, and intramuscular delivery is recommended for optimal onset of action. Two epinephrine autoinjectors are commercially available to adult patients in Canada: Epipen® and Twinject®. Epipen® has a needle length of 14.3 mm. Each Twinject delivers 2 doses of epinephrine; the needle length of the first dose is 12.7 mm, and the second dose is 14.3 mm. Little is known about the adequacy of these autoinjector needle lengths in delivering epinephrine intramuscularly in adult patients at risk for anaphylaxis.
Method: Fifty nine consecutive adult patients (21 male and 38 female) with confirmed food or venom allergy requiring prescriptions or refills of epinephrine autoinjector at an Allergist's office were recruited for the study. Skin to muscle depth (STMD) at the right mid-anterolateral thigh was measured using ultrasound by a single operator under minimal (min) and maximum (max) pressure, estimated to be 2–8lbs. The needle length is considered adequate if $STMD_{max}$ was ≤14.3 mms. Two groups of patients with:
1) $STMD_{max}$ ≤14.3 mms and
2) $STMD_{max}$ >14.3 mms were compared.

Baseline characteristics including age, gender, ethnicity, allergen, nature of reaction, concurrent medical problems, BMI and medications were compared.
Results: Baseline characteristics such as age and weight did not significantly differ among the two groups. The mean $STMD_{max}$ among those with ≤14.3 and >14.3 mm were significantly different (8.20 ± 2.78 and 17.58 ± 4.46 mm respectively; P value = 0.0001). Under maximum pressure, the standard needle length is inadequate for intramuscular delivery of epinephrine in 18 (30.5%) patients, all of whom were female. In the multivariable regression analysis, BMI was found to be the strongest predictor of STMD (OR: O.82, 95% CI: 0.71–0.94; P value = 0.005).
Conclusion: Our pilot study suggests that in one-third of adult patients, the commercially available epinephrine autoinjectors do not reach the intramuscular space. This is particularly concerning in those with an elevated BMI.

1604
Peanut and tree nuts allergy in a Portuguese pediatric cohort

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Background: Food allergy is extremely common in the pediatric group, with a wide range of clinical features and some might be life-threatening. When compared to adults, children have a limited number of foods responsible for allergy. In fact, as many as one third of overall anaphylactic episodes are associated with peanut or tree nut ingestion. Eviction diet is sometimes difficult to achieve and can alter quality of life, the reason why the diagnosis must be well established and allergen sensititization must be differentiated from real allergy.

Since nut allergy is more well documented in adults, we aimed to characterise a cohort of children with suspected allergy to peanuts and/or nuts, referenced to a food allergy pediatric Unit.
Methods: Twenty-two children with food allergy observed between 2004 and 2012 were retrospectively reviewed. All patients underwent skin prick (or prick-prick) tests and specific IgE determination. Unambiguous history, response to eviction diet and oral food challenge confirmed the diagnosis.
Results: Mean age was 9 years old (range 3–15) and male to female ratio was 2.4. Family history of atopic disease was found in 20%; individual history of respiratory atopy was found in 53% of patients (9% suffered from rhinitis and 53% rhinitis and asthma). Allergens most commonly involved were peanut (66.7%) and cashew (14.3%), followed by hazelnut (4.76%), walnut (4.76%), pistachio (4.76%) and Indian chestnut (4.76%). The clinical manifestations included anaphylaxis (41%), urticaria (24%), angioedema (20%) and atopic dermatitis (6%); 9% were asymptomatic. Mean specific IgE for the culprit allergen involved was 28.3 kU/l (range 0.35–100 kU/l). Four patients revealed a value of >100 kU/l for peanut IgE: 2 suffered from anaphylaxis, 1 had facial angioedema, and 1 was asymptomatic. The majority of patients had symptoms on the first known ingestion. Two oral provocation tests were performed: one was positive for peanut (oral allergy syndrome and

urticaria) and one was negative for hazelnut. Mean wheal diameter was 10.5 mm.
Conclusion: This study points to the existence, in Portugal, of allergy not only to peanut but also to tree nuts in very young children and highlights the emergence of tree nuts allergy as being responsible for severe reactions.

1605
Health related quality of life in children with perceived food allergies vs. those with a physician diagnosed food allergy

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Background: There have been some reports recently on how food allergy impacts on Health Related Quality of Life (HRQoL) of children. The effect of food challenge outcomes on HRQoL has also been studied. We determined HRQoL in children with a diagnosed food allergy vs. those who were avoiding a food due to a perceived food allergy, using a validated questionnaire (FAQLQ-PF) by DunnGalvin et al.
Method: We recruited 41 children (age 10 years); 23 with diagnosed food allergies and 18 children who were avoiding a food due to a perceived food allergy into this study. All these children are enrolled in the FAIR birth cohort study. Those with a diagnosed food allergy were either diagnosed by the FAIR study team in the past or the David Hide Asthma and Allergy Research Centre on the Isle of Wight. We compared the effect of food allergy vs. perceived food allergy using the domains specified in the FAQLQ-PF questionnaire: Food Anxiety, Emotional Impact, Social and Dietary Limitations and also HRQoL.
Results: Using the Independent sample T-test, we found no significant difference between the two groups (diagnosed food allergy vs. perceived food allergy) in terms of Emotional Impact (mean: 1.39, SD: 0.99 vs. mean: 1.17, SD: 1.43; $P = 0.5$), Social and Dietary Limitations (mean: 1.78, SD; 1.36 vs. mean: 1.24, SD: 1.47; $P = 0.3$) and HRQOL (mean: 1.75, SD; 1.44 vs. mean 1.6, SD; 1.33; $P = 0.15$). However, Food Anxiety scores were significantly higher in those with diagnosed food allergy compared to those who were avoiding a food due to a perceived food allergy (mean: 1.92, SD: 1.43 vs. mean: 0.95, SD; 1.21; $P = 0.03$).
Conclusion: Children with perceived food allergies seem to show similar results in terms of HRQoL compared to those with diagnosed food allergy. However, anxiety scores were significantly higher in those children with diagnosed food allergies.

1607
Early cow's milk challenge in infants presenting with bloody stools after birth

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Background: Allergic proctocolitis has been recognised as one of the most common causes of rectal bleeding in infants. This disorder is characterised by the onset of rectal bleeding, generally in children younger than 2 months of age. The majority of infants will tolerate cow's milk products by 1 or 2 years of age. The aim of the study was to investigate the rate of milk tolerance in infants who are under 12 months of age.
Method: Twenty-seven infants were studied who presented bloody stools, due to allergic proctocolotis after birth and had a cow's milk challenge at a mean age of 6 ± 2.43 months. Twenty-four infants at a mean age of 17.7 ± 4.34 months who also presented allergic proctocolotis, after birth and were challenged after the first year of life served as controls. Statistical analysis: Fisher's Exact test was used to compare rates between patients and controls.
Results: Three out of 27 patients had a positive cow's milk challenge and 1 out of 24 children among the controls had a positive challenge ($P = 0.6123$).
Conclusion: Early cow's milk challenge caused a higher reaction rate of 11, 1% compared to the control rate of 4, 16% (not statistically significant results could be attributed to the low study sample). Reintroduction of cow's milk in previously allergic infants who presented bloody stools shortly after birth is possible around the 6 month of life and does not carry a high risk for reaction.

1608
Quality of life in food allergic patients in Israel

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Background: Prevalence of food allergy is estimated to be 2–8% in infants and young children and 1–4% in the adult population. The current approach includes strict avoidance and emergency treatment for accidental exposures. Parents and patients must be vigilant about food allergen avoidance in multiple settings. This burden and fear of accidental ingestion can lead to reduced health-related quality of life. The purpose of the study was to examine the quality of life in food allergic patients in Israel.
Patients and methods: The population study includes patients registered in the 'Israel Foundation of Food Allergy' A validated separate questionnaires for children and adolescents were used. Questions were divided into three main groups: food anxiety, dietary limitations and emotional impact.
Results: One-hundred and nineteen patients were included, 71 (60%) males. Average age 6.5 ± 2 years. Food anxiety score is significantly greater in children with more than one food allergy ($P = 0.037$). Dietary limitations (DL) is significantly greater in children with cow′s milk allergy as compared to other food allergies ($P = 0.036$). Significantly greater food anxiety among sesame and peanut allergic patients ($P = 0.029$, 0.024, respectively). No difference in any of the scores by anaphylaxis. Dietary limitations score were significantly higher and emotional impact (EI) score marginally higher in children with asthma/bronchitis. (DL $P = 0.031$, EI $P = 0.056$)
Conclusions: Food allergy clearly affects quality of life of patients and their families in Israel. The parameters that have the most significant impact include cow′s milk allergy, allergy to more than 1 food, allergy to sesame or peanuts, but surprisingly not anaphylaxis.

1609
Eosinophilic esophagitis: a rare side effect after a specific oral tolerance induction

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Background: Disposition towards severe allergic reactions to basic food is usually being treated by dietary measures although significantly diminishing the quality of life. Despite a diminished allergen exposure, patients will still remain at risk, however, if hidden traces of the culprit allergen are known to elicit symptoms.
Case report: A 21-year old female patient presented with a history of anaphylactic reactions which had been associated with the consumption of milk, and which had occurred for the first time soon after birth. Subsequently, the patient's parents were instructed to strictly avoid milk products,

and were provided with an emergency kit. In the following years, the patient occasionally experienced only mild symptoms when consuming an apparently milk-free diet within a family-based setting. Later on, the patients moved into a flat-sharing community and started a job training necessitating the consumption of workplace meals. Although the patient had explicitly informed all persons involved into meal production and serving, she repeatedly experienced minor to moderate allergic reactions (asthma).

Laboratory examinations revealed specific IgE-antibodies to milk protein, lactalbumin and casein (all CAP class 2); furthermore, we found positive prick test reactions to casein and cow milk solutions. Subsequently, we started a specific oral tolerance induction (SOTI) using long life milk at a dose of 100 ml (customary skimmed long life milk). During up-dosing, the patient repeatedly developed urticaria. Since pre-treatment by fexofenadine and omeprazole eventually caused an agonizing nausea and aversion, we reduced the daily milk dose to 50 ml. One and a half years later, we modified our therapy now switching to ultra-heat treated milk (ESL-milk). During this time, the patient no longer had problems when eating out. Half a year later, daily intake of milk doses became irregular during vacation. After returning home the patient complained about repeated throat and chest pain. Histological examination of mucosa biopsies taken endoscopically revealed an eosinophilic esophagitis (EO). This finding prompted us to terminate SOTI.

Conclusion: EO is a rare disease. There is now solid evidence that food allergy may cause this inflammatory disorder. As demonstrated by our case, development of EO may also be a side effect of SOTI performed in patients with a history of anaphylaxis.

1610
Effects of omalizumab therapy on multiple food allergies

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Background: Omalizumab has been currently used in severe asthma and rarely in other allergic diseases. However data on its efficacy for food allergy is limited. In this case report we evaluated the effect of omalizumab on multiple food allergies in 12 years old boy.

Case report: The patient was 12 years old boy with past history of asthma at 1 year, severe atopic dermatitis at 2 years, anaphylaxis due to wheat at 6 years, vernal conjunctivitis and multiple food allergies. Total IgE level was 3450 IU/ml. Skin prick test revealed reactions to house dust mites, grass pollens, tree pollens, milk, egg, wheat and peanut. He had high specific IgE levels for milk, egg, wheat, peanut, soy, carrot, orange, strawberry, banana, apple, potato, spinach, and garlic. Oral food challenge was found to be positive for milk, egg and wheat. He had been treated for asthma, atopic dermatitis, rhinitis and vernal conjunctivitis. His symptoms were not under control even with medical therapy and strict diet. He was put on omalizumab 150 mg every other week. After 3 months his symptoms were improved. Skin prick test was found to be negative for food allergens and food spIgE levels were decreased. Moreover, oral food challenges for milk, egg and wheat were found negative.

Conclusion: In this case we showed that omalizumab had positive effects on both clinical symptoms and laboratory findings in patients with multiple food allergies. Further studies in larger series are needed.

1611
IgE mediated food allergy (urticaria and angioedema) treated with omalizumab a recombinant humanised anti-immunoglobulin E antibody

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Background: Omalizumab, a recombinant humanized monoclonal antibody has been currently used in the treatment of patients with severe or mild asthma, with a serum IgE ranging from 30 to 700 IU/ml, which are not controlled by normally performed drugs. Few observations suggest the use of omalizumab for patients with the food allergy.

Method: In one of our patient, male, 36 years old, with severe attacks of IgE-mediated was treated with Omalizumab. Before of treatment with monoclonal antibody the patient experienced severe attacks of IgE-mediated asthma with contact to peach associated to urticaria and angioedema. This patient was admitted to the emergency room several times during the last year; (2 times for Urticaria and Angioedema with following to anaphylaxis and to attack of severe asthma) with an asthma symptom score of 8 [scale from 0 (least) to 9 (severe)]. He had previous several episodes of oral allergy syndrome and contact urticaria. The total IgE concentrations were 342 IU/ml; specific IgE against Dermatophagoides Pteronyissinus (91 kU/l), Dermatophagoides Farinae (79 kU/l), Perennial Rye Grass (rLol p1: 78 kU/l), Birch pollen, (rBet v1: 64 kU/l and rBet v2: 45 kU/l) and to allergen of Peach (Prunus p3:16 kU/l).

Results: The patient was treated with Omalizumab every four weeks 0.016 mg/kg/IU (IgE/ml). After 16 weeks of treatment with Omalizumab, the total IgE in the serum were 210 lU/ml. No visits to intensive care unit were necessary during the treatment and the asthma symptom score decreased to 3.The peak of expiratory flow (PEF) in the morning increased each four weeks with a stable value of 620 l/min (EU Scale). The patient tolerated a diet including peach fruit (300 g) and its corralates fruits (i.e.: pears, walnuts, almonds, hazelnuts, apples, apricots, plums, cherries, kiwi, carrots, potatoes, peppers, celery, fennel, parsley, parsnips and coriander).

Conclusion: This study suggests a novel approach to the treatment patients with atopic asthma and Urticaria and Angioedema to peach fruit. Omalizumab is a recombinant humanized monoclonal anti-IgE antibody approved for treatment of moderate to severe IgE-mediated asthma, it could be useful also to treat IgE mediated Urticaria-Angioedema and as it may be also a reduction of risk to suffering a life-threatening reaction to other correlated foods.

1612
Predictive value (tolerance induction) of IgG and its subclasses in allergic patients to cow milk protein

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Background: Allergic reactivity to cow milk protein (CMP) could develop allergy no mediated by IgE, a process less known. That's why we had been evaluated the possible role of Immunoglobulin G (IgG) and its subclasses in allergy to CMP and its possible role in tolerance induction in allergic patients.

Method: A transversal study was done in 129 allergic patients and 29 healthy individuals among 0 and 45 years old. Patients with allergic rhinitis (AR), bronchial asthma (BA), atopic dermatitis (AD) and/or immunodeficiency, who attended the consultation of allergy, among January to May 2012 were included. International criteria were applied during clinical trials. An automated ELISA instrument was used to determine specifics IgE, IgG and IgG4. A

comparative study was done using McNemar method.
Results: Among all allergic patients (76 women, 53 men), prevalence of BA was 24%, AR 36%, BA+AR 57%, BA+AD 23%, BA + Immunodeficiency + AR 20.9%; BA+ AD+ atopic march 11.3%; while the prevalence of BA+AR+AD+ atopic march was 18%. 61.2% of atopic patients showed high IgG levels against CMP and 29.5% of them showed high level of specific IgG4. There was significant differences with respect to healthy population (p 0.05), 3.4% of them showed high IgG levels and none of them showed high IgG4 levels. Twenty-five percent of atopic patients high IgE and IgG levels, and a higher percentage showed high IgG levels and normal IgE levels ($P = 0.003$). Seven individuals showed high IgE and IgG4 levels and twice of them showed high IgG4 levels and normal IgE levels ($P = 0.054$).
Conclusion: Sensitivity of 57.26% and specificity of 88.90% have been reported for IgG; while sensitivity and specificity for IgG4 was 20.20% and 100%, respectively. These data suggest that these biomarkers are more specific and less sensible for the diagnosis and follow of allergic pathology, and can play a predictive role (tolerance induction) in the course of illness.

1613
Burning mouth syndrome and oral allergy syndrome – is there an overlap?

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Background: Burning mouth syndrome (BMS) is regarded as having a lack of recognised therapies and relief for patients. Oral allergy syndrome (OAS) can present with a similar disease profile and is much better understood with much more helpful and directed advice. There are some similarities between the two conditions which has never previously been explored or recognised and which we would like to investigate.
Method: A cohort of patients from a specialist oral medicine unit have been recruited to complete an initial telephone survey regarding their symptoms and allergic profile. Skin prick allergy testing will be carried out on all patients to see if there is an allergic cause for their BMS. The following nine allergens will be tested; grass, tree, dog, cat, dermatophagoides pteronyssinus (dust mite), dermatophagoides farina (dust mite), mugwort (fungus), alternaria (fungus) and aspergillus (fungus).
Results: There was a high percentage of patients with a positive allergy profile. This included hayfever (23.5%), eczema (23.5%), food allergies (17.6%), asthma (11.8%) and grass (5.8%). A history of allergic symptoms was also identified in this cohort including nasal symptoms at a time besides which the patient had a cold (47.1%), night time coughing (41.2%), wheezing in the chest (29.4%) and an itchy rash lasting longer than 6 months (29.4%).
Conclusion: Patients with BMS will benefit from the greater understanding and potential treatment options currently available within OAS and this could lead to further research in a wider cohort of patients with this research not having been performed before.

1614
Allergy to cow's milk associated with allergic dermatitis and chronic diarreha

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Background: Allergy to cow's milk (CM) is one of the most common causes of allergies in childhood. This produces multiple organic disorders such as eczema, diarrhea, vomiting, respiratory disorders, and other manifestations associated with food allergies.
Material and Methods: We studied five children of 4 years old diagnosed with allergic eczema, chronic diarrhea and cow's milk allergy by clinical history (atopic background); type of feeding (maternal, artificial); age of beginning of symptoms; time passed between the cow milk ingestion and appearance of symptoms (Dry skin, itching, vesicles, exudation, and frequency increasing in stool (volume and amount liquid). Prick Test was performed with cow milk standardised protein extracts (Casein, A-lacto globulin and B-lacto globulin). A Histamine concentrate (1 mg/ml) was used as positive control, being considered positive a 5 mm papule, and a Saline Solution was used for negative control giving non papule a result. Serum IgE and Specific IgE to Cow Milk in International Units milliliters was quantified by enzyme bioassay. We consider Diarrhea volume above10 g/Kg/day.
Results: Old of the 5 children studied presented atopic family antecedents, eczema and chronic diarrhea symptoms after cow milk dietary supplement. As a result of this research, three children presented the some symptoms the first year of life, and two of them during the second month. Three from the five children studied showed moderate Specific CM IgE levels: two of them during their first year of life and one during the first month. These three children presented Alfa Lacto globulin Positive Prick Test and Negative Beta Lacto globulin and Casein. The Seric IgE levels was above 100 UI/ml.

In the case of the other two children the Seric IgE and Specific CM Ig E levels were non significant (50 UI/ml). The Prick test from Cow Milk gave a negative resold.
Conclusion: According to these results it is possible to be determined that the cow mil is present in the allergic eczema and chronic diarrhea of smaller children to the four years old, and that his replacement could improve the clinical sintomatology of the patient with medication saving for such.

1615
Anaphylaxis due to oat milk ingestion

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Background: The common oat (*Avena sativa*) is a cereal commonly used for human consumption. Skin or inhalatory sensitisation has been described in cases of oat allergy. We present a case of anaphylaxis after ingestion of oat milk with no cross-reaction with other cereals.
Method: A seventy-year-old man with a history of essential hypertension and rheumatoid arthritis, presented 10 min after ingestion of 200 ml of oat milk, an episode of palmoplantar pruritus, generalised exanthema, nausea, vomits, thoracic and laryngeal oppression and systolic hypotension. The episode resolved after adrenaline, corticosteroids and antihistaminic treatment. The allergic study included: basal tryptase, blood count cell, biochemistry and coagulation; skin test with usual pneumoallergens, oat milk and oat seed; serum specific IgE determination (immunoCAP) to oat, barley, rye and grass pollen; IgE determination (EAST) to oat milk and oat seed, as well as to 102 allergens (immunocap ISAC) were performed; SDS-PAGE immunoblotting with extracts from oat milk and oat seed was carried out.
Results: Laboratory results were normal including tryptase (6.99 μg/ml). Skin prick -prick test to oat milk and oat seed was positive. Specific IgE EAST was positive (0.4 kU/l) while serum specific IgE levels by immunoCAP and ISAC were negative (<0.35 kU/l). SDS-PAGE Immunoblotting with patient serum, in non reducing conditions, revealed a 45 kDa IgE binding band in oat seed extract. This band disappeared when the electrophoresis was performed in reducing conditions (with 2-mercaptoethanol).
Conclusion: We describe a case of unusual selective *Avena sativa* allergy. There are no previous reports involving a 45 kDa-allergen from oat as the possible responsible of anaphylaxis after oat ingestion.

Poster Session 72

The clinical challenge of allergy diagnosis

1616
Determination of cross-reactivity between hazelnut and grass pollen allergens by immunoblotting and inhibition experiments among children with hazelnut and grass pollen allergies

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Background: Hazelnut allergic patients usually suffer from tree pollen associated oral allergy syndrome (OAS) caused by cross-reactivity. In our clinic we observed high prevalence of hazelnut allergy in children with grass pollen allergy. In this study we aimed to investigate the cross reactivity between hazelnut and grass pollen allergens among children with sensitivity to both hazelnut and grass pollen.
Method: In this study 17 sera from patients suffering from pollinosis to grass and sensitisation to hazelnut were studied. Sensitivity of patients to hazelnut and grass pollen was determined by skin prick tests and sIgE (ImmunoCAP). Study group divided to 'hazelnut reactive' and 'hazelnut non reactive' according to DBPCFC tests. Hazelnut and grass pollen allergens (*Phleum pratense*) were identified by means of SDS-PAGE and IgE immunoblotting. Assessment of cross-reactivity with grass pollen allergens is shown by immunoblotting inhibition experiments.
Results: A band smaller than 10 kD was found in the patients with (+) DBPCFC but not in patients with (−) DBPCFC. In the SDS-PAGE gel for Phleum pratense allergens 32kD band (presumably Phl p5b) was found as a major allergen. In SDS-PAGE gel by using serum pool of DBPCFC (−) and DBPCFC (+) groups, we determined bands between 50–60 kD (Group 4 and 13 grass pollen allergens), these bands were present only in DBPCFC (−) but not DBPCFC (+) group. As similar to grass pollen allergen gel, in the gel with hazelnut allergen extract we found bands between 40 50 kD in DBPCFC (−) group, but not in DBPCFC (+) group. Inhibition experiments showed that the bands between 40–50 kD, observed in DBPCFC (−) group, were inhibited by *Phleum pratense* allergenic extracts. Moreover bands between 50–60 kD (Group 4 and 13 grass pollen allergens) observed in grass pollen gel of DBPCFC (−) group, inhibited by hazelnut allergenic extracts.
Conclusion: Our results suggest that the band in hazelnut allergen gels smaller than 10 kD (presumably Cor a8) may be useful for discrimination of hazelnut reactive patients from non reactive ones and the specific IgE response in DBPCFC (−) group might be as a result of cross-reactivity between hazelnut allergens (40–50 kD) and grass pollen allergens (50–60 kD) by means of homolog antigen structure.

1617
A study of the prevalent sensitising allergens in India

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Background & objectives: This study was conducted to identify the most common sensitising food and inhalant allergens in physician-diagnosed allergic children and adults in North India.
Methods: Two-hundred and seventy four allergy-diagnosed patients aged 6–65 years were enrolled in the study. They were classified as atopics if had at least one positivity when screened with ImmunoCAP® Phadiatop and fx5 (Food mix 5; 6 common foods), a technology considered as the gold standard for IgE antibody blood testing worldwide. For identification of the sensitising allergens atopic patients were further tested by ImmunoCAP® Specific IgE using a broad panel of common Indian allergens covering 17 foods and 19 inhalants (singles/mixes).
Results: Phadiatop/fx5 determined 59% (162/274) of the patients as atopic, whereof 159 were included for further evaluation. Thirty-six percent of the patients had the medical history of urticaria followed by atopic dermatitis (26%), asthma (23%) and rhinitis (23%). The commonest sensitising food allergen was banana (68%) followed by sesame seeds (66%), lemon (45%), rice (31%), wheat (24%), cashew (23%) and peanut (21%). Among inhalants, house dust mite, Dermatophagoides farinae (83%) was the most prevalent sensitising allergen followed by cockroach (79%), weed pollens (29–50%), tree pollen (16–29%), grass pollen mix (26%) and mold mix (25%).
Interpretations and conclusions: Phadiatop/fx5 results revealed that the physicians' diagnosis of IgE mediated allergy was accurate only in 59% of cases and thus showed the importance of using allergy tests in conjunction with clinical findings for a correct allergy diagnosis. This is the first Indian sensitisation data of this dignity analyzed by ImmunoCAP®; a WHO standardised allergy blood test. Besides high rates of mite and cockroach sensitisation, useful native information of other prevalent sensitising Indian allergens was collected that would improve cost effectiveness of the allergy treatment and increases the quality of life of patients with allergy in India.

1618
Large scale serum IgE determination from various patients with suspicion of allergy within one year covering Hungary

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Background: The incidence of allergic diseases increased in recent years due to many reasons, including air and water pollutions, artificial food consumption, increasing traffic. Our laboratory receives samples nationwide from selected disciplines. Doctors send samples for IgE based *in vitro* tests besides *in vivo* testing their patients. The aim of this study was to analyze all material in order to get insight into factors determining prevalence of allergy in Hungary.
Method: Serum samples (3178) sent in by laboratory network were analyzed according demand of the doctors. Five panels and 80 different nutritive and inhalant

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allergen specific IgE (sIgE) threshold positivity was Class 2, together with total IgE were measured by IMMULITE 2000 and Modular E respectively.

Results: Out of all samples 1463 were directly linked to allergic diseases. These included allergic rhinitis 39%, asthma 19%, allergic urticaria 15%, atopic dermatitis 11%, allergic gastroenteritis 8%, and 'allergy' 8%. The remaining 1715 samples belonged to 24 different diagnostic categories out of which 9 (with 676 samples) could be related to allergy as well. About 1039 samples (15 diagnostic categories) were sent upon different acute conditions (879; 27.6%). The pediatric allergic cases could be divided into age categories 0–7.9; 8–14 years with 542 and 189 cases. The remaining 732 cases represented adults (>15 year) and were females 509 (69.5%) and males 223 (30.5%). Within the allergic group according to diagnosis at 95% sensitivity for total vs sIgE, the cutoff value was 30 kU/l; negative predictive value 96% (by ROC curve). Out of the total 1463 allergic samples 448 (30%) reacted at least one inhalant allergen. Similarly, 218 (15%) were positive to at least one nutritive allergen. Moreover, a mixed positive group could be generated with 28 out of 135 demands containing both inhalant and nutritive sensitivities.

Conclusion: Among many unnecessary test, that represent over estimation of allergy or poor decision by the sender, the low cutoff value established for sIgE in relation to total IgE deserves attention. In our study Ragweed is the most common allergen in Hungary.

1620
Natural course of atopy detected with skin prick test

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Background: Skin prick testing is a practical method widely used in the diagnosis of allergic diseases. Repeated skin prick tests can be used to demonstrate the new sensitisations or natural sensitisation. The aim of this study is to investigate sensitisations to common enviromental antigens over time in children.

Method: Sixty children who were followed up with diagnosis of allergic rhinits and/or asthma in Dokuz Eylul University Faculty of Medicine division of Pediatric Allergy and Immunology. Participants were the children who had skin testing second time during 2010. Skin prick test allergens involved grass, grass/cereal, weeds, tree pollens, fungi, animal hair and dander, olea, pinus, and house dust mite. Induration more than 3 mm at the side of the test was considered as positive response. In statistical analyses, categorical variables of dependent groups evaluated with chi-square test. Comparison of values between groups gathered from measurements were assessed with Mann-Whitney U test.

Results: 60% of the patients were male and the mean age was 7.3 ± 3.7 and the average time elapsed between the two skin test was 2.2 ± 1.4 years. When the first skin test were compared to second skin test, grass sensitisation increased from 38.3% to 51.7% ($P = 0.058$), grass/cereal sensitisation increased from 38.3% to 51.7% ($P = 0.059$) and pinus increased from 1.7% to 8.3% ($P = 0.046$). While increase in sensitivity to grass and grass/cereal mix was non significant, the increase in pinus sensitivity was statistically significant. Mean eosinophil count among individuals with increased sensitivity (431.81 ± 318.30) was significantly higher than individuals with no increase in sensitivity (295 ± 331) ($P = 0.03$). Mean IgE values among individuals who presented increase in sensitivity (572.77 ± 575.15) were significantly higher compared to ones showing no increase in sensitivity (212.22 ± 215.90) ($P = 0.03$).

Conclusion: Sensitivity detected by skin tests could increase by time. Skin tests could be repeated among patients presenting high IgE and total Eosinophil values in their first visit and if new symptom and findings occur during follow-up.

1622
Evaluation of a new multiplex assay system for the simultaneous detection of total and specific IgE and IgG4 against established immunological assay methods

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Background: As a joint-venture of Dr. Fooke Laboratorien GmbH and the Engelhardt Institute of Molecular Biology of the Russian Academy of Sciences (EIMB) a prototype of a multiplex test-system for the simultaneous quantitative determination of 21 allergen-specific antibodies and total IgE was developed. The Biochips are manufactured using EIMB technology. The architecture of the chip is an array of hemispherical gel elements (microdrops 0.1 nl in volume), each containing an individual immobilised molecular probe. The main advantage of the three-dimensional hydrogel Biochip is a high immobilisation density, the absence of contact of protein molecules with the hydrophobic surface of the carrier and an aqueous environment of immobilised molecules prevents protein denaturation.

Method: A set of purified allergen extracts which fulfill the requirements of manufacturing for the hydrogel-based Biochips were prepared for 21 very common allergens and total IgE and >300 serum samples of allergic patients and healthy donors were tested. The measurement and calculation of the signals was performed using *ImaGelResearch* software (developed in EIMB).

We compared the results produced with the novel AllergoChip with established assay methods like ALLERG-O-LIQ (DFL) and ImmunoCAP (Thermo Fisher).

Results: Good correlation of the results of simultaneous determination of 21 sIgE and total IgE on biochips with the results of individual assays using ALLERG-O-LIQ test for specific and total IgE-HRP EIA (both from Dr. Fooke company) has been demonstrated: correlation coefficients were 0.89–0.99 for sIgE and 0.99 for the total IgE.

Conclusion: Due to the nature of the chip and the immobilisation technology the capability of this biochip technology allows for an unlimited widening of analyzed allergens.

1623
IgE – antibodies to cats's allergens in allergic patients in Russian Federation

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Background: The sensitisation to pet's allergens is one of the main causes of provocation of allergic respiratory symptoms. There are more than 50% of Russians keep the pets in their dwellings, predominantly cats (in 69%) according to the study «Romir Monitoring». The aim: to investigate frequency of IgE-aB to cat's allergens among patients with allergic rhinitis and bronchial asthma.

Method: The study was conducted in Moscow' and Yekaterinburg' (538) atopic residents aged from 1 to 58 years old during period 2008–2012 years. IgE-aB to cat and dog allergens were determined by ImmunoCap (ThermoFisher Scientific, Sweden). Component-resolved diagnosis was provided by ImmunoCap ISAC in 18 sera of pts with high evidence of cat's allergy.

Results: The frequency of IgE-aB to cat's allergens among all (538) allergic patients amounts – (53.25%). From them cat's IgE-aB were revealed in (53.67%) of atopic children up to 7 years, and in (65.9%) aged from 7 to 14 years old. The occurrence of IgE-aB to cats in adults with respiratory allergic diseases made (63.67%) in pts aged from 14 to 20 and (32.14%) – in those from 20 to 58 years old. From 18 of pts's sera 16 (88.9%) were positive to major cat allergen's component uteroglobin rFel d 1. IgE-aB to lipocalins rFel d 2 and rFel d 4 were determined in 9/18 (50%) and 4/18 (22.2%), respectively.
Conclusion: The frequency of serum IgE-aB to cat's allergens among patients with allergic rhinitis and bronchial asthma in residents of two capitals Moscow and Yekaterinburg is high – up to in children and – up to in adults. The majority of sensitised to cat pts (89%) are reactive for rFel d 1.

1624
Factors affecting the sensitivity of skin prick test

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Background: Skin prick tests are widely used to determine sensitivity in allergic diseases. Skin test reactivity may vary over time. There is limited information about the natural history of skin sensitisation tests and factors that affect it.
Method: 170 patients' skin tests among the patients who underwent skin tests between 2005–2007 in Clinic of Pediatric Immunology and Allergy, were repeated after an interval of at least 3 years. Skin-prick tests with the same allergens were repeated in all patients. Pulmonary function tests, immunoglobulin E and peripheral blood eosinophil levels were evaluated.
Results: The mean age was 10.7 ± 3.1 (5–18) years and 70% of the patients were male. In the present skin tests 95 (55.9%) cases had skin reactivity to at least one allergen, while 89 (52.4%) patients had skin prick-test reactivity in first skin test. In the comparison of sensitivities of the two test, there was a statistically significant alteration for grass pollen mixture, cereal pollen mixture and dog epithelium sensitivity ($P = 0.01$, $P = 0.08$, $P = 0.00$). 14 (17%) with non sensitivity in the first tests showed changes in sensitivity while the change of sensitivity had in 52 (58%) patients with sensitivity in the first tests. In total, 66 (39.0% of the study population) had a different skin tests result at follow up compared with first. Alterations: loss of sensitivity in 18 (11%) patients, the formation of a new sensitivity in 37 (22%) patients, and 11 (6%) both gained and lost sensitisations. The presence of atopy in the family, the presence of allergic rhinitis and IgE elevation (respectively, odds ratio = 5.88; 95% confidence interval = 1.7 to 20.6, $P = 0.005$, odds ratio = 20.91; 95% confidence interval = 3.4 to 130.4, $P = 0.001$, odds ratio 7.97 = 95% confidence interval = 1.6 to 39.9, $P = 0.012$) significantly predicted incidence of new sensitisation. The presence of sensitisation of multipl allergen (Odds ratio = 7.97; 95% confidence interval = 1.6 to 54.6, $P = 0.035$) significantly predicted incidence of loss of sensitisation.
Conclusion: It is found that there was an alteration of sensitisation in 4/10 children at the end of the average 4-year period. These alterations have been mostly in the form of new sensitisation. The presence of family history, the presence of allergic rhinitis and IgE elevation were the risk factors for development of new sensitisation besides sensitisation of multipl allergen were the risk factors for loss of sensitisation.

1625
Serum markers which could predict the risk of anaphylaxis in mastocytosis patients

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Background: Patients suffering from mastocytosis are at risk of anaphylactic reactions which occur in 50% of patients with systemic and 15% of patients with cutaneus disease. There are no *in vitro* methods available which could be used to predict the risk of the reaction so far. The aim of the study was to analyze the cytokines levels in the serum which could indicate patients at risk of anaphylactic reaction.
Method: Eighty-five patients suffering from systemic mastocytosis and 20 controls were included in the study. Among the mastocytosis patients 54 (63%) declared anaphylactic reaction in the medical history, while 31 (37%) did not suffer from such reaction so far. Cytokine levels (GM-CSF, IL-13, IL 1 beta, IL-3, IL-4, IL-6, IL-8, MCP-1, RANTES, TNF-alfa, VEGF, bFGF) were measured in the serum of the patients using flow cytometry and microbead flex set.
Results: The significant difference was found in the level of IL8 (mean 23.6 ± 16.6 ng/ml in patients with anaphylaxis) vs (mean 31.3 ± 63.7 ng/ml in patients without anaphylaxis) $P = 0.038$.

MCP1 (mean 156.4 ± 165 ng/ml in patients with anaphylaxis) vs (mean 86.2 ± 45.6 ng/ml in patients without anaphylaxis) $P = 0.016$.

The levels of other measured cytokines did not differ in analyzed populations.
Conclusion: IL8 and MCP1 levels might be used in the further studies to create an *in vitro* method assessing the risk of anaphylaxis in mastocytosis patients.

1626
Frequency of sensitisation for food and aero-allergens in 6600 patients received in a Venezuelan laboratory during 2010–2012

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Background: The prevalence of allergic diseases has grown in recent years. A food allergy is often the first manifestation of allergy in childhood, predisposing to further development of respiratory allergy so the importance of early diagnosis to implement preventive measures. The determination of sensitisation to food and respiratory allergens may prevent future allergic diseases. The objective was evaluate the behavior of the frequency of foods and respiratory allergens sensitisation in patients referred to Corpodiagnostica Laboratory (Caracas, Venezuela, ISO 9001:2008 certified laboratory) in the period 2010–2012.
Method: There were a total of 6600 patients with a request of specific IgE against some foods and aero-allergens. We measured the specific IgE to each patient by the *in vitro* RIDA® Allergy-screen immunoblot method (r-biopharm®, Germany).
Results: The frequency of sensitisation to aero-allergens were 41.48% in 2010, 62.18% in 2011 and 63.17% in 2012, being most frequent dust mites. In the case of food allergens the frequency of sensitisation were 25.99% in 2010, 45.41% in 2011 and 44.93% in 2012. Cow milk is the most common food allergen in the children group in each period evaluated.
Conclusion: In Venezuela has been increasing the total sensitisation rate for the aero and food allergens during the 3 years we examined. These frequencies of aero-allergens are consistent with others studies that suggest that climate change and exposure rate may contribute to increasing development of respiratory allergy. On the other hand, the increasing obtained for the

frequency of sensitisation to food allergens could be relate with the introducing of cow milk, cheese, wheat, egg white and corn in the early diet of Venezuelan children; in fact these kind of allergens are the most frequency food in the Venezuelan diet. Furthermore, the specialists have more laboratory tools for the determination of specific IgE for allergy diagnostics.

1627
Urticaria and rhinoconjunctivitis in a hunter

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Background: Although scattered reports have been published on roe deer allergenicity, we present a case of rhinoconjunctivitis and contact allergy urticaria to roe deer dander on a hunter.
Method: A 38 year old man, with subclinical hypothyroidism and slight pollen rhinitis on January and May-June, refers sneezing, rhinoconjunctivitis and urticaria on contact with roe deer, for the last 2 years. He has contact with this animal 3 days a week from April to July and in September-October. We performed functional lung test, skin prick test (SPT) and immunological studies to disclose the relationship between exposure to this animal, sensitisation and symptoms.
Results: Baseline spirometry revealed a FEV_1 of 4.870 mmL (100% predicted), that was normal. We performed a bronchial challenge (BC) with methacholine, without any kind of bronchial response. FE_{NO} was of 33 ppb, and the nasal nitric oxide determination was of 3175 ppb. SPT to a standard panel of inhalants was positive to grass, olive and *Cupressus* but negative to other pollens, dust mites, fungus and dog-cat dander, confirming the cause of his pollen rhinitis. Also we did SPT to some epithelia allergens, that was positive to horse and goat, doubtful to cow and sheep, and negative to others (rabbit, mouse, cat, dog, hamster, goose, mixture of feather, …). We made an extract with the patient′s roe deer hair and dander and when tested in prick test a weal of 15 mm was obtained (positive control wih histamine test a weal of 5 mm, and negative control with saline was negative). We performed a nasal provocation test with this extract on different concentrations, and we obtain a positive result with the first one (less concentrated one): the patient began with runny, sneezing and falled of peak inspiratory flow rate nasal. The immunoblot revealed IgE in the patient′s serum that bound to a protein around 19 kDa and another around 22 kDa.
Conclusion: This study confirms than roe deer can act as an allergen on hunters, with an IgE mediated reponse.

1628
Bird-egg syndrome

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Background: Bird-egg syndrome is a known cross-reactive syndrome firstly described in 1985. We present a case report of a 55-year-old woman referred to our outpatient clinic because since six years ago she suffered sneezing, nasal blockage and nasal pruritus with conjunctival erythema and ocular pruritus. She also suffered since two years ago dyspnoea, cough and wheezing episodes that need budesonida, salmeterol, montelukast and salbutamol inhaled treatment with oral corticoids each month.. Moreover she complained of lingual pruritus immediately after eating hen's egg that last for an hour. She had a cockatoo at her home.
Method: We performed skin prick test with canary, duck and parakeet feather and excrement, complete hen's egg, egg yolk, egg white, ovoalbumin, ovomucoid and lysozyme Alk-Abello extracts. We also performed espirometry after and before bronchodilator.
Results: Skin prick tests were positive to canary, duck and parakeet feather, complete hen's egg, egg yolk, egg white and ovomucoide. It was negative to the rest of allergens tested. Bronchodilation test was positive.
Conclusion: We present a case report of a bird-egg syndrome with rhinoconjunctivitis, asthma and oral allergy syndrome. This case underlines the importance of ask about food allergy in asthma suspected patients and on the other hand, exposure to cross-reacting antigens by ingestion might also influence the allergic manifestations to inhalant allergens.

1632
Total serum immunoglobulin E and allergy

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Background: Immunoglobulin E (IgE) mediated immune responses seem to be directed against parasites and neoplasma, but are best known for their involvement in allergies. However, after having been widely used in clinical practice, the limit of evaluating total IgEs levels in the diagnosis of allergic disease has emerged. In fact, the determination of reference values is difficult due to problems in defining possible overlaps of IgE values between atopic and non atopic patients and the multiplicity of factors influencing their levels. The aim of the study was to characterise allergy patterns and the relationship between total serum IgEs and medical history in young patients.
Method: We enrolled 266 patients: 188 presented with allergic rhinitis or asthma, 86 with cutaneous symptoms and 12 with food allergy. The patients were then stratified into four age groups at baseline (0–2, 3–5, 6–10 and >10 years). Total IgEs were measured by fluoroenzymeimmuno-assay and expressed in kU/l. Descriptive statistics were calculated and reported as medians (md). Comparison of variables was performed by the non-parametric Mann-Whitney U test. A P-value ≤ 0.05 was considered as statistically significant.
Results: Out of 258 patients, 145 (54.5%) showed an increased total IgE level. Total serum IgE levels were significantly higher ($P < 0.0001$) across age groups with the highest levels in the >10 year group (0–2 years – md: 22.5 kU/l, 3–5 years – md: 64.55 kU/l, 6–10 years – md: 142 kU/l and >10 years – md: 164 kU/l). If we consider the patients showing IgE levels over the range by age, the highest median value was in the 6–10 years group. Patients with allergic rhinitis or asthma showed a significant (P value < 0.0001) increase of IgE levels until 5 years of age, while the total value tends to decrease with age. The same findings were highlighted in patients with cutaneous symptoms. Total IgE values showed an increase through age in the food allergy group.
Conclusion: Total serum IgE levels seem to be helpful to diagnose a predisposition to allergy in children. The clinical utility of total serum IgE measurements in the diagnosis of allergic disease has always been limited by its age dependent concentration and the wide overlap in concentrations in serum between atopic and non-atopic populations. Our preliminary results require further confirmation in larger cohorts and a study of correlation between total IgE levels and clinical severity of disease.

1634
Allergy to sugar? A diagnostic challenging case

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Background: Type I hypersensitivity reactions are mediated by specific IgE to proteins, polysaccharides or glycoproteins. Saccharose or fructose intolerances and malabsortions are usually due to enzymatic deficiencies and manifest with gastrointestinal symptoms.

Case presentation: A 52-year-old male patient was admitted to our department to study the occurrence of several episodes of systemic muco-cutaneous reactions (urticaria, angioedema and pharyngeal constriction) soon after ingestion of foods/drinks with a high content of rapid absortion sugars. He also had previous episodes of anaphylaxis 5 min after hymenoptera sting, and describes long-lasting asthma symptoms during the spring pollen season, both conditions without convenient medical diagnosis and treatment.

The study was conducted after more than month in complete absence of symptoms. Skin prick tests to aeroallergens (GA^2LEN panel) was positive only for *Parietaria judaica* 5 mm (histamine = 5), and negative to fresh fruits and other food-allergens. Prick-prick test to regional honey = 4, purified fructose = 3 and saccharose = 3 (all negative in healthy volunteers using the same sources). Intradermal tests to hymenoptera were positive to *Apis mellifera* only. Serum specific IgE to *Apis m* was 1.26 kU/l and negative for honey, cross-reactive carbohydrate determinants (CCD) and *Parietaria*. Basal tryptase and complement factors were normal, as well as the global laboratorial assessment, including glycemia. Functional bronchial tests demonstrated mild distal obstruction.

An open oral challenge test was performed with saccharose in fasting conditions, starting with 2 g dissolved in 20 cc of water, and 2 g increasing doses at each 30 min. About 10 min after the 8 g dose (cumulative 20 g) the patient developed facial flushing and widespread urticaria, treated by parenteral clemastine.

Conclusion: The absence of sensitisation to CCD argues against the eventual association of these atypical clinical symptoms to the hymenoptera sting allergy. The mechanisms involved in this presumably IgE-mediate reaction to simple sugars require further studies.

1635
Vesicular contact reaction, progressing towards erythema multiforme of a dermal type in a 27-year old patient after cesarean section

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Case presentation: The authors present a case of a 27-year old patient, who developed severe erythemato-vesicular reaction 24 h after cesarean section. Within the time period of 48 h we could observe progression towards erythema multiforme-type of skin lesions (histopathological examination revealed erythema multiforme of a dermal type). Skin lesions were localised on the abdomen and thighs. Due to the severity of the reaction methyloprednizolone in pulse therapy, together with cyclosporine A (350–400 mg per day) were administered. A slow, systematic alleviation of symptoms was achieved. Pemphigoid gestationis was excluded on the basis of an immunopathological examination. Three months after the remission, the patient was hospitalised again to perform the diagnostics toward hypersensitivity reaction against disinfectants and textiles used during surgical procedure.

Poster Session 73

Clinical rhinoconjunctivitis: treatment options

1636
Recalcitrant nasal polyposis treated with omalizumab

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Background: The incidence of nasal polyposis asthma increases probably because eosinophilic inflammation which characterises these diseases. Surgery is indicated when medical treatment is not effective, but does not prevent recurrences. Omalizumab is a monoclonal antibody anti-immunoglobulin E used to reduce the severity of bronchial asthma.
Method: A 67 year-old female, with severe asthma, admissions in the intensive care unit, NSAID intolerance, sensitised to mites and dog epithelium. Nasal poliposis history for over 10 years. In four years has been surgically intervened three times by the recurrence of polyps despite repeated topical steroids and oral steroid cycles. Omalizumab treatment begins with 300 mg/month in February 2009.
Results: After Omalizumab therapy is appreciated progressive improvement of nasal symptoms and lower respiratory tract, without emergency visits or need for oral corticosteroids, smell gradually recovers, and is results in a reduction of the dose of inhaled corticosteroid nasal and bronchial. During treatment showed no relevant changes in the blood count, biochemistry, skin tests, total and specific IgE, tryptase, immunoglobulins, and complement. ECP values decreased from 32.8 to 18.2 μg/l. The FEV1 improved from 68.5% to 89% of the theorist. After the last surgical cleansing, in rhinoscopy not been shown the reappearance of nasal polyposis. Marked decrease is seen naso-sinus polyps in radiological images.
Conclusion: In our patient with anti-IgE therapy Omalizumab improved asthma, as has been described in the literature and suggested also be very effective in the control of the recurrence of polyposis, which may have therapeutic utility in this disease.

1638
Non-interventional study comparing treatment of acute rhinosinusitis with SNS01 (ectoine nasal spray) or BNO-101

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Background: Acute rhinosinusitis is one of the most common upper respiratory tract diseases. In Germany, treatment of the disease with the herbal substance BNO-101 (Sinupret forte tablets) is very common. This non-interventional trial aimed to compare the treatment with BNO-101 and with the nasal spray SNS01 which contains the natural osmolyte ectoine. In contrast to most pharmaceutical treatments, ectoine is not metabolised but acts rather by stabilisation and moisturisation of cell membranes.
Method: Patients diagnosed with acute rhinosinusitis in a specialist clinic were asked to participate in this non-interventional trial. Based on their personal preference, they were either treated with SNS01 or BNO-101 for 14–16 days. Treatment was applied in accordance with the instructions for use. Symptoms during the course of the study were evaluated by nasal endoscopy by ENT (ear nose throat) experts. Additionally, both physicians and patients scored the predominant disease symptoms using a rating system based on EPOS recommendations. A disease-specific quality of life questionnaire was used to document the impact of symptom improvement on daily life. Statistical analyses were carried out with SPSS 20; significance levels were set to 5% for all tests.
Results: Following two weeks of treatments, endoscopy results reflected a comparable symptom decrease of 57.8% ($P < 0.001$) in the SNS01 group and of 49.3% ($P = 0.004$) in the BNO-101 group. In line with this, Sinusitis Symptom scores decreased similarly by 58.1% in the SNS01 group and by 53.5% in the BNO-101 group ($P < 0.001$ for both groups). Quality of life in patients treated with SNS01 improved by 15.81 points, and in patients receiving BNO-101 by 18.32 points ($P < 0.001$ and $P = 0.033$). Local tolerability of the nasal spray was judged very well by the patients. At the end of the treatment, both physicians and patients rated the efficacy of both products as good without differences in treatments. Tolerability of SNS01 was regarded as good to very good with comparable scores, and only one adverse event occurred during the course of the study.
Conclusion: Treatment of acute rhinosinusitis with the nasal spray SNS01 showed equivalent efficacy as treatment with the herbal substance BNO-101. As SNS01 was also well tolerated and showed a very good safety profile, it might present a promising new treatment strategy for acute rhinosinusitis.

1639
Protective efficacy of pranlukast dry syrup, a leukotriene receptor antagonist, against Japanese cedar pollinosis in children

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Background: We have reported the efficacy and safety of pranlukast dry syrup (PLK-DS), a leukotriene receptor antagonist (LTRA), in children from 10 to 15 years old with Japanese cedar (JC) pollinosis by the double-blind, placebo-controlled, cross-over study used an artificial exposure chamber (OHIO Chamber) [1)]. It is ideal that the treatment of pollinosis can be started as early as possible to alleviate symptoms. We examined whether PLK-DS have a protective efficacy against the priming state, the artificial pollen-exposure and the natural pollen-exposure of JC pollens by the double-blind, placebo-controlled, comparative study, in which medication was started on the date of pollen-observation before the defined start date of pollen dispersal.
Method: Thirty children with JC pollinosis who had positive skin tests for JC pollens, had suffered from pollinosis for at least two years, and had severe nasal blockage when exposed to JC pollens were enrolled in the double-blind, placebo-controlled, comparative study. Over 8 weeks, a double-blind study was conducted by randomly allocating

the children to two groups (the placebo group and the PLK-DS group). PLK-DS or placebo was administered orally after breakfast and dinner for 8 weeks in the season of JC pollen dispersal. Before the defined start date of pollen dispersal, all subjects underwent the exposure of 3 h to a specific amount of JC pollens ($8000/m^3$) in the OHIO Chamber. The efficacy of PLK-DS was evaluated based on nasal symptoms (sneezing, rhinorrhea, or nasal blockage), and eosinophil cationic protein (ECP).

Results: In the PLK-DS group, scores for symptoms of pollinosis were lower compared to the placebo group in the medication period of the priming state, the artificial pollen-exposure and the natural pollen-exposure of JC pollens. Especially PLK-DS significantly improved the score for nasal blockage, compared to the placebo. Furthermore, the correlation was confirmed in change between scores for symptoms of pollinosis and ECP.

Conclusion: Our results confirm a protective efficacy of PLK-DS against the priming state, the artificial pollen-exposure and the natural pollen-exposure of JC pollens. We conclude that PLK-DS, a LTRA, is a more effective drug as primal therapy when administered as early as possible in the season of JC pollens.

Reference: Wakabayashi K et al, Allergy Asthma Proc. 2012;33:102–109.

1640
The effect of rebamipide eye drops on allergic conjunctivitis with giant papilla

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Background: Rebamipide, a gastroprotective drug, has been prescribed for the treatment of gastritis and gastric ulcers because it suppresses gastric mucosal inflammation and increases gastric mucus production. In Japan, rebamipide eye drops have been approved for the treatment of dry eye disease. We previously reported that rebamipide can suppress polyI:C-induced cytokine production in human conjunctival epithelial cells and that the topical administration of rebamipide suppresses conjunctival allergic eosinophil infiltration in a murine experimental allergic conjunctivitis model. It has also been reported that dry eye with only decreased tear break-up time is sometimes found in allergic conjunctivitis patients. In this study, we examined the effect of rebamipide eye drops for allergic conjunctivitis with giant papilla.

Methods: This study involved 5 allergic conjunctivitis patients with giant papilla (vernal conjunctivitis or atopic keratoconjunctivitis) accompanied by dry eye with decreased tear break-up time. In this study, rebamipide eye drops were prescribed for the treatment of dry eye in the 5 allergic conjunctivitis patients with giant papilla, and the alterations of their giant papilla were then observed. This study protocol was approved by the Ethical Review Board of Kyoto Prefectural University of Medicine.

Results: For all five patients, a 3–4 times daily administration of rebamipide eye drops was prescribed, and attenuation of the giant papilla was observed in all of the 5 patients.

Conclusions: Administration of rebamipide eye drops was found to might suppress the giant papilla in allergic conjunctivitis, and might possibly be an effective treatment for allergic conjunctivitis as well as dry eye.

1641
Inhalation therapy with vibrating aerosols – an advanced approach for the treatment of acute and chronic rhinosinusitis?

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Background: About 10–15% of the US and EU population have CRS which leads to an enormous health economic burden. The paranasal cavities are non-ventilated areas. Hence a desirable topical drug delivery e.g. by usual inhalation is not very successful. With an innovative inhalation technology providing a pulsating aerosol a significantly improved particle deposition in the paranasal sinuses – compared to an inhalation which does not present the vibration – has been shown. The patients' acceptance and the clinical benefits of the treatment have been evaluated.

Method: Multicentric, non-interventional, retrospective survey including a 2-page-question-naire completed by community ENT-specialists after the pulsating aerosol therapy (PARI SINUS, PARI GmbH, Germany) with saline solution. Therapeutic effects on the main ARS and CRS symptoms and the acceptance of the device and the treatment option were assessed on a 7-point scale from −3 (very negative) to +3 (very positive).

Results: Data from 81 rhinosinusitis patients (33 ARS patients, 17 female (f), 16 male (m) average age 39.3 ± 18; 48 CRS patients, 29 f, 22 m, average age 49.8 ± 12) receiving the treatment twice daily (mean 2.05 ± 0.92) have been evaluated. The effect on the symptoms was rated +2.27 ± 0.36 for ARS and +1.76 ± 0.43 for CRS patients. The acceptance of the therapy and the handling of the inhalation technique were valued as +2.46 ± 0.95 and +2.27 ± 0.98. An impact on facial pain (ARS +2.17 ± 0.89; CRS +1.55 ± 1.18) was reported as well as a reduction of the post nasal drip (ARS +2.16 ± 0.73; CRS +1.74 ± 0.93). The effect on quality of life (QoL) was graded +2.39 ± 0.84 for ARS and +2.18 ± 0.76 for CRS. The course of the disease was marked +2.48 ± 0.81 (ARS) and +2.05 ± 1.01 (CRS). For ARS patients the therapy led to a reduced need for oral antibiotics rated +1.63 ± 1.31and nasal steroids rated +1.42 ± 1.26. CRS patients also needed fewer oral antibiotics (+1.49 ± 1.06) and nasal steroids (+1.19 ± 1.19). A decrease in sick leave days was reported (ARS +1.70 ± 1.07, CRS +1.26 ± 1.23).

Conclusion: Vibrating aerosol inhalation for rhinosinusitis is well accepted by ARS and CRS patients. Symptom relief, reduction of oral antibiotics and nasal steroids, improvement of QoL and declining sick leave days make this painless and non-invasive treatment an interesting therapy option. For the investigation of the full potential of this treatment option further studies on this topical therapy for ARS and CRS are desirable.

1642
Clinical data from usage of an isotonic solution of hyaluronic acid and sea water in ENT inflammatory diseases

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Background: Consensus guidelines recommend saline nasal irrigation as an option for the treatment of a variety of upper respiratory conditions, such as acute and chronic rhinosinusitis, allergic rhinitis, nasal polyposis and for postoperative treatment. Seawater nasal irrigation may improve nasal mucosa function through several physiologic effects, including direct cleansing, removal of inflammatory mediators and increased ciliary beat frequency leading to improved mucociliary function.

Recent evidence suggests that hyaluronic acid may exert important effects against injury in a number of respiratory diseases. Thanks to its high water-binding capacity it hydrates nasal mucosa and maintains the mucociliary function. Moreover, it improves healing of nasal mucosa micro-injuries and in post-operative conditions.

Aim of this study is to collect clinical data from usage of an isotonic solution of hyaluronic acid and sea water from Bréhat island, in ENT inflammatory diseases.

Method: Data were collected from 30 subjects (mean age 46 ± 15 years, 17 female – 13 male) with ENT inflammatory diseases (rhinosinusitis) treated with Ialumar (Rottapharm|Madaus), as nasal application, 2–4 times a day, for 6 days.
Results: The patients performing nasal application showed significantly better conditions of nasal secretion, obstruction, and rhinorrhea. Doctor's judgment on treatment efficacy was positive for all subjects. All the patients performing nasal irrigation reported improvement of rhinitis symptoms. Only one case reported of unchanged condition. No adverse event was recorded.
Conclusion: These data indicate that Ialumar nasal application is a safe and effective option for ENT inflammatory diseases (i.e. rhinosinusitis).

1643
Side effect of Timolol 0.5% treating open angle glaucoma, at the same patient suffering from chronic asthma bronchialis and diabetes mellitus type II. Case report

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Purpose: To evaluate the side effect of Timolol 0.5% long term used for glaucoma treatment at patient suffering from chronic asthma bronchialis.
Method: A 64 years old women D.B was presented for check – up to the Ophthalmology service with complains of low vision. She use to be diagnosed and treated regularly for glaucoma since 2004 but for medical reasons she present to the clinic after 4 years of missing. During the interview and objective examination she refer her treatment for a long period with sol. Timololi 0.5% twice daily, sol. Brinzolamide 1% twice daily. She was suffering from diabetes mellitus Type 2, Sarcoidosis, HTA also Asthma Bronchialis since 2008 all treated with the specific protocols. She is taking Salbutamol oral disc inhaler 2 mg/5 ml 100 mg two times daily, Seretide two times daily for asthma. When specifically asked she complain of exacerbation of asthma lately the 4 last year's beside the regular treatment and check – up to Allergology service.
Results: The Timolol 0.5% was stopped used and switched with sol. Betoptic -S twice daily. The patient was asked to come for check -up every 2 weeks after changing the therapy of Glaucoma. On presentation she referred no more heavy attacks of asthma and better breathing. After 2 months of switching the glaucoma therapy she was feeling even better.
Conclusion: It is well known the side effect of sol. Timololi 0.5% at asthma bronchialis. Better information is need for the patients using this drug for the side effects. Also the physician must be more careful when taking the disease history of the patients, just to prevent complication and discomfort for the patients.

1644
The impact of endonasal sinus surgery on patients with chronic sinusitis and chronic pulmonary disease

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Background: Co-incidence of chronic sinusitis and bronchial asthma is well known. New studies indicate also a common incidence between chronic obstructive pulmonary disease (COPD) and chronic sinusitis. The present study compares the impact of the sinus surgery on the upper and under respiratory system at patients with bronchial asthma and patients with COPD.
Method: Forty-three patients with chronic sinusitis were enrolled in this study (32 patients with bronchial asthma and 11 patients with COPD) at the Department of Otorhinolaryngology, University Medical Center in Homburg. In all patients endonasal sinus surgery was performed. To evaluate the successes of surgery, we used the SNOT-20 (Sino-nasal outcome Test 20) and the SGRQ (St. Georges Respiratory Questionnaire) preoperative and at least 6 months after surgery.
Results: Improvements of sinonasal symptoms were clearly proved postoperative in both groups. The SNOT-20 index was improved from 44 (preoperative) in both groups to 20 (postoperative) in patients with bronchial asthma and to 33 (postoperative) in patients with COPD. The preoperative SGRQ index was improved about 8.3% in patients with asthma bronchial and 7.9% in patients with COPD. The Wilcoxon-test was significant ($P = 0.021$). The medications intake was unchanged in both groups.
Conclusion: The surgical therapy on patients with chronic sinusitis and chronic pulmonary disease improved the nasal symptom as well as the symptom of respiratory tract and the quality of life in patients with COPD or bronchial asthma.

1645
Dry eye syndrome and allergy

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Background: Eye allergy is often associated with the pathology of the surface of the eye, including dryness. An insufficient production of tears and/or a poor quality of the tears, favors the accumulation of allergens on the eye surface and limits their natural evacuation. Allergy and eye dryness involve inflammatory mechanisms that sustains one an other. The symptoms of dry eye may be similar to eye allergy: redness of the eyes, burning or itching in the eyes, blurred vision, sensation of foreign body, tired eyes.
Method: Prospective study on a group of 30 patients with dry eye syndrome, during one year. Inclusion criteria: signs of eye dryness, lamp examination revealed conjunctival folds, Schirmer test pozitiv and / or test But low, ocular allergy symptoms: itching, red eyes; symptoms and signs of other allergic diseases: rhinitis, atopic dermatitis, asthma; positive specific IgE or skin prick tests. Exclusion criteria: patients with dry eye syndrome who respond well to the use of artificial tears, negative specific IgE or skin prick tests.
Results: Of the 30 patients, 23 (76.6%) had IgE- mediated sensitisation. Among patients with allergic sensitisation, allergens were: house dust mite-11 patients (47.82% of allergic patients, 36.6% of total), grass pollen-6 patients (26.08% of allergic patients, 20% of total), Ambrosia elatior pollen-5 patients (21.73% of allergic patients, 16.6% of total), cat dander -2 patients (8.69% of the allergic patients, 6.66% of total); molds mix-1 patient (4.34% of allergic patients 3.33% of total); birch pollen-1 patient (4.34% of allergic patients 3.33% of total). Three patients showed sensitisation to more than one allergen: two patients to house dust mites and grass pollen and one to cat dander and Ambrosia elatior pollen. From 23 patients with dry eye syndrome and allergic sensitisation, 18 patients are urban, which supports the idea, according to which there is an interaction between pollution and allergens with increased aggressiveness of the allergens, the more so as the film normal tear is not quantitatively or qualitatively (positive Schirmer test and / or test BUT extended). Local treatment received: artificial tears without preservatives and olopatadine. General treatment: desloratadine. Efficacy of the treatment was 86.9%.
Conclusion: Dry eye syndrome is a risk factor for the development of ocular allergies. Quality of life is significantly higher

when patients receive full diagnosis and appropriate treatment.

1646
Chronic blepharoconjuntivitis: importance of the differential diagnosis

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Background: Allergic eye diseases are frequent and usually of mild severity. Its diagnosis is easy and can be done based only on the symptoms and simple complementary tests, although, it is important to carry out a complete differential diagnostic that discard other not so frequent process.
Method: Our patient is a woman 55 years-old with edema, redness and crusting in eyelids, ulcers in the palpebral margin, fragmentation of eyelashes, photophobia, epifora and gummy whitish, since several months ago. In the physical examination we could see erythema and detritus when we turned around her eyelid. She had been in treatment with antibiotics, corticoids, oral and topical antihistamines without improvement.

To reach de diagnosis we did a Prick-test and Microbiological studies.
Results: The prick-test with standard aeroallergens was negative. We did a cytology of the bottom of lacrimal sac and we saw abundant bacteria, cells epithelial and neutrophils, but without eosinophils. The cultivation of the eye secretion developed infestation by *S. Aureus* and a parasitological study done showed infestation by Demodex Foliculorum. With these data we reached the diagnosis of demodicidosis. We prescribed permethrin 5% cream applying it at night on the eyelids and the morning washing his face and eyelids with mild soap and the patient improved slightly.
Conclusion: Demodex Folliculorum is a mite than should be suspected when blepharitis chronic be resistant a antibiotics and antiallergic. This mite belongs to the Aracnida class, and their size varies from 0.1–0.4 mm. They live in the hair follicles and sebaceous glands. During their life cycle they destroy skin and eyelashes laying eggs and dying within the follicles.

It's a vector for bacterias as *Staphylococcus Aureus* (*S. Aureus*).

The incidence of demodicidosis increases with age and its treatment is very complicated due to his recurrent course (a chronic inflammatory State is combined with superinfections to *S. Aureus*).

1647
Incidence of allergic conjuctivitis at patients with diabetes mellitus TIP II, retrospective study

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Purpose: The aim of the study is to describe the incidence of allergic conjunctivitis at patients diagnosed with diabetes mellitus type II.
Methods: Forty three patients diagnosed with diabetes mellitus type II, underwent ocular examinations. Twenty male and 23 female, aged from 47–75 years old. History of disease duration of diabetes other systemic diseases, age, sex was obtained by reviewing the medical records and direct patient interview. Visual acuity with correction, slit-lamp examination with special attention to upper tarsal conjunctiva for the presence of hyperemic papillae. The medical rewiev of the patients complains like tearing, fotofobia, red eye, itching, palpebral edema, swelling of conjunctivae, conjuctival injection and discharge was recorded.
Results: Twenty patients were diagnosed with Allergic conjunctivitis. Nine male /13 female. Fifteen patients refer to suffer from Asthma Bronchialis. The diagnosis was made by referring to patients complains and the presence of papillae at upper tarsal conjunctiva.
Conclusion: In our study the Allergic conjucivitis showed to have a high correlation with diabetes mellitus type II (about 47%). About 76% of the patients diagnosed with Allergic conjunctivitis use to suffer from asthma bronchialis. Age and sex didn't seem to play any role in this condition.

1648
Allergic conjunctivitis due to food allergy? A case report

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Background: A 27 year-old male patient suffered from perennial conjunctivitis without seasonal exacerbation. No improvement was obtained with the use of topical antihistamines, mast cell stabilisers, non-steroidal antiinflammatory drugs (NSAIDs), local corticosteroids or tobramycine eyedops. When he ate peach, watermelon and melon he presented oral itching and lip swelling. A first allergologic study was made (1). A few months later, the patient carried out a restriction diet. He stopped drinking milk and eating tomato, cucumber, zuchinni and eggplant. The symptoms disappeared. A new allergologic study was carried out (2).
Method: The following tests were carried out: 1-Skin prick tests (SPT) with a battery of common inhalants, peach, watermelon, melon, profilin and peach LTP (Pru p 3). Specific IgE to pollens, mites, peach, watermelon and melon. 2- SPT with whey fractions of cow's milk, whole milk and casein from goat, sheep and cow. Prick-to-prick tests with vegetables. Specific IgE to pumpkin, onion, garlic, tomato, eggplant, cow's milk proteins, whole cow's, sheep's and goat′s milk.
Results: SPT were positive to grass, olive tree, plane tree, cypress, cat and dog dander, profilin, melon and watermelon. Prick-to-prick tests were positive to cucumber, zucchini, onion, garlic and eggplant. Specific IgE was >0.35 kU/l to olive tree, grass, Artemisa, Cupressus arizonica, Platanus acerifolia, peach, melon, watermelon, garlic, pumpkin, onion and tomato. The patient refused oral challenge tests.
Conclusion: The coexistence of allergic symptoms to certain plant-derived foods and pollen allergy has been defined as oral allergy syndrome (OAS). IgE cross-reactivity between pollen and food allergens represents the molecular basis for this phenomenon. OAS is considered a form of contact allergy confined almost exclusively to the oropharynx and rarely affects other target organs. The plant proteins involved in OAS belong to plant protein families, including profilins, pathogenesis-related proteins (PRs) and lipid transfer proteins (LTPs). We report a case of a patient with chronic allergic conjunctivitis probably caused by the daily ingestion of certain vegetables. By stopping the consumption of these foods, the conjunctivitis resolved completely. We hypothesise that in our case, sensitisation to profilins in plant aeroallergens might cause allergic conjunctivitis due to the ingestion of vegetables. More studies need to be done to confirm such hypothesis.

1650
Type 1 allergy to ophthalmic preservatives (Benzalkonium chloride)

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Benzalkonium chloride, also known as BAC, is a quaternary ammonium, which is

a highly hydrosoluble bipolar compound with surfactant properties. Numerous cases of contact sensitivity have been reported, including alarming cases of paradoxical bronchoconstriction and anaphylaxis (an acute multi-system and very severe Type I hypersensitivity reaction) with BAC in nebuliser solutions.

We have described a case of rare allergic reaction to a preservative contained in ophthalmic drops.

Case report: A15-year-old female patient with genarilized urticaria and angioedema was examined at the emergency service She didn't have wheezing, dizziness, vomiting or diarrhoea, and her blood preesure was normal. The symptoms began 20 min after using Ketorolac trometamol 5.0 mg/ml ophthalmic antiinflamatuar prescription drops (Acular; ALLERGAN AUSTRALIA). These drops were prescriped for bilaterally for dryness with contact lenses as empiric treatment of inflamation. She was taken to the nearest hospital where she was treated with systemic corticosteroids and antihistamines intravenously. She recovered completely thereafter. She had had a similar episode 6 moths ago. Approximately 60 min after receiving tropikamid% 0.5 (Tropamid% 0.5 Mefar Drug, Turkey) eye dilator drops, she experienced genarilized urticaria and angioedema. Consequently, she had to visit the emergency service where she was given a antihistamin as a treatment. She reported no other allergies and no significant family history. She asked for a probable reason for this allergic condition. A common preservative found in both eye drops of benzalkonium. Therefore we conducted Skin prick tests with benzolkonium the results of which were strongly pozitive.

Conclusion: It's known that ocular hypersensitivity reactions to different types of preservatives in different chemical classes of topical ophthalmic treatments are mentioned in the literature including IgE-mast cell mediated, cell mediated. Quaternary ammoniums (benzalkonium chloride) are most commonly associated with irritant toxic reactions.

We have described a case of rare allergic reaction to a preservative contained in ophthalmic drops with confirmatory testing. In these cases, the most effective way to both prevention and treatment is to inform the patient about the avoidance of BAC-containing products and to ask the patient to report similar reactions to other agents immediately.

1651
Role of hyaluronic acid in non allergic rhinitis

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Background: Hyaluronic acid is a component of extracellular matrix that is considered as a regulator of inflammatory responses and tissue damage. Non-Allergic Rhinitis (NAR) is a non-IgE-mediated group of disorders that are characterised by nasal congestion, rhinorrhea, sneezing, and/or postnasal discharge and by distinct inflammatory cell infiltrate: NAR infiltrated by eosinophils (NARES), by mast cells (NARMA), by neutrophils (NARNE) and by eosinophils and mast cells (NARESMA). The aim of this study is to evaluate the cytological characteristics of nasal tissue in patients with NAR before and after treatment with an isotonic solution of hyaluronic acid and seawater.

Method: Ten patients with non allergic rhinitis were enrolled. NAR was defined on the basis of the allergological exam (prick test for common aeroallergen and IgEs negative). All the patient underwent nasal cytology. Nasal cytology was performed by scraping the middle one-third of inferior turbinates with Rhinoprobes. Samples were fixed by air drying and stained with Wright-Giemsa stain and were examined under an optical microscope. Five patients were randomly treated with an isotonic solution of hyaluronic acid and seawater (group A) and Five patients without therapy (group B) for 60 days. Nasal cytology was repeated after 60 days.

Results: In the group A at time 0 different immunological inflammatory patterns were detected: 2 cases of metaplasia mucipara, 1 of NARMA, 1 of NARES and 1 of NARNE, after treatment with the isotonic solution of hyaluronic acid and seawater we observed a significant decrease of globet cells in the two patients with metaplasia mucipara; in 1 case of NARMA any mast cell was detected after the treatment. In 1 case of NARES and 1 of NARNA any cytological modification was observed. In the group B at time 0 were 3 cases of NARES, 1 of NARMA and 1 normal. Any difference was detected in the group B after 60 days.

Conclusion: The treatment with the isotonic solution of hyaluronic acid and seawater led to an improvement of the cytological features of the rhinitis, that appeared more clear due to the reduction of the globet cells. The treatment seems to be more effective in rhinitis with globet cells metaplasia. Previous observations with these findings confirm the role of hyaluronic acid in the regulation of the nasal inflammatory responses and his role in the repairing of nasal epithelium.

1652
Modification of cytokine-secretion through antihistaminic and steroidal drugs in hyperplastic and polypoid nasal mucosa in an ex-vivo short-time-tissue-culture with oxygenation

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Background: To characterise cytokine-expression in hyperplastic and polypoid nasal tissue (NT) after application of antihistamines and topical steroids through the establishment of an ex-vivo short-time-tissue-culture of faultless functional NT via oxygenation with ambient air.

Methods: Intraoperatively assessed NT was divided in pieces of approximately 2 mm^3 and subsequently oxygenated in culture medium up to 48 h at 37°C through insufflating of air blisters. After stimulation with Lipopolysaccharide and Staphylococcal enterotoxin B (SEB), the released cytokines Il-5, Il-8 and MCP-1 from tissue were verified via ELISA in incubation medium as well as their modifications through addition of cromoglycic acid, levocabastine, rupatadine, budesonide, fluticasone and mometasone furoate.

Results: Compared to conventionel tissue-culture in dishes, an up to 4.3 times higher expression of cytokines in course of time could be detected. Secretion of IL-8- and MCP-1 in hyperplastic NT was less suppressed through cromoglycic acid, levocabastine, budesonide and fluticasone furoate than through mometasone ($P < 0.01$) und rupatadine ($P < 0.01$). Cytokine-secretion in polypoid NT was up to 4 times higher and mostly suppressed through rupatadine ($P < 0.01$) followed by mometasone ($P < 0.01$).

Conclusion: The presented ex-vivo short-time-tissue-culture of NT with oxygenation represents an easy to use sensitive assay for further examination and characterisation of (patho-) physiological procedures after different stimulations and applications of agents respectively. Comparable distinct suppression of cytokines could be shown best in polypoid NT for rupatadine and mometasone, a fact which could be of clinical interest in comorbid patients with chronic rhinosinusitis with nasal polyps and allergic rhinitis.

Poster Session 74

Clinical studies in allergen-specific immunotherapy I

1653
Vaccination during concurrent subcutaneous immunotherapy: safety of simultaneous application

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Background: As per the EAACI task force paper (2006) allergen injections should be separated from vaccinations for infectious diseases by at least 1 week because it is assumed that adverse reactions can result from the additional activation of the immune system. Many manufacturers recommend interrupting subcutaneous immunotherapy (SCIT) for a total of 3 weeks in case of vaccination.
Method: A total of 1364 persons (approximately 23% children/adolescents up to 18 years of age) receiving SCIT and/or vaccination in a German ENT-practice between 2007 and 2012 were included and analyzed retrospectively. About 766 patients had received vaccination (e.g. influenza, pneumococcus, tetanus/diphtheria, hepatitis, TBE, MMR), 431 patients with severe allergic disease received only SCIT while 151 patients had received vaccination and SCIT injections simultaneously on one day in different locations. Additionally, 16 patients inadvertently received SCIT injections within up to 4 days after vaccination because they had not informed the doctor about their previous injections. Allergoids as well as native allergen extracts were used for SCIT, predominantly in a perennial application mode. Some of the patients were observed for consecutive years receiving several vaccinations during SCIT. Adverse drug reactions (ADR) were evaluated according to the World Allergy Organization (WAO) grading system (WAO-grading). This survey was neither initiated nor sponsored by industry.
Results: Patients exclusively receiving vaccinations did not report any drug-related ADR. One ADR third grade and two second grade occurred in 3 asthmatic patients exclusively receiving SCIT. None of these patients were admitted to hospital and all recovered in the physician's rooms within 2 h. The 151 patients simultaneously receiving vaccination and SCIT did not have any ADR. This was also the case for a subgroup of 36 of them who consecutively received SCIT and vaccination for up to 5 years. Furthermore, there was no reported ADR in patients receiving inadvertent SCIT within 4 days of vaccination.
Conclusion: The international guidelines for SIT recommend an intermission of at least one week between SCIT and the administration of vaccines, however our findings demonstrate the possibility to shorten or abolish this interval without increasing the risk of ADR. It should be further clarified how similar the immunological mechanisms of 'allergen vaccination' (SCIT) and vaccination against pathogens are.

1654
Custom made sublingual immunotherapy tablets for allergy disorders

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Background: Desensitisation of Type-1.IgE mediated allergy disorders is known over a century. SLIT (sublingual immunotherapy) emerged in recent times in place of SCIT (Subcutaneous immunotherapy) with merits of patient friendly, least life threatening side effects and increased adherence for a long term treatment. Recent literature search has shown that SLIT tablets containing grass & mites extract with fixed dose showed a good clinical response. Our research team made an attempt to formulate SLIT tablets for custom made prescriptions.
Method: SLIT Tablets are designed to deliver antigen via sublingual route. Tablets were prepared by wet granulation method using starch paste as a binder. After drying the granules at 36°C, prescribed quantity of standard allergen was added and mixed. Latter Granules were blended with lubricant and glidant and compressed to 100 mg tablets. The custom made, personal medicine dossier details of SLIT tablets are presented. Formulation details (actives and excepients), evaluation (tablet hardness, disintegration time, weight variation, mouth dissolution time and assay) and the clinical details of adverse events of SLIT tablets are described.
Results: SLIT Tablet complied with the requirements. Tablet thickness varied from 2.65 to 2.74 mm, weight Varied from 97–103 mg and diameter of 6 mm. Content uniformity of 90–110% of the label claim was observed. Surface pH study showed pH ranging from 6 to 7. The tablets dissolved rapidly within 30 to 60 s. SLIT tablets had a greater power of releasing allergens. SLIT Tablets contact with sublingual mucosa attained dissolution in 2 min and possessed the feeling of freshness with least allergen bitter taste or smell.
Conclusion: The sublingual tablet formulations showed promising response with less adverse effect and the results were comparable to SLIT drop formulations and to our research module SLIT STRIPE (Abstract # 339, EAACI 2009, Abstract # 659 EAACI 2010).

1655
Specific sublingual immunotherapy in respiratory allergy patients

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Background: The prevalence of allergic asthma and rhinitis is increasing worldwide. It is a growing medical, social and economic problem. The therapeutic management of allergy currently involves: allergen avoidance, symptomatic medication and specific immunotherapy. Only specific immunotherapy targets the underlying disease. Traditionally, immunotherapy has been administered subcutaneously. The development of immunotherapy as sublingual drops has provided a safer and more convenient alternative to the subcutaneous route.
Method: Sixty patients suffering from grass pollen, house dust mites-induced rhinoconjunctivitis with or without asthma underwent specific immunotherapy with appropriate standardised allergen extract (Sevapharma, Czechrepublic) administered sublingually for two years. The diagnosis of respiratory allergy was made by clinical history, positive skin prick test to standardised pollen, house dust mites extract and

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the presence of specific IgE to the mixture of grass pollens, mites with class 3 as minimum value. Sublingual immunotherapy (SLIT) involved a build-up or induction or updosing phase and maintenance phase with the maximum dose (10000 JSK, PNU; 10 drops 3 times in the week). Efficiency was estimated clinically (very good/good/moderate/poor/no effect) and laboratory (specific IgE and IgG4) to and in 2 years of treatment. Serum specific IgE were detected by immunoblots (R-Biopharm, Germany. Specific IgG4 levels were measured by ELISA DR FOOKE).

Results: It was found that SLIT is effective according to subjective clinical parameters and drug consumption, with a highly significant reduction of symptoms and drug intake favoring sublingual administration where a reduction of more than 80% was achieved. After 2 years of SLIT of specific serum IgE to the respiratory allergens of grass pollens, house dust mites level was significantly decreased. Levels of specific IgG4 to the allergens of grass pollens, house dust mites showed increase (p 0.001). Adults with rhinitis only have lower specific IgE and IgG4 than adults with both rhinitis and asthma (P 0.05). Laboratory results corresponded to the clinical improvement. Adverse effects were limited to a small number of mild local reactions.

Conclusion: SLIT drops for adults with rhinoconjunctivitis, asthma is a highly effective treatment for carefully selected patients with respiratory allergy and can be given at home.

1658
Clinical effects of sublingual immunotherapy in comparison with medication in the allergic rhinitis: an interim report of 3-year case-control study

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Background: Recently there have been couple of Korean reports demonstrating the superiority of sublingual immunotherapy (SLIT). In this study, the clinical effects of 3-year results were compared and analyzed dividing allergic rhinitis patients into the two groups of 'SLIT group (patient)' and 'medication group (control)'.

Method: From 2009 to 2012, among persistent or severe allergic rhinitis patients visited Trinity ENT allergy center, 126 patients with SLIT after skin prick test were included as 'patient group' and 32 patients with 3-year medication without SLIT were included as 'control group'. Each group was recorded pre- and 3-year post-therapy state as symptom scores (0–5), and analyzed the clinical effects using scoring system and rescue medication during 1 month (medication scores).

Results: Total of 350 patients were registered, and SLIT was performed with 126 patients (mean age, 20[4–50]; M:F = 68:58; adults:children = 74:52). Among 126 patient group, 90 patient (71.4%, 1-year follow-up), 75 patients (59.5%, 2-year follow-up) and 54 patients (42.9%, 3-year follow-up)) were maintained treatments after 3-year follow-up. At the point of the end of the treatment, symptom scores were as followings: nasal discharge, 3.1–1.7; nasal obstruction, 3.1–2.1; sneezing, 2.0–1.4 ($P < 0.05$). Rescue medication were decreased from 12.2 for pre-treatment into 2.8 for post-treatment ($P < 0.05$). Control group was included 32 patients [mean age, 23.1 (4–46); M:F = 20:12; adults:children = 21:11]. At the point of the end of the follow-up, mean symptom scores were as followings: nasal discharge, 3.6–3.0; nasal obstruction, 3.4–3.1; sneezing, 3.1–2.6 ($P < 0.05$).

Conclusion: In the allergic rhinitis patients, successful compliance for 3-year SLIT compared with control was approximately 43%. It is expected for sublingual immunotherapy to be the standard therapy of allergic rhinitis in the future from the point of view that demonstrated significant improvement of symptom scores and remarkable decrease in the scores of the mean number of rescue medication days after 3-year treatment.

1659
In vitro immunomodulatory effects in the ALUMITES study, a randomised, controlled, multicenter phase IV study with house dust mites subcutaneous immunotherapy for allergic rhinitis. A six months interim analysis

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Background: ALUMITES study was designed to assess the efficacy of house dust mites (HDM: *D. pteronyssinus* + *D. farinae*) subcutaneous immunotherapy (SCIT) for the treatment of allergic rhinitis patients along one year. Here we report an interim analysis done after 6 months of treatment.

Method: In this controlled multicenter phase IV study, HDM allergic adult patients were randomised to receive SCIT with a 10 IR/ml depot extract plus symptomatic treatment (group A) or only symptomatic treatment (group B) (2:1). Total IgE and Der p 1 and Der p 2 specific IgG_4 were measured at baseline and after 6 months of treatment.

Results: Total IgE and IgG_4 were collected from 46 of the 57 patients enrolled in the study. The difference between basal and 6 months visit total IgE was 37.4 [95% CI: (15.4, 59.6), $P = 0.0002$] in active group and 19.4 [95% CI: (−12.6, 51.3), p = NS] in control group. The increase for Der p1 IgG_4 was 0.2 [95% CI: (0.1, 0.3), $P < 0.0001$] in active group and 0.0 [95% CI: (−0.1, 0.0), p = NS] in control group. Similar results were obtained for Derp p 2 IgG_4, it increased 0.4 [95% CI: (0.3, 0.6), $P < 0.0001$] in active group and 0.0 [95% CI: (−0.1, 0.0), p = NS] in control group. Total IgE increased in both groups without any statistical difference between them, however specific IgG_4 for Der p 1 and Der p 2 increased significantly in active group vs control group ($P < 0.0001$).

Conclusion: Six months of SCIT treatment with a 10 IR/ml depot HDM extract showed an objective immunomodulatory effect as demonstrated by the fact that both specific IgG4 increased their levels in patients receiving active treatment compared to patients in control group.

1660
Quality of life improvement with subcutaneous immunotherapy

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Background/introduction: Achieving a better quality of life should be the first objective of etiological treatment with immunotherapy (IT) in patients with specific diseases such as allergic rhinitis symptons and IgE-mediated asthma. The aim of this study is to assess the perceived effectiveness of the patients' quality of life after a year of IT treatment.

Methods: Twenty-five Subjects were recruited during the years 2010/11 from the Allergy Department at the Hospital Central de la Defensa 'Gómez Ulla' in Madrid, Spain. These 25 participants were comprised of 19 females and six males with rhinitis and/or asthma, with ages ranging from 12 to 48 and a mean age of 30.4 years. They were treated with subcutaneous inmunotherapy depot pollen hypoallergenic (olive and /or grasses). We used an Analog Display Scale (ADS) to assess and evaluate the quality of life before and after a year of treatment with SCIT. Descriptive

statics were performed using SPSS software statistical significance, that was assesed using the Shapiro-Wilk test.

Results: 25 patients were enrolled in the present study. Perennial IT 13/IT 12 seasonal The mean total ADS pretreatment was 3.68 ± 2.17; medium 3.0 (0.5–9.0), 95%. While the mean total ADS after treatment was 7.58 ± 1.68; medium 8.0 (3.0–10.0), 95%. Mean difference 3.9, 95% CI (between 3.13 and 4.67 points), these values being significant ($P < 0.0001$).

Conclusions: It was seen a statistically significant reduction of symptoms and improvement of quality of life ($P < 0.0001$) demonstrated by the ADS, during the initial first year period of SCIT. After the first year it continued decreasing.

These data support the efficacy and undeniable value of SCIT for allergic patients with specific diseases.

1661
Analysis of the causes of a sudden adverse events increase in patients with *alternaria alternata* allergen-specific immunotherapy

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Introduction: AIT (allergen-specific immunotherapy) can cause adverse events (AE) due to different factors such as:

1 Administration technique,
2 Poor patient's disease control
3 Increased environmental allergenic exposure and
4 Variability of the potency or allergen content in the AIT extract.

Objective: Analysis of causes of a sudden increase of AE coinciding with a specific time period, geographic location and a new batch of AIlergovac depot Alternaria alternata ® (Arístegui, Bilbao, Spain) AIT.

Methods: We estimated the environmental concentration of alternaria spores in that time period. AE data were analyzed in relation to be specific batch: overall allergenic potency and quantitative composition of the problem batch by means of SDS-PAGE. We analyzed the clinical characteristics and the sensitisation profile (IgE Immunoblotting) of every patient receiving the AIT batch.

Results: Thirty-one patients received the first maintenance dose of this batch. Eleven (35% of the patients) exhibited AE (3 Large local reactions and 8 systemic reactions). All the reactions occurred between June 22 and July 18 of 2011, coinciding with the greatest annual concentration of Alternaria spores (36).The relative potency of the batch was within the interval established by the European Pharmacopoeia of 50–150% in relation to the reference preparation. The qualitative composition showed no differences with other batches. Immunoblotting results detected that 6 of 11 patients who exhibited AE and only 1 of 20 without AE, showed a protein of approximately 11 kDa. Its molecular weight was consistent with those described for the P1 and P2 ribosomal proteins (Alt a 5, Alt a 12), in whose content the extract is not standardised. Our AE incidence was in sharp contrast with the national rates, showing figures of 5.5% of AE for initial and maintenance treatments in the same time period and with the same AIT product.

Additionally, the results in an unvaccinated group and in another group of patients from a different geographic location will be presented in order to compare the observations.

Conclusion: Although various factors may have contributed to this sudden accumulation of AEs, sensitisation to a minor allergen could have been decisive in these events.

1662
Safety in immunotherapy with dust mite allergens in asthma and allergic rhinitis

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Background: Mite allergens are among the most prevalent in worldwide sensitisation. In patients with asthma and allergic rhinitis they are one of the main causes that trigger and aggravate symptoms. That is why immunotherapy (IT) with mites is present in most allergy services.

Objectives: To evaluate the safety of IT for the treatment of allergic rhinitis and bronchial asthma using DEPOT extracts and lyophilised extracts from different types of mites.

Methods: Active monitoring was performed on 1291 patients with asthma and / or allergic rhinitis who attended the Allergy Service of Previsora Camagüey, sensitised to allergens of Dermatophagoides pteronyssisus, Dermatophagoides farinae, Blomia tropicalis, Acarus siro, Lepidoglyphus destructor, Tyrophagus putrescentiae, Glycyphagus domesticus, Blomia kulagini, and Chortoglyphus arcuatus. About 839 received subcutaneous immunotherapy (SCIT) and 452 sublingual immunotherapy (SLIT). Of those who received SCIT: 374 (44.5%) were from lyophilised extracts, 422 (50.2%) Depot extracts, and 43 (5.1%) with a mixture of one or the other. Adverse reactions, local and systemic, were recorded on both tracks. The adverse reactions to treatment were classified according to the degree of systemic allergic reactions (I, II, III and IV) and criteria of severity (mild, moderate, severe, and fatal). Tables, graphs, and percentages were then calculated.

Results: 12 (0.9%) patients left IT. Of the 442 who received SLIT, 27 (6.1%) had a local reaction and 12 (2.7%) a systemic reaction Grade I. Mites were more involved in adverse reactions in B. tropicalis and Dermatophagoides pteronyssisus with 7.1% and 6.5% respectively. Of the 837 patients who received SCIT 78 (9.3%) had mild to moderate local.

1663
Specific immunotherapy efficacy: which route is better?

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Background: Allergen specific immunotherapy (ASIT) is a treatment capable of modifying the natural course of allergy. The aim of our study was to evaluate the clinical efficacy and adverse reactions of ASIT in adults with allergic rhinoconjunctivitis with/without asthma.

Method: Data were collected using our made questionnaire for patients who were treated in the Center of Pulmonology and Allergology of Vilnius University Hospital with subcutaneous (SCIT) or sublingual (SLIT) immunotherapy. All patients were asked about duration, route of the treatment, changes in allergy symptoms and adverse reactions during the treatment course. A total of 47 patients (28 females/ 19 males), 30 ± 7.2 years old were enrolled. 15 (31.9%) patients had asthma symptoms. 30 (63.8%) patients received SLIT, 17 (36.2%) – SCIT. All patients were treated with Stallergenes preparations: house dust mites mix – 21 (44.7%) patients, five grass polen mix – 17 (36.2%) patients, other allergens – 9 (19.1%) patients. Mean duration of ASIT was 16.9 ± 14.5 months.

Results: The majority of patients indicated clinical improvement. Symptoms improved on the average after 7.2 ± 4.6 months: in SCIT group after 5.7 ± 5.4 months, in SLIT group after 8.1 ± 3.9 months ($P = 0.018$). There was no statistical significant difference between SCIT and SLIT groups in nose itching, sneezing, rhinorrhea, nasal congestion, palate's and eyes' itching and asthma symptoms. Eyes' tearing significantly improved in SLIT group after half a year ($P = 0.032$). Adverse reactions were mild in both groups. The main reaction in SLIT group (11 (36.7%) patients) was transient slight sublingual oedema in the built-up phase.
Conclusion: ASIT is effective and safe treatment. The faster effect of ASIT was in SCIT group. There was no statistical significant difference between SCIT and SLIT groups in changes of allergy symptoms. Both ASIT routs were well tolerated.

1664
Grass pollen carbamylated monomeric allergoid administered by injective route for allergic rhino-conjunctivitis: preliminary data on safety and efficacy

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Background: Monomeric carbamylated allergoids are chemically modified allergens featured by a reduced IgE-binding activity conferring reduced allergenicity, but preserved structural conformation and immunogenicity. Their safety profile, efficacy and tolerability have been extensively documented after sublingual administration. Purpose of this study was to obtain data on the safety and efficacy when these extract are delivered subcutaneously.
Method: Patients 5–70 year-old with moderate to severe allergic rhino-conjunctivitis with/without asthma due to grass pollen and positive skin test mean diameter, were recruited after a run-in spring season to receive, from November 2011 to June 2012, grass carbamylated allergoid with a monthly dose of 0.80 ml, (10 BU equivalent to 5 μg/ml of major allergen), following an induction phase (0.10-0.20-0.40-0.60-0.80 ml with weakly increase). Outcomes were patient's allergic condition self-assessed and evaluated by doctors by means of a visual analogue scale (VAS 0-10), symptomatic drugs consumption (scarce, no more than 5 days with the need ofa rescue therapy in that month; moderate, no more than 10 days; elevated, more than 10 days), frequency of adverse reactions.
Results: Thirty nine patients (mean age 29.6, 44% males, mean disease duration 8.5 years, were treated. Their allergic condition largely improved after 8 months of treatment with a significant mean VAS improvement (+3.3, SE = 0.5, $P < 0.0001$) from spring 2011 to spring 2012, consistent with doctors' judgment (mean VAS change +4.05, SE = 0.5, $P < 0.0001$). Drugs usage was scarce (<5 days a month with the need of antihistamines, nasal corticosteroids or other drugs) during the period. During the build-up phase, 15 adverse reactions overall occurred (12 local and 3 systemic), respectively 3 with 0.1 ml, 2 with 0.2 ml and 0.4 ml, 6 with 0.6 ml, 2 with 0.8 ml. Patients experiencing at least one reaction were 8 (20%). The maintenance phase was well tolerated with no signaled adverse reactions. Non serious reactions occurred.
Conclusion: Carbamylated monomeric allergoid of grass pollen appears well tolerated and effective in improving the allergic condition when delivered subcutaneously for 8 months. Rare adverse reactions, mainly local, may occurs during the induction phase in particularly susceptible patients.

1665
Tree pollen allergic patients can be safely treated with cluster immunotherapy

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Background: Subcutaneous specific immunotherapy (SCIT) is the 'gold standard' when using the causal treatment of specific immunotherapy, and the majority of patients' starts with the therapy before or after the pollen season. For this presentation the safety of the cluster-immunotherapy initiated intra-seasonally or outside of the pollen season was retrospectively analysed for patients treated with highly polymerized allergens from tree pollen.
Method: From 122 patients (73 female, 49 male; aged 8–74 years) treated with highly polymerized allergen mixtures of tree pollen (birch, alder, hazel; CLUSTOID; 10 000 TU/ml) any documented reactions related to the injections were graded as local or systemic side effect according to EAACI position paper (1993), described by Pfaar et al. (Eur Arch Otorhinolaryngol 2009). The treatment started with the cluster schedule: two injections within an interval of 15 min (0.2 + 0.5 mL in one and the other arm) on the first treatment day, the maintenance injections of 0.5 mL were applied once a month.
Results: 27% of the patients started the treatment during the tree pollen season (February to April), 34% during the summer months (May to August) and 39% during autumn and winter. Of all injections ($n = 647$) 6.2% resulted in side effects like local reactions of grade 0 (5.4%) and grade 1 (0.6%) and one systemic reaction (0.2%, headache and symptoms like common cold). All were reported for patients who started treatment outside of the tree pollen season, but no side effects were documented for patients who started treatment initiation during the tree pollen season. Overall, no severe reactions were observed.
Conclusion: Cluster immunotherapy with highly polymerized allergen extracts of tree pollen (birch, alder, hazel) was shown to be a safe treatment for tree pollen allergic patients starting before, after or even during the tree pollen season.

1666
Compliance and safety of perlingual spray application with an aqueous allergen extract of grass pollen

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Background: Grass pollen are the main cause of allergic diseases during summer time in Germany. Specific sublingual immunotherapy (SLIT) as a causal treatment is of increasing interest for many patients as they can apply this treatment by themselves. For this purpose a proper way of application should enhance the acceptance and compliance by the patients. Retrospectively, data of grass pollen allergic patients using the perlingual spray application could be analysed with respect to safety and patients' compliance.
Method: For 25 grass pollen allergic patients between 18 and 66 years of age (16 female; 9 male) using an aqueous allergen extract (SULGEN Spray; 30 000 TU/ml) of grass pollen the compliance has been retrospectively assessed using a scale from 0 = very bad; 1 = bad; 2 = satisfactory; 3 = good; 4 = very good as well as the safety of the treatment for a time period of 2 months after initiation. The treatment started with two puffs at the first day and was continued daily with the same dose.
Results: For 60% of the patients the compliance was rated as *very good*, for 32% as *good* and as *satisfactory* for 8%. All patients wished to continue the treatment.

The perlingual treatment was well tolerated. Only one patient described a mild local reaction (itchiness and swelling in the mouth), one patient reported about

headache and indisposition, but had no reactions later on. However, no severe side effects had been observed.
Conclusion: The perlingual spray application with an aqueous allergen extract of grass pollen is a safe treatment for grass pollen allergic patients. A good patients' compliance could be shown.

1667
Perlingual spray application with a mixture of tree pollen is a safe treatment for patients suffering from allergy during spring time

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Background: The use of specific sublingual immunotherapy (SLIT) as causal therapy of IgE-mediated allergic disease is of increasing interest for many patients. The compliance as well as the safety profile may be reasons for prescription of this kind of treatment. These aspects were retrospectively assessed in this presentation by analyzing data of tree pollen allergic patients using a spray application for perlingual treatment.
Method: Data from 61 patients (18–73 years; 41 female; 20 male) treated with an aqueous allergen extract of a tree pollen mixture (birch, alder, hazel) according to their allergic disposition (SULGEN Spray; 30 000 TU/ml; two puffs daily from the first day on) were retrospectively analysed during the first 8 weeks after starting of the treatment. The documented safety and reasons for choosing this application form were evaluated and the patients' compliance was rated on a 5-point-scale from *very bad* to *very good*.
Results: The evaluation of the patients' compliance resulted in *very good* for 59%, *good* for 31.2% of the patients, in *satisfactory* for 9.8%. For 48 out of 61 patients reasons for using the perlingual application were documented, in 37.5% the treatment form was the patients' wish. Four patients were afraid of injections and 13 patients favoured the flexibility in time. A mild local reaction in the mouth was documented for one patient, no systemic reaction occurred at all during the observation period.
Conclusion: A good compliance as well as a good safety profile was shown for tree pollen allergic patients treated with an aqueous allergen extract of tree pollen by using the perlingual spray application.

1668
Cluster immunotherapy can be safely initiated for mite allergic patients and results in good compliance

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Background: Besides taking measures for allergen avoidance for example by using encasings subcutaneous specific immunotherapy (SCIT) can be applied as causal treatment for mite allergic patients. To assess the patients' compliance as well as the safety using the cluster immunotherapy as a fast variant of SCIT with highly polymerized allergen extracts of house dust mite data of adequately treated patients were retrospectively analyzed.
Method: Data were evaluated from 43 patients (18–70 years of age; 26 female; 17 male) with clinical sensitisation to house dust mite allergens who have been treated with a highly polymerized allergen extract from 50% *D. pteronyssinus*, 50% *D. farinae* (CLUSTOID; 10 000 TU/ml) using the cluster schedule with two applied injections (0.2 + 0.5 ml) on the first treatment day within 15 min in one and the other arm, followed every four weeks by a maintenance injection of 0.5 ml. The compliance has been assessed on a scale from 0 = very bad to 4 = very good. The documented reactions to the injections were differentiated as local or systemic side effect according to EAACI position paper (1993) and graded as described by Pfaar et al. (Eur Arch Otorhinolaryngol 2009).
Results: The patients' compliance was assessed as 'very good' for 44.2%, 'good' for 51.2% and 'satisfactory' for 2.3% of the patients. One patient stopped treatment due to a bad compliance. Altogether, for 95.7% of all injections ($n = 234$) no reactions were described; 4.7% resulted in local reactions, 4.3% of grade 0 and 0.4% of grade 1. No systemic reactions and no severe side effects have been reported.
Conclusion: Cluster treatment with a highly polymerized extract of house dust mites has been shown to be a safe treatment for mite allergic patients with good compliance.

1669
The effect of standard regiment of specific immunotherapy on grass pollen induced allergic rhino-conjunctivitis

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Background: We have evaluated the influence of specific immunotherapy (SIT) on the clinical symptoms and inflammatory response in patients with allergic (grass pollen induced) rhino-conjunctivitis.
Method: Twenty-six patients (age range 18–44 years) with positive history for more than 2 years and skin-prick test ≥5 mm underwent conjunctival provocation tests before and after 1 year of SIT. Clinical severity of nasal and conjunctival symptoms during the season was assessed by 4-point arbitrary rating scale from 0 to 3. Conjunctival provocation were done out of the season until allergic symptoms occurred achieving the allergen threshold dose (ATD).
Results: After 1 year of SIT we found reduction in clinical symptoms of allergic conjunctivitis (burning, itching, lacrimation and hyperemia) $P < 0.05$ as well as reduction in clinical symptoms of allergic rhinitis (secretion, irritation, itching and nasal blockade) $P < 0.01$. Significantly higher allergen doses in provocation test (out of season) were tolerated after 1 year of performed SIT, reaching new ATD.
Conclusion: Grass pollen SIT reduces clinical symptoms of allergic rhinoconjunctivitis and modifies the inflammatory response after specific allergen challenge.

1670
May immunotherapy during childhood suppress the occurrence of adult asthma?

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Background: Specific immunotherapy (SIT) is a therapeutic cornerstone of respiratory allergy (RA) diseases. The aim of this study was the assessment of RA development in early adulthood in subjects with allergic rhinitis and bronchial asthma, treated with SIT during their childhood.
Method: Twenty-three children with RA (7–13 years old) were treated with subcutaneous SIT (Lofarma, Milano) for a period of 4–5 years after diagnosis with skin prick or specific IgE tests. Of them, 9 were treated with house dust mites extracts, seven with grasses, three with alternaria, two with cat, one patient with wall pellitory, and one patient with combination of grasses, birch, hazelnut and plantago. Subjects were under clinical evaluation about symptoms and medication needs up to 5 years after SIT interruprion. Twelve asthmatic children who matched in age and clinical status with mentioned subjects served as control. They were only under inhalatory treatment.

Results: Pharmacological needs were halved within first year of SIT in 20 patients, and at the end of treatment, this subjects' proportion was symptom free. Sixteen patients were symptom free five years after SIT interruption, four remained patients reported for asthmatic symptoms after respiratory infections and inhalatory treatment needs for a period of 1–2 months after infection-related exacerbation. In contrast to them, 9 out of 12 subjects who did not become SIT had the same medication's need because of persistent symptoms even during their early adulthood.

Conclusion: SIT is efficient in symptoms and medical needs reduction. The introduction of therapy during childhood may suppress the development of adult asthma at least for a certain period of time.

1671
Subcutaneous immunotherapy with mite allergen extracts in bronchial asthma. Multicenter, double-blind, placebo controlled study

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Summary background: There has been a confirmed efficacy in reducing asthma symptoms and use of medications in 42 clinical trials of immunotherapy with mites; studies in Latin America are still insufficient.

Objective: Check the efficacy of subcutaneous immunotherapy with mites in bronchial asthma in four countries in Latin America and the Caribbean.

Materials and methods: A Phase IV multicenter clinical trial in asthmatic patients from Venezuela, Cuba, Ecuador, and Mexico. The study included November 2010 to October 2012. The sample consisted of 40 patients from each of the services with intermittent asthma and mild to moderate persistent associated with allergic sensitisation to Dermatophagoides pteronyssinus, Dermatophagoides farina, and B. tropicalis. Mono-sensitised and polysensitised patients of both sexes ranging from 18 to 60 years of age were included. Randomised double-blind groups were formed with immunotherapy (IG) and placebo (PG). The IG received Depot vaccines from Diater laboratories, the PG received a diluent. The plan used was four standardised PNU / cc bottles were applied in ascending order (10, 100, 1000 and 10 000), beginning with the 10 PNU / cc bottle. Five weekly subcutaneous injections (0.10, 0.20, 0.30, 0.40 and 0.50 cc) were applied. Once the

five weekly increases were completed, the fourth subcutaneous injection 0.50 cc was left as a maintenance dose every 30 days. Efficacy was evaluated in the first week and at 12 months. Efficacy endpoints included reduction in the frequency and severity of asthma

symptoms (RFSS), drug consumption behavior (CCM), evidence of reduced sensitivity to the allergen (PRHA), and quality of life questionnaire (AQLQ).

Results: The frequency of asthma symptoms was 0.5 before the study in both groups, and at 12 months of 0.1 and 0.3 in the IG and PG respectively. Severity in the IG was 2.1 before and 0.7 after the study, the PG 2.2 and 1.9 respectively. The CCM in both groups was

94.3% before the study and after the study 28.8% in IG and 63.7% in PG. Mean PRHA was lower (3.1 mm) in IG than in the PG (4.2 mm) at 12 months. The quality of life of living increased in the IG from 4.1 to 6.4 score and 4.2 to 5.1 in the PG.

Conclusion: Immunotherapy with Depot vaccines is effective in the treatment of bronchial asthma.

1672
Trans-continental survey on allergen immunotherapy in patients with cancer in remission or stable cancer under treatment

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Background: Little data exists on allergen immunotherapy (AIT) in patients with cancer in remission (CaREM) or cancer in stable stage, but still under treatment (CaTx). In this context the experience of practicing allergists might yield very useful information.

Methods: A survey (Surveymonkey®) was sent out to all AAAAI members in and outside US to explore their experience with AIT in patients with specific medical conditions. We defined minor problems as 'some dose-reduction or doses postponed, but no major problems'. AIT could be continued' and major problems as 'activation of underlying disease and/or AIT not well tolerated (systemic adverse events) and/or AIT discontinued for medical reasons'. Results are expressed descriptively.

Results: 1061 of the 5148 (20.6%) surveys were sent back. Practice characteristics: 86–14% US-outsideUS, 44% urban, 51% suburban and 5% rural with a third of all responders working in an academic setting. Fifty-four percent of the surveyed had clinical experience of more than 16 years with an even distribution over small/ middle/ large practices.

671/963 (69%) responding experts have experience with AIT in CaREM patients, 25% have no experience but would treat, while 7% considers CaREM a contraindication. 146/681 (21%) report experience with >10 patients in their clinics, summing a total of over 2400 CaREM patients treated by all respondents together. Ninety one percent of responding allergists found no special problems, 8% minor and 0.6% major problems (2 from Europe, 1 from LA; Ca of GI tract/kidney). Three-hundred and sixteen allergists gave AIT to breast CaREM patients without major problems, 115 prostate, 77 colon, 70 lymphoma and 60 skin.

346/976 (36%) responding experts have experience with AIT in CaTx patients, 32% have no experience but would treat, while 33% considers CaTx a contraindication. 33/680 (5%) report experience with >10 patients in their clinics, summing a total of over 700 CaTx patients treated. Eighty-two percent of respondents found no special problems, 14.4% minor and 3.6% major problem:, 6US, 1LA and 2EU allergists, reporting problems with a melanoma/GI-tract/kidney malignancies, breast Ca on chemotherapy (problems not specified) and possibly increased growth of a desmoid tumour. One hundred and two allergists gave AIT to breast CaTx patients without major problems, 36 prostate, 19 colon, 18 lymphoma and 9 skin.

Conclusion: our data show a vast experience of AIT in CaREM and CaTx patients. It should be re-considered if CaREM is a contraindication for AIT.

Poster Session 75

Biologics and immune regulation

1673

Long-term follow up (5–7 years) of omalizumab treatment in patients with indolent systemic mastocytosis

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Background: Several case studies have presented evidence that omalizumab treatment controls spontaneous and venom-immunotherapy (VIT) induced anaphylactic reactions in systemic mastocytosis patients; the follow up period in these studies has been limited to 2 years or less. The aim of this study is to present a 5–7 year follow up of continuous omalizumab treatment in three patients with indolent systemic mastocytosis (ISM).
Method: Three adult patients (2 males, 1 female, aged 45, 48 and 44, respectively) with life threatening venom-induced anaphylaxis were studied. Bee venom sensitisation (positive skin tests and RAST/CAP) was confirmed in the first male and vespid in the female patient; the second male with three of unprovoked and three bee venom induced life-threatening anaphylaxis episodes was found to be IgE negative for venom allergy. On further workup, which included bone marrow biopsies and genetic studies too, they fulfilled the WHO criteria for ISM. A trial of VIT in the first two patients failed because of systemic reactions. All three patients consented to omalizumab treatment (+VIT in the 2 patients); 300 mg has been administered at monthly intervals through today (the first 2-year follow up has already been published).
Results: Patients have been free of anaphylaxis (spontaneous or VIT induced) and have tolerated omalizumab without any adverse effect. A stage I renal cell carcinoma was diagnosed post-nephrectomy in the IgE negative patient at 2.5 years of omalizumab treatment; general anaesthesia was well tolerated despite his previous history of three unprovoked anaphylaxis-episodes. Patient remains free of any recurrence 2.5 years post-nephrectomy. All three have been repeatedly stung by the offending insects (H.bee, Vespids) without reactions. Routine laboratory evaluation is within normal limits; serum tryptase (ImmunoCAP) remains lower than the pre-omalizumab values and has normalised (<15 μg/l) in the longest treated patient (7 years).
Conclusion: Long term (5–7 years) omalizumab treatment in patients with systemic mastocytosis and venom-induced anaphylaxis – with or without demonstrable specific IgE – appears to be a well tolerated and efficacious treatment.

1674

Improving anti-tumor immune response in breast cancer patients using dendritic cell based immunotherapy

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Background: Antitumor cellular immune response in patients with breast cancer is impaired. Dendritic cell function and tumor antigen presentation to CD4+ and CD8+ T-cell subsets are very important in the disease course and prognosis. This study assesses anti-tumor immune response in patients during dendritic cell (DC) based adjuvant immunotherapy.
Method: Since 2010 there were 43 patients included in the trials, 19 patients in the main group (treated with DC) and 24 patients in the control (C) group. DC were obtained from peripheral blood monocytes, primed with four p53 peptides and injected into the patient sub-cutaneously three times. T-regs and antigen-specific T-cell (ASC) count was evaluated before and 6 months after the therapy in 14 patients from the main group and 12 patients from the C.
Results: The median number of ASC was 0.29 (0.06–0.77)% in the DC treated group and 0.53 (0.14–0.89)% in the C ($P = 0.28$). The increase of ASC was seen in 80.0 ± 12.6% of patients after the DC immunotherapy. After the treatment the number of ASC increased in the DC treated group up to 0.81 (0.38–1.47)% ($P = 0.001$), while in the C there was no significant difference before and after treatment ($P = 0.21$). The level of T-regs before the treatment was 4.7 (2.9–6.7)% in patients from DC treated group and 3.6 (1.7–4.6)% in the C ($P = 0.06$). During course of DC immunotherapy T-regs in these patients were decreased in 71.4.0 ± 12.1% ($P = 0.006$) and only in 25.0 ± 12.5% of the C ($P = 0.2$). The ratio of ASC/T-regs in patients from the DC treated group was 0.04 (0.01–0.06)% before and 0.23 (0.19–0.43)% after the DC treatment ($P = 0.001$). However in the C group ASC/T-regs ratio did not change significantly during treatment period being 0.06 (0.01–0.32)% and 0.02 (0.00–0.21)% ($P = 0.67$).
Conclusion: Elevated numbers of T-regs in cancer patients correlate with worse survival while a decrease of T-regs with treatment is a good prognostic factor. These results indicate the restoration of anti-tumor immune response in the patients with breast cancer due to treatment with the dendritic cellsvacine.

1676

Acute infusion reactions to infliximab: safety and efficacy of a standardised rapid desensitisation protocol

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Background: Infliximab is a chimeric anti-TNFa monoclonal antibody useful in the treatment of chronic inflammatory diseases. The Acute Infusion Reactions (AIRs) reported at its administration, represent a treatment impediment, compelling alternative, usually less efficient therapeutic choices. The aim of our study was to provide data on the efficacy and safety of re-administrating infliximab to a well selected population by applying a standardised Rapid Desensitisation (RD) protocol.
Method: Patients (pts) selected for RD fulfilled the following inclusion criteria: (i) AIR clinically consistent with immediate hypersensitivity reaction, during or within 1 h after a slow-rate (≥2 h) infliximab infusion, (ii) documented moderate or severe systemic (Brown grading system for hypersensitivity

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reactions) AIR and/or C)positive *in vivo* Skin-Prick or Intradermal testing in non-irritant infliximab concentrations. The RD protocol involved three solutions (each 250 ml) delivered in 12-consecutive steps, each step increasing the rate of infliximab administration by 2- to 2.5-fold. Solution 1 was a 100-fold dilution of the final target concentration (steps 1–4), solution 2 a 10-fold dilution (steps 5–8) and the concentration of solution 3 (steps 9–12) was calculated by subtracting the cumulative dose administered in steps 1–8 from the total target dose. Steps 1–11 each took 15 min, and step 12 was prolonged to complete the target dose.

Results: Eight pts (5♀), at a mean age of 44.7 years (range 33–63), with AIRs to infliximab administered for Crohn's disease (2/8) and psoriasis (6/8) were included. The AIRs had occurred from the 2nd to the 12th (median 6.5) infusion and the mean time of reaction onset was 20.2 min from the beginning of the infusion. Referring to severity, 4pts reported mild and four moderate AIR, while only one was on concomitant immunosuppressive therapy. Positive intradermal testing was observed in 4/8 (50%) pts, all with a history of mild AIR. Atopy was documented in 2/8 pts. Twenty-six RDs were performed; in all of them (26/26) the total target dose was successfully administered. In four pts, four AIRs (3mild/1moderate), all at the 12th step, were recorded; thus the reaction rate during RD was 15.98% (4/26).

Conclusion: RD through the use of this 12 step-protocol, under the supervision of trained allergists, appears to be a safe and efficient method for re-administrating the full therapeutic dose of infliximab to a well selected population of pts with AIRs.

1677
Passive anti-EGFR immunotherapy in canine cancer patients – a comparative medicine study

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Background: Companion dogs (*Canis lupus familiaris*) are prone to develop spontaneous cancers, with comparable incidence rates as humans. Additionally numerous studies have reported highly conserved molecular expression patterns of the disease. In human medicine, passive immunotherapy with monoclonal antibodies, like the chimeric human-mouse anti-EGFR (ErbB-1) IgG1 antibody cetuximab is well established in clinical oncology. In contrast, the therapy options in veterinarian oncology are limited to surgery, radiation and chemotherapy.

We could previously reveal high sequential, structural and functional homology between the human and canine EGF receptors. Moreover, we could confirm the specific binding of cetuximab to the canine EGFR leading to similar effects, i.e. silencing of growth signals and tumor growth inhibition. Frequent overexpression of ErbB-1 for example in canine mammary carcinomas proposes that it might be effectively targeted in passive anti-tumor immunotherapy.

Method: We employed the variable regions of cetuximab 225 to generate a dog-mouse chimeric IgG antibody (can225IgG) targeted against EGFR. CHO DUKX-B11 cells were used for production of the antibody, which was then purified with *Streptococcal Protein G*. Biochemical integrity and folding of the recombinant antibody was assessed by immunoblots and CD-spectroscopy. Specificity of the can225IgG was tested via flow cytometry, immunofluorescence microscopy, immunohistochemistry, immunoblotting and ELISA. Viability assays were carried out to assess tumoricidic properties.

Results: The recombinant can225IgG was proven to be intact and correctly assembled. Its specificity towards the naturally expressed canine EGFR and recombinant human EGFR could be confirmed repeatedly in several assays. Proliferation and viability trials verified the *in vitro* functionality of the antibody, showing significant tumor cell growth inhibition upon can225IgG treatment.

Conclusion: We report in this study the first generation of a recombinant canine anti-tumor IgG for subsequent clinical studies in dog patients with EGFR-overexpressing cancers.

Furthermore, this study additionally emphasizes the essentiality of comparative medicine to reveal connections between conserved pathological processes between different species. Thereby, the development of novel therapeutic approaches could be speeded-up in human as well as veterinarian oncology.

1678
Skewing of SAG mediated therapy for a predominant Th1 during Visceral Leishmaniasis on triggering CD2 epitope

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Background: Visceral leishmaniasis is a macrophage associated disorder which is linked with a profound decrease in the immunotherapeutic potential of the infected subjects leading to a marked reduction in the CD4 linked Th1 protective immune response. It greatly affects the liver leading to abnormal levels of SGPT and SGOT. Also the patients suffering from VL have been reported to be coinfected with Hepatitis C during some circumstances. Simultaneously the patients in Bihar are showing unresponsiveness towards SAG which is still a first line of drug in many countries around the world against Visceral Leishmaniasis. We have previously reported down regulation of CD2 co receptor on the surface of CD4 cells in patients suffering from Visceral Leishmaniasis. Stimulation of CD2 epitope with antiCD2 antibody has led to a remarkable increase in the Protein kinase C alpha mediated phosphorylation on CD2 co receptor on CD4 T cells, induction of IFN-γ led Th1 dominated immune response, a substantial increase in the lymphoblast population and this response remained Th1 dominated even in the presence of Th2 predominant conditions signified with rIL4. Studies in the 1980s showed that biological immunomodulators such as interferon (IFN)-γ can provide a missing signal and enhance the activity of antimonials in the treatment of VL and CL.

Methodology/principal findings: In the present part of the study we have tried to evaluate the use of CD2 antibody as an immunotherapeutic agent along with SAG in ensuring treatment of BALB/c mice induced with experimental Visceral leishmaniasis. It has been found in the present set of studies that stimulation of CD2 co receptor along with along with therapeutic dose of SAG has led to the enhancement in the release of IFN-gamma which leads to the release of TNF-alpha and activates the macrophages. An increase in the NO mediated killing further observed by the activated macrophages leading to the reduction in the parasitic load.

Conclusions/significance: The results indicate that enhancing the immune potential of a VL patient will help in the better response of Sodium Antimony Gluconate which is the first line of drug against VL in many countries.

1680
Altered white matter tracts in the thalamus is associated with dyspnea in Gulf War illness

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Background: Gulf War Illness (GWI) subjects have many systemic complaints including shortness of breath. Dysfunctional central mechanisms have been associated with the perceptions of dyspnea. This has not been studied in GWI.
Method: 24 GWI subjects who met Chronic Fatigue Syndrome and Fibromyalgia criteria and 10 controls completed fMRI scans, WHO Dyspnea severity and UCSD Shortness of Breath scores. No subjects had airflow limitations. White matter structure was analyzed by non-invasive diffusion tensor imaging (DTI) to identify potential correlates of dyspnea. Reduced fractional anisotropy (FA) indicates compromised white matter integrity. Increased axial diffusivity (AD) and radial diffusivity (RD) measure axonal injury and demyelination respectively.
Results: Dyspnea scores were higher ($P = 0.0002$, 2-tailed unpaired t-test) in GWI [8.5 (6.2–10.8)] [M; (95% CI)] than controls [0.8 (0.04–1.6)]. UCSD scores were comparable ($P = 0.008$). Multivariate regression identified a positive correlation with the Dyspnea ($R^2 = 0.28$, $P = 0.008$) and UCSD ($R^2 = 0.20$, $P = 0.028$) scores as dependent variables with RD of the right anterior thalamic radiation (ATR) in GWI. Correlations were absent in controls. This suggests demyelination, oligodendrocyte dysfunction, or neuroinflammation.
Conclusion: Lung and phrenic sensory afferents project to the thalamus. The ATR conveys fibers from the thalamus and prefrontal cortex for interoceptive processing. Loss of myelin integrity in the right ATR may contribute to the subjective perception of dyspnea in GWI.

1681
Early child vaccination and incidence of acute respiratory infections and atopic dermatitis

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Background: Vaccination is one of the most important and effective preventive measures in modern medicine, but in recent years the number of people, especially children's parents, doubted the usefulness and necessity of vaccination. It is feared that vaccines can increase atopy and allergic diseases complicate the immune system or even weaken it. The aim of this study was to compare the incidence of infectious respiratory diseases and atopic dermatitis (AD) among vaccinated and unvaccinated children during first 2 years of age.
Method: The study was conducted retrospectively by selecting and evaluating health care cards. The chosen statistical significance level was $P < 0.05$. Subjects were followed from 6 months up to 2 years and retrospectively evaluated the incidence rate (incidence times during the observation period) of upper and lower respiratory tract infections, as well as the incidence of AD. The study population ($n = 78$) was divided into two groups according to vaccination (until 6 months of age) peculiarities. The first group comprised 45 children (29 girls/16 boys) fully vaccinated according to the Lithuanian children preventive immunisation schedule; the second (control) group comprised 33 unvaccinated children (18 girls/15 boys).
Results: Vaccinated children morbidity rate of upper respiratory tract infections (4.64 ± 0.46) did not differ from the disease incidence rate (4.36 ± 0.49, $P = 0.68$) of unvaccinated children. The morbidity rate of lower respiratory tract infections in vaccinated children group was 0.24 ± 0.08, but not significantly lower than in the group of unvaccinated children (0.3 ± 0.09, $P = 0.63$). There was no significant difference in the incidence of AD among unvaccinated children (72.7%) and vaccinated children (66.7%, $P = 0.54$).
Conclusion: 1) Children, vaccinated until 6 months of age by the child preventive vaccination calendar, during 2 years of age were not characterised by a higher susceptibility to upper or lower respiratory tract infection than non-vaccinated children.

2) Frequency of upper or lower respiratory tract infections in vaccinated and unvaccinated children groups did not differ by gender.

3) There was no significant difference in the incidence of AD among unvaccinated children and vaccinated children. To confirm the observed tendencies and results found, further larger studies are needed.

1682
Preventive immunisation against equine insect bite hypersensitivity: comparison of injection sites using recombinant allergens with or without IC31® adjuvant

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Background: Insect bite hypersensitivity (IBH) is an IgE-mediated dermatitis of horses caused by bites of insects of the genus Culicoides, that do not exist in Iceland. The prevalence of IBH is much higher in horses born in Iceland (where Culicoides are absent) and exported to the continent as adults, compared to Icelandic horses born in a Culicoides rich environment. The specific allergens causing IBH have recently been identified and expressed as recombinant proteins in *E coli*. The objective of this pilot study was to compare intradermal and intralymphatic vaccinations using four purified recombinant allergens, with and without Th1 focusing adjuvant. The final aim is the development of a preventive immunisation against IBH in Icelandic horses.
Methods: Twelve healthy horses living in Iceland were vaccinated three times with a combination of four recombinant (r-)allergens (Culn1, Culn2, Culn5 and Culn9). Six horses were injected intralymphatically, three without and three with IC31® (kindly provided from Intercell, Vienna). Six additional horses were immunised intradermally, three without and three with IC31®. Serum was collected for analysis of antibody responses in western blot and ELISA. The horses were tested for potential sensitisation in a sulfidoleukotriene release test (CAST®) and in intradermal tests.
Results: The r-allergens in IC31® adjuvant gave much stronger specific IgG responses to the allergens. Intralymphatic was slightly more efficient than intradermal immunisation. The IgG induced against all four allergens was mainly of the IgG1 and IgG4/7 subclasses and to a lesser extent IgG5. Postvaccination serum was able to block binding of serum IgE from IBH-affected horses to the respective r-allergen. The immunised horses did hardly produce any detectable specific IgE. There were also no indications of induction of IgE-mediated reactions as the horses did not respond to Culicoides extract stimulation in the CAST® or to the recombinant allergens in intradermal tests.

Conclusion: Vaccination of horses previously not exposed to the allergens both intralymphatically and intradermally with r-allergens in IC31® adjuvant was well-tolerated and induced immune response without IgE production. The horses produced IgG that could inhibit r-allergen-specific IgE-binding. We therefore conclude that both the injection methods and the IC31® adjuvant are strong candidates for further development of immunotherapy in horses.

1683
Blood eosinophil levels, proteomics patterns of strail and CXCL8, correlated survival with bevacizumab (anti-VEGF monoclonal antibody) treated stage-4 colon cancers

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Background: Colorectal cancer (CRC) belongs to the most common malignancies and accounts for almost 10% of all cancer deaths in the Western World. In the study, 69 metastatic stage-4 colorectal (MRCR) patients who had been used bevacizumab plus various chemotherapy regiments were assessed retrospectively. During the past decade, considerable progress has been made in understanding and defining the molecular basis of CRC. The development of CRC is characterised by a sequence of events during which normal colonic epithelium gradually transforms to carcinoma tissue, in most cases via the development of colorectal adenomas.

Method: TRAIL, CXCL8, CEA, LDH, CRP levels together with Complete Blood Count parameters were recorded in the beginning and evry three months afterwards for a period of two years. sTRAIL and CXCL8 levels were measured by ELISA in the sera of 45 bevacizumab-treated MCRC patients.

Results/Conclusion: Median age of the patients were 57.3 (29–81) and 36 of the patients were male. Majority (23) of the tumors were localised primarily in the rectosigmoidal region. Progression free survival was 245 days and overall survival was 1038 days.

Overall survival was higher in patients whose Karnofsky Performance scores were above 85% ($P = 0.003$).

Overall survival was higher in patients whose Hemoglobin levels at 6 months were were higher than the mean Hb level ($P = 0.03$).

There were significant changes prior to treatment and 6 months later for sTRAIL ($P = 0.0060$) and CXCL8 ($P = 0.0002$). Progression free survival was higher in patients whose blood eosinophil counts at 0, 6 and 9 months were were higher than the mean levels of corresponding values (P values are 0.016, 0.032 and 0.019 respectively). Another significant correlation was found between the platelet levels at 9 months and progression free survival ($P = 0.019$).

Poster Session 76

Latex and occupational allergy

1685
Associated factors with sensitisation and allergy to latex

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Background: Patients with spina bifida are at increased risk of allergy to latex. The aim of this study was to further analyze the factors associated with latex sensitisation and allergy.
Method: This cross-sectional study involves 400 patients with spina bifida, aged 0–18 years, from a Reference Hospital of São Paulo, Brazil. A questionnaire to identify immediate symptoms of latex allergy, as well as associated factors with sensitisation or latex allergy, was developed by experts and applied to the patients. Patient's blood was drawn for detection of serum specific IgE to latex, through ImmunoCAP® technique. Symptomatic patients with positive specific IgE were considered allergic to latex, and asymptomatic patients with positive test were regarded as sensitised. The patients without allergic symptoms and with negative serum specific IgE to latex were the negative control group. The associations were analyzed by Mann-whitney test and chi-square test.
Results: Patients mean age was 7.68 years, and 201 (50.25%) were female. Latex allergy was associated with: greater total number of surgeries (5 surgeries), greater number of orthopedic surgeries (3 surgeries), ventricular-peritoneal shunt (10 years of use), and intermittent bladder catheterization (5 years of use). When the allergic patients were compared with those sensitised, the former had the first surgery earlier (11 h of life), and a greater total number of surgeries (4 surgeries). These differences were statistically significant, with $P < 0.05$.
Conclusion: Time of the first surgery and total number of surgeries differentiate patients sensitised and allergic to latex.

1686
Clinical SCORE for screening of latex allergy

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Background: Screening patients in risk groups for latex allergy is an important but neglected procedure that must be standardised. The aim of this study was to develop a clinical SCORE of symptoms for screening of latex allergy.
Method: This cross-sectional study involves 400 patients with spina bifida, aged 0–18 years, from a Reference Hospital of São Paulo, Brazil. A questionnaire to identify immediate symptoms of latex allergy was developed by experts and applied to the patients. Cutaneous, nasal, ocular, oropharyngeal and pulmonary immediate symptoms were investigated. Patient's blood was drawn for the detection of serum specific IgE to latex, through ImmunoCAP ® technique. Symptomatic patients with positive specific IgE were considered allergic to latex. Discrepancy between the number of symptomatic patients and the number of sensitised patients with positive serum specific IgE to latex brought the proposal to establish a SCORE of symptoms. The SCORE was set inductively by values in accordance with the frequency of symptoms.
Results: Patients mean age was 7.68 years, and 201 (50.25%) were female. There were 91 (22.75%) symtomatic patients, but only 49 (12.25%) of them were positive for serum specific IgE to latex. A SCORE equal to or <40% was associated with the diagnosis of latex allergy. The questionnaire had a sensitivity of 45% and a specificity of 85.3%. Symptomatic patients who had negative serum specific IgE to latex had low SCORES in the questionnaire of symptoms.
Conclusion: The development of a clinical SCORE of symptoms can help in screening for the diagnosis of latex allergy. The SCORE showed good specificity being able to exclude the nonallergic patients with nonspecific symptoms.

1687
Do heat labile panallergens cause latex allergy in patients who are negative to both latex sIgE and skin prick tests?

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Background: To investigate grass and tree pollen sensitisation in patients diagnosed with latex allergy following latex provocation testing.
Method: A retrospective case note study of adult patients presenting to a Leicester (UK) based allergy clinic. Data from a four year period (2008 and 2012) were reviewed and latex positive challenge patients identified.
Results: Twelve patients had a positive latex challenge. 8/12 and 4/12 patients reacted to latex following cutaneous and mucosal exposure, respectively. 10/12 patients had a negative latex skin prick text (SPT) (<3 mm) and sIgE. Of these, 3/9 patients had positive SPTs to one (or more) of grass, birch and three tree (Hazel, Alder and Birch). All three of these patients had a history of seasonal rhinitis and 2/3 and 1/3 had a clinical history of oral allergy syndrome and latex fruit allergy, respectively. Latex allergy in 1/3 of these patients was diagnosed following a mucosal challenge.
Conclusion: One case would have been missed without mucosal challenge and we propose that both cutaneous and mucosal provocation tests are required to exclude latex allergy. Without mucosal exposure the risk posed by intraoperative exposure to latex cannot be fully excluded. Heat labile panallergens such as the profilin Hev b 8 may cause latex allergy in a proportion of patients who have negative latex SPT and sIgE. Hev b 8 has previously been associated with latex sensitisation rather than latex allergy and further studies using challenge data and component resolved diagnostics are needed. Finally, although the incidence of latex allergy in health care workers is decreasing, it remains important to assess patients for latex allergy including those who have pollen related allergic disease.

1688
Latex exposure and its allergies among Albanian healthcare workers

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Background: The frequent and extensive use of latex gloves is known to noticeably impact the increasing prevalence of latex allergies among the health care workers. At the same time skin prick test is routinely used to evaluate the sensitivity to latex. The present study aims to evaluate the relationship between latex exposures its allergy, and skin prick test positivity in Albanian healthcare workers.
Method: We conducted a cross-sectional study, at a university hospital centre, involving 662 nurses filling up a questionnaire. Simultaneously, we performed a skin prick test with latex and negative control solutions, on the forearm of each participant. From among them, 639 participants accepted to answer the questionnaire; while 602 accepted to undergo the skin prick test. RR and the chi-square test were used to test the differences. PASW Statistics 18 and MS Excel 2007 were used to analyze the data.
Results: 2.33% (14) participants showed positive results for latex skin prick test; while 0.5% (3) participants showed positive results for both skin prick tests. On the other hand, 9.39% (60) participants reported at least one symptom related to latex exposure. In fact, those who used more than nine pairs of latex gloves were at a higher risk of developing allergy symptoms compared to those who used 5–9 and less than four pairs of gloves (RR 3.49, $P < 0.05$ and 2.48, $P < 0.05$ respectively). No significant differences were observed in the skin prick test positivity between these subgroups.
Conclusion: These are the first ever reported data on latex allergy among Albanian healthcare workers. Besides, this study supports the evidence that exposure to latex gloves carries the risk of developing latex allergies.

1691
Role of natural rubber latex sensitivity follow up survey in dentistry students

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Background: Latex is considered as a major cause of contact dermatitis. In healthcare workers the prevalence of latex sensitivity is threefolds higher compared with the general population. Latex is a risk factor for type I, IV allergic reaction and irritant dermatitis. There are no studies in Albania related to latex gloves sensitivity, even though the healthcare providers regularly use them.
Objective: To evaluate the latex sensitivity, to emphasize the need of questionnaires before the first years of practice and follow up evaluation of latex sensitivity.
Method: Dentistry students based on a large randomised and still in process study are being investigated for immediate or late reaction. Other allergy patterns like rhinitis, asthma, urticaria-related to latex-sensitivity are being evaluated. Students of the last year of Dentistry Faculty have been working at least 2–4 h a day with latex gloves for about 2 years. They were provided with latex sensitivity questionnaires. The skin prick test (commercial latex, other environmental and food allergens), challenge test and patch tests were performed.
Results: In a group of 24 students three of them had immediate allergic reaction: one of the students developed symptoms like itching, urticaria, the other one facial rush and the last one severe allergic reaction with asthma and cutaneous symptoms on exposure to latex gloves. The last mentioned student had been suffering from contact dermatitis for 2 years.
Conclusion: Re-evaluation of latex sensitivity in dentistry students after the first year of practice is needed. Repeated information, questionnaires, etc for latex allergy symptoms for these practitioners or students are also necessary. And as long as the prevention is the key, the need for latex safe protocol, early diagnosis and appropriate environmental changes (vinyl gloves) are important factors with the final intention that healthcare providers can work under safe conditions.

1693
Occupational asthma and rhintis due to type I hypersensitivity to ash wood dust with negative skin prick tests

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Background: Several studies have been published reporting that occupational exposure to wood dusts can induce allergy with respiratory and nasal disorders but only a few to ash wood dust are reported. This exposure has been shown to cause a type I hypersensitivity; nevertheless an IgE-mediated sensitisation has not always been elucidated so it is important to make a complete detailed study.
Method: We present a case of a 30-year-old man without atopic backgrounds who has worked in a furniture factory for over 10 years and was referred to our clinic with a 2-year history of nasal and respiratory symptoms after working with ash wood that he used frequently.

These symptoms disappeared out of work and were not related with other wood dust.
Results: Skin prick tests (SPT) were negative for a battery of common allergens and commercial extracts of different woods (ash, pine, samba, framire, iroko, embero, sapeli).

The spirometry was normal but the methacholine challenge was positive (PC20: 5.16 mg/ml). Fractional exhaled nitric oxide (FENO) was also positive (89 ppb). Serial peak flow monitoring showed a fall in peak expiratory flow rate during work with ash wood.

Specific inhalation challenges were carried out with ash and sapeli (control) wood dust. The results showed rhinorrea (15 min) after the exposure with sapeli and decrease in nasal peak inspiratory flow rate (33%), severe rhinorrea, sneezing (1 min) and decrease in forced expiratory volume (FEV1) of 23% (15 min) with ash.

Bronchial provocation tests with dyalized ash wood dust extract induce a decrease in FEV1 in 18% (15 min) and 26% (10 min) with non dyalized extract.

Because of the lack of correlation between the challenge tests and the SPT we realised intradermal testing (ID) with dyalized and not dyalized ash extracts that elicited positive responses (1:100). They were negative in two controls (1:10).

He was treated with nasal corticosteroids, antihistamines and irrigation and the recommendation to use anti-allergen mask during work.

A control inhalation challenge test using an anti allergen mask was realised after 3 months when he showed improvements in symptoms and serial peak flow monitoring with negative results.
Conclusion: We report a case of a patient with occupational asthma due to hypersensitivity type I to ash wood dust with negative SPT that was confirmed with serial provocations and ID tests.

1694
Occupational contact dermatitis due to Alstroemeria and Gerbera in a florist

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Background: Many plants and flowers can cause dermatitis in florists. Alstromeria,

also called Peruvian Lily, has frequently been reported to cause hand eczema in floral workers, But only few cases of allergic contact dermatitis from Gerbera has been reported in florist. We present a case of contact dermatitis to Alstromeria and Gerbera. Our Patient was a 46 years old woman with previous history of allergic rhinoconjunctivitis due to Parietaria judaica pollen, who has been working for over 4 years in a florist shop where handles and makes bouquets with Alstroemeria, Gerbera and Lilium. In the last 18 months, she developed fingertips erytema, scaling and peeling of thumb, index and middle hand right fingers which improves on holidays.

Method: Patch tests with the International Contact Dermatitis Reserch Group standard series, Plants and essences series (Bial- Aristegui) and stem, leaf and flower portions of the suspected ornamental plants (Alstroemeria, Gerbera and Lilium) were performed.

Results: Patch tests lecture were performed on the second and third day. The International Contact Dermatitis Research Group standard series were negative. Patch test performed with the plants, essences series, stem, leaves and flowers with positive results to Tulipalin A, Alstroemeria and Gerbera stems, being negative to leaves and flowers. All Path test with Lilium portions were negative.

She remains asymptomatic after avoid Gerbera and Alstroemeria.

Conclusion: We present a female patient with occupational allergic contact dermatitis like 'tulips fingers' clinical picture due to Gerbera and Alstroemeria flowers.

Patch tests with ornamental portions were helpful.

The responsible allergen was Tulipalin A lactone.

1695
Occupational asthma and urticaria in a hairdresser

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Background: Persulphate salts are chemical compounds of low molecular weight that cause infrequently allergic pathology. They are currently used at hairdresser's for bleaching the hair in the form of white powder. We report the case of a hairdresser with occupational rhinitis and bronchial asthma by persulphate salts demonstrated by skin tests and specific bronchial challenge.

Clinical case: A 23 year-old woman, haidresser, nonsmoker, was referred to our Unit with symptoms of sneezing, nasal obstruction, facial edema and generalised urticaria after handling bleach product in April 2010. Although she didn't personally handle the bleach product at work, she still had symptoms of rhinitis with nasal obstruction, wheezing and spasmodic cough daily, predominantly at night. She also had scalp itching after application of hair dye. She was asymptomatic during the bank holidays and holiday periods.

Method: We made allergological study using skin tests to inhalants to pneumoallergens and sodium persulphate, peak flow records during working days and not working days, patch tests (European Standard Baterry and Hairdessing Battery), unspecific bronchial hyperreactivity test (Methacholine) and specific bronchial challenge with sodium persulphate.

Results: We demonstrated sensitisation to grass pollen (*Lolium perenne*) and sodium persulphate (100 mg/ml) by skin testing, positive patch testing to Nickel sulphate, Cobalt chloride and Phenylenediamine, positive methacholine test to PC20FEV1 = 6.61 mg/ml and positive specific bronchial challenge test with sodium persulphate to 0.01 mg/ml (FEV1 declined in 21.8%).

Conclusion: We report a case of occupational asthma and allergic rhinitis by sodium persulphate demonstrated by positive skin test and positive specific bronchial challenge test with sodium persulphate. We show that kind of etiological diagnosis can be realised in an Allergic Unit without a specific challenge chamber. The patient also was diagnosed by occupational contact dermatitis.

1697
Occupational allergy to *Plantago ovata* like laxative

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Background: It is known that Plantago ovata seeds (ispaghula), use as laxatives, produce occupational allergy in health care and pharmaceutical workes. Cross reactivity of plantago lanceolata- pollen has been suggested.

Case: Two woman, both auxiliaries nurses in a handicapped center seek advice for suffering rhinoconjuntivitis and asthma symptoms during or after handing laxatives containing *P. ovata* seeds (Plantaben®). One of then also describes a rash and an anaphylactic reaction. We made a study protocol that included: a medical history which includes allergies and the type of *P. ovata* seeds exposition, physical examination, functional respiratory tests, prick test to common inhalants (house dust mite, fungi, animals danders, latex, common pollens included *P. lanceolata* plus LTP and profilin), prick test with commercial laxatives (Plantaben®) 1/10, 1/100 and 1/1000 dilution, total and specific IgE determination and controlled exposition test which consist in mixing the laxative with water and observe if symptoms appear. It is used an visual analogue scale and spirometric controlPrick test, specific IgE determination and exposition test with *P. ovate* were positive in both patients. When patient 1 prepared plantaben she suffered ocular and nasal itching within obstruction, cough and dysnea finding a 20% decrease FEV1. Patient 2 presented similar syntoms, nevertheless FEV1 didn't drop. All the other tests were negative. We realised prick test with Plantaben® to 20 non allergic patients, and these were negative. It was recommended avoid the manipulation of *P. ovata* in their workplace. They staywithout symptoms since these suggestions.

Conclusion: Plantago ovate seeds are a frecuent cause of occupational allergy in healthworkes, primarily at cronic care hospitals. It is quite easy to diagnose, could produce important syntoms and avoidance measures should been recommended. Atopic status and *P. lanceolata* pollen sensibilition had been described before for risk factor to *P. ovate* allergy. We presented two patients without this factors.

1698
Occupational asthma due to *Capsicum annuum* fruit harvesting

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Background: Occupational allergy in horticulture is not common, but it has been described as a consequence of bell pepper pollen allergy. Inhalation of paprika (dry powder of *Capsicum annuum*) is also a known cause of occupational asthma.

Case presentation: We present an 18-year-old woman, vegetables harvester, that developed rhinitis and asthma symptoms when gather hot pepper fruits into a greenhouse. She tolerated their intake. Bronchial hyperresponsiveness, sputum eosinophilia

and peak expiratory flow during working periods inside and outside the greenhouse confirmed asthma related to work. Skin prick test with perennial and seasonal common aeroallergens were negatives. Skin prick test with a battery of in-house-made vegetables extracts were only positive to green, red and hot bell pepper. Serum IgE (Enzyme Allergosorbent Test) and flow cytometric basophil activation test to hot bell pepper fruit were positive. ImmunoCAP to MUXF3 (the bromelain-type N-glycan) was also positive. SDS-PAGE Immunoblotting in reducing conditions (Laemmli) with hot bell pepper fruit extract showed IgE binding bands at approximately 40, 34, 30, 24, 19 and 17 kDa. The most intense was the 30 kDa one, that according to its molecular weight could correspond to the l-ascorbate peroxidase decribed as a cross-reactive allergen with latex extract. Blotting inhibition assay using bromelain in inhibition phase as a source of N-glycans structures (cross-reactive carbohydrate determinants [CCDs]) showed persistence of a unique band at 30 kDa, meaning that its recognition is based on peptic epitopes.

In our knowledge this is the first case reported of occupational asthma by fresh hot pepper fruits.

1699
Occupational asthma in a hairdresser due to formaldehyde

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Background: Formaldehyde is a low molecular weight chemical used in many industrial processes such as textile, manufactoring of plastics, rubbers, adhesives, nail polish, etc. It is also used as disinfecting, preserving and embalming agent, as well as a hair stabiliser and straingthner. Despite of its widespread use, cases of formaldehyde-induced occupational asthma has not frequently been reported.

Case report: We report a 37 year-old smoker woman who had been working as a hairdresser for 20 years. In the last year she developed pruritic micropapular exudative eruption and vesicles located in hands, being diagnosed of allergic contact dermatitis by dermatologist. Moreover she complained of work related symptoms of rhinoconjunctivits and episodes of cough, dyspnea and wheezing, when she worked with SALERM® blisters (25% formaldehyde solution) in the hairdressing. which are used for hair straighteing. These symptoms subside over holidays and dissapeared after she stopped working.

Material, methods and results: Skin prick tests were negative to common inhalants. Patch testing using standard TRUE-TEST® and hairdressing MARTI TOR® series showed positive reactions (++) at 48 and 96 h to kathon CG, formaldehyde, p-phenylenediamine, quaternium 15, ammonium persulfate, as well as the SALERM® formaldehyde blister. A baselyne spirometry was normal and a metacholine inhalation test was negative in the period away from work. Initial FeNO measurement was 41 and 17 ppb after she stopped working. No eosinophils were found in a induced sputum sample. A specific inhalation challenge test with the SALERM® blister (formaldehyde) was performed in a 7 m^3 dymamic closed-circuit chamber by means of opening and manipulating the blister simulating working condition. 7 h after the inhalation test, a 20% fall in FEV1 was observed, reaching a maximum fall in FEV1 of 45% at 9 h, with recovery after inhalation of beta2-adrenergic agent. 24 h after the specific inhalation test, the metacholine test became positive (PC20 3.5 mg/ml) and induced sputum samples showed an intense 30–40% eosinophilia.

Conclusion: To the best of owr knowledge this is the first case of occupational asthma due to formaldehyde in the hairdresser industry, used as a hair straightner and stabiliser, and demonstrated by positive specific inhalation challenge test. Moreover, the patient suffered allergic contact dermatitis due to formaldehyde and other hairdressing chemicals.

Poster Session 77

The novel mechanisms of contact dermatitis

1701
Colophony as a cause of Riehl melanosis: a case series

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Background: Riehl melanosis or pigmented contact dermatitis, is usually seen in persons with a dark complexion. It is clinically characterised by dark-brown pigmentation distributed on the chest, face and neck. The hyperpigmentation is caused by frequent and repeated contact with sensitising allergen. The allergen is hypothetically too low in concentration to produce typical eczematous dermatitis. Mostly fragrances and chemicals in cosmetics cause Riehl melanosis. Colophony is uncommon sensitiser of pigmented contact dermatitis. The accumulation of allergen results in allergic contact dermatitis. Histopathology showed vacuolization of basal cells, pigment incontinence and lymphocytic infiltrate in the dermis.
Method: We performed patch test and photo patch test to five patients with Riehl melanosis in our clinic. Patch test and photo patch test of these patients used the standard, cosmetic, and fragrance series. A biopsy was taken from one patient.
Results: Patch test and photo patch test of these patients using standard, cosmetic and fragrance series hardly showed positive reaction to suspected sensitisers. The only positive reaction in photo patch test was found in 1% colophony. Irritation was found in one patient by paraphenylene diamine. The biopsy taken from one patient demonstrated inextensive vacuolization of basal cells.
Conclusion: Here we reported five cases of Riehl melanosis, with colophony as a sensitiser. Colophony is known as a sensitiser of allergic contact dermatitis. However, it is uncommon to cause pigmented contact dermatitis. Colophony can be found in several every day products, such as adhesive tapes, sealant, polishes, and waxes. Avoidance to related sensitiser results in significant clinical improvement in our patients.

1702
Pharmacotherapy of allergic contact dermatitis – how many drug licenses are in keeping with current guidelines for treatment?

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Background: The therapy of allergic contact dermatitis is not just a pharmacological challenge. It may also have legal and administrative consequences for the doctor. Using medications whose effectiveness has been proven by scientific studies, yet are not licensed for a given indication, may be interpreted by law as a 'therapeutic experiments', which has a range of consequences for the treating physician. The aim of this study was to confront up-to-date recommendations for the treatment of allergic contact dermatitis (ACD) with the scope of licensed use of recommended drugs according to the Summary of Product Characteristics (SPC).
Method: The analysis was based upon the recent Polish and international recommendations regarding ACD treatment. A list of recommended drugs was compiled and confronted with the Official List of Medicinal Products that is in force in Poland. Medicinal products both recommended by expert bodies and allowed for ACD treatment in terms of SPC were indentified.
Results: Only a half of the drugs recommended by experts for the therapy of ACD are officially licensed in Poland for treating this condition. Among drugs recommended for ACD treatment (topical and systemic glucocorticosteroids, topical and systemic immunosuppressants, barrier drugs and psoralens), only some topical and systemic glucocorticosteroids, as well as topical barrier drugs were licensed in Poland for the treatment of this disease. On the other hand, SPC of some old antihistamines (cyproheptadine, hydroxizine, clemastine) contained the indication for ACD treatment, despite lack of expert recommendation and scientific evidence that would support their effectiveness in this disease.
Conclusion: There are considerable discrepancies between current expert recommendations for the treatment of allergic contact dermatitis and the licensed use of medicines as determined by the official product characteristics. The 'off-license' use of such drugs may be interpreted as 'therapeutic experiment' with a range of legal and administrative consequences, including the requirement for a patient's written consent, lack of reimbursement from the health insurance, no liability of the producer for adverse drug reactions, and no coverage of a possible damage from the physician's liability insurance.

1704
Prevalence of mercury allergy and treatment of adverse events to dental materials

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Background: We did a cohort study of adverse health outcomes to dental materials to investigate the association between alloy dental treatment and the risk of potential adverse events.
Method: Cohort study of 759 individuals diagnosed as having dental alloy adverse events.
Results: We evaluated 491 (491 of 759, 64.6%) symptomatic dental patients with systemic and/or oral diseases associated with mercury amalgam. Median age was 44, 359 were female (73.1%), woman to man ratio 2.7:1. Of 491 patients with adverse clinical events to mercury amalgam, 325 underwent the patch testing (325 of 491, 66.1%). The current prevalence of allergy to mercury was 28.6% (in aggregate, as metallic mercury, ammoniated mercury, thimerosal, dental amalgam, all in petrolatum). Median urinary mercury levels in 70 patients was 1 μg/l. The most common adverse effects of amalgams are burning mouth syndrome (17.9%), contact dermatitis (16.9%), neurologic disorders (12.6%), oral lichen planus (10.0%), endocrine alterations (5.9%), chronic fatigue (4.1%). nine patients (1.8%, eight woman and one men) had positive serum

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anti-nuclear and all nine ANA-positive patients became ANA negative after mercury amalgam removal. Serum prolactin levels were elevated in six patients (1.2%) and return to normal levels after amalgam removal. Five patients (1.0%) had thermal regulation disorders (low cold tolerance) and reversed after amalgam removal. Three (3 of 491, 0.6%) patients had type III hypersensitivity reactions to mercury with elevated immune complexes. Two women with selective IgG subclass deficiency reversed after blood Hg fell to undetectable levels. One had mercury-induced low serum ACTH concentrations that returned to normal range after amalgam removal. Endo-osseous titanium dental implants were associated with oral and/or systemic conditions in 24 of 759 (3.1%). Clinical presentation included hemifacial edema, burning mouth syndrome, atypical facial pain, lichenoid stomatitis, leukopenia. Serious adverse events that were considered to be related to titanium dental implants placed in the vicinity of mercury amalgam were paraproteinemia, demyelinating disease, motor neuron disease. Treatment consists of safe amalgam and dental implants removal (*en bloc* technique).

Conclusion: Allergy and exposure to dental alloys can adversely affect individuals more than previously estimated.

1705
Toothpaste-associated labial allergic contact dermatitis

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Background: Allergic contact dermatitis (ACD) is an antigen specific, cell-mediated delayed type hypersensitvity. Unlike classic type IV reactions which occur in the dermis and are mediated by CD4+ T- lymphocytes, ACD is characterised by epidermal involvement with an infiltrate composed of CD4+, CD45RO+, TCR alpha beta T-lymphocytes. The sensitisation period may vary from days to years. In the acute phase, ACD is characterised by erythema, edema, papules, vesicles, oozing, and crusting. In the chronic stage, involved areas are lichenified and fissured. We report a case of a patient with a two year history of chronic labial dermatitis.

Methods: Ten-year-old boy with no significant past medical history who presented for allergy evaluation. Two years prior to presentation, he developed 'yellow lesions,' foul-smelling breath, along with intermittent bleeding and peeling of his top and bottom lip. He denied mucosal involvement or rash elsewhere. He was afebrile and did not experience systemic complications such as joint pain, respiratory or gastrointestinal symptoms. There was no history of food or seasonal allergies, asthma, or eczema. The family reported routine use of a toothpaste containing mini breath strips as well as mint flavoring.

Results: Allergen patch testing was performed using the family's toothpaste containing the mini breath strips and mint flavoring, a regular tartar protection toothpaste, and a ready-to-use patch test system containing 29 allergens and allergen mixes. Positive result was obtained for the toothpaste containing the mini breath strips and mint flavoring. The remainder of items tested negative (including the regular tartar protection toothpaste). Comparison of the toothpaste ingredients indicates that possible allergens are PEG-12, cocamidopropyl betaine, and methylcellulose. Our patient′s symptoms resolved completely after avoidance of all products containing PEG-12, cocamidopropyl betaine, and methylcellulose.

Conclusions: We report a novel case of toothpaste-associated allergic contact dermatitis caused by PEG-12, cocamidopropyl betaine, or methylcellulose. To our knowledge, none of these contact allergens have been reported in association with toothpaste ACD. The most common toothpaste ACD triggers include cinnamic aldehyde, spearmint, peppermint, menthol, and carvone. Physicians need to consider ACD as an etiology for lip eruption.

1706
Why we must not call haptens the 'a-names'

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Background: The use of scientifically correct terminology both determines and reflects our understanding of the surrounding world. From immunological point of view, small molecular weight substances that cause contact allergy are haptens, and not 'allergens'.

Method: An analysis of the differences between the terms 'hapten' and 'allergen' and of the possible scientific and administrative consequences of using the incorrect terminology, based on literature search and analysis of legal documents.

Results: There are substantial differences between these two types of sensitising agents: Haptens can penetrate through intact epidermal barrier, while allergens cannot. After entering the body, allergens are instantly recognised by the immune system, while haptens have to undergo complicated processes resulting in creation of antigens consisting mainly (>99%) of body's own proteins. As a results, there are more similarities of contact allergy to autoimmunity than to immediate-type allergy. Skin tests to allergens (e.g. prick tests or intracutaneous tests) are connected with a considerable risk of anaphylaxis, while it is exceptionally rare in case of haptens. Regardless substantial differences, the tendency of referring to haptens as 'allergens' seems to be more widespread nowadays than a century ago, hinting on a decline in clinicians' understanding of the underlying mechanisms. This seems to encourage some allergists to copy their knowledge about allergens (e.g. in allergic rhinitis) while diagnosing or treating contact allergies, e.g. treating contact dermatitis with antihistamines or attempts at 'desensitising' to haptens. Most unfortunately, the improper terminology has also influenced regulatory bodies, which now mistake haptens for allergens, too. As a consequence, without much consideration they tend to classifying nowadays haptens as 'therapeutic drugs', in analogy to therapeutic allergens for immunotherapy. With estimated 3.5 thousand environmental haptens, most of them relevant each to a relatively small group of people, the cost involved in a registration of such haptens as 'drugs' would make production of most patch test substances economically unsustainable, thus taking away from millions of patients the chances for having the cause of their disease identified.

Conclusion: Using imprecise and incorrect terminology may affect both doctors′ and regulators′ understanding of a medical problem, and directly or indirectly decrease patients′ chance for cure.

1707
Trends and developments in two decades of patch testing

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Introduction: Allergic contact dermatitis is a common condition with an estimated lifetime prevalence of 19.5%. The diagnosis is confirmed by patch tests.

This study aims to visualise trends and developments in patch testing over 23 years and to evaluate the influence of legal restrictions with special interest in chromate. Chromate was a notorious allergen in cement, but in 2003 the European Council issued chromate restrictions for cement, which might influence the frequency of sensitisations.

Methods: Retrospective study to evaluate the patch test results of the dermatology department of the University Medical Center Groningen between January 1989 and January 2012. Patch tests were performed with the extended European Baseline series according to the guidelines of the International Contact Dermatitis Research Group and results were read on day 2 and day 3 or on day 3 and day 7.

Results: In 23 years 11 983 consecutive patients were patch tested with the extended European baseline series. The patch tested population became significantly older, with a growing female preponderance, but a relative stable influence of occupational factors. Overall, the three most frequent contact allergens were nickel (18.2%), fragrance mix I (5.6%) and cobalt chloride (4.9%). Over two decades, the prevalence of nickel, paraphenylene diamine (PPD), methylchoroisothiazolinone/methylisothiazolinone (MCI/MI) and, paratertiary butylphenol formaldehyde (PTBF) sensitisations increased, while a significant decrease was observed in the number of sensitisations to fragrance mix I, colophonium, quinoline mix, formaldehyde and thiuram.

The number of sensitisations to potassium dichromate did not significantly decrease since 2003; however the patient characteristics of those reacting to potassium dichromate did change.

Discussion: The influence of the legal chromate restrictions was not visible in this study. Chromate might have been restricted in cement; however it is not restricted in leather, which might explain the absence of a decline in sensitisations to chromate. Furthermore, a number of patients might have been sensitised before legal restrictions were introduced. The same is true for nickel restrictions.

Conclusion: This study demonstrates that the patch test results of the baseline series are subject to trends and other developments over time, but respond slowly to legal restrictions.

1708
Perineal allergic contact dermatitis postpartum

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Background: Vaginal birth has been recognised as being potentially traumatic but allergy contact in vulvar and perineal regions has rarely been reported. Perineal contact dermatitis by obstetric surgical procedures as a vaginal birth can be involved multiple causes such as latex, antiseptics, metals, sutures, local anaesthetics, urinary catheter, lubricant and medicaments.

Method: A 35 year-old woman who presented erythematous and pruritic plaques on perineal region and upper inner thighs that began after vaginal birth. She had had contact with providone iodine, latex gloves, antiseptics (chlorhexidine) and urological lubricant Organon® applied on the vesical catheter for urinary retention, containing the topical anesthetic, Tetracaine. She received treatment with corticosteroids and antihistamines with improvement. We performed allergy study.

Results: Skin prick test with standarized extracts of latex resulted negative.

Patch tests were conducted according to the International Contact Dermatitis Research Group criteria, using the TRUE Test® system (Stallergens®). We also tested the urological lubricant Organon® (Organon Española, S.A., Barcelona Spain), chlorhexidine digluconate 0.5% and providone iodine.

Readings at 48 and 96 h, patch test results showed intense positive reaction with caine mix (benzocaine, tetracaine and dibucaine hydrochloride), lubricant Organon® ointment; Tetracaine hydrochloride was contained in the urological lubricant applied on the vesical catheter. We perfomed patch test with tetracain hydrochloride 5%, resulted positive.

The patient was diagnosed with contact dermatitis due to Tetracaine.

Conclusion: We present a case of allergic contact dermatitis due to Tetracaine, contained in a urological lubricant. Tetracaine hydrochloride, is a local anaesthetic, and it has been demonstrated to be a strong sensitiser. Local anesthetics are widely used in clinical practice and adverse effects are not uncommon. Delayed hypersentivity reactions are among the most common effects, but immediate-type reactions may also occur.

A Spanish study found positive patch test to tetracaine in 1.2% of a large series of tested patients which corresponded to almost 20% of those positive to caine mix. Cross-reactivity with other anaesthetics of the amine group does not occur and they can therefore be used as a safe alternative in sensitised patients.

1709
Plasma cell gingivitis due to allergy to dental metals

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Background: Here we report the first case of plasma cell gingivitis associated with allergic sensitisation to intra-oral metals. In 2012, a 56-year-old nonsmoker female reported gingival bleeding and white patches on the maxillary buccal mucosa accompanied by commissural cheilitis. She had received 8 dental alloy crowns and six endosseous dental titanium implants.

Method: The patient was evaluated for allergological, immunological, and toxicological assessment.

Results: Skin patch testing showed weak allergic reaction (+) to gold thiosulfate at 0.5% at 96 h. Lymphocyte blastization test (LTT) revealed strong sensitisation to nickel (29.2), cadmium (6.6), molibdenum (2.4), inorganic mercury (2.8), zirconium (2.3), and LTT confirmed the sensitivity of gold (8.0). Biopsy of the maxillary buccal gingiva was consistent with plasma cell gingivitis with moderate vacuolization in circumscribed areas of epithelial basal membrane. There was no cytological evidence of malignancy in the dorsal mucosa of the tongue nor visible tongue mucosal lesions. Culture of the lesions grew Escherichia coli in four occasions. Gold and nickel concentrations in saliva sample were 68.2 and 2.8 micrograms per gram, respectively (Au limit value, 0.2; Ni limit value, 7.9). After removal, we measured the emission of mercury vapor from the largest mercury filling and it was 42.3 $\mu g/m^3$. Laboratory investigations revealed leucopenia, eosinophilia, and modest hypercalcemia as well as hyperomocysteinemia. After amalgam-treatment removal (two dental amalgams) and complete removal of 17 root-canal metal-based posts, and three alloy crowns she achieved a complete remission of plasma cell gingivitis after 9 months of treatment. The patient has never been subjected to pharmacological treatments with topical and/or systemic corticosteroids. Plasma cell gingivitis has been associated with use of chewing gum, candy, food, and oral hygiene products (e.g. toothpaste). The exact mechanism by which mercury

amalgam may cause plasma cell gingivitis is not known.

Conclusion: This case demonstrates that allergic plasma cell gingivostomatitis was due to allergic sensitisation to intra-oral metals.

1710
Glyceryl caprylate – a new contact allergen

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Background: Glyceryl monoesters (monoglycerides) are common ingredients of cosmetics and are used mostly as skin conditioning agents. There are no reports about allergic reactions to the monoester glyceryl caprylate (2,3-dihydroxypropyl octanoate).

Case report: A 39 year-old woman presented with a several year history of recurrent eczema of her face. She had used various skin care products in the past and suspected, among others, Linola face cream (Linola Gesicht®) of having induced her dermatitis.

Methods: Patch testing was performed according to the guidelines of the German Contact Dermatitis Research Group (DKG) using allergens provided by Almirall, Reinbek, Germany (German baseline series, external products series, preservatives series, fragrances series) and several of the patient's own cosmetics.

Results: Positive reactions were observed to potassium dichromate, nickel sulfate, rosin, fragrance mix and its ingredient oakmoss (evernia prunastri), propolis and to several of the patient's own cosmetics, among them Linola Gesicht®. Patch testing with the single ingredients of Linola Gesicht® revealed a 3+ reaction in the 2D, 3D, 4D readings to glyceryl caprylate (5% pet.). In a further patch test positive reactions were observed also to lower concentrations of glyceryl caprylate (1+ to 0.1% pet., 3+ to 1% pet. in the 3D reading). None of the three healthy control persons reacted to glyceryl caprylate. Upon avoiding contact with cosmetics containing this substance the patient has remained symptom free.

Conclusions: To the best of our knowledge this is the first report regarding contact allergy to the glyceryl caprylate. The patient's own products should always be considered for patch testing when contact dermatitis to cosmetic ingredients is suspected.

1711
Oral lichen planus due to allergy to mercury dental amalgam

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Background: Chronic exposure to mercury dental amalgam may have serious adverse reactions in oral tissues. We report the case of a 48-year-old woman who developed oral lichen planus (OLP) after receiving air polishing and ultrasonic scaling. Concurrent mercury-related disorders were right acute otomastoiditis, burning mouth, xerostomia, dysgeusia (metallic taste), atypical facial pain, and gingival bleeding, and weight loss. She had seven mercury-containing dental amalgams and OLP lesions were located in close topographical association with four amalgams. She had three high-palladium metal ceramic crowns.

Method: We did biopsy, allergological, and toxicological investigations.

Results: November 2011, on inspection, OLP involving right buccal mucosa and tongue, on the right latero-dorsal surface. The patient's medical history included cholecystectomy. OLP had started 15 days after dental hygiene as tongue lesions and rapidly progressed into right buccal mucosa. OLP lesions had has been present for one month and biopsy specimen of buccal mucosa lesion revealed oral lichen planus. Skin patch-testing disclosed allergic reactions to metallic mercury 0.5% (+) and mercury ammonium chloride 0.1% (+) at 96 h. Lymphocyte transformation test showed sensitisation to cadmium (3.64), molybdenum (2.40), nickel (2.42) [limit stimulation index <2]. Nickel was elevated even in serum (2.83 μg/l). Her saliva mercury level was 8.8 μg/l. Intraoral mercury vapor was 47 μg/l. Blood mercury concentrations was 1.50 μg/l, whereas urinary mercury levels was 1.40. She had two amalgam tattoos. Fish consumption occurred about six times per month. We removed all ($n = 7$) amalgam fillings by using a safe procedure (lift-on technique), decreasing the levels of exposure to mercury vapor. Six months after total amalgam removal, complete resolution of the oral white patches – OLP lesions – was noted and follow-up laboratory tests showed that mercury in blood, urine, intraoral air, and saliva fell below quantifiable levels. Mercury released from amalgam is deposited into oral mucosa, eliciting an intense inflammatory response sensitisation. Early diagnosis is paramount in the successful treatment of OLP related to allergy and exposure to mercury amalgam and we do not recommend steroids before amalgam removal.

Conclusion: OLP in this patient was caused by mercury amalgam fillings released in massive quantities during dental hygiene procedures.

1713
Contact dermatitis induced by beclomethasone dipropionate

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Background: Corticosteroids, topical and systemic, are drugs commonly used in allergic disease's treatment. However, corticosteroids allergy is a common finding, being most frequent delayed-type reactions. The incidence of corticosteroids allergy varies between 0.5% and 5%. The corticosteroids, contact is increasingly globally, being recognised as a significant clinical and therapeutic problem. The occurrence of cross-reactions between different steroids is not uncommon.

Method: We report the case of a 66 years old woman who presented after application of beclomethasone dipropionate on genital, dermatitis in the contact area. She had no previous problems with other corticosteroids.

Results: Pach test: betamethasone dipropionate and valerate, budesonide, dexamethasone, prednisone, triamcinolone acetonide, methylprednisolone, tixocortol, hydrocortisone, prednisolone, amcinonide, fluocinolone, betamethasone, clobetasol, desoxymethasone:48–72 h negative (beclomethasone ointment application on the forearm, 3 days): dermatitis in contact area.

Hydrocortisone and dexamethasone use test: no injuries.

Conclusion: Corticosteroids had been classified into four cross-reacting groups. Recent studies have proposed the division of corticosteroids into three groups according to their cross-reactivity patterns based on patch testing and molecular models: Group 1: the non-methylated, most often non-halogenated molecules; Group 2: the halogenated molecules with a C16/C17 cis ketal/diol structure; Group 3: the halogenated and C16-methylated molecules (integrated by Alclomethasone dipropionate, Beclomethasone dipropionate, Betamethasone, Betamethasone 17-valerate, Betamethasone dipropionate, Betamethasone

sodium phosphate, Clobetasol propionate, Clobetasone butyrate, Desoxymethasone, Dexamethasone, Dexamethasone acetate, Dexamethasone sodium phosphate, Diflucortolone valerate, Diflorasone diacetate, Flumethasone pivalate, Fluocortin butyl, Fluocortolone, Fluocortolone caprylate, Fluocortolone pivalate, Fluprednidene acetate, Halomethasone, Meprednisone, Fluticasone propionate, Mometasone furoate). We report the case of a patient with contact dermatitis secondary to topical application of beclomethasone, without cross-reactivity with other steroids (of difererent and similar group). It is necessary to know the patterns of cross-reactivity in each patient individually.

1714
Contact allergic dermatitis exacerbated by enalapril

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Background: Inhibitors of Angiotensin Converting Enzyme (ACEI) are largely used worldwide, with approximately 40 million patients exposed to them for treatment of hypertension. A considerable number of patients experience Adverse Drug Reaction (ADR) in their skin; although there are few references in the literature of exacerbation of inflammatory skin diseases associated to these drugs, the systemic treatment with ACEI results in an increased cutaneous inflammatory response to allergens, together with increased manifestations of allergic contact dermatitis which is one of the most common inflammatory skin diseases in the industrialized worl. Nickel is the allergen routinely found during patch testing.
Method: Two females, 72 and 69 years, attended to Hospital Central de la Defensa. They were under treatment with enalapril. They were treated at emergencies department several times (more than five each one) showing an extreme pruritus and erythematous papules, edema and vesiculation in arms, legs, face and neck, after contact with metal objects: jewellery, coins, snaps and buttons. The lesions spred beyond the areas of initial contact (submental neck as well as medial arms or areas covered by jewellery).

Allergologic study: immediate and delayed prick test with standard allergens and food. Epicutaneous test with standard sensitisers and enalapril (International Contact Dermatatis Group); the patch test was performed taking enalapril and four months after withdrawal. Blood count, biochemistry, total IgE, eosinophil cationic protein, complement and immunoglobulins were performed.
Results: Patch test with nickel sulphate 5% was positive 3+ vesicles and bullae, and negative with enalapril in both of them.

Blood count biochemistry and standard skin tests were normal. Total IgE were 12.4 and 23 kU/l. Eosinophil cationic protein was normal. Complement and other immunoglobulins levels were normal.

Acute episodes disappeared after enalapril was withdrawn. Patch test persistied positive with nickel but only 1+/− macular erythema.
Conclusion: Patients subject to ACEI enalapril have an increased cutaneous inflammatory response of type IV hypersensitivity to nickel. The morbidity from ADR can be considerable, antihypertensive drugs are widely used and they should be taken into account in severe contact dermatitis. ADR caused by these drugs is resource-consuming and has a direct effect in the patients' quality of life.

1715
Allergy contact dermatitis by bronopol: case report

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Background: The bronopol (2-bromo-2nitropropane-1,3diol) is an antimicrobial compound used as a preservative, most commonly in drugs and cosmetic formulations like cleansing preparations, body milk, eyebrow pencil, shampoos, etc. These products contain bronopol in concentration from 0.01% to 1%, because over 1% is irritative. Over time it is degrading and forming formaldheido.

We present a case of allergic contact dermatitis by bronopol and the process carried out to reach that diagnosis.
Method: The patient is a woman 46 years-old with a personal history of atopic dermatitis.

On several occasions, after the use of a body milk, she's presented pruritic erythema and eczema injuries in the areas of application on her body, that improve with corticoids i.m and antihistamines, althought the injuries persist during 2 months. Last time she showed similar symptoms after using a hidrophilic ointment (Eucerin®).

We did a True test® patch test because is ready and easy to use, and includes the most common allergens, in accordance with the recommendations of the International contact Dermatitis Research Group (ICDRG).
Results: After removed the patch testing (true test®) at 48 and 96 h, the patient showed papules and erythema on the location of bronopol, being negative the rest of allergens (incluiding formaldehyde). With the symptoms of the patient and this result we reached the diagnosis of allergy contact dermatitis by this allergen (bronopol). We recommended to avoid products containing bronopol in their formulation.
Conclusion: Bronopol is an antimicrobial active against gram-positive, gram-negative bacteria, yeast and funghi. There are few cases described about contact dermatitis to bronopol without the coexistence of sensitisation to formaldheido. One reason could be that bronopol is an uncommon allergen.

1716
Eight month follow up of patients suffering from systemic nickel allergy syndrome after a year of oral nickel desensitisation

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Background: Oral nickel administration has been demonstrated useful in treating patients suffering from Systemic Nickel Allergy Syndrome (SNAS). In the published trials, the treatment lasted one year maximum and ended in general with a safe reintroduction of nickel rich foods in the diet by the majority of patients. At present, no follow up studies were published. In the present work we report a 8 month follow up of a group of patient previously treated by 1 year of oral nickel therapy.
Methods: Eight months after the discontinuation of a successfully oral nickel therapy, 20 patients were administered a questionnaire asking questions similar to the those to which they answered at the time of enrollment in the therapeutic trial. In particular, patients were asked to report cutaneous and gastrointestinal clinical symptoms, the tolerance to nickel rich foods (during the therapeutic trial they were provided three lists of foods according their nickel content, from the lowest to the highest) and to indicate in a VAS their clinical condition in relation to the SNAS, as they did at the end of the nickel desensitisation.
Results: Fifteen patients reported the reappearance of both cutaneous and gastrointestinal symptoms after 5–7 month from the discontinuation of the treatment when

ingesting the foods with the highest nickel content. In particular, they reported generalised itching, urticaria, meteorism and intestinal colic. Four patients were had gastrointestinal and cutaneous symptoms with the highest nickel containing foods after 4 months and of the medium nickel containing foods after 7 months. One patient still tolerated all nickel containing foods. VAS values were consistent with the answers to the questionnaires.

Conclusions: Oral nickel treatment in SNAS patients has been demonstrated clinically useful. However, one year treatment seems to be insufficient in maintaining the obtained beneficial effects as many patients progressively experience a reappearance of symptoms in relation with the food nickel content. Longer trials are needed to determine the optimal duration of the oral nickel treatment.

1717
Nickel may induce type I hypersensitivity

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Background: Nickel is a well-known hapten as an etiologic factor in type IV hypersensitivity reactions. Our aim was to evaluate the type of T helper cell response by determining the secreted cytokines in Ni-stimulated primary peripheral blood mononuclear cell (PBMC) cultures in nickel allergic patients.

Method: Patients who were determined as sensitive to nickel sulphate according to their patch test results and healthy subjects were enrolled into the study. Atopy, symptoms, familial history of nickel allergy, complaints with wearing jewellery were determined with detailed history. Lymphocyte transformation test (LTT) was performed with various concentrations of nickel sulphate in PBMCs. The LTT was considered as positive when the stimulation index was 2 or higher. IL-4, IL-10 and IFN-γ levels were detected in the culture supernatant by ELISA.

Results: Thirty-nine patients (30 female, mean age: 45.17 ± 15.03), ten healthy controls (eight female, 34.9 ± 12.06) were evaluated. Atopy, familial history, complaints with jewellery were determined in 13, 8 and 30 patients respectively. Various oral symptoms were reported in 27 patients. Skin symptoms and respiratory symptoms were found in 7 and 2 patients respectively. Three patients reported both oral and skin symptoms. The LTT stimulation index was significantly higher in the patient group than the control group ($P < 0.001$). Similarly IL-4 levels was found significantly higher in the patient group than the control group ($P = 0.035$), whereas IL-10 and IFN-γ levels were not different.

Conclusion: The significant increase of IL-4 found in the patient group suggests that the T helper 2 cells were the predominant responsive cells. This finding may be an evidence for Type I hypersensitivity to nickel in nickel allergic patients.

1718
A case of nickel allergy syndrome with extracutaneous symptoms

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Background: Nickel is the most common metal that causes contact dermatitis which is a long life disease. But apart from this form of hypersensitivity, patients may manifest systemic nickel allergy syndrome with cutaneous and extracutaneous signs like respiratory ones.

Case report: Hereby we present the case of a 34 year old female with dispnea and cough from 6 weeks. She referred also for angioedema and rash related to the usage of expensive creams, or another one that had nickel among its ingredients. After cream application she had eyelid angioedema and facial rash. The patient mentioned to have episodic dipnoea after almonds or cans of Red Bull energy drink consumption. The woman had suffered before from contact dermatitis after the usage of cheap earrings. Her son had atopic dermatitis during childhood. The skin prick test with food and inhalant allergens resulted negative. Patch test revealed positive results (+++) for nickel. We recommended her to avoid contact with metals and food with high concentration of nickel like almonds, canned food and beverages. We also prescribed her antihistamines, glucocorticoids. After 2 months she rarely had symptoms.

Discussion: Low concentration nickel diet lead to the improvement of the symptoms in some patients. But nickel is a kind of metal that is found in soil, water and food, so it not always easy to respect the physician advices. In some cases avoidance of metal contact is not sufficient because signs are not only locally seen only but even as o form of a systemic reaction (respiratory and cutaneous signs).

Conclusions: As nickel may aggravate contact dermatitis or even the symptoms of systemic nickel allergy syndrome, low concentration of nickel in diet plays an important role apart from the traditional treatment with antihistamines and corticosteroids.

Poster Session 78

Novelties in urticaria and its management

1719
Omalizumab treatment in patients with refractory chronic autoimmune urticaria-angioedema

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Background/purpose: The aim of this study is to investigate the efficacy and safety of omalizumab, evaluating the clinical course in three patients with refractory Chronic Autoimmune Urticaria- Angioedema (CAU-A).
Introduction: CAU-A affects about one third of all patients with urticaria. The mechanism leading to chronic urticaria often remains unclear. Up to half of patients are thought to have functional circulating IgG auto antibodies against the high- affinity IgE receptor (FceR1) or, in a few cases, even against IgE. These antibodies are able to release histamine in vitro from basophils and mast cells. The disease becomes uncontrolled despite the high doses of antihistamines and corticosteroids or additional immunomodulators, that are known to be unsafe and less desirable when used for prolonged terms. Taking into account that autoimmune aetiology is often related to severe urticarial cases, treatment with omalizumab may be an alternative regimen in patients who do not respond to conventional treatments.
Methods: We conducted an analysis of three patients with refractory CAU-A, who were recruited from the Department of Allergy at 'Hospital Gómez-Ulla' in Madrid, Spain. On an initial dose of omalizumab 225 mg every 2–4 weeks, the three patients achieved remission. The dose of antihistamines required to control CAU also decreased. No serious adverse events was noted.
Results: The respond to treatment in our cases was compared with reports from PubMed. Down regulation of FceR1 was observed in association with significant improvement and discontinuation of other immunosuppressive medications. The study demonstrates the effectiveness of omalizumab in treating this condition. However, the duration of disease is not related to treatment response. Instead, it is known to be a higher prevalence of personal or family history of allergic diseases in those who follow remission; which indicates that allergic diseases may be a favorable factor for predicting remission after omalizumab treatment.
Conclusion: The collective evidence points to omalizumab as a safe and effective treatment option for patients with CAU-A who do not sufficiently respond to standard therapy as recommended by the existing guidelines.

1720
Efficacy of omalizumab treatment in patients with refractory chronic urticaria

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Background: Chronic urticaria is usually controlled by sustained high doses of antihistamines either associated with leukotriene receptor antagonists or on their own. On some occasions symptomatology may persist, which requires the uninterrupted use of oral corticoids, assuming their consequent side effects. Here we present our experience in the treatment of this type of urticaria applying anti-IgE (Omalizumab).
Method: Six patients (three males and three females aged between 44 and 66) suffering from long-term urticaria (within the range of 2–37 years) and poorly responding to treatment have been treated. The initial dosage of Omalizumab was calculated on the basis of the patients' weight and total serum IgE level. Anti-IgE was administered every four weeks in all cases. In three patients the dose was increased up to 300 mg due to worsening during the days previous to scheduled dose administration.
Results: All the patients experienced marked improvement, which started at the beginning of the first week after the first dose. All the patiens discontinued oral corticoids and in four of them antihistamines were also withdrawn. The three patients who exhibited slight exacerbation symptoms during the days previous to the Omalizumab administration dose completely improved after increasing the dose up to 300 mg every four weeks. No adverse reaction was detected and presently the six patients remain asymptomatic and following the anti-IgE treatment.
Conclusion: Patients with long-term and poor outcome chronic urticaria responded favourably to Omalizumab treatment in all cases, achieving not only suspension of corticoid treatment but also withdrawal of remaining medication in most cases. It should be noted that in some cases the dosage calculated according to weight and IgE-levels seems to be insufficient, in which instance it is necessary to increase it up to 300 mg every 4 weeks.

1721
Effectiveness of omalizumab in a series of 114 patients with refractory chronic spontaneous urticaria

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Background: Chronic Spontaneous Urticaria (CSU) is a condition that impairs quality of life. Available treatments are symptomatic and there is not cure for this disease. It has been published the efficacy of Omalizumab to control CSU, even if patients are refractory to conventional treatments as H1 antihistamines (over half of patients).
Methods: We performed A retrospective descriptive analysis on data of 114 patients suffering refractory CSU that were treated in 9 Spanish hospitals with omalizumab as off-label treatment from Oct-2009 to Sep-2012. A total of 2032 of 150 mg Omalizumab doses were administered. The primary endpoint was the effectiveness in symptoms control and use of medication.
Results: Of 93 (81.6%) patients referred a complete or significant response. Of 13 (11.4%) patients showed a partial response and eight patients (7%) showed no

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response. In a subgroup of 38 patients urticaria activity score was measured and a significant decrease (5.34 ± 0.88 to 0.66 ± 1.3; $P < 0.005$) upon treatment was recorded. The use of concomitant medication significantly decreased ($P < 0.005$). Of 68 (59.6%) patients were able to withdraw all medication remaining asymptomatic just using omalizumab. Forty one patients stopped omalizumab (after 1–18 months) due to a good response but it had to be reintroduced in 20 (47.5%) because of relapse upon stopping Omalizumab controlling again 18 patients. No serious adverse events were reported.

Conclusions: This real life study shows that Omalizumab have an excellent profile in terms of efficacy/adverse events, with a response rate of 81% and only 7% of refractoriness in patients with CSU not controlled with high doses of antihistamines.

1722
Treatment of severe cold contact urticaria with omalizumab

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Case report: Cold contact urticaria (CCU) is a common subtype of physical urticaria. It is characterised by the development of wheal and/or angioedema within minutes after cold contact. We report 2 patients with cold urticaria with different response to treatment with omalizumab (Xolair®).

Clinical manifestation of CCU can range from mild, localised whealing to life-threatening anaphylactic shock reactions. Omalizumab has been described to be useful in cases of chronic urticaria and may be an interesting option for treatment of CCU. We describe one patient with significant and long-lasting improvement of symptoms and one without any improvement after anti-immunoglobulin E therapy. In our case reports, we want to highlight that there is still a small group of patients without benefit from omalizumab treatment. It is necessary to identify this minor subgroup of patients where omalizumab does not represent an effective treatment possibility.

1723
A case of idiopathic cold urticaria and anaphylaxis

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Background: Cold urticaria (CU) is a subtype of physical urticaria characterised by development of urticaria and angioedema after cold exposure. Symptoms typically occur in minutes after skin exposure to cold air, liquids and objects. Most common method to confirm the diagnosis of CU is ice-cube- challenge test but %20 of patients with CU have negative ice-cube challenge tests. The greatest risk with this kind of urticaria is development of systemic reaction resulting in a hemodynamic collapse during generalised cold exposure. We present a case who developed CU and anaphylaxis during swimming and diving in the sea.

Case: A 13-year-old girl was admitted to our hospital with history of multiple episodes of generalised urticaria while swimming in the sea. On the last episode she experienced feeling of fainting and dizziness after diving into the sea. She did not have any symptoms in warm water. There was no family history of cold urticaria. Her physical examination was normal. An ice cube challenge test was performed and it resulted a wheal within 10 min. Her laboratory tests were normal except for antinuclear antibody (ANA) titer. Her ANA titer was found 1/320 positive. Management of her condition involved avoidance of swimming in cold water and carriage of an adrenaline auto-injector.

Conclusion: Cold urticaria is a uncommon form of physical urticaria that can cause life threating reactions. We presented this case in order to draw attention to these systemic reactions and prevention strategies of cold urticaria.

1724
A case of progesterone-induced recurrent urticaria in a patient with polycystic ovary syndrome

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Background: Progesterone and its analogues have many medical applications in various obstetric and gynecologic conditions. Progesterone-induced urticaria is a rare disorder and typically occurs in females due to an autoimmune phenomenon to endogenous progesterone production, but it can also be caused by exogenous synthetic progesterone. Here, we present a case of recurrent urticaria that occurred after progesterone administration.

Case: A 32-years-old woman with polycystic ovary syndrome visited an allergy clinic due to whole body urticaria that occurred about 1 h after taking one table of oral progesterone. Previously, the patient had been treated with oral and injectable progesterone intermittently for anovulation and pregnancy without any side effect and allergic reaction. However she had experienced urticaria over a period of 1 month after an intra-muscular injection of progesterone 3 months ago. Intradermal testing revealed a positive progesterone reaction after 15 min, and subsequently, she complained of injection site swelling and pruritic urticaria that persisted for several days. The patient then underwent ovulation induction to evaluate response to endogenous progesterone and a mild but non-significant urticarial reaction developed.

Conclusion: We suggest that the potential risk of autoimmune progesterone-induced urticaria caused by exogenous progesterone be recognised and included in the differential diagnosis of recurrent urticaria that develops after progesterone administration.

1725
Comparison of the urea breath test with bacteriological investigation in detecting of *Helicobacter pylori* in patients with chronic urticaria

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Background: It is known, that Helicobacter pylori (*H. pylori*) is linked the pathology of the gastrointestinal tract. According to some authors, *H. pylori* may be the cause of the urticaria. But some patients with chronic urticaria have no clinical signs of gastroduodenal pathology.

Purpose: To compare the efficacy of diagnostic methods for detecting of Helicobacter pylori (*H. pylori*) in patients with chronic urticaria (CU).

Method: Forty-four patients were observed with CU, who had clinical and specific allergic examination and additional consultation of other specialists, including a gastroenterologist. During examination in all patients with CU pathology of the gastrointestinal tract was found. *Helicobacter pylori* infection was diagnosed with non-invasive method – urea breath test, and invasive method of bacteriological investigation during fibrogastroduodenoscopy. Gastric mucosal biopsy specimens were incubated at 37°C in nutrient substratum during 5 days. The amount of *H. pylori* was calculated in colony forming units per gram of gastric mucosa (CFU/g).

Results: Analysis of the data showed that 20 patients had positive urea breath test (45.5%). During bacteriological examination 17 patients had level of *H. pylori* contamination more than 104 CFU/g. This result had match with urease test in 85% of patients. Twenty-four patients had negative results of *H. pylori* urease test. In this case, bacteriological method did not confirm *H. pylori* infection also. All in all urease test showed sensitivity of 100% and a specificity of 89%.
Conclusion: Urease test has high sensitivity and specificity. We can consider that a non-invasive method for diagnosing infection *H. pylori* is sufficiently informative and can be recommended for screening in patients with CU to identify *H. pylori*, even if the patient has no clinical signs of gastroduodenal pathology.

1726
Features of chronic urticaria in patients with autoimmune thyroid disease

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Background: Patients with chronic idiopatic urticaria (CIU) very often have autoimmune thyroid disease (ATD). However, the impact of this disease on the urticaria has not been studied.
Purpose: To evaluate the features of chronic idiopathic urticaria (CIU) in patients with autoimmune thyroid disease (ATD).
Method: Sixty-five patients with CIU were examined clinically and for specific allergologic examination. Additionally they underwent Autologous Serum Skin Test (ASST). Severity of disease was determined by presentation of the main symptoms of the disease (number of urticarias and intensity of pruritus) and evaluated on a scale from 0 to 6. Patients were assigned to counseling other specialists, including endocrinologist.
Results: Twenty-eight patients (43%) with CIU were diagnosed with ATD, they had high level of antithyroid peroxidase antibodies (TPOab). Patients with a combination of CIU and ATD were included into investigation group, and the comparison group was consisted of patients (37 men) suffering from urticaria, but do not have a high level of TPOab. The median severity of chronic urticaria in patients with autoimmune thyroiditis was four points (2.38, 5.11), while in the comparison group this figure was equal to only three points (2.0; 4.0) ($P = 0.047$). In addition, in the study group ASST was positive in 64% patients, in the comparison group in 16% of patients, respectively. Should be noted that between the level of TPOab and the severity of the CIU, a direct correlation of medium strength ($r = 0.541$, $P = 0.048$), and between the same indicator and positive samples with ASST correlation was not valid ($r = 0.51$, $P = 0.079$).
Conclusion: Patients with CIU are very often diagnosed with autoimmune thyroid disease. The patients with combined CIU and ATD had more severe urticaria. The higher the level of antibodies to thyroid peroxidase linked to more severe CIU clinical course. In addition, patients with ATD more often diagnosed with autoimmune urticaria.

1727
Aetiologies of severe chronic urticaria in Reunion Island

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Background: Urticaria is a common disease in the dermatological-allergological outpatient clinic in daily practice. The aetiologies of chronic urticaria (CU) in tropical countries remains incompletely understood because of limited data. The aim of this study was to examine some of the possible etiologies of severe therapy resistant CU in a tropical island.
Method: We evaluated 63 patients, who had problems in controlling their urticaria by antihistamine drugs, referred from January 2005 to December 2011 to our unit. Complete history and physical examination were performed in all patients. Patients were investigated for complete blood count, erythrocyte sedimentation rate, blood chemistry, liver function tests, serum levels of complement C3, C4, and C1 inhibitor, free thyroxin, TSH, IgE total, infective panel, *H. Pylory* IgG antibodies, stool examination, Skin Prick Test (SPT) with inhalant and food allergens, patch test with European Standard Series. All patients were tested also to acetylsalicylic acid.
Results: One inducing factor has been found in 52.8%. Aspirin has been identified as urticaria provoking factor in 9%, atopy-18%, infection-14%, stress-7%, dermographism-9%, and pressure-6%. Parasites were found in 4% with clinical correlation. SPT to foods was positive in 6%, to inhalants-4%, positive reaction to patch test- 8%. 14 patients (22%) had positive *H. Pylory* antibodies. None of the patients had abnormal thyroid function test.
Conclusion: Half of our patients have multifactorial etiology. We present clinical clues and tips that can validate potentially relevant laboratory and allergy test to explore etiologies of CU in patients living in tropical countries.

1728
Cyclosporine in the management of chronic urticaria: the efficacy and safety data in Koreans

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Background: Cyclosporine has been proposed as next line treatment for H1-antihistamine refractory chronic urticaria (CU). There are limited data which support cyclosporine treatment in Korean CU patients. This study aims to evaluate the efficacy and safety of cyclosporine in the management of CU.
Method: The electronic medical records at the Seoul National University Bundang Hospital (Jan. 2003–Oct. 2012) were reviewed to identify CU patients treated with cyclosporine. Clinical characteristics and cyclosporine doses were compared between responders and non-responders. Outcomes and adverse reactions were also investigated.
Results: Total of sixty four patients was enrolled. Fifty four (84.4%) patients showed the improvement of symptoms; 25 (39.1%) achieved complete absence of urticaria. Ten (15.6%) of 64 showed no response. The clinical characteristics including total serum IgE, specific IgE to common allergens and autoantibodies were not different between the groups. The mean starting dose of cyclosporine was higher in responders than in non-responders (2.3 ± 0.9 vs 1.5 ± 1.1 mg/kg, $P < 0.05$). In 11 patients (20.4%) of 54, remission was sustained more than 3 months without any medication. Twenty nine patients (53.7%) required anti-histamine to sustain remission and 9 (16.7%) experienced symptom-aggravation and recurrence after the cessation of cyclosporine. Adverse reactions occurred in 42.2% ($n = 27$). Most common adverse reaction was gastrointestinal symptom. In four patients, cyclosporine was discontinued within first 1 month because of adverse reactions. Adverse reactions were tolerable in other 23 patients after dose reduction. Four (21.1%) of 19 patients who received cyclosporine for more than 6 months

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showed adverse reactions such as edema, hirsutism, nephrotoxicity and hepatotoxicity, respectively.

Conclusion: Adverse reactions were generally mild and reversible by dose reduction even in long-term treatment. With adequate starting dose and treatment period, cyclosporine could be an effective and safe therapeutic option for those with uncontrolled or steroid-dependent CU in Korea.

1730
Chronic idiopathic urticaria is associated with a high incidence of antibodies anti-IgE receptor

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Background: According to the research, auto-antibodies appear under the guise of etiology of chronic urticaria (CU) 'unknown' etiology. Among them, anti-IgE antibody deserves special interest. It is found that the etiologic factors of non immune form of chronic urticaria are: physical, psychological, infectious, autoimmune, etc. and various natural factors. Today, some doctors pick out so-called 'idiopathic chonic urticaria.' It is doubtful that the bases of this type of urticaria are autoimmune processes.

Objective: To study antibodies against IgE receptors in patients with idiopathic chronic urticaria.

Study Group: The investigation was made on 67 patients with chronic urticaria, 41 women and 26 men, from 18 to 54 years old.

Diagnosis was made with a comprehensive study of patients. Among them were: medical history, the whole range of instrumental and laboratory researches, selected for each of them separately. Analysis of these results showed that 21 patients – (31%) from 67 patients had a idiopathic chronic urticaria, almost one-third. Patients were divided into two groups: chronic urticaria (G1) and idiopathic chronic urticaria (G2). In control group (G3) were 11 women and seven men, age 15–42 years, who did not have various allergic diseases.

Method: All 86 patients were studied on carrying anti-IgE receptor antibody. For this ELISA kit was used, which sensitivity was from 0 to 200 ng/ml. Plasma were taken for analysis of acute period of the disease before treatment.

Results: G3 of Anti-IgE receptor ab amount were 0–5 ng/ml. In groups G2 105–362 ($m = 275 \pm 23$, 8, $P < 0.001$) ng/ml; in G1 – of 21–47 ($m = 34 \pm 4$, 5, $P < 0.035$) ng/ml.

Conclusion: Results show that in the group with idiopathic chronic urticaria 'autoimmune' indexes were statistically significant. This fact increases our suspicion that 'idiopathic chronic urticaria' is not always a truly idiopathic.

1731
Acute urticaria presenting in the emergency room of a general hospital

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Background: Many patients with acute urticaria are treated by their family physician, but acute urticaria is a common disorder that often prompts patients to seek treatment in the Emergency Department (ED). There are few data on acute urticaria presenting in emergency department. The aim of this study was to provide the demographic and clinical data of patients presenting with acute urticaria at the Emergency Department of Dimiccoli Hospital, the only acute care general hospital of Barletta, a 90 000 inhabitants town of South Italy. The predictive factors of the length of stay in the ED had also been investigated.

Method: The ED patients database was searched for urticaria by ICD-9 code and by keywords in the diagnosis description. All the medical records of the identified patients, in a period of 1 year of observation, were reviewed and the length of stay in ED was noted.

Results: A total of 459 patients (226 female, mean age 35 years) were admitted to ED with acute urticaria, out of a total of 44 112 attendances in 2011, corresponding to 1.01% of total ED visits and to 1.2 admission per day. The mean length of stay was 155 ± 74.9 min (range 20–420 min). Angioedema was present in 139 cases (30.3%), fever in 55 (12%) and associated symptoms in 73 cases, 29 of them fulfilled the criteria of anaphylaxis. Triggers could be identified in 193 cases (42%): drugs in 20.7%, followed by insects bites (10.2%), foods (7.4%) and contact urticaria in 3.7%. Patients were treated mainly with i.v. glucocorticoid (93%) and parenteral anti-histamine drugs (78%). Oral therapy was seldom administered Only one patient received oral glucocorticoid and 40 patients (8.7%) oral anti-histamine drug. Adrenaline was used only in 15 out of 29 cases of anaphylaxis (52%). Anaphylaxis ($P < 0.002$), food ($P < 0.05$) and drugs ($P < 0.05$) were significant and independent predictive factors of the length of stay in ED at multivariate regression analysis.

Conclusion: Patients with acute urticaria are frequently referred to the emergency room, but only in a few cases urticaria is associated with severe allergic manifestations. Drug and food hypersensitivity, together with anaphylaxis, are the best predictors of the length of stay in ED.

1733
Chronic urticaria associated with primary biliary cirrhosis in a patient with normal liver function tests

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Background: Chronic urticaria (CU) is a disorder defined as the presence of pruritus and urticaria over a duration of 6 weeks or longer. Currently, an etiology for CU is identified in only 5–20% of patients. According to recent ABIM and AAAAI Choosing Wisely Guidelines, clinical history and physical examination are necessary for the diagnosis of CU but routine laboratory evaluation is discouraged. We present a 44-year-old female with CU and normal initial laboratory values. However, further evaluation led to the diagnosis of Primary Biliary Cirrhosis (PBC).

Case presentation: The patient is a 44-year-old female with a history of Hashimoto's thyroiditis presenting with daily pruritus and urticaria for 6 weeks. The rash was refractory to treatment with OTC antihistamines but resolved after starting methylprednisolone therapy. Because the rash recurred one week after discontinuation of corticosteroid therapy, additional laboratory evaluation was pursued. The patient was started on colchicine and experienced complete resolution of her pruritus and urticaria.

Results: Initial laboratory work-up demonstrated a normal CBCD, ESR and negative histamine release assay, but her thyroperoxidase antibody and CRP were both elevated at 306 IU/ml and 0.69 mg/dl respectively. Following her second visit, hepatic panel, including GGT, were within normal limits, however the ANA panel was mildly positive at 1:40 and anti-mitochondrial titer (AMA) was positive at

1:640. Additionally, her mitochondrial M2 antibody was significantly elevated at 131 IU/ml. Given the positive AMA and M2 antibody titers, she underwent liver biopsy which showed granulomatous portal inflammation and bile duct inflammation diagnostic of PBC.

Conclusion: We are aware of only two case reports describing urticarial rash as the presenting symptom of PBC. This is the first case report of PBC with normal hepatic panel and GGT presenting with pruritus and urticaria. Current recommendations suggest minimising laboratory evaluation in uncomplicated cases of CU, however, this case describes an uncomplicated patient who after laboratory evaluation for CU was diagnosed with PBC. Therefore, we suggest a broader laboratory assessment should still be considered in patients with CU even in the absence of other signs or symptoms.

1734
Higher monocyte counts and increased erythrocyte sedimentation rates in severe chronic spontaneous urticaria

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Background: A uniform approach to severe chronic allergic and related diseases has been recently proposed in a MeDALL – GA(2)LEN – ARIA position paper (Int Arch Allergy Immunol. 2012). Concepts of disease severity, activity, control and responsiveness to treatment have been proposed as a way to streamline research and routine management. From the point of view of chronic spontaneous urticaria (CSU) a severe and refractory to treatment phenotype requires characterisation and identification of specific biomarkers.

Method: In search of such markers we carried out a study on 210 patients (mean age 42.4 years; range 18–81; 141 women): 130 patients with a mild CSU (mCSU) and 80 patients with difficult-to-treat severe CSU (sCSU). We investigated differences in demographics, clinical course (disease duration, age of onset, presence of angioedema and signs of delayed-pressure urticaria, corticosteroids use), autologous serum skin test (ASST) positivity, intolerance of non-steroidal antiinflammatory drugs, thyroid autoimmunity, Helicobacter pylori (HP) infection, blood hematology and biochemistry. In addition to these variables, 41 responders (R) to antihistamine treatment and 39 non-responders (NR) in the sCSU group were more extensively examined using physician-assessed symptom scores (0÷3) for wheals and itch, 100 mm visual analogue scales (VAS) for disease-related discomfort and for urticaria specific quality of life (UQoL).

Results: We did not find any differences in disease duration, presence of angioedema, signs of delayed-pressure urticaria, ASST positivity and HP infection. However, among the blood indices erythrocyte sedimentation rate (ESR) ($P = 0.005$) and monocyte counts ($P < 0.001$) stood out as distinct delimiters between mCSU and sCSU. In addition a trend was outlined for higher monocyte counts in NR sCSU ($P = 0.06$). As expected corticosteroid use was significantly increased in sCSU vs mCSU ($P < 0.001$), and in NR vs R groups; ($P = 0.004$); the NR sCSU patients had higher symptom scores ($P < 0.001$) and poorer UQoL ($P = 0.003$).

Conclusion: Higher symptom score, corticosteroid use and low UQoL are characteristic features of sCSU. Our data do not confirm observations that autoimmune CSU is related to the severity of the disease. Increased ESR and monocyte counts suggest that characteristic systemic inflammation is present in those patients. To our knowledge this is the first report of increased monocytes in sCSU.

1735
Association between blood coagulation and chronic urticaria

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Background: Chronic urticaria (CU) is a rather frequent skin disorder with an estimated prevalence of 0.5–1%. Recently, some evidence of the possible involvement of the coagulation cascade in the pathogenesis of CU has suggested. We evaluated the association of blood coagulation and CU.

Method: Twenty-one patients with CU were prospectively collected from January 2012 to July 2012. Platelet count, prothrombin time (PT), activated partial thromnboplastin time (aPTT), Fibrinogen, antithrombin III, FDP and D-dimer were measured.

Results: Of the total study patients, the mean age was 42.1 years and the mean disease duration of CU was 25 weeks. All the coagulation markers were within normal range. There were no significant correlation between coagulation markers and clinical parameters including disease duration, the presence of angioedema, atopy, except that disease severity of CU was inversely correlated with antithrombin III ($r = -0.531$, $P = 0.023$).

Conclusion: Blood coagulation markers in CU patients were within normal range. Disease severity of CU was inversely correlated with antithrombin III.

1736
Chronic urticaria and coeliac disease: suggestions from a clinical case

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Background: Many studies report an association between chronic urticaria (CU) and autoimmune disorders. In literature a link between CU and Coeliac disease (CD) has been previously reported, mostly in pediatric population. A 47 year old woman came to our observation reporting chronic urticaria with daily flares since the age of 42. No other symptoms were reported. She had only been diagnosed with autoimmune thyroiditis at the age of 41.

Method: A detailed hystory was collected. Blood tests, microbiological screening, autoimmunity blood markers, chest X-rays and head CT, abdominal echo scan, prick tests for common food and aero allergens were performed. Autologous serum skin test (ASST) was also carried out, following EAACI/GA^{2}LEN guidelines.

Results: The patient's history did not suggest any possible trigger factor for urticaria. All the investigations described above were negative. ASST were clearly positive ($ASST_{mean\ weal} - normal\ saline_{mean\ weal} \geq 1.5$ mm). Immunologic investigations confirmed autoimmune thyroiditis and surprisingly showed positive IgA antihuman tissue transglutaminase (hTTG) antibodies. Endoscopy with bowel biopsy was then performed, and CD was diagnosed. Our patient was put on a gluten-free diet with complete recovery of urticaria. Three months later she was reassessed. She had no urticarial lesions, normal value of hTTG antibodies was detected while positivity of serum antithyroid antibodies persisted. During the same follow-up assessment, ASST was performed both with the same day serum (negative result) and with the serum collected at the time of the first assessment (positive result).

Conclusion: Our report shows the importance of CD screening in patients with CU. CD screening should be performed whenever a positive ASST is detected, not only in children but also in adults, even in the absence of gastrointestinal symptoms and even in the presence of other known autoimmune diseases. In fact in our patient CD rather than autoimmune thyroiditis seems to play a role as the autoreactive component of urticaria, since the persistence of positivity of antithyroid antibodies only coexists with CU resolution and ASST shift. From a pathogenic perspective, persistence of skin reactivity to the serum collected at the time of first assessment, suggests that exclusion of an exogenous trigger rather than reduction in autoreactivity is at the basis of CU resolution.

Poster Session 79

Angioedema: a multifaceted health disorder

1738
Clinical similarities among different subtypes of non-hereditary angioedema

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Background: Non-hereditary angio-edema (AE) is characterised by local swelling due to self-limiting, subcutaneous or submucosal extravasation of fluid, and is divided in several subtypes. Clinical features of these subtypes are not profoundly described. We investigated the clinical characteristics of symptoms and potential differences in clinical presentation of AE subtypes.
Method: Patients presenting with AE at our tertiary outpatient clinic filled out a questionnaire to document clinical characteristics, potential triggers, location and severity of AE using visual analogue scales (VAS).
Results: 106/165 (64%) returned the questionnaire. Twenty-five patients had idiopathic AE, 64 urticaria-associated AE, 15 drug-associated AE, and two had AE due to other causes. Most patients reported prodromal symptoms (60%) and multiple locations for an attack (63%). Face and oropharynx were main locations of AE attacks of any subtype, swelling was the dominant symptom. Overall severity of the last attack was indicated as severe by 69% of the patients. There were no differences between the subgroups.
Conclusion: In spite of different aetiology clinical manifestations of non-hereditary AE subtypes are similar. These findings point to a final common biochemical pathway.

1739
A case of acquired angioedema associated with Waldenstrom's macroglobulinemia treated with rituximab

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Case report: We report a case of Waldenstrom's macroglobulinemia causing an acquired deficiency of C1 esterase inhibitor in a 40-year-old woman. She initially presented with an episode of angioedema followed by many episodes of abdominal distention associated with pain, vomiting, and diarrhea for 1.5 years. Work-up revealed low C1 esterase inhibitor levels, normal C3, and nonexistent C4. A diagnosis of acquired C1 esterase inhibitor deficiency was proposed at the time. However, it was also noted that her IgM was very elevated with an IgM monoclonal gammopathy with kappa light chains, and an enlarged spleen. Bone marrow biopsy and aspirate revealed clonal B-cells staining positively for CD20. She was diagnosed with Waldenstrom's macroglobulinemia in association with C1 esterase inhibitor deficiency. Although the association is recognised, it is extremely rare, and likely secondary to antibodies against C1 esterase inhibitor. After treatment with rituximab, cyclophosphamide, and prednisone, her paraprotein levels fell to normal range, and her autoimmune parameters normalised with significant clinical improvement. She has not had any further episodes of angioedema. She will continue on rituximab as maintenance therapy for two more years. In summary, acquired deficiency of C1 esterase inhibitor is quite rare with fewer than 150 cases in the literature. Given that most cases are related to antibodies against C1 esterase inhibitor, rituximab may be the treatment of choice.

1740
Hereditary angioedema with the signs of acute urticaria: a case report

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Background: Hereditary angioedema (HAE) is a rare autosomal dominant genetic disorder characterised by localised or diffuse swelling of an affected patient's face, neck, larynx, visceral organs, extremities, and trunk.
Purpose: To present a case with hereditary angioedema misdiagnosed like acute urticaria.
Method: Thirty-two year-old woman was presented to our hospital with 12 days of generalised skin purit and burning sensation of the whole body, breathing difficulties, abdominal pains with liquid on percussion, erythematous rash, facial and eyelid swelling with signs with palpebral conjunctivitis. She refers that she use to take oral contraceptives since 4 months. We treated her for acute urticaria with levocetirisine 5 mg at bedtime, fexophenadine 180 mg morning time, and methylprednisolone 125 mg intravenously every six hours without results on clinical icon, symptoms still persist. She was treated for the ocular conjunctivitis.
Results: Laboratory testing was performed and she had a low C4 level 13 mg/dl a low C1-INH level 5 mg/dl and an elevated CRP level 1.4 mg/dl. ECHO- abdomen shows the presence of liquid on abdominal cavity. The low levels of C4, low C1-INH levels, increased CRP, use of oral contraceptive pills, also no response to high dose steroid therapy, the diagnosis of HAE was made and she start treatment with intravenous infusion of C1-INH Berinert 20 U/kg of body weight/4 ml/min. She had totally improved with the this therapy.
Conclusion: Some times HAE may be misdiagnosed like acute urticaria and the physician must pay attention to the laboratory tests to confirm the proper diagnose and treatment.

1741
Angioedema: clinical review of the diagnosis, risk factors and management

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Background: Angioedema is a sudden, transient swelling of well – demarcated areas of the dermis, subcutaneous tissue, mucosa and submucosal tissue that can occur with or without utricaria. It is now generally accepted that the swelling is mediated by either histamine or bradykinin.
Method: We evaluated the clinical characteristics of patients treated for angioedema and determined the risk factors as well as management. We performed a review of 476 patient charts with primary or secondary diagnosis of angioedema over the per-

iod between January 2007 and December 2011 at University Hospital of Biaystok, Poland. The chart selection was conducted according to the International Classification of Diseases (ICD-10).

Results: The mean age of patients was 55.4 ± 20.1 years. There was a female predominance (65%) in our study. We found that 53% of the episodes occured without utricaria and 47% with utricaria. In aproximately 55% of cases the probable cause has been determined. Angioedema occurred most commonly in patients treated with NSAIDs, antibiotics ACE inhibitors. Other possible inciting risk factors include such as food, cosmetics, and insect bites. In 45% of cases it was unable to determine the cause. Moreover we have distinguished certain co-morbidities such as hypertension and thyroid diseases that accompanied angioedema more often than the others. Most patients were treated with intravenous steroids and histamine 1 or histamine 2 receptor blockers. Of these patients 7 presented low serum C1- inhibitor concentration and low serum C1-inhibitor activity.

Conclusion: The number of angioedema-related hospital visits had been increasing over the 5 year study period. Angioedema occured more often among female patients. The most common reason for an angioedema episode were drugs.

1743
Recurrent angioedema without urticaria – our experience

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Background: Angioedema (AE) is defined as nonpruritic, nonpitting areas of swelling that involves subcutaneous tissues or mucosa. Pathogenic mechanisms of AE without urticaria are poorly understood. The aim of our study was to characterise all patients with history of recurrent AE without urticaria observed in our outpatient clinic during 2011.

Method: Retrospective analysis of clinical data recorded during appointments for AE without urticaria in order to assess gender, age of symptoms onset, personal and family history of atopy, family history of AE, clinical manifestations, triggers, laboratory work-up, treatment, diagnosis and clinical evolution.

Results: Eighty-three patients were included, 60% female; median age of symptoms onset 45 years (5–85); 28% atopic; 41% had family history of atopy and one patient of AE. Face was the most common affected site (88%) and respiratory symptoms were present in 22% of patients. 56% were able to identify a trigger and drugs were the most frequent (62%). Thirty-three percent of patients were medicated with angiotensin-converting-enzyme inhibitors (ACEI) or angiotensin-receptor antagonists (ARA). These drugs were stopped in 37%, with resolution of AE in 70%. Abnormalities of autoimmune study were found in 13%; autoimmune thyroiditis was the most frequent associated disease (60%) but AE did not improve despite its treatment. Infections were found in 11% and appropriate treatment improved AE in two patients. One patient had low levels of C4 and C1q with normal C1-INH. The episodes resolved spontaneously in 21% of the patients. Antihistamines, corticosteroids or both were the main drugs used to treat attacks (94%). Epinephrine was used in three patients due to upper airway compromise. From the 54 patients (65%) that concluded the work-up, idiopathic AE was diagnosed in 46%, drug-induced AE in 28%, an association of both in 6% and autoimmune diseases or infections in 15%. Three patients were diagnosed Melkersson–Rosenthal syndrome, acquired AE with underlying LES and peripheral AE. The remaining miss appointment before completing the work-up (18%) or did not complete it during 2011 (17%).

Conclusion: In our study, as described in the literature, AE was more prevalent in women and face was the most common affected site. More than half of the patients identify a trigger and drugs were the most frequent one. Autoimmune diseases and infections were the main associated diseases. It was possible to establish a plausible diagnosis in 65% of patients.

1745
Follow-up of patients with drugs targeting the renin-angiotensin-aldosterone system-induced angioedema

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Background: Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are drugs that target the renin-angiotensinaldosterone system. Both drugs are widely used in patients with hypertension or ischemic heart disease. ACEIs or ARBs-related angioedema (ACEIs/ARBs-AE) is a well-documented condition, which seems to occur in up to 1% of treated patients. The aim of this study is to describe the clinical aspects of a cohort of ACEIs/ARBs-AE patients.

Method: We conducted a retrospective, observational, cohort study of 36 patients diagnosed of ACEIs/ARBs-AE. We studied the items: sex, toxic habits, familial or personal history of angioedema, onset of symptoms, characteristics of attacks (duration, frequency, treatment), antihypertensive involved, response to stop treatment and other relevant pathologies or treatments.

Results: Sixty-four percent of patients are male and 28% smokers. Personal history of histaminergic AE and/or chronic urticaria was finded in 33%. Just two patients presented family history of non-histaminergic AE. Median of onset of symptoms was 64 years old. ACEIs-AE were 67% of the total and the drugs most frequently involved were perindopril and ramipril. Just 8% of patients presented ACEIs plus ABRs-AE. Drug was prescribed from 7 days to 20 years before first attack. Attacks on the ORL region were observed in 97% of patients, with 30% of larynx attacks. Duration of attack was 24–96 h, with a frequency from one single attack to 5 episodes/month during several years. Treatment with corticoids and antihistaminics were ineffective in all attacks. Twenty-eight percent of patients were treated at least for one attack with Icatibant, C1inhibitor concentrate or tranexamic acid with improvement in every case. Icatibant was especially successful with an improvement of symptoms in 1–2 h. Only 19% of patients presented symptoms until 9 months after stopping drugs involved. Two patients also took gliptines with ACEIs. Two patients' attacks were also facilitated by the use of hormonal therapy to treat prostate cancer.

Conclusion: This study shows the clinical characteristics of ACEIs/ARBs-AE, in a French patients' cohort and the efficacy of specific treatments as icatibant or C1Inhibitor concentrate. Regarding of the frequency and the severity of this drug-induced disease, diagnosis and treatment have to be well known to improve care assistance.

1746
Report on a case of hereditary angioedema and pregnancy

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Background: Hereditary angioedema (HAE) is a genetic disease featured by either low levels of C1-inhibitor (type I) or

normal levels of ineffective C1 protein (type II); also, a type III is described as being associated with high estrogen levels or mutations in coagulation factor XII. Clinically, HAE presents with episodic attacks of swelling that may affect the face, extremities, genitals, gastrointestinal tract and upper airways, namely the larynx, which may lead to throat tightness. Possible precipitant factors include infection, trauma, extreme anxiety and pregnancy; the latter becomes important as estrogen levels significantly rise thereby increasing the risk of crisis. In pregnancy, prophylactic modified androgens, the recommended therapy when swelling attacks are frequent, becomes troublesome due to teratogenecity and are contra-indicated. Therefore, during pregnancy and breast-feeding, alternative therapies must be considered.

Case report: The authors present the case of a 38 year-old woman diagnosed with type II HAE at the age of 31. For the last 7 years she has been complaining of sudden and recurrent edema of upper/lower extremities and face mainly associated with minor trauma or dentistry intervention, respectively. Also, chronic abdominal colicky pain was described. This patient started on a daily androgen regimen (danatrol 100 mg) and aminocaproic acid as rescue medication, with complete disease control. At the age of 35, due to pregnancy attempting, this therapy was discontinued and she was started on weekly C1-inhibitor concentrate at Immunoallergology Day Care Unit. During the next 3 years, she suffered from three consecutive spontaneous abortions (before 12 weeks), with no known relation to disease progression. During the last pregnancy, positive antithyroid peroxidase antibodies were found (with normal thyroid function) and the patient was prescribed levothyroxine. Under this therapy combined with biweekly C1 concentrate infusions (due to increasing abdominal crisis), pregnancy was carried out and she delivered a healthy baby by cesarean section. She is now again taking the androgen regimen, with complete crisis remission, not needing C1 concentrate infusions.

Conclusion: This case highlights the importance of C1 concentrate during pregnancy. In this particular case, the therapy with levothyroxine appears to have been beneficial, but its specific role in the success of the pregnancy remains unclear.

1747
Case report of hereditary angioedema with anaphylaxis after hornet sting and consequent venom immunotherapy

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Background: Both hereditary angioedema (HAE) and venom anaphylaxis are potentially fatal conditions. Patients with HAE are at risk of mainly subcutaneous and submucosal oedema, laryngeal oedema being the most dangerous. Patients with anaphylaxis are at risk of cardiovascular collapse during systemic allergic reaction. Our patient was diagnosed with HAE several years ago. She experienced symptoms of erythema, urticaria, chills, fever, dysarthria, shortness of breath and faints in 2011 after hornet sting. Consequently she was hospitalised at the Intensive Care Unit and an examination for allergy to insect stings was recommended.

Method: We performed skin prick tests, examined specific IgE and IgG4 to venom extracts and their components and basophile activation test (BAT) with venom extracts was performed as well.

Results: Skin prick tests to venom extracts were negative; IgE to wasp venom 1.361 kIU/l; IgE to bee venom 1.811 kIU/l; IgE to rVes v5 2.3 kIU/l; IgE to rVes v1 0.401 kIU/l; IgE to rApi m1 0.00 kIU/l; IgE to CCD 0.001; BAT wasp venom 17%; BAT bee venom 11%. IgG4 specific antibodies: IgG4/wasp 1.71, IgG4/rVes v5 2.431, IgG4/rVes v1 1.521, and IgG4/bee 0.29.

Historically diagnosed HAE was confirmed by decrease C4 and C1 INHIBITOR (C1INH) levels impaired C1 INH function and mutation of C1 INH gene.

Conclusion: We confirmed allergy to wasp venom and we recommended venom immunotherapy (VIT) for this patient. However, we were concerned that VIT might cause attacks of HAE and so this treatment could be dangerous for the patient. Therefore we searched for similar experience with VIT in patients with HAE in the literature but unfortunately we failed to find relevant cases.

Nevertheless, given the history of Muller reaction grade III and examination results, we decided to administer wasp VIT. We began administering VIT Alutard (ALK-Abelló) in the standard regimen. The patient obtained a prophylactic dose of cetirizine 10 mg and danazol 200 mg on the day of VIT administration. During the treatment the patient has showed no adverse reaction to the VIT and she has had no HAE attacks in connection with this VIT. We therefore present this case report as our experience with this unusual and potentially hazardous combination of HAE and VIT.

1749
Hereditary angioedema: clinical differences among countries

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Background: Differences in the health care conditions and in the availability of specific treatments in different countries may influence the Health related quality of life (HRQoL) in hereditary angioedema due to C1-inhibitor deficiency (HAE-C1-INH) patients.

Method: From 2008 to 2010, within a study for development of an international specific HRQoL questionnaire for HAE-C1-INH, a self-administered clinical questionnaire was completed by patients from different countries. Data regarding last 6 months were collected. The results were analysed with statistical software SPSS v 9.0.

Results: Of 290 patients from 11 countries participated: Argentine (AR) 16 patients, Austria (AU) 18, Brazil (BR) 34, Canada (CA) 21, Denmark (DE) 27, Germany (GE) 42, Hungary (HU) 38, Israel (IS) 9, Poland (PO) 22, Romania (RO) 19 and Spain (SP) 44.

Home availability of plasma-derived C1-INH concentrate (pdC1INH) ranged from 0% (BR) to 97.4% (HU), self-administration of pdC1INH from 0% (BR, PO, RO, AR) to 7.4% (CA), administration of antiallergic drugs for HAE-C1-INH attacks from 0% (CA) to 35.6% (BR), patients with missed work days due to the disease from 21.1% (RO) to 66.7% (AR) and with

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missed school days due to the disease from 0% (CA) to 18.8% (AR). Patients with long term prophylaxis (LTP) varied from 27.8% (AU) to 73.5% (BR) and treated patients, used the following drugs: attenuated androgens 33.3% CA-100% AR, antifibrinolytics 0% (AU, GE, RO, AR)- 50% DK and pdC1INH 0% (HU, DE, PO, RO, AR, BR)- 66.7% (CA).

We also compiled data about rate of affected HAE-C1-INH children per patient (mean 23.3% IS-58.3% BR), age at onset of symptoms (mean 8.5 years. IS-14.0 years GE), age at diagnosis (mean 11.3 years IS-34.2 years RO, BR) and mean delay at diagnosis (2.9 years IS-23.3 years BR).

Conclusion: Although in the last years, knowledge about HAE-C1-INH and availability of new specific drugs for the disease have increased, and currently data are probably dissimilar from those shown, variability between countries with different socioeconomic and health care conditions still remain. Data presented may contribute to increase awareness of HAE-C1-INH situation in different countries and be useful for comparing with new data expressing the desirable improvement in managing this disease worldwide.

1750
Burden of hereditary angioedema for patients in Sweden; results from a retrospective patient registry survey implemented by a population based census SWEHA of patients with HAE type 1 and 2

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Background: C1INH deficiency causing hereditary angioedema (HAE) type 1 and 2 are rare orphan diseases characterised by spontaneous attacks of edema that interrupts the normal attack-free state. The quality of life (QoL) and productivity are affected by these attacks but there is a shortage of data to quantify these effects.

Method: A retrospective registry study of Swedish patients with HAE captured by the Sweha-Reg census. Questions related to patient demographics for age and sex and parameters as attack duration, location and severity were included. Inclusion criteria were at least one attack within the last 12 months. Utilities were calculated using EQ5D-5L and patient-reported sick leave was also analyzed to understand the factors responsible for productivity loss in patients with HAE. Patients completed EQ5D-5L questionnaires both for attack-free and acute HAE attack states. The EQ5D-5L answers were analyzed using the British references.

Results: From an initial mailing of 139 surveys a total of 103 valid responses were analyzed (74% response rate). Of the 103 patients 54 were females, 12 were under 12 years of age and 7 were 12–18 years of age. During the last 12 months 79% of these patients reported an attack. The total number of attacks reported per patient during 1 year ranged from 1 to 120 (geometric mean 7.23; SE 0.89). The EQ5D-5L scores for acute HAE attacks were associated with a significant utility decrement for all attacks ($P < 0.0001$). The HAE attack severity showed differences between the 'EQ5D today' and 'EQ5D attack' scores observed for mild (0.07, $P < 0.05$), moderate (0.369, $P < 0.0001$) and severe attacks (0.486, $P < 0.0001$). Increased attack frequency had also a negative impact on patients with HAE. The difference in 'EQ5D today' scores between the two populations with <30 and ≥30 attacks per year suggested that increased attack frequency had a negative impact even on 'between attack' patient quality of life (0.841 vs 0.679, $P < 0.02$). Thirty out of the 103 reported time off work with 75 days all together. Absenteeism was found to be significantly more likely with increasing severity of attack ($P < 0.05$). No significant relationship was found between the location of attack and patients' absenteeism.

Conclusion: Results from the Sweha-Reg study provide an insight to the burden on life for patients and society measured as significant impact on QoL and productivity loss that HAE has on patients in Sweden.

1751
The influence of age at first clinical manifestation of hereditary angioedema on the clinical course of the disease

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Background: Hereditary angioedema (HAE) is a rare disorder caused by functional C1-esterase inhibitor (C1-INH) deficiency and characterised by recurrent episodes of swelling. Initial symptoms usually occur during the first decade of life. There is uncertainty, however, as to whether disease severity is correlated with the age at first clinical manifestation.

Method: The relationship between age at first clinical manifestation of HAE and frequency of recurrences was retrospectively evaluated for 69 patients (group 1: early onset of symptoms at an age of 0–6 years [$n = 47$], group 2: later onset of symptoms at an age of >6–18 years [$n = 22$]). The course of the disease was defined based on the number of attacks per month (severe: ≥4 attacks/month, moderate: 1 to <4 attacks/month, mild: <1 attack/month). Attacks were treated with human pasteurised C1-INH.

Results: Overall, patients with an early onset of symptoms tended to be more likely to suffer from a severe course of the disease. In 6 patients (8.7%), who suffered from the most severe courses of HAE, the first clinical manifestation was at an age of <3 years. Treatment with human pasteurised C1-INH concentrate was efficacious and safe irrespective of disease severity.

Conclusion: The severity of the course of HAE seems to be associated with the age at first clinical manifestation. The threat of developing a severe course with early onset of symptoms underlines the importance of early diagnosis in families with a history of HAE to allow for an optimal management of the disease.

1752
Angioedema due to bradykinin in childhood. Early diagnosis of C1 inhibitor deficiency, a case report

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Background: Hereditary angioedema (HAE) by deficit of C1 inhibitor (C1-INH) is a rare autosomal dominant disorder characterised by recurrent episodes of subcutaneous edema and/or submucosa of the digestive and upper airway. Rarely these episodes are preceded by non-itchy rash (erythema marginatum). Its incidence is estimated at 1:10 000–50 000 people worldwide with no racial or gender predilection. Clinical presentations usually manifest in the second decade of life. There may be a 30% mortality in laryngeal edema attacks untreated.

Case: Seven year old girl referred to our Service by recurrent episodes of rash not itchy on the trunk and upper extremities. Abdominal pain and isolated episodes of angioedema of hands.

Previous diagnoses were virus diseases. She was once visited by the Surgery Department for abdominal pain, ruling out surgical pathology. Family History: Two

siblings. Father with a history of angioedema.

Method:

Skin tests (prick test) aeroallergens and food screening: negative.

Analysis: Normal blood count, total IgE 5.18 U/ml,

Immunoglobulins: A, G, M normal.

Study of complement: C3 133 mg/dl (85–180), C4 6 mg/dl (10–40)

C1-inh 4 mg/dl, (15–35), C1-inh functional UC1-In/ml 0.22. (0.70–1.30).

Study: thyroid, Autoimmunity: (ANAS, Anti-thyroglobulin and anti-microsomal): normal.

Family genetic study: SERPING1heterozygous mutation c.685 + 2 T> A (intron 4) in patient, father and sister.

Diagnostic: Hereditary angioedema type I C1 inhibitor deficiency (Quantitative and qualitative). Mutation previously undescribed.

Conclusion: HAE is a usually underrecognised and misdiagnosed disease, often the diagnosis occurs in later life. In this case the diagnosis was made in the child at an early age and later the father's diagnosis.

In the family genetic study shows a mutation not previously known.

Both the father and the girl in the clinical picture presented erythema marginatum manifestation only about 26% of patients.

It is important to establish an early and appropriate treatment of acute episodes, given its potential mortality (treatments antihistamines, corticosteroids, adrenaline is ineffective), a short-term prophylaxis in special situations and avoid certain triggers.

1754
How familiar are doctors in Turkey with hereditary angioedema?

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Background: Hereditary angioedema (HAE) is a rare but serious autosomal dominant disorder marked by swelling attacks in the extremities, face, trunk, airways, or abdominal areas that can be spontaneous or the result of several factors such as trauma. Attacks can be serious; the risk of dying from airway obstruction, has been estimated at 30%. In Turkey, the mean time between the onset of symptoms and the established diagnosis of the disease is as long as 26 years. One can argue that this unacceptable delay may arise from the relatively low level of awareness of the disease between doctors. In this study, we aimed to investigate the level of awareness of the doctors on HAE.

Method: A questionnaire consisting of 20 questions was performed in 155 persons randomly selected from internal medicine specialists participated in the XIV. National Congress of Internal Medicine in Turkey. In this questionaire, the basic questiones such as 'Have you ever heard of HAE?', 'Have you ever faced with a patient diagnosed with HAE?' as well as more specified questions like 'What is the name of the deficient protein in HAE?' were included.

Results: The responders were 71% male and 29% female; mean age 36.72 ± 9.02 years, range 24–64. The majority of the doctors (145 of 155, 93.4%) reported that they were aware of the presence of HAE and 42.8% of them (66 of 155), had followed at least one time a patient with HAE (67.7% of the doctors working in university vs 36.4% of the doctors in state hospitals, $P = 0.002$). 38.6% of the doctors did not have any idea about the pathogenesis of the disease. Only 22.2% knew that HAE was due to C1-INH deficiency. Doctors working in university facilities were more familiar with the pathogenesis of the disease than doctors in other institutions (38.7% vs 18%, $P = 0.014$). HAE was more frequently heard (known) among younger doctors (35.98 ± 8.23 vs 45.70 ± 13.26, $P = 0.047$). 62% of all doctors stated that urticaria could have accompanied attacks in HAE. Only 6% of the responders knew that the screening test for HAE was C4 level measurement. The screening test was also known more correctly among newer graduated doctors (9.87 ± 7.31 vs 12.99 ± 9.04, $P = 0.033$). A percentage as small as 6% reported that C1-Inh levels or function had to be checked for a correct diagnosis.

Conclusion: Our study showed that because of lack of awareness of the clinicians about HAE, the patients can be left undiagnosed for many years. Therefore, a national educational programme is required.

1755
Current practice with self-administration in the management of hereditary angioedema: the results of a survey

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Background: Hereditary angioedema (HAE) is an autosomal dominant disorder caused by partial deficiency of C1 inhibitor (C1-INH). Treatment regimens may involve short- or long-term prophylaxis and on-demand treatment for acute attacks. Therapy options include; pasteurised-nanofiltered (pnf) C1-INH (CSL Behring [CSLB] or ViroPharma [VP]); a bradykinin receptor blocker, icatibant; a kallikrein inhibitor, ecallantide (not approved in Europe [EU]) and recombinant C1-INH. pnfC1-INH and icatibant are indicated for self-administration. The aim of the survey, and follow-up international HAE expert meeting was to capture current practice for self-administered HAE treatment in the United States (US), Canada and the EU.

Method: A 16-question survey about self-administration of HAE therapy was sent to 21 centres (in the EU, US and Canada); 10 completed surveys were returned. Survey responses and discussions from the follow-up international HAE expert meeting were used to determine current practice for self-administered HAE therapy.

Results: All responding centres offer self-administration for HAE treatment and have observed that as awareness of this option grows, an increasing number of patients are being offered and are using it. Nine of ten centres provide patient training, however, training programme development varied between countries. Patient and physician benefits from self-administration include earlier treatment which may reduce attack length and severity, lower doses of medication and healthcare resource use as well as improved quality of life. The most widely used products were icatibant (49%), pnfC1-INH (CSLB) [47%] and pnfC1-INH (VP) [4%]. However, pnfC1-INH (VP) was not available in some countries at the time of the survey.

Conclusion: An increasing number of patients are being offered and are opting for self-administration therapy. Patient benefits include shorter time to symptom relief and shorter attack duration; physicians benefit from cost savings, a decrease in healthcare use and fewer emergency room visits. The two most widely used products, pnfC1-INH (CSLB) and icatibant, are used equally by patients opting for self-administration; however, national preferences are notable. The key to successful on-demand therapy appears to be patient training alongside robust nurse/physician support. Additional work is required to increase the number of patients opting for self-administration and thus maximise the benefits to HAE patients and healthcare providers.

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Poster Session 80

Atopic dermatitis and other dermatoses

1756
Severe atopic dermatitis treated with methotrexate

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Background: Atopic Dermatitis (AD) is a chronic disease with variable severity. Although most of the patients need only topical agents and sedating antihistamines, about 10% are refractory to these conventional modalities. Methotrexate (MTX) is an immunosuppressive drug, familiar to dermatologists, which has been used particularly in the treatment of psoriasis for more than four decades. In the past few years its eficiency in severe atopic dermatitis has been reported.

Case report: We report the case of an 24 year old male patient with 6 years history of atopic dermatitis refered to our clinic in a flare of eczema. In the first stage of disease symptoms were controlled with topical corticosteroids. In the past 2 years the patient had multiple severe flares requiring hospitalisation and prolonged systemic corticosteroids with early and frequent relapses after tapering off. Narrowband UVB phototherapy gave poor results.

Clinical examination revealed the presence of pruritic generalised erythematosquamous plaques, lichenification on the arms, scratching lesions, infraorbital folds, marked xerosis.

Blood tests were within normal limits except elevated levels of eosinophils. Due to extensive skin lesions, skin prick test could not been carried out. Specific IgE for house dust mites and animal dander (cat and dog) were extremely elevated (>100 UI/ml).

We started systemic treatment with corticosteroids, H1 and H2 antihistamines. After remission of skin lesions treatment with MTX was started as a weekly single 10 mg oral doze. Dose escalation was tolerated untill 22.5 mg/week was reached. The patient received 5 mg of folate every second day after MTX intake. After 12 weeks we achieved complete disease control.

Conclusion: MTX could be an efficient and safe alternative for treatment of moderate to severe AD with low response to conventional treatments. Prescribed during episodes of peak disease activity, MTX would be either tapered off when the disease subsided in response to therapy or maintained at the lowest efficient dosage. Placebo-controlled clinical trials are needed to demonstrate the effectiveness and safety of MTX in AD and to define its place as systemic therapy in moderate to severe AD.

1757
Allergen immunotherapy in severe atopic eczema – case report

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Background: Atopic eczema (AE) is a chronic inflammatory relapsing skin disease, often diagnosed in childhood (15–30%). It has a multifactorial etiology: skin barrier dysfunction, immune deregulation and IgE-mediated mechanisms. In the latter, aeroallergens and food allergens are the most important. Reports show that allergen immunotherapy (AIT) benefit these patients, leading to a sustained SCORAD decrease and reduced therapeutic needs, including steroids. The authors present a case report of a child with severe AE that improved after AIT.

Case report: Eleven-year old child with family history of asthma and history of persistent eczema since the age of 3 months in the retroauricular, malar, flexural, gluteal regions and inner thighs. As aggravating factors he mentioned heat, dust and irritant exposition, and nocturnal worsening. The progressive worsening of the lesions led to referral to Dermatology where he was treated with emollients, steroids, cyclosporine (for 2 years) and tacrolimus (for 6 months) with no improvement.

By age 6 his behavior disturbed school performance (need to leave the classroom to rub and hit his face for pruritus relief) and he presented sleep disturbance (awoke hourly), leading to evaluation by Psychology.

At age 8 he was referred to Immunoallergology for severe AE. He had cutaneous xerosis, erythematous lesions with scoriations at the malar and cervical regions, and erythematous and lichenified lesions with bacterial impetiginization in the back and flexural regions. At that time, SCORAD index was 90.2. He also had mild persistent rhinitis. Skin prick tests were positive for dust mites, cat dander, grass and artemisia pollens. Laboratory evaluation revealed eosinophilia (1500/μl), total IgE 5516 U/ml and specific IgE for *D. pteronyssinus* (D.pt) and *D. farinae* (D.f) >100 kU/l. He started flucloxacillin (qid), loratadine (bid), oxatomide (id), tacrolimus ointment (id) and emollients.

After clinical improvement was observed (SCORAD of 41.2 after 1 year of therapy with no need for oral steroids) he started sublingual AIT (50%D.pt + 50%D.f) with further improvement of the eczema, sleep pattern and scholar performance. Currently he is treated with AIT (2 years), loratadine bid and emollient, with a SCORAD of 23.8.

Conclusion: The authors present a case report of severe AE, with markedly reduced quality of life. Patient's clinical evolution demonstrates the benefits of an integrated immunoallergic approach, including AIT in selected cases.

1758
Atopic dermatitis and sexual behavior of women

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Background: Women with atopic dermatitis (AD) often suffer poor self-esteem, difficulties in social interactions, and significant psychological distress, which has an impact on their sexual and reproductive behavior. The aim of this research was to make a detailed assessment of AD impact on quality of life (QOL), with the focus on sexual behavior which contributes to an overall adults' well-being.

Method: One hundred and two female patients with AD (without exacerbation), age 16–55 years, were examined at the Occupational Diseases Outpatient Clinic and the Allergology Centre of Saratov

Medical University. Russian-language versions of validated Dermatology Life Quality Index (DLQI), Dermatology Specific Quality of Life (DSQL) and Women's Health Questionnaire (WHQ) were used. The impact of AD on QOL was measured on a scale, where higher index represents more significant behavioral problems and lower QOL.

Results: Respondents' QOL (according to DLQI and DSQL) was 31.3–65.7% lower in comparison with the best basic indexes of other dermatology patients. AD even without exacerbation decreased work productivity and had adverse effect on daily activities. The major negative impacts of AD were in the areas of socializing, self-esteem and sexual behavior. The most significant decrease of sexual activity was among young females (19–25 years) – only 50% were active vs 87% in other age groups. Sexual satisfaction of respondents (standard index of sexual behavior, according to WHQ) was 0.546 – lower in comparison with average 0.473 regional and 0.4 European indexes ($P < 0.05$). Self-perception of 'appearance' among patients was the lowest – index of 0.66 vs 0.56 in European and 0.44 in regional populations ($P < 0.05$). It is important to mention that DSQL proved to be more sensitive than DLQI (on the basis of data comparison of 52 respondents who filled both questionnaires) in describing clinical phases of AD, a better representation of behavioral characteristics and having more QOL scales.

Conclusion: Results confirmed statistically significant differences in AD female patients' QOL, as well as sexual behavior, which often depend on the level of patient's self-perception. It is suggested that clinicians should address these QOL issues via: better clinical management and therapy, patient education and being more alert to sexual behavior problems in female AD patients.

1759
Atopy patch test in children with atopic dermatitis

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Background: Atopic dermatitis (AD), a chronic intermittent inflammatory disease of skin, is frequently associated with allergy to foods and aeroallergens. The aim of this study was to study the result of atopy patch test and skin prick test with local lyophilised allergen extracts, Siriraj Mite Allergen vaccine (Df, Dp) and American Cockroach allergen extract in atopic dermatitis children.

Method: A cross-sectional study was carried out in atopic dermatitis children aged less than 18 years old. Atopy patch test (APT) and skin prick test (SPT) using local lyophilised cow's milk, egg white, egg yolk, wheat, soy and shrimp extracts, Siriraj Mite allergen vaccine and commercial extracts of American cockroach were evaluated. Oral challenge test were performed in the cases with informed consent from their parents.

Results: Fifty six atopic dermatitis children with median age of 2.08 years were included into this study. The APT and SPT were positive in 25.5% and 22.6% of the tests for food allergens respectively. The sensitivity, specificity, positive predictive value and negative predictive value of atopy patch test from this study were 40%, 90.2%, 65.2% and 76.6% respectively and those of SPT were 40%, 93.9%, 75% and 77.3% respectively. Positive APT for Df, Dp and American cockroach were 33.9%, 35.8% and 21.8% respectively. No serious complication from APT occurred.

Conclusion: The atopy patch test with lyophilised allergen extract in atopic dermatitis children showed high specificity, median positive predictive value but low sensitivity. The atopy patch test was safe, no severe reaction was found.

1760
A puzzlingly low incidence of atopic dermatis in Romania

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Background: The objective of this study was to evaluate the prevalence of atopic dermatitis in kindergarten children in Iasi-Romania, examined in December 2011. Six kindergartens were randomly selected and a total of 912 children were examined by the same dermatologist over a period of one month, in winter period (December 2011). Atopic Dermatitis was diagnosed according to UK Working Group criteria (accepted in Romania) and other skin modifications were noted and evaluated.

Method: The study was performed over one month period, in December 2011.To eliminate all variations regarding the diagnosis, the clinical examination was carried out by the same dermatologist, in the same period of time, between the 8 and 15 o clock, every day, with the exception of weekends. Six kindergartens were selected by the criteria of location (the same region of the city), the age of the children (pre-school children with ages between 3 and 7 years old), the type of kindergartens (prolonged stay-day care centers: from 8 am until 18 pm, two meals).

Iasi is the biggest city in the north-eastern part of Romania, with a population around 400 000 inhabitants.

All the children from the selected kindergartens were examined (in the presence of medical supervisor: GP doctor and nurses), with the written consent from the parents and the managers of the kindergarten. Questionnaires were not distributed not prior the examination nor after to the selected children and families.

A total of 912 children had an entire skin examination, all the skin lesions were observed and written down and all the data collected and sent to the Statistics Department.

The target population was based on age variable: 3–7 years old (pre-school children).

Results: The age range of the children was 3–7 years, but most of the children were aged 4–5 years (31.5%). Of all the children examined 95.94% of them were with normal skin evaluation at the date of medical exam, no history of allergies, with equal distribution related to gender.

Xerosis (in winter time) was noted to 23 children (2.52%), keratosis pilaris to eight children (0.88%), followed by a few cases of keratosis elbows (2 cases–0.22%), pityriasis alba (1 case–0.11%), xerosis palmaris (1case–0.11%) and two children with Atopic Dermatitis (0.22%).

Xerosis was prevalent in small children (3–4 years) with 4.60% and 6–7 years (3.57%).

Conclusion: The point prevalence of Atopic Dermatitis in this study was 0.22% overall.

1761
A new pharmaceutical formulation of cyclosporine A for topical administration: skin penetration and safety studies in Beagle dogs

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Background: Dogs are frequently affected with atopic dermatitis (AD). Nonetheless, the pathogenesis of AD has not been fully elucidated and the available treatment options are limited. Oral cyclosporine A (CsA) has been used to control canine AD, but adverse effects have been reported. A new formulation of CsA (2.25%) based on

chitosan nanoparticles has been recently developed in order to enable epidermal absorption, avoiding systemic side effects. The main objectives of this study were to evaluate the ability of CsA to penetrate into canine skin and to assess the safety of this new formulation.

Method: Skin penetration of CsA was performed in two Beagle dogs. Two milli litre of the new formulated CsA labelled with tritium, was topically applied to a 4 cm^2 cutaneous surface. Skin biopsies were obtained from control (before treatment) and treated areas, after 1, 6 and 24 h of CsA topical application. Skin samples were freeze-mounted in tissue holders and 8-μm frozen sections were cut and dipped in nuclear emulsion diluted 1:1 with distilled water. They were exposed in the dark at 4°C for 4–6 months, developed in Kodak D19 for 5 min, and fixed in Ilford Hypam fixer.

Safety analysis was carried out applying topical CsA ($n = 6$) and placebo ($n = 8$), two times a day for 45 consecutive days. Before and after treatments, blood samples were taken to perform haematological and biochemical analysis. Moreover, serum samples were collected after 1, 2, 4 and 6 weeks to quantify the CsA blood levels.

Results: The autoradiographic images showed that the new formulation of CsA was able to penetrate the epidermis and reach the upper layer of dermis. Moreover, CsA was observed in the hair follicles. Notwithstanding, only traces of CsA were detected in the dermis. Not quantifiable levels of CsA were detected in blood samples at any of the times studied. No changes in haematological and biochemical analysis were evidenced in any animal, during the study.

Conclusion: This study demonstrated that this new topical CsA formulation could be an effective and safe topical treatment for localised AD skin lesions, avoiding systemic side effects.

1762
The sensitivity and specificity of hypersensitivity tests with common aeroallergens in atopic dermatitis patients

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Background: We carry out the study on clinical relevance of hypersensitivity to common aeroallergens in patients with atopic dermatitis (AD).

Method: We tested 29 children and adults with AD for hypersensitivity to grass and birch pollen and house dust mites (HDM) using atopy patch test (APT), skin prick test (SPT) and specific IgE measurement. A history of AD exacerbation as a result exposure to allergen was obtained. Clinical score of AD (SCORAD) and the number of days with need of topical anti-inflammatory treatment (AITD) were recorded during 1 year. The period covered pollen season as well as 6 weeks of mite avoidance regimen. Sensitivity (SE) and specificity (SP) of the tests were calculated on the basis of history, SCORAD and AITD changes.

Results: Up to now, 29 subjects completed the whole study period. APT was positive in 18 patients, mostly to HDM ($n = 13$). SPT and/or specific IgE were positive in 16 subjects, in most cases to grass pollen ($n = 12$). SE and SP calculated on the basis of history or SCORAD changes were higher: SE of APT 13–67%, SP 43–75%; SE of SPT and specif. IgE 0–67%, SP 62–88%; if calculated on the basis of SCORAD changes SP of HDM hypersensitivity tests was higher. SE and SP of hypersensitivity tests calculated on the basis of AITD were inconsistent. Clinical relevance of detected hypersensitivity was higher in patients positive to the same allergen both in APT and SPT/specif. IgE.

Conclusion: AD is often associated with hypersensitivity; however, its influence on AD is clinically significant only in minor group of patients. The clinical relevance assessment of hypersensitivity test on the basis of SCORAD changes looks promising, especially in HDM allergy. The clinical relevance assessment based on changes in need for antiinflammatory treatment seems to be unsuitable.

1763
Targeting of GATA-3 by DNAzymes as therapeutic approach for the treatment of atopic dermatitis

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Background: GATA-3 represents the master transcription factor in the development of allergic immune reactions and is the central regulatory molecule in the differentiation and activation of Th2 cells. It is necessary and sufficient for Th2 cytokine expression in CD4-positive T cells. Thus, it represents a promising target for therapeutic intervention.

DNAzymes are catalytically active single-stranded DNA molecules that consist of two binding domains flanking a central catalytic domain. They represent a particular class of antisense molecules combining the superior specificity of antisense molecules with an inherent catalytic activity making them an attractive tool for the specific interference with disease-causing target molecules. For therapeutic intervention with GATA-3-mediated immune reactions we have developed a GATA-3 specific DNAzyme – called hgd40.

Method and results: In the studies presented here we demonstrated the efficacy of hgd40 formulated in a newly developed water-in-oil-in-water (W/O/W) emulsion in a model of oxazolone-induced allergic contact dermatitis in mice. This model is designed to induce prolonged skin swelling reactions thereby enabling the analysis of treatment effects on T cell-mediated pathomechanisms.

Treatment with topically applied hgd40 significantly and dose-dependently reduced oxazolone-induced skin swelling reactions. Infiltration of inflammatory cells into the skin was also reduced by treatment with hgd40. No adverse effects due to hgd40 or the emulsion were detected, while treatment with dexamethasone, though very effective with respect to skin swelling and infiltration, showed clear adverse effects like scaling and skin atrophy.

Conclusion: In summary, targeting of GATA-3 by the DNAzyme hgd40 represents a new and promising therapeutic concept for the topical treatment of allergic skin diseases.

1764
Prevalence of vitamin D deficiency and clinical efficacy of vitamin D supplementation in Korean patients with atopic dermatitis

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Background: Vitamin D deficiency was associated with increased prevalence of atopic dermatitis (AD). Vitamin D supplementation resulted in significant clinical improvements in patients with AD in a few studies. We evaluated the prevalence of vitamin D deficiency and the clinical efficacy of vitamin D supplementation in Korean patients with AD.

Method: Serum levels of 25-hydroxyvitamin D [25(OH)D] were measured by radioimmunoassay in 102 patients with AD (mean age: 23.2 years, range 4–64 years). Vitamin D deficiency was defined when serum levels of 25(OH)D were <20 ng/ml. Fourteen adult patients with AD were

supplemented with 2000 IU of vitamin D (cholecalciferol) daily for 2 months.
Results: Vitamin D deficiency was observed 88 (86.3%) of 102 patients with AD. In 14 adult patients with AD, the clinical severity score of atopic dermatitis (SCORAD) significantly decreased from 45.2 ± 27.6 (mean ± SD) at baseline to 30.3 ± 20.5 at 2 months after supplementation of vitamin D ($P = 0.01$). Mean decrease in SCORAD value at 2 months compared to baseline value was 28.0%. Serum levels of 25(OH)D were significantly increased from 12.4 ± 5.3 to 26.6 ± 7.8 after supplementation of vitamin D ($P = 0.001$). There was no significant changes in peripheral blood eosinophil counts before (414.7 ± 258.9) and after (351.6 ± 212.2) supplementation of vitamin D ($P > 0.05$).
Conclusion: Vitamin D deficiency was prevalent in Korean patients with AD and vitamin D supplementation resulted in significant clinical improvements.

1767
Adult atopic dermatitis and allergic asthma treated with omalizumab: case series

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Omalizumab is an established add-on therapy efficacious in allergic diseases with additional antiinflammatory activity in the treatment of asthma. Isolated case report show the efficacy of anti-IgE in recalcitrant atopic dermatitis, a skin disorder characterised by elevated levels of IgE, a disease with significant morbidity.

We report of five adult patients with chronic severe atopic dermatitis and moderate bronchial asthma treated with oral steroids and immunosuppressive therapy such as cyclosporine or Methotrexate. The patients two male and three women, mean age 34.6 (range 19–48) started treatment with Omalizumab 375 mg every 2 weeks. Pretreatment IgE levels ranged from 282–5390 IU/ml (mean 2501 IU/ml). After 16 weeks the serum IgE levels resulted lower mean 1146 IU/ml,(range 147–3088) and a significant clinical improvement was registered in all patients with reduction of skin lesions and pruritic score (from nine indicating severe itching to 3) and asthmatic exacerbations were reduced. After 1 year follow-up of Omalizumab therapy, the IgE levels were 620 IU/ml (range 140 to 1000) and the patients experienced no adverse events.

Conclusions: Anti IgE Omalizumab is effective in improving atopic dermatitis unresponsive to conventional therapy in patients with concomitant asthma after few weeks of treatment. Further studies and biological effects of this treatment are required in this setting.

1768
Successful treatment with anti-IgE (omalizumab) in child with severe atopic dermatitis

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Background: Treatment options in severe atopic dermatitis in childhood are limited and adverse effects of systemic immune suppressive treatments are extremely high. Omalizumab is a humanized monoclonal antibody against IgE and has been approved for the treatment of severe asthma in children above 12 years or adults in most of countries. There are few case reports that omalizumab can be successful in severe atopic dermatitis in children above 6 years of age. But there is no report in the literature about the use of omalizumab in children under 6 years of age. Here we emphasized the successful treatment of omalizumab in a 4-year old child with severe atopic dermatitis who did not respond to the conventional treatments. The patient partial responded to the systemic steroid and cyclosporine.
Case: Four-year old girl was diagnosed with severe atopic dermatitis since 14 months of age in our outpatient department. She had a concomitant food allergy and mild asthma without aeroallergen sensitisation. She was previously treated conventionally including emollients, topical steroid and topical calcineurin inhibitors but her lesions did not respond. She had benefit from systemic steroid treatment but steroids were interrupted because of suppressed hypothalamic-pituitary-adrenal axis. Thereupon cyclosporine treatment was given to her. She had benefit from cyclosporine treatment but the severity of atopic dermatitis increased quickly after cessation of cyclosporine therapy. Because of long time using of cyclosporine than suggested by literature we decided to find out an efficient and safe systemic treatment option for controlling her dermatitis. Finally she was treated with 150 mg of omalizumab subcutaneously, repeated at 2-week intervals. Absolute eosinophil count was 500 and total IgE level was 216 kU/l at the beginning of the treatment. After three months of omalizumab, her SCORAD index was decreased from 71.5 to 44.6 (37.6% reduction according to the initial) and her treatment is still continuing without need of any topical steroid. Although she was monitored closely there were no potential adverse effects of treatment.
Conclusion: This is the youngest case demonstrating the success of omalizumab treatment in severe atopic dermatitis in childhood. Based on this case we suggest that omalizumab may be a useful and safe treatment option for severe atopic dermatitis in young children.

1769
High risk IgE food sensitisation to egg, milk and peanut in young children with moderate to severe atopic dermatitis in a large, single centre cohort

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Background: We aimed to explore the relationship between high levels of IgE food antibody responses and atopic dermatitis (AD) in a large, single-centre cohort of young children with predominantly moderate to severe AD.
Method: Consecutive patients presenting to a dedicated AD pediatric outpatient clinic were recruited. A detailed clinical history was recorded. The Nottingham Eczema Severity Score (NESS) and CAP FEIA measurements for total IgE and IgE antibodies to the three most common food allergens: cow's milk, egg and peanut were measured. Previously reported age and allergen specific 95% positive predictive values (PPVs) associated with positive food challenge outcomes and food allergy (FA) were used to define subjects as having high risk IgE food sensitisation (FS).
Results: One thousand four hundred subjects (mean age 3.3 years) were recruited. Complete data was available on 1354 patients. All patients were atopic (total IgE >0.35KU_A/l). The mean NESS was 11 (moderate AD). Patients with severe AD were significantly more likely to have high risk IgE FS to cow's milk, egg and peanut compared to those with mild AD. Egg was the most commonly identified food allergen, with patients with severe AD being most at risk. The total IgE score was also significantly higher in the severe AD group. For a subset of 400 patients the age of onset was recorded. The frequency of high risk IgE FS to milk, egg and peanut was the greatest in patients who's AD developed in the first 6 months of life compared to those who developed AD after 6 months of age.

Conclusion: Patients with moderate and severe AD, with onset before 6 months of age should be treated with a high level of suspicion for food allergy.

1770
Sucessful use of colchicine in refractory normocomplementemic urticarial vasculitis

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Background: Colchicine, a microtubule polymerization inhibitor, has been shown to decrease mast cell degranulation, suppress leukotriene generation and decrease leukocyte adhesiveness and migration. It is considered as second-line therapy in chronic urticaria.
Method: We describe the case of a 40-year-old woman referred to our clinic with daily pruritic wheals, periorbital and lips swelling, difficulty in swallowing and episodic dypsnea of 1 year duration. The lesions lasted more than 24 h and resolved without sequels. The urticaria activity score was (UAS) 6. She had a history of epilepsy, anemia, hypothyroidism and celiac disease. The patient was treated with daily anti-H1-antihistamines (maximum doses) and periodic cycles of corticosteroids with no adequate control.
Results: Skin tests were negative from aeroallergens and commercial extracts of food, latex, Anisakis, profilin and peach LTP. Laboratory: complement (CH50, C3, C4, C1-inhibitor), renal and liver function, antithyroid and antinuclear antibodies, stool parasite exam, hepatitis B and C serology, immunoglobulins and thorax X-rays were all within the normal range. Erythrocyte indices in blood count and thyroid function revealed lower values. Skin biopsy revealed acute inflammatory perivascular infiltrate mainly consisting of eosinophils. We introduced colchicine (1 mg/24 h) and within the first month the patient elicited a rapid improvement of her symptoms so dose of antihistamines was decreased (cetirizine 10 mg each 2 days) and oral corticosteroids were discontinued.
Conclusion: Our patient suffered from severe, longstanding and persistent urticaria symptoms. We use colchicine because no other alternative medications could be used due to her co-morbidities. Colchicine appears to be an effective and economic treatment in non-responding patients with urticarial vasculitis in order to avoid side effects resulting from long term use of corticosteroids.

1771
A case of hypocomplementemic urticarial vasculitis due to coxsackievirus type A9

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Background: Urticarial vasculitis is characterised by episodes of uncontrollable urticaria and by biopsy evidence of leukocytoclastic vasculitis. It has been reported to accompany infection, malignancy, connective tissue diseases such as systematic lupus erythematosus(SLE), viral hepatitis, and cryoglobulinemia, and the administration of certain drugs. Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a type III allergic reaction characterised by urticaria with persistent hypocomplementemia. HUVS has been frequently been described in adults, but is very rare in children.
Method: We examined a 1-year-old girl who presented with continuous fever and multiple urticarial rashes and wheals on her face, trunk, back and limbs. Treatment with an antihistamine was ineffective. We performed a skin biopsy to examine pathologic tissue, and collected specimens by nasopharyngeal swab specimens as well as stool and blood specimens for microbiological examination using MRC-5 (human embryo lung fibroblast) cells.
Results: Laboratory tests revealed the following findings: white blood cell (WBC) count, 21 200/μl (neutrophilis 76%), total protein, 5.6 g/dl, albumin, 2.8 g/dl, FDP 12.8 μg/dl, D-dimer, 9.1 μg/dl, and C reactive protein, 13.55 mg/dl. The C3 level, (16 mg/dl), C4 level, (1 mg/dl), CH50 level, (5.9 mg/dl), and C1q level (1.5 μg/ml) were extremely low. Antinuclear antibody (ANA) was not detected. At first, we thought that the patient had Kawasaki disease, but a skin biopsy revealed early lesion of leukocytoclastic vasculitis. Permeation of lymphocytes and histocytes with nuclear dusts (products of the destruction of neutrophil nuclei), eosinophiles and neutrophils had occurred around the superficial dermal blood vessels, and leakage of the blood cells from the capillary vessels was observed. These findings led to a diagnosis of HUVS. We therefore treated her with prednisolone 2 mg/kg/day, gradually reducing the dose after the urticaria had disappeared. We isolated coxsackievirus type A9 (CA9) from the all samples (nasal fluid, blood, and stool). The neutralising antibody against CA9 in the convalescent phase serum was significantly more elevated than that in the acute phase serum.
Conclusion: Infection by the coxsackievirus type A9 may cause HUVS.

1772
A case of atypical cutaneous urticarial vasculitis associated with thrombosis

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Introduction: Urticarial vasculitis (UV) is characterised by pruritic, burning or painfully raised, superficial, erythematous or edematous, circumscribed wheals, foci of purpura and induration. The individual urticarial lesions last frequently more than 24 h and leave a residual transient hyperpigmentation. Urticarial vasculitis is most commonly idiopathic and it may be systemic or localised to the skin.
Case: Seventeen year-old boy admitted our hospital because of rashes on his various body region, angioedema and edema on his left arm. He had no fever, weakness and other symptoms of systemic involvement. On his physical examination he had some erythematous, painfully rashes without wheal formation on his palm, soles of the right feet and left elbow. Left arm had diffuse minimal edema but there was no hyperemia and pulselessness. Other physical examination was normal. He had not any history of chronic disease and there was no medical history of thrombosis in his family. Laboratory tests for etiology of UV were normal except for erythrocyte sedimentation rate and C-reactive protein. He underwent doppler USG and it revealed thrombosis of left axillary vein. Ethiological causes of thrombosis were investigated and heterozygous Factor 5 Leiden mutation was detected. Biopsy of skin revealed urticarial vasculitis. He diagnosed as idiopathic urticarial vasculitis and venous thrombosis. He was treated with low molecule weight heparine and a oral antihistamine.
Conclusion: We present an atypical case of UV without wheals which is associated with venous thrombosis. These are two distinct entities that are not reported together previously. Urticarial vasculitis may present without wheal formation and it may be confused with other situations. If there is any clinical suspicion of UV, skin biopsy must performed although C3–C4 complements are normal.

1774
The efficacy of immunotropic agents in the treatment of psoriasis

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Background: Psoriasis is a chronic immunologically mediated genetically determined dermatosis. Hyperactivity of the immune system and metabolic disorders are known to be its essential pathogenic mechanisms. The aim of our study is to find out the efficacy of *S*-adenosyl methionine and *γ-glutamyltryptophan in a complex therapy of psoriasis*.

Method: Twenty-six patients of 20 to 50 years old presented with 1 to 5-year moderate psoriasis history were under study. The mean PASI index was 53. Eleven patients were given 800 mg of S-adenosyl methionine every other day (total 14 doses). Another ten patients were given two 7-day courses of 1 ml of γ-glutamyltryptophan intramuscularly, with a 2-day interval between them. Five patients were given γ-glutamyltryptophan and S-adenosyl methionine simultaneously. All these patients also applied zinc pyrithione cream on the lesions two times a day. The assessment of the course effectiveness was made on the 7th and the 28th day.

Results: On the 7th day the mean PASI index was noted to have decreased by 15% in S-adenosyl methionine taking group, it appeared to have decreased by 26% in γ-glutamyltryptophan taking group. In patients taking both γ-glutamyltryptophan and S-adenosyl methionine PASI index has decreased by 40%. On the 28th day of therapy in one patient of the latter group the regressing stage of psoriasis was noted, with the mean PASI index being 5. Marked clinical effect was also registered in the group of patients taking γ-glutamyltryptophan, with the mean PASI index being 20. The course with S-adenosyl methionine showed less effect, with the mean PASI index being 35.

Conclusion: Thus, the simultaneous course of γ-glutamyltryptophan and S-adenosyl methionine showed maximal clinical effect when given with conventional therapy. These patients demonstrated maximal remission duration for a year. The combination of immunodepressants and hepatoprotectors, therefore, seems worth of using in psoriasis therapy.

Allergy © 2013 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd, **68** (Suppl. 97), 498–636

Poster Session 81

Pediatric asthma and rhinitis

1775
Exhaled transforming growth factor-β1 levels after exercise challenge in children with asthma

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Background: Transforming growth factor-β_1 (TGF-β_1), is believed to be involved in the pathogenesis of asthma by promoting the fibrosis and remodeling in asthma. Besides its pro-fibrotic property, TGF-β_1 has antiinflammatory activity related with its induction of T regulatory cells. There is conflicting data concerning the role of TGF-β_1 in the pathogenesis of airway hyperreactivity (AHR).
Objective: To investigate the role of exhaled TGF-β_1 and interleukin (IL)-4 in EIB in asthmatic children.
Method: Fifty-six asthmatic children were evaluated with exercise challenge and exhaled TGF-β_1 and IL-4 levels. Exhaled breath condensate was collected before and 30 min after exercise challenge. TGF-β_1 and IL-4 concentrations were determined using a specific immunoassay kit.
Results: At baseline, no significant difference in EBC TGF-β_1 levels was found between the EIB group ($n = 25$) and the non-EIB asthmatics ($n = 31$). After exercise challenge, a significant difference in EBC TGF-β_1 levels was found between the EIB group and the non-EIB asthmatics (106.4 pg/ml [91.4–126.4] vs 125.4[104.2–186.65], respectively; $P = 0.04$). There was a statistically significant increase in TGF-β_1 levels after exercise challenge in the non-EIB asthmatics (before exercise: 117.9 [36.7–181.3]; after exercise: 125.4 [104.2–186.65]; $P = 0.008$). A statistically significant increase in the concentration of TGF-β_1 levels was not noted after exercise challenge in the asthmatics children with EIB (before exercise: 124.1 [20.7–149.1]; after exercise: 106.4[91.4–126.4]; $P = 0.56$). Pre-exercise TGF-β_1 levels strongly correlated with ACT score, baseline FEV_1%, and IL-4 levels ($P = 0.01$, $r = 0.49$; $P = 0.02$, $r = 0.35$; $P = 0.001$, $r = 0.51$; respectively). Post-exercise TGF-β_1 levels negatively correlated with eosinophil percentage ($P = 0.005$, $r = -0.42$) and positively correlated with maximal post-exercise decrease in FEV_1 ($P = 0.047$, $r = 0.31$). There was no significant increase in the concentration of IL-4 levels after exercise challenge in the asthmatics with or without EIB.
Conclusion: Our study showed that TGF-β_1 may have a role in the suppression of EIB which is a physiological example of the AHR. It has been shown that blockage of TGF-β_1 may result in an increase in AHR in an animal study. Our findings showed that TGF-β_1, the cytokine associated with regulatory T cells, may have a role in well asthma control and better pulmonary function tests.

1776
ST13 polymorphisms increase the risk of exacerbations in steroid-treated asthmatic children and young adults

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Background: The clinical response to inhaled steroids in asthma varies between children and might be associated with single nucleotide polymorphisms (SNPs) in various genes.
Method: We performed a meta-analysis of three cohort-studies: PACMAN ($n = 357$, age: 4–12 years, the Netherlands), BREATHE ($n = 818$, age: 3–22 years, United Kingdom), PAGES ($n = 391$, age: 2–16 years, United Kingdom). Genes were selected based on their role in the glucocorticoid signaling pathway or a previously reported association with asthma. Two outcome parameters were used to reflect exacerbations:
1 asthma-related hospital visits and
2 short course(s) of oral corticosteroid (OCS) use in the previous year.

The model was adjusted for age, sex and treatment step. ORs were meta-analyzed assuming random effects with the inverse variance weighing method. *Q*-values were calculated to account for multiple testing. Identified associations were replicated in a fourth study: CAMP ($n = 172$, age: 5–12 years, USA). CAMP was included in a second meta-analysis to test the robustness of the findings.
Results: In a meta-analysis of PACMAN, BREATHE and PAGES two SNPs in *ST13* were associated with severe exacerbations despite corticosteroid treatment. An additive genetic model was assumed. *ST13* SNP rs138335 increased the risk of asthma-related hospital visits (OR = 1.35 per G allele; 95%CI 1.07–1.70, OR: 1.35, $P = 0.01$, $q = 0.25$). Rs138337 had a similar effect (OR = 1.36 per G allele; 95% CI: 1.11–1.67, $P = 0.003$, $q = 0.11$). In addition, rs138335 was associated with OCS use in the previous year (OR = 1.33 per G allele; 95% CI: 1.11–1.59, $P = 0.002$, $q = 0.11$). The two SNPs were not associated with risk of severe exacerbation in CAMP. However, when CAMP was included in the meta-analysis the two SNPs were significantly associated with both outcomes. In the meta-analysis of the four studies rs138335 increased the risk of hospital visits (OR: 1.28 per G allele; 95% CI: 1.03–1.59, $P = 0.02$, $q = 0.36$), as did rs138337 (OR: 1.31 per G allele; 95% CI: 1.07–1.59, $P = 0.007$, $q = 0.19$). Furthermore, both SNPs were associated with OCS use in the previous year (rs 138335: OR per G allele: 1.18; 95% CI: 1.01–1.38, $P = 0.03$, $q = 0.41$; rs138337: OR per G allele: 1.28; 95% CI: 1.09–1.54, $P = 0.003$, $q = 0.10$).
Conclusion: A novel susceptibility gene, *ST13,* which codes for a chaperone of the glucocorticoid receptor, is associated with the occurrence of exacerbations in asthmatic children and young adults despite corticosteroid treatment.

1777
Asthma exacerbation in childhood – sputum profile and pulmonary tests

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Aim: To describe the changes in the indicators of pulmonary function tests (PFT) and sputum cytology characteristics in children with bronchial asthma (BA) during exacerbation.
Method: Forty-one children with confirmed BA (21 girls and 20 boys, median age 12, 12 years), admitted in the hospital due to exacerbation, defined by GINA criteria (2008 modification). Multiple PFT during treatment period were performed. All children provided spontaneous or induced sputum for investigation.
Results: An upward trend in indicators FEV1, FVC and MMEF with increasing of the age ($P = 0.06$) was noted. No statistically significant correlation between age and sex of patients and PFT was found. Characteristic findings of sputum cytology were the presence of eosinophils in all of the tested materials, the percentage of eosinophils ranged from 1% to 15%. Twenty-nine patients (70.73%) had ≥3% eosinophils. We could not find inverse correlation between the percentage of neutrophils and eosinophils, which is probably due to the fact that during the exacerbation, sputum cytology characteristic is heterogeneous. A reverse correlation has been demonstrated only in studies of patients with asthma in a stable, controlled state, also gender difference with higher eosinophil percentage in boys by some authors, was confirmed in our results, but the data were not statistically significant (boys-3.9%, girls- 2.8%, $P = 0.27$).
Conclusion: PFT and sputum cytology examination in exacerbation of BA are informative and safe.

1778
The combined leucotrienes inhibitors and vitamin D3 treatment with viral induced bronchial asthma children

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Background: To increase the effectiveness of viral induced bronchial asthma treatment in children.
Method: Under our observation were 126 children with viral induced bronchial asthma, where more than 80% of all exacerbation cases were present not due to atopic allergens, but with simultaneous respiratory infections. The age of all patients was from 3 to 14 years. The all study population was divided into two groups – the first one with moderate – severe bronchial asthma history inhalant glucocorticosteroids standard treatment with additional leucotrienes inhibitors (Montelucast Natrium) ($N = 64$), and the second – standard treatment with leucotrienes inhibitors and additional vitamin D prescription 2000 IU during 20 days ($N = 62$). Only moderate severity cases were included. Clinical examination also included peak flow rate investigation, computed spirometry and X-Ray examination when it was necessary. Laboratory examination included general blood tests, serum immunoglobulines with allergen specific IgE level determination and specific allergen skin tests.
Results: Our research results showed that in children of the second group who were treated with additional Vitamin D the incidence of viral induced bronchial asthma was reduced in 24 (37.5%) cases and the frequency of exacerbations decreased in 21 (33.8%) cases. Laboratory data revealed that in this group significantly decreased the level of IgE in 1.2 times – 239.33 ± 53.12 compared to children without such treatment ($P < 0.01$).
Conclusion: Thus, in conditions of increased viral infections in autumn-winter period children with bronchial asthma living in conditions of extremely continental climate are recommended preventive treatment with vitamin D additionally to standard and antileucotriene treatment.

1779
Acute obstructive bronchitis as a risk factor for bronchial asthma in children

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Background: The frequency of occurrence of bronchial asthma (BA) in children with acute obstructive bronchitis (AOB) was analysed quantitatively on the basis of a follow-up study.
Method: One hundred and sixty-four children (av. age 5 years, 62.34% male and 37.66% female) admitted to hospital with AOB symptoms were supervised during 1 year in a children's clinic after discharging from hospital. Based on initial diagnoses, it was distinguished between a main group (I) of 114 children with AOB and a control group (II) of 50 children with BA.
Results: The analysis of anamnestic data showed that half (49.12%) of all children fell ill with AOB symptoms for the first time during the first year of their life and the share of such children was statistically significant greater ($P < 0.05$) in II than in I. Children of II showed genetic predisposition toward allergies five times more often than those of I (60.0% vs 12.5% resp.). Children of II were born from pregnancies accompanied by mothers' viral respiratory tract infections and acute attacks of chronic somatic diseases 4 times more often than those of I (32.0% vs 8.8% resp.). The majority of children observed (77.1%) were full term born and had normal birth weight, 19.1% of children observed were born SGA and only 3.8% of children observed were born LGA; there were no statistically significant differences concerning these criteria between both groups. The latter applies to the type of feeding as well: the majority of children received breast feeding up to the age of 4 months, and only 14.0% of children were switched to artificial feeding during their early months. Among the children of II, 1/3 were proven to have food allergies; 1/3 were proven to have house dust mite allergy; the etiology of asthma could not be established for the remaining 1/3. Children of II had concomitant allergic diseases: allergic rhinitis (20.0%) and atopic dermatitis (55.0%). During continuous ambulatory supervision of children, BA was diagnosed in 25.4% of children of I, worth mentioning these were children with complicated allergic histories. These children were prescribed basic therapy. Remaining children of I had no symptoms of AOB. As a result of rehabilitation measures, the frequency of acute respiratory diseases decreased among the latter ones. The analysis of all identified BA cases showed that BA was diagnosed on an average as late as 4 years after onset of its first symptoms.
Conclusion: Based on the study, on average, every fourth child diagnosed as having AOB also has BA.

1780
Bronchial hyperresponsiveness in a pediatric population with persistent rhinitis

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Background: Nonasthmatic subjects with allergic rhinitis often have bronchial hyperresponsiveness (BHR), a risk factor for later development of asthma. The presence and degree of atopy is correlated with the presence of BHR in patients with asthma. The present study was aimed to compare BHR to methacholine and to exercise

challenge testing in children with persistent rhinitis and its relationship with the presence of atopy.

Method: We evaluated the presence of BHR in a sample of non-asthmatic children with persistent rhinitis by means of methacholine challenge and exercise challenge testing (ATS protocol). Bronchial hyperresponsiveness to methacholine was considered if PC (20) was <14 mg/ml. Positive result in exercise challenge testing was defined as a 15% decrease in forced expiratory volume in 1 s (FEV(1)) post-exercise. Clinical examination and skin prick tests to inhalant allergens were performed in all patients.

Results: Forty children with persistent rhinitis allergic to house dust mite (23 male/17 female), aged from 7 to 17 years, were enrolled. BHR to methacholine and exercise challenge testing was observed in 34 (85.0%) and 7 (17.5%), respectively. There was no association between BHR post-exercise and the presence of atopy, whereas BHR to methacholine was more frequent in atopic patients. All patients with positivity in exercise challenge test were also positive in methacholine challenge test. Moderate to severe HBR to methacholine was only present among the atopic group (28.6%), while mild HRB was similar between atopic and non atopic group (46.4% and 50.0%, respectively).

Conclusion: HRB to methacholine was found in a significant proportion of children suffering from persistent rhinitis, independent of the atopic status. Severe BHR was detected in allergic pediatric patients and may be a marker of early bronchial involvement. In this study, the exercise challenge was not a suitable test for the detection of HRB. We recommend a systematic evaluation of HRB, in pediatric patients with persistent rhinitis.

1781
Exhaled nitric oxide and asthma control in children and adolescents: a cross-sectional study

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Background: Asthma is a chronic respiratory disease characterised by hyper-responsiveness and bronchial inflammation. It is the most common chronic disease among children and has an important personal, family and socio-economic impact. The bronchial inflammation in these patients can be monitored by measuring the fractional exhaled nitric oxide (FENO).

The aim was to determine the FENO association with therapy, peak expiratory flow (PEF) and disease control inferred by the Global Initiative for Asthma (GINA).

Method: Observational, analytical and transversal study of children with asthma, 6–12 years-old, followed in the Outpatient Respiratory Pathology of Braga Hospital. Sociodemographic and clinical information were collected through a questionnaire. FENO and PEF were determined by portable analyzer Niox Mino® and flow meter, respectively.

Results: The sample is constituted by 101 asthmatic children, 63 (62.4%) of males and 38 (37.6%) females. The mean age (SD) of participants in the sample is 9.18 (1.99) years. The logistic regression performed with the cutoff value obtained by ROC curve, revealed that FENO ($b_{\text{FENO Levels}} = 0.85$; X^2_{Wald} (1) = 8.71; OR = 2.33; $P = 0.003$) has a statistical significant effect on the probability of changing level of asthma control. The ratio of chances of going from 'controlled' to 'partly controlled/uncontrolled' is 2.33 per each level of FENO.

Conclusion: The probability of an asthmatic children change their level of asthma control, from 'controlled' to 'partly controlled/uncontrolled', taking into account a change in their FENO level, increases 133%.

FENO, in asthmatic children, appears to have a predictive value in the inference asthma control.

1783
Features of clinical symptoms of asthma in children with different phenotypes of connective tissue disorders

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Background: Changed clinical symptoms of asthma (A) in children with symptoms of connective tissue disorders (CTD) are the source of various medical errors, inappropriate care, development of complications.

Aim: To study the features of the current clinical course of A in children with manifestations of CTD.

Method: Sixty-three pediatric patients with A aged 1–3 years (group A, $n = 8$), 4–7 years (group B, $n = 28$), 8–12 years (group C, $n = 18$), 13–18 (group D, $n = 9$) were observed during a 1-year period. Moderate persistent asthma occurred in 90.4% of the studied patients, in 3 (4.8%) and 3 (4.8%) – mild persistant and severe persistant respectively. All patients had multiple phenotypic signs of CTD.

Results: In 25 patients (39.7%) long-term exacerbation was caused by community-aquired pneumonia (CAP) caused by atypical pathogens: in 44.4% – by Mycoplasma pneumoniae (MP), in 12.7% – by combination of MP with Cytomegalovirus (CMV). In 32 patients (50.8%) prolonged bronchial obstruction in A exacerbation occured together with allergic rhinitis (AR). Development of pulmonary hypertension (PH) in 8 (12.7%) patients, pulmonary fibrosis – in 7 (11.1%), emphysematous bullae (EB) – in 4 (6.3%) and spontaneous pneumothorax – in 1 (1.6%) was revealed in C and D groups. 42 (66.7%) patients had unclassifiable phenotype of CTD (UP-CTD) (children of groups A and B), 17 (27%) patients – Ehlers-Danlos-like CTD phenotype (EDP-CTD), (patients of groups B and C), four patients of group D(6.3%) had Marfan-like CTD phenotype (MP-CTD). Adolescents of group D in six cases (66.7%) had PH, in 5 (55.6%) – PH and PF, three patients of which (33.3%) – EB and 1.6% – SP. In patients with MP-CTD were observed all the mentioned complications.

Conclusions:

1. Close relationship is revealed between A and CTD.
2. More severe A occurred in patients with CAP, AR with EDP-CTD and MP-CTD.
3. Development of complications – PF, PH, EB, SP, was in all adolescents with the MP-CTD.
4. Assessment and identification of the following A clinical phenotypes in children: an infectious-associated; AR-associated; CTD associated – is perspective.
5. The occurance of MP-CTD suggests more severe A with the development of complications, such as PF, PH, EB, SP.

1784
Impact of the family on childhood asthma

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Background: The relation between socio-economic status and allergic diseases in childhood is controversial. Some studies have proposed childhood asthma to be more common in families with low socio-economic status.

Aim: To assess the impact of the family on asthmatic children as the relation between socioeconomic status, parental smoking and family history of allergic diseases and asthma control.

Method: A case control study of 230 asthmatic children (6–18 years) residing in

Assiut, Egypt were enrolled. The database included data on demographics, health status, asthma control, and health-related quality of life. Socioeconomic status: the following characteristics were used to define socioeconomic status: level of education of father and mother. Information was also collected on their occupation and income. Maternal and paternal diagnosed as asthma, or other allergic conditions were examined as a risk for developing childhood asthma. Indicators of disease severity including symptom scores, attack frequency, medication use, hospital attendance, and life threatening bronchospasm were correlated to socioeconomic status, smoking and the family history of allergic diseases.

Results: Asthma was common among males (62.2%), most of them lived in poor rural areas. Only 10% of patients met the requirements for acceptable control, while 22% had intermediate control, and 68% had unacceptable asthma control. Children from families in lower income had poorer control. Impact of socioeconomic status; parental education and their jobs; there was a decreasing risk of asthma with good control with increasing socioeconomic status. The OR for asthma was 2.33 (95% CI 2.17–5.66) comparing the highest and the lowest socioeconomic groups. Parental smoking history, Asthma in general positively related to household smoke exposure. Parental smoking was more strongly associated with wheezing among non-atopic children OR 2.2 (1.3–3.8).

Family history of asthma or other allergic diseases, maternal asthma was most strongly associated with asthma in the child (OR = 2.2, 95% CI = 4.9 to10.5). Paternal asthma was weakly associated with childhood asthma. Similarly family history of other allergies significantly increases risk of childhood asthma.

Conclusion: Asthma was more common in lower socioeconomic groups with poor asthma control. Parental smoking was associated with more severe disease. The odds of having a child with asthma were three times greater in families with one asthmatic parent.

1785
Adolescence, atopic disease and quality of life: a comparative study

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Background: The importance of quality of life in health care practice and research is steadily growing and in the last decades an increasing effort has been made to understand the impact of atopic disease on Health-Related Quality of Life (HRQL) in children and adolescents.

Purpose: To assess the HRQL of adolescents with controlled atopic disease and compare the results with healthy controls in an urban area of northern Portugal.

Material and methods: Cross-sectional study involving adolescents (10–18 years old) with controlled atopic disease from hospital outpatient clinic and healthy students. A self-administered generic questionnaire (KIDSCREEN-52®) was used. A confidence level of 0.05 was considered.

Results: Of 364 participants, 122 with controlled atopic disease (62 – asthma, 27 – rhinitis, 30 – asthma and rhinitis, 3 – food allergy) and 242 healthy controls. The age median was 13 years in the atopic disease group and 15 years in the healthy group. There was a significant male predominance in the atopic disease group (62.9% vs 51.3%, $P = 0.034$). Compared to healthy controls, atopic adolescents presented lower HRQL scores in the physical well-being ($P = 0.015$) and social support and peers ($P = 0.038$) domains, but higher scores in the psychological well-being ($P = 0.014$), moods and emotions ($P = 0.005$) and self-perception ($P = 0.004$) domains. Despite there was no significant difference in the school environment domain, we found a higher school retention rate among atopic adolescents ($P = 0.027$). There were no significant differences in any domain comparing asthma and rhinitis groups or comparing adolescents with one atopic disease and those with asthma and rhinitis.

Conclusion: Similarly to previous studies, controlled atopic adolescents presented lower HRQL scores concerning to physical well-being and peers relationship. Unexpectedly, they presented higher HRQL scores related to psychological well-being, emotions and self-perception issues. This can be explained by a good disease control or reflect a limitation of the study by using a generic instrument. We were unable to demonstrate a deleterious effect of atopic disease in HRQL regarding family relationship or economic issues. Further studies could contribute to the long-term implementation of measures to improve the HRQL of adolescents with atopic disease.

1786
Humoral immune status in children with recurrent wheezing associated with ENT disorders

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Aim: Evaluation of total IgE and serum levels of immunoglobulins A, M, G in children with recurrent wheezing associated with ENT.

Method: The study included two groups of children aged 6–12 years. The study group was consisted of 68 children (13.7%: 95% CI 11.1 to 16.6) with recurrent wheezing associated with ENT (otorhinolaryngology) and control group of 544 children (86 3%: 95% CI 83.4 to 89.9) with recurrent wheezing solitary. The total concentration of IgA, IgM, IgG and serum level of IgE was determined by ELISA. The accumulated material was processed in the database of Statistical Epi Info program.

Results: The serum level of IgE in the study group permitted us to found the increased concentration (174.5 ± 37.6 ME /ml) in children with recurrent wheezing associated with ENT disorders compared with children only with recurrent wheezing (83.6 ± 7, 6ME/ml, $P < 0.02$). The level of IgA (0.8 ± 0.1 mg/ml) has tendency to be reduced in the study group (children from the control group – 0.9 ± 0.04 mg/ml, $P > 0.05$). The serum concentration of IgM in the basic group does not differ from the values of control group (1.74 ± 0.1 mg/ml, 1.73 ± 0.1 mg/ml, respectively, $P > 0.05$). It was highlighted increased levels of IgG equal to 10.8 ± 0.5 mg/ml at the basic group (7.2 ± 0.1 mg/ml, $P < 0.01$ in children in the control group).

Conclusion: Humoral immune changes are confirmed by increasing levels of IgG in children with recurrent wheezing associated with ENT diseases which are influenced by the negative impact of chronic infectious process, allergic mechanisms are presented by increased values of total IgE.

1788
Prematurity, low birth weight, cesarean, and pediatric allergy, their role in chronic respiratory disease and the bronchial hyperresponsiveness

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Background: In a retrospective study that included children from birth to age ten, we investigated the association between low birth weight, prematurity and cesarean section compared with the control group and role in the hygiene hypothesis.

Method: Period of investigation from 2002 to 2012. Of 173 children were monitored with discernment exclusion, compared with the control group with clinic, biochemical respiratory function and skin prick test were used, complemented with X-ray diagnosis, allergy personal family history.

Results: Term infant: 32.36% of which at normal birth were: 30.35% and cesarean section: 69.64%, Preterm: 67.63%: Neonatal hospitalisation: 67.63% with oxygen requirements: Halo O_2: 58.97%; mechanical ventilation: 41.02%; Sepsis: 41.02%; History family allergy: positive: 78.03%, unknown: 21.96%; one allergic parent: 45.18%, both allergic parents: 54.81%; IgE: normal: 15.02%, elevation: 84.97%; Skin Prick Test: 17.91 negative: 82.08% positive for aeroallergens; Age of mother at birth: <20 years: 13.87%, between 20 and 39 years: 84.97% >39 years: 1.15%; Socioeconomic Status: Low: 50.28%; Medium: 46.82%; Height: 2.89%.
Conclusion: Prematurity, low birth weight, and cesarean section, they are linked with chronic respiratory disease and/or airway hyperresponsiveness in postnatal life. Perinatal events, may play a role in the lack of response to maintenance therapy or rescue for bronchial obstruction at various stimuli, opening one of the paths to the allergic march. So it is important to identify this risk group from the birth because it allows us to anticipate with therapeutic agents, the changes in the airway and in this way eliminate or decrease the impacts and as a consequence a better quality of life.

1790
Evaluation of relationships between birth-related factors and asthma

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Background: Asthma is the most common chronic childhood disease responsible for a significant impairment in physical, emotional, psychological and spiritual aspects of life. Currently, there is a controversy regarding risk factors of asthma, specially birth-related factors. The aim of this study was to evaluate relationship between asthma and birth-related factors.
Method: In this case-control study, 30 children between 3 and 12 years old with asthma were selected as the case group, and 90 non-asthmatic children were included in the control group after matching based on age and sex. Data about birth-related factors affecting asthma for both groups was collected and compared between two groups.
Results: The results showed that the majority of the children in the case group were boy and born by cesarean section. There were significant differences in factors such as pre-term born (OR = 2.53 CI 95% 0/98–6.75), family history of asthma (OR = 3.52 CI 95%: 1.03–10.16) and residency in the city (OR: 16.28 CI 95%: 5. 99–44.28) between two groups.
Conclusion: This study showed family history of asthma, residency in city and preterm born are associated with susceptibility to asthma. But there was not any relationship between asthma and type of delivery and time of breast feeding periods.

1791
Nasal symptom score as a predictor of nasal obstruction in children affected by persistent allergic rhinitis

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Background: Allergic Rhinitis (AR) is a chronic inflammation of the nasal mucosa clinically defined by itching, sneezing, nasal blockage or congestion.

Nasal obstruction is known to be a relevant symptom exerting an important role on the impairment of quality of life, sleep disordered breathing, school and children's cognitive performance.

Anterior rhinomanometry is an objective method to predict nasal patency reduction.

Many subjective methods have been proposed to assess the perception of nasal blockage.

Although nasal obstruction may be difficult to quantify accurately, a valid subjective score could be useful to select the patients with an higher reduction of nasal patency.
Objective: To evaluate Nasal Symptom Score (NSS) as a predictor of nasal obstruction measured by an objective method such as anterior rhinomanometry.
Methods: This study was performed at the Immunology and Allergology service of the Pediatric Department, Policlinico Umberto I Hospital, Rome. One hundred and six children (70 males and 36 females) aged between 4 and 10 years of age (mean age 8 years) affected by Persistent Allergic Rhinitis (PAR, defined as symptoms that occur on >4 days/week and for >4 consecutive weeks) and sensitised to mites were enrolled.

All children underwent anterior rhinomanometry. Its results were considered related to nasal flows of 150 Pascal (Pa) and compared with pediatric reference values reported in literature.

The same day the Nasal Symptom Score (NSS, maximum 24) was obtained for each patient. This clinical score expresses severity and duration of nasal symptoms (stuffy nose, runny nose, sneezing and nasal itching) through a 4-point scale calculated as follows: 0 = absent/never; 1 = mild, lightly annoying/once in a while; 2 = moderate, somewhat annoying/often; 3 = severe, very annoying, always or almost of the times.
Results: In our sample NSS mean value was 14.45 ± 3.64 and mean flow was 60.50 ± 26.83. A negative correlation was found between NSS and the fraction of predicted values of Nasal flows ($r = -0.29$; $P < 0.03$).
Conclusions: The relationship between subjective and objective assessment of the severity of nasal obstruction is still considered a matter of debate. Our findings seem to suggest that in children affected by PAR, NSS might be a valid predictor of nasal obstruction. NSS was significantly higher in children with lower nasal patency and hence with severe nasal obstruction.

1792
Rhinitis in children

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Background: Rhinitis in children is a very common disease, yet not sufficiently studied. We aimed to study it's pathology in a population that visited our Rhinitis Outpatient Clinics, a conjunct clinic, which takes place as collaboration between our Allergy Unit and the ENT Department of the 'P & A. Kyriakou' Children's Hospital.
Method: Children and adolescents that visited our Rhinitis Outpatient Clinics with median age 6.9 years (0.9–15 years) participated in this study. Their records have been studied retrospectively, recording main rhinitis symptoms, IgE sensitisation to common aeroallergens and egg white by means of serum IgE and Skin Prick tests, presence of asthma and atopic dermatitis. Their rhinitis' symptoms have been classified as mainly blockers, mainly sneezers/runners, and mixed, while concerning the cause their rhinitis has been classified as allergic, infectious or other cause. Statistical analysis has been performed using SPSS 17.0
Results: Among 130 children, 56 (43%) children were mainly blockers, 29 (23%) mainly sneezers/runners and 44 mixed (34%), while concerning the possible cause, in 76 children rhinitis was classified as infectious and in 51 as allergic. Of the 130 children, 57 (43.8%) had a diagnosis of atopic dermatitis (past or current) and 58 (44.6%) had a diagnosis of asthma (past or current), 28 (21.5%) children had both, while 27 (20.7%) children had a diagnosis of asthma without atopic dermatitis. Pre-schoolers were mainly blockers ($P = 0.005$). Children

with atopic dermatitis presented more often IgE sensitisation ($P = 0.033$), less often a congestive phenotype ($P = 0.008$), while those without atopic dermatitis had less often a mixed phenotype ($P = 0.015$). Having any IgE sensitisation, children presented more mixed ($P = 0.007$) and less congestive rhinitis ($P = 0.004$). Older children were higher sensitised than pre-school children ($P = 0.003$).

Conclusion: Rhinitis symptoms in childhood change with age and so does IgE sensitisation. Atopic dermatitis and asthma often coexist with rhinitis. The congestive symptoms seem related to younger age; they are less related to IgE sensitisation, and/or atopic dermatitis, while mixed symptoms relate to IgE sensitisation.

1793
Cognitive function in adolescents with persistent allergic rhinitis

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Background: The purpose of this study was to investigate the status of cognitive functions in adolescents with persistent (long-lasting) allergic rhinitis (PAR) to work out a correction strategy.

Method: Of 108 adolescents aged 14–15 years with PAR were included in the study. Clinical examination, allergic tests, blood oxygen concentration measurement were used. Cognitive functions characteristics/indices, including memory, attention, perception, analytic-synthetic processes, and delicate motor activity (over ten metrics in total) were investigated using quantitative computer-based tests on the device 'Psychomat' developed by the Research Institute of Medical Instrumentation under RAMS (Russia). Moreover, the quality of life in the study group was measured using questionnaires.

Results: PAR in adolescents was associated with deficiency of cognitive functions (memory capacity by 10.7%, short-term visual memory by 27.4%, attention concentration by 51.5%, attention level by 56.2%, attention switching by 20.7%, decision-making efficiency by 63.2%, maximum speed of motive reactions by 98.4%, delicate coordination by 15.3%, efficiency of motive-coordination activity by 61.1%) and deterioration of the quality of life including sleep disturbance, variable moods, poorer school performance. Intranasal GCS mometasone furoate (Nasonex) was administrated to the study group for 4 weeks and proved highly effective in relieving AR symptoms and improving cognitive functions.

Conclusion: Measurement of quantitative cognitive function indices in adolescents with PAR can be used to determine the degree of cognitive deficiency. The role of computer-based testing of cognitive functions in measuring treatment effectiveness was determined. The link between PAR and social disadaptation was identified. After a 4-week period of treatment, cognitive functions in 89% of the adolescents studied normalised or became closer to the norm. All the above allows for the selection of an appropriate antiinflammatory treatment strategy for allergic rhinitis (intranasal steroids, e.g. mometasone furoate), a major factor in both correcting cognitive deficiency in patients with PAR and improving the QoL in adolescents and their families.

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Poster Session 82

Pediatric allergy prevention and risk factors II

1795
Rhinovirus genotypes in the first wheeze

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Background: The susceptibility to human rhinovirus (HRV) associated wheeze has been linked to biased immune functions, mainly atopy, and to the development of asthma in children, but the data on the first wheeze are scarce. Our aim was to study HRV genotypes, other virus etiology, and their links to patient characteristics in the first wheeze.
Method: Nasopharyngeal aspirates and blood samples were collected from 111 first-time wheezing children (88 inpatients, 23 outpatients) in Turku University Hospital. The virus etiology was analyzed from the aspirates by in-house PCR tests for HRV, respiratory syncytial virus (RSV), enteroviruses and human bocavirus-1 and by a multiplex PCR test for HRV A and B, RSV A and B, parainfluenza virus types 1–3, metapneumovirus, adenovirus, coronavirus (229E, NL63, OC43 and HKU1) and influenza A and B virus. HRV genotypes were analysed using a 397-bp variable sequence in the 5′ UTR of the HRV genome. Bocavirus-1 infections were serologically confirmed. Atopy was defined as positive immunoglobulin E antibodies to any of common allergens (>0.35 kU/l).
Results: The mean age of the study patients was 12 months (SD 6.0, range 3–23). Male gender predominated (67%), 29% had dermatitis, 23% were sensitised, 20% had parental asthma and 16% had atopic dermatitis. At least one respiratory virus was detected in 100% (111/111) of the cases. HRV was most commonly detected (76%), followed by RSV (28%), bocavirus-1 (17%), parainfluenza virus (9%), metapneumovirus (6%) and each other virus <5%. Of the HRV-positive samples, HRV-C was detected in 43%, HRV-B in 23%, HRV-A in 13% of cases, and 21% of the cases were untypable. Virus co-infection occured in 37% of cases; most commonly with HRV and bocavirus-1 (31%). Four children were only bocavirus-1 positive. Blood eosinophil count $>0.4 \times 10^9$/l (OR 14.5), atopic dermatitis (OR 6.1), dermatitis (OR 4.2), parental smoking (OR 3.0) and age (per month, OR 1.1) were positively associated with HRV etiology. RSV etiology was positively associated with inpatiency (OR 5.2 compared to non-RSV etiology). Of the HRV positive cases (n = 84), the proportions for hospitalisation were as follows: HRV-A 91%, non-typable HRV 83%, HRV-C 81% and HRV-B 58%.
Conclusion: Respiratory virus can be detected in all young children suffering from their first wheezing episode using PCR. HRV was clearly the most common finding, and it was associated with atopic characteristics. HRV-C was the most common HRV genotype.

1796
Human rhinovirus species C infection is associated with higher sensitisations to aeroallergens in infants and children as determined by allergen biochip

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Background: Asthma exacerbations in children have been shown to be strongly associated with human rhinovirus (HRV) infection and allergic sensitisation. As HRV species C (HRV-C) was recently associated with more severe wheezing attacks, we hypothesised that HRV-C infections would influence allergen sensitisation in children with asthma exacerbation, wheezing and acute lower respiratory illness (ALRI).
Method: Children were recruited from the Emergency Department at Princess Margaret Hospital for Children, Perth, Western Australia, between June 2003 and November 2010 and were followed-up in convalescence. HRV was detected and typed from nasal specimens using molecular methods. Specific IgE antibodies to 103 aeroallergens and food allergens were measured in patients' serum with the ISAC® allergen biochip (ThermoFisher Scientific, Uppsala, Sweden).
Results: Of 81 children were studied: 51 (63.0%) male; median age 4.87 years (range 1.8 months–15.56 years). At recruitment, most children were infected with a respiratory virus (90.1%), 69 (86.2%) were positive for HRV and 45 (65.2%) of these were HRV-C. 62 (76.5%) children were already sensitised to at least 1 allergen at recruitment. Of 77 who were followed-up, 14 (18.2%) remained negative at follow-up and only two children (2.6%) developed a sensitisation after recruitment. The most common sensitisation at recruitment (n = 50, 61.7%) was to dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Storage Mites*), then animal dander (n = 32, 39.5%) and grass pollens (n = 31, 38.3%). For the 69 children whose HRV infection was successfully typed, HRV-C infection was associated with a significantly higher number of sensitisations at recruitment (median 6, 25th to 75th percentile = 2.5–12) than children who were not infected with HRV-C (median = 3, 25th to 75th percentile = 0–7, P = 0.032, n = 80).
Conclusion: In conclusion, aeroallergen sensitisation is common in children with virus-induced acute exacerbations of wheeze or asthma and HRV-C infection may be associated with a higher degree of allergen sensitisation.

1797
Exposure to visible mold at home during infancy increased the risk of current atopic dermatitis in adolescents with TLR4 polymorphism

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Background: Prevalence of atopic dermatitis (AD) has been increasing worldwide. Gene-environmental interaction can contribute to increased prevalence of AD. Mold exposure has been reported to be one of the leading causes of the development of AD in children. We investigated the risk factors for AD and the gene-environmental interaction.
Method: A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was used to investigate the prevalence of AD in 7144 middle school students. Environmental factors and *TLR4 + 8595C/T* (*rs1927911*) polymorphism were analyzed to investigate the risk factors for the development of current AD who have ever been diagnosed as AD and also had AD symptoms in the past 12 months.
Results: Prevalence of current AD was 7.62%. After controlling for potential confounders, female sex, parental history of AD, maternal smoking history, living in a new house before 1 year of age, and exposure to visible mold at home during infancy and past 12 months were associated with increased prevalence of current AD. Adolescents who were exposed to visible mold during infancy and had *TLR4 CT + TT* polymorphism showed increased risk for the development of current AD compared to those who were unexposed and had *CC* genotype (aOR 2.31, 95% CI 1.03–5.21).
Conclusion: Adolescents who were exposed to visible mold at home during infancy are associated with the development of current AD, especially in genetically susceptible subjects.

1798
In vitro evidence for immune modulatory properties of non-digestible oligosaccharides

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Background: The combination of specific lactic acid bacteria with oligosaccharides is considered to selectively manipulate the composition of the microbiota of the host. This is of special interest regarding the growing application of lactic acid bacteria in combination with a mixture of non-digestible oligosaccharides in prevention and treatment of diseases. Aim of the study was to investigate the impact of different bacterial strains in combination with oligosaccharides on cytokine release by human monocyte-derived dendritic cells (MoDC).
Method: Immature MoDC prepared from peripheral blood monocytes of healthy non-atopic volunteers were stimulated with a *Lactobacillus* and *Bifidobacterium* strain in different concentrations in the presence of different combinations of GOS (galacto oligosaccharides), FOS (fructose oligosaccharides) and AOS (pectin derived acidic oligosaccharides). IL-12p70 and IL-10 release was analyzed after 24 h in cell-free supernatants.
Results: Incubation of MoDC with different concentrations of the *Lactobacillus* and *Bifidobacterium* strains in combination with neutral or acidic oligosaccharides revealed that GOS/FOS (9:1) and GOS/FOS/AOS (9:1:2) had a significant additive effect on bacteria-induced IL-10 release by human MoDC, while the ability of these oligosaccharides to increase IL-12p70 production was less pronounced.
Conclusion: Enhanced release of IL-10 by bacteria-treated human MoDC in the presence of GOS/FOS and GOS/FOS/AOS suggests specific immune regulatory capacities *in vitro*. Thus, the tested *Bifidobacterium* and *Lactobacillus* strains in combination with oligosaccharides might be considered as potential health promoting providing new strategies for the therapeutic treatment of diseases including immune regulatory disorders, such as skin diseases, allergy or infection and open new aspects for the application as allergy preventing ingredients in food.

1799
Systematic review of formulas containing hydrolysed protein for prevention of allergy

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Background: Formulas containing extensively hydrolysed proteins (EHF) have been used to treat infants with allergy. It is unclear whether partial (PHF) or EHF can be advocated for prevention of allergy.
Method: The standard methods of the Cochrane Review Group were used. Searches were updated January 2013. Randomised trials that compared the use of a hydrolysed infant formula to human milk (HM) or cow's milk formula (CMF) with >80% follow up of participants were eligible for inclusion.
Results: Four trials compared early, short term hydrolysed formula to HM feeding and CMF. No significant differences in infant allergy or childhood cow's milk allergy (CMA) were reported. One large study reported a reduction in infant CMA of borderline significance in low risk infants (RR 0.62, 95% CI 0.38, 1.00). 10 eligible studies compared prolonged feeding with hydrolysed formula vs CMF showed a significant reduction in infant allergy (seven studies, 2514 infants; RR 0.79, 95% CI 0.66, 0.94). There was no significant difference in infant eczema (eight studies, 2558 infants, RR 0.84, 95% CI 0.68, 1.04), or asthma, rhinitis and food allergy. One study reported a significant reduction in CMA (RR 0.36, 95% CI 0.15, 0.89).

Comparing PHF vs CMF, it was found a significant reduction in infant allergy (six studies, 1391 infants; RR 0.79, 95% CI 0.65, 0.97) but not asthma, eczema or rhinitis. Infants fed EHF compared with PHF had a significant reduction in food allergy (two studies, 341 infants; RR 0.43, 95% CI 0.19, 0.99). Comparing EHF with CMF, one study (431 infants) reported a significant reduction in childhood allergy incidence (RR 0.72, 95% CI 0.53, 0.97). Meta-analysis found a significant reduction in infant eczema (three studies, 1237 infants; RR 0.71, 95% CI 0.51, 0.97). One study reported a significant reduction in childhood eczema incidence (RR 0.66, 95% CI 0.44, 0.98).
Conclusion: There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy compared to exclusive breast feeding. In high risk infants who are unable to be completely breast fed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a CMF reduces infant and childhood allergy and infant CMA. In view of methodological concerns further large, well designed trials comparing formulas containing PHF whey or EHF casein to CMF are needed.

1800
Allergen-induced cytokine production in allergic and non-allergic women during and after pregnancy

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Background: A successful pregnancy and allergic disease have been postulated as Th2 phenomenons, but little is known about the impact of allergens on the

T-helper (Th) 1, Th2 and antiinflammatory cytokine and chemokine production during pregnancy and after delivery in allergic and non-allergic women. The total IgE levels, but not the allergen-specific IgE levels were increased at gestational week 10–12 as compared to 12 months after delivery in the allergic, but not in the non-allergic women. The aim of this study was to characterise the allergen-induced Th1/Th2/antiinflammatory immune responses in allergic and non-allergic women by measuring birch and cat allergen induced cytokines and chemokines during pregnancy and postpartum.

Method: Twenty women with and 36 women without allergic symptoms were included in the study, of whom 13 were sensitised with allergic symptoms and 30 were non-sensitised without allergic symptoms. Peripheral blood mononuclear cells (PBMC) collected at gestational week 10–12, 15–16, 25, 35 and 2 and 12 months after delivery were stimulated with birch and cat allergen extracts and phytohemagglutinin (PHA), as positive control. The interleukin-4 (IL)-4 and IL-10 production was measured with enzyme-linked immunosorbent assay (ELISA). Interferon-γ, IL-5, IL-13, the Th1-associated chemokine CXCL10 and the Th2-associated chemokine CCL17 will be quantified using an in-house Luminex-assay.

Results: The sensitised women with allergic symptoms produced higher levels of IL-4 in response to birch allergen at gestational week 25 and in response to cat allergen at gestational week 15, 25, 35 and 2 and 12 months after delivery compared to the non-sensitised women without allergic symptoms. The allergen-induced levels of IL-4 and IL-10 were similar during pregnancy and after delivery in both groups.

Conclusion: The sensitised women with allergic symptoms showed increased allergen induced IL-4 levels during pregnancy and postpartum as compared to the non-sensitised women without allergic symptoms, supporting an increased allergen-specific Th2 immune response in the allergic group. The birch and cat induced IL-4 and IL-10 levels were similar during and after pregnancy in both groups, indicating that the previously observed Th2-deviation during pregnancy in the allergic group is not caused by immune responses to allergens.

1801
Maternal and cord blood miR-223 expression associates with prenatal tobacco smoke exposure and with low Treg numbers

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Background: There is evidence that miRNAs are sensitive to environmental stressors including tobacco smoke. On the other side miRNAs are involved in immune regulation, e.g. regulatory T cell (Treg) differentiation. The aim of the present study was to investigate the association between prenatal tobacco smoke exposure, miRNAs and Treg numbers.

Method: Within a prospective mother-child study (LINA) we analysed the expression of miR-155 and miR-223 together with Treg numbers in maternal blood during pregnancy as well as in cord blood. Tobacco smoke exposure was assessed by questionnaires and maternal urine cotinine levels. Additionally, the concentration of smoking related volatile organic compounds (VOC) was measured in dwellings of study participants.

Results: Both maternal and cord blood miR-223 expression were positively correlated with maternal urine cotinine levels. An association was also found between maternal miR-223 and indoor concentration of benzene and toluene. High miR-223 expression was associated with lower Treg numbers in maternal and cord blood. Furthermore, children with lower Treg numbers at birth had a higher risk to develop atopic dermatitis during the first 3 years of life. The concentration of the toluene metabolite SBMA (S-benzylmercapturic acid) in maternal urine was associated with decreased cord blood, but not maternal blood, miR-155 expression. A relationship between miR-155 expression and Treg numbers was not found.

Conclusion: We show for the first time that maternal tobacco smoke exposure during pregnancy correlates with the level of miRNA-223 expression in blood with an impact on children's cord blood Treg numbers and the subsequent allergy risk.

1802
National allergy programmes relieve the disease burden for patients and society. Patient associations take action to share best practices

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Background: The prevention and management of allergic diseases are changing because of scientific evidence questioning old truths. An approach involving healthcare professionals, and patients and relatives is needed to enable everyone to benefit from best practices (WAO White Book, 2011). National Allergy Programmes that integrate these sectors, namely the Finnish and Czech Republic Programmes (Haahtela, Allergy 2008; www.ginasthma.org/CzechInitiativeForAsthma), have proven effective in improving patients' quality of life (QoL) and reducing costs despite the increasing allergy incidence. In 2011, the European Federation of Allergy and Airways Diseases Patients' Associations (EFA) surveyed their member associations in 18 European countries to learn about national respiratory allergy policies. The data showed a greatly improved patients' QoL in countries with a robust national programme, but not in countries in which the national programme fails to involve all stakeholders (e.g. involving only specialists) or is not adequately implemented and sustained (EFA Book on Respiratory Allergy, 2011).

Methods: EFA has launched, within its 4-year allergy awareness programme, an initiative to promote adoption of allergy programmes throughout Europe. Since EFA recognises the Finnish Allergy Programme (FAP) as gold standard, the first step was to share best practices via meetings between FAP experts and national delegations. The FAP involves professionals and the public, is implemented by NGOs and needs to reach both target groups.

Results: From the Helsinki 2012 meeting it emerged that allergy health should be endorsed and tolerance (immunological and psychological) promoted. Programme financing is a challenge, but the work is mostly done by already paid healthcare professionals, who are now trained to set common goals to reduce the disease burden. Programmes must be tailored to local needs and the organisational characteristics of National Health Systems.

Conclusion: Actions to implement Allergy Programmes are underway and will be promoted in countries participating in the EFA initiative. Cooperation between NGOs, the scientific community and authorities is mandatory.

1803
Allergy: environmental and nutritional programming in childhood

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Background: Allergic diseases (AD) are increasing in frequency and severity, and represent a global health problem. The EAACI reported that about 25% of children in Europe show allergic reactions to inhalant or food allergens. Although genetic predisposition is an important risk factor, the rise in prevalence happened within a too short time period to be explained by genetic changes in the population. There is convincing evidence that lifestyle factors (e.g. smoking, diet, and air pollution) are important contributors to allergy risk. Prenatal and early life exposures have attracted attention to study the mechanisms involved in the environment-driven epidemic of AD. The underlying molecular mechanisms are still unclear, but epigenetic changes are a plausible mechanism to alter gene expression, which can establish a different phenotype and thereby altering the risk of AD later in life. Therefore, we hypothesise that prenatal exposures (e.g. air pollution and mother's diet) affect the fetus by changing the intra-uterine environment, leading to epigenetic changes that can influence a child's risk for AD later in life.
Method: The current study is embedded in an ongoing birth cohort follow-up in Flanders (Flanders Environment and Health Surveys FLEHS1). Questionnaires (asking for e.g. allergy status, life style, diet) and blood samples are available from 595 mother/child pairs with children followed until 10 years of age. Currently we are collecting additional data on DNA methylation to correlate with the prevalence of AD, involving measurement of total DNA methylation status via HPLC as well as gene-targeted DNA methylation in allergy-related genes via pyro-sequencing techniques. A case-control study design will be applied.
Results: Preliminary results from a subcohort of the FLESH1 birth cohort showed an association between prenatal exposure to air pollutants (NO_2, benzene and PM10) and the development of allergies and/or wheezing problems in 3-year old toddlers. At 10 years of age, 65.21% of the children developed some form of allergy, of which 13.78% airway allergy. For the DNA methylation studies we selected 49 allergy cases with matched controls.
Conclusion: The outcomes of this project will encourage the development and use of predictive biomarkers which assess epigenetic changes as modulating factors in allergy pathogenesis. Ultimately this work will improve the development of prevention strategies, particularly in children.

1804
Taking dietary supplements by the child and the symptoms of allergies

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Background: The use of dietary supplements is widespread in society, including children. Their objective is to supplement the diet affects the development of the child. Evaluate the relationship between the intake of dietary supplements by children in early school age, and the incidence of allergic symptoms (including skin and food).
Method: The study comprised children aged 6–7 years attending primary school in the capital of Poland Warsaw. Of 1801 questionnaires were collected and verified (54% female, 46% male); Response Rate = 53.5%. Children under 6 years of age accounted for 40% of the study group, and at the age of 7 years were 60%. Systematic sample selection was applied in the study. All children from first classes in selected schools were invited to the survey. Questionnaires were distributed to parents of studied subjects. Questions were based on Epidemiology of Allergic Disease in Poland (www.ECAP.pl), European Community Respiratory Health Survey II (ECRHS II), International Study of Asthma and Allergy in Childhood (ISAAC) and questions of author. Questionnaire consisted of questions pertaining to the type of lifestyle, symptoms of allergies and taking dietary supplements by the respondents and their children.
Results: In children who in the past six months took dietary supplements, adult respondents declared that children suffered from symptoms of: shortness of breath, stuffy nose, rhinitis, itchy nose ($\chi^2 = 6.04$, $P < 0.05$, OR = 2.1), wheezing or whistling in the chest ever during the past 12 months ($\chi^2 = 5.95$, $P < 0.05$, OR = 1.7), problems with sneezing, rhinitis or blocked nose simultaneously deprived of evidence of flu or fever ($\chi^2 = 26.03$, $P < 0.001$, OR = 2.11). Children taking dietary supplements in the past 6 months, more than 1.7 times more likely to have ever had a food allergy ($P < 0.0001$, OR = 1.7) and was more common in these rash, itching, burning skin ($P < 0.001$, OR = 2.6).
Conclusion: The administration of supplements to children in early school age, positively correlated with the occurrence of allergy symptoms. The test requires further analysis confirming the nature and direction of the observed relationships.

1805
Fish consumption in infancy and development of allergic disease up to age 12 years

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Background: Fish intake in infancy has been associated with a reduced risk of allergic disease in early childhood, but it is unknown if this effect remains as the children grow older. The aim of this study was to investigate the possible effect of fish consumption in infancy on prevalent and incident allergic disease up to the age of 12 years.
Method: Of 3285 children from a prospective Swedish birth cohort (BAMSE) were included in the present study. At 1, 2, 4, 8 and 12 years, parental questionnaires were used to obtain information on lifestyle factors, environmental exposures and symptoms of allergic disease. Frequency of fish intake in infancy was assessed in the 1-year questionnaire. Serum IgE levels to common allergens were obtained at age 8 years. Generalised estimating equations and multivariate logistic regression were used to examine the associations between fish consumption in infancy and prevalent, as well as incident, allergic disease at ages 1–12 years, including sensitisation and IgE-associated disease at age 8 years.
Results: At 1 year of age, 80% of the children consumed fish regularly (i.e. at least twice a month). Regular fish consumption in infancy reduced the overall risks, from 1 to 12 years, of prevalent and incident allergic disease (adjusted odds ratio for incident rhinitis: 0.78; 95% CI 0.67, 0.91

($P = 0.01$), and for incident eczema: 0.66; 95% CI 0.57, 0.77 ($P < 0.001$).

Conclusion: Regular fish consumption in infancy may reduce the risk of allergic disease up to age 12 years, including the risk of IgE-associated allergic disease at age 8 years.

1807
Increase in vesicular hand eczema after house dust mite inhalation challenges

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Background: It was reported in two studies that inhalation challenges with HDM aggravated skin lesions in patients with atopic dermatitis, especially in those with concomitant allergic asthma. The effect of HDM inhalation on aggravating skin responses in patients with hand eczema had never been investigated.

Method: Of 18 patients with vesicular hand eczema and HDM allergy (positive SPT to *D. pteronyssinus*) were investigated in a randomised, double-blind, placebo-controlled, cross-over study. Increasing concentrations of standardised HDM (80, 400, 2000, 10 000 BU/ml) were inhaled for 1 min at intervals of 15 min. The FEV_1 was measured immediately before and after each dose, after the last challenge every 10 min for 1 h, and thereafter every hour for 7 h. The placebo challenge procedure was the same as described for the active suspension. The time interval between HDM and placebo was 2–4 weeks. Early asthmatic reactions and late asthmatic reactions (LAR) were defined as a placebo-corrected fall of 15% or more from baseline of FEV_1. Hand eczema was scored according to the Dyshidrotic eczema Area and Severity Index (DASI) at baseline, 1, 6, 24 and 48 h. Total IgE was measured at the start of the first provocation day and serum eosinophils on both provocation days before the first challenge and 24 h later.

Results: Significant increases in median DASI score and median DASI sub-scores were seen only after HDM provocation. After placebo provocation, no significant differences from baseline were seen. The median DASI increased significantly as compared with baseline at 6 and 48 h after HDM inhalation. This increase was significantly different between the provocations at 6 h. The median vesicles score increased significantly from baseline at 24 and 48 h. Patients with a placebo-corrected increase of vesicles at 24 and 48 h had significantly more often a LAR than those without an increase of vesicles. Patients with a placebo-corrected increase of the DASI at 24 h had as a group a higher mean total IgE level than those without an increase of the DASI. The increase in serum eosinophils 24 h after HDM provocation was not significantly different between the placebo-corrected skin responders and non-skin responders.

Conclusion: Hand eczema increased significantly more after HDM provocation than after placebo provocation. An increase of vesicles was preceded by a LAR. The group patients with an increase of hand eczema tended to have a higher mean total IgE level.

1808
Neurological clinical manifestations of hay fever in conditions of different pollen load

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Background: Nervous system disorders caused by pollen allergens at hay fever are not life threatening, but are not good in prognostic aspect of the disease.

The aim of the study: To investigate the incidence of nervous clinical manifestations in children with pollinosis in the conditions of different pollen load.

Method: The study conducted in 2011. Under our observation were 114 children at the age of 10–15 years. Study population was divided into two groups. The first one ($N = 59$) consisted of children, living in the central region of the city with the average pollen load 31.6 ± 1.4 grains per one air liter^3, the second group ($N = 55$) consisted of children, living in the outskirts area with the average pollen load 57.4 ± 1.2 grains per one air liter^3. Pollen count was assessed by the standard method. The special allergological questionnaires, including the data about neurological manifestations and presence of headache were completed.

Results: Pollinosis were diagnosed in all 114 patients on the basis of clinical and laboratory data. The term of 'pollen intoxication' were introduced. It was found that 47 children (85.4%) from the second group had complaints for periodical headache, whereas only 34 (57.6%) of the first group had the same complaints. Severe headache were found in 9 (16.3%) children of the second group and only in 2 (3.38%) patients of the first one. The difference between two groups in ear stuffiness and tinnitus were not statistically significant 15 ± 1.4 and 17 ± 1.2, respectively ($P \geq 0.05$). Complaints for the memory impairment and concentration were the most common in both groups, 51 (86.4%) of the first group and 49 (89.1%) of the second one. Impaired mood and apathy were found in 54 (98.1%) of the second study group, whereas in 47 (79.6%) from the first one.

Conclusion: The term of pollen intoxication were introduced for the first time and were determined in children living in the outskirts areas with increased pollen load. In children with neurological clinical manifestations of hay fever psychological inferiority complexes due to impaired study ability should be prevented.

Poster Session 83

Progress in venom immunotherapy

1811
Influence of vitamin D on treg population of hymenoptera venom allergic patients

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Background: A growing number of experimental data recognises the role of vitamin D in the modulation of innate and adaptive immune responses. Vitamin D receptors (VDRs) have indeed been identified in almost all immune cells including B lymphocytes, neutrophils, antigen presenting cells and were highly expressed on CD4+ and CD8+ activated cells (1).

Our aim is to study the hypothetic correlations between the administration of vitamin D and the response to specific allergen immunotherapy in patients with reactions to Hymenoptera venom.

The primary objective is to analyze the changes in the T regulatory cell population after *in vitro* stimulation with the allergen and treatment with vitamin D.

Method: We enrolled patients with Hymenoptera venom allergy undergoing injective immunotherapy and healthy controls.

Blood samples were collected pre-treatment and assays for vitamin D in its biologically active form (1,25 $(OH)_2$ D_3) and in its most frequently circulating form (25 (OH) D_3) were carried out.

PBMCs were isolated from the blood by means of Ficoll-Hipaque gradient centrifugation and fresh PBMCs were cultured for 48 h in 24-well round-bottom microtiter plate at 1×10^6 cells/well with the specific allergen, PHA (5 mg/ml) and in the absence or in the presence of vitamin D (10^{-8} M).

PBMCs were analysed by flow cytometry using the following mAbs: CD4, CD25 and CD127. Treg lymphocytes were assessed as CD4+ CD25+ CD127− cells. According to the results obtained in this first phase, additional tests, such as the analysis of cytokines production (IL-10, IFN-γ and IL-4) will be performed by means of ELISA.

Results: In our results 1,25-Dihydroxy and 25-Hydroxy vitamin D basal levels did not differ between healthy subjects and patients.

Treg cells from both healthy controls ($n = 7$) and patients ($n = 5$) showed no significant response to treatments with respect to untreated cells. We however noticed a significant difference ($P < 0.05$) in Treg cells percentage when we compared untreated cells from controls and patients.

Conclusion: Our preliminary data suggest that Treg cell population is not differently influenced by vitamin D in basal conditions in both healthy subjects and Hymenoptera venom allergic patients. It is presently under investigation the study of Treg population after the induction phase of allergen specific immunotherapy.

1812
Does the sting localisation play a role for the severity of symptoms in hymenoptera venom allergy?

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Background: Systemic symptoms after a sting vary from skin symptoms to life-threatening reactions like anaphylactic shock and ultimately, cardiac or respiratory arrest. Various risk factors have been described: among others, elevated basal tryptase levels, higher age, cardiovascular diseases, and severe preceding reactions were associated with more severe reactions. Stings in the head and neck region have been discussed to account for most of the fatal reactions; however, there is no recent data available. The aim of the study was to evaluate if there is a correlation between sting localisation and symptom severity.

Method: Of 270 patients with confirmed hymenoptera venom allergy were included in the study. Patients were asked about the sting localisation and symptoms using a standardised questionnaire. We hypothesised that stings in skin areas which are well supplied with blood could lead to more rapid and severe reactions. Furthermore, we used excess skin after excision of skin tumors in two persons to perform sting challenges to determine the stinger's depth of penetration.

Results: In areas with a thin reticular dermis like in facial skin the stinger reached the deep arteriovenous plexus of the subcutis. In regions with a thick skin like on the back it got stuck in the reticular dermis. However, in the 270 patients, symptom severity was not correlated to the sting localisation: We observed severe reactions (grad III and IV according to Ring and Messmer) in 21.9% of patients after facial stings, in 31.6% after stings in the trunk, in 34.9% after stings in the upper extremities, and in 37.8% after stings in the lower extremities ($P = 0.207$). Interestingly, 37.7% of patients aged under 50 reported stings in the lower extremities compared to 20.0% of patients aged above 50 years ($P = 0.002$).

Conclusion: Although there was a difference in the stinger's depth of penetration, we did not observe a correlation between sting location and symptom severity. We thus were not able to confirm previous reports of a higher risk for severe reactions after facial stings.

1813
The relative delta bound in serum tryptase concentration even below 11.4 μg/l is not an indicator of systemic hypersensitivity side reaction during venom immunotherapy in children

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Background: An increase in serum tryptase concentration has been proven a good mast cell activation predictor/marker during systemic allergic reactions to field insect stings (FIS) and insect venom immunotherapy (VIT) in different age groups[1,2,3]. In a prospective adult study, the relative increase (relative delta bound – RDB) to ≥135% of tryptase concentration even below 11.4 μg/l in response to FIS or VIT, indicated subjects with systemic hymenoptera venom allergy (HVA) reactions[4]. We attempted to evaluate RDB relevance in VIT-treated children.

Method: Serum tryptase levels were measured (ImmunoCAP system) prospectively 1 h before (baseline I) and after the last dose of rush-VIT (delta I) or 1 h after

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symptoms presentation in patients with systemic side reaction (SSR) to VIT, as well as after a year-long maintenance treatment – 1 h before (baseline) and after the regular dose of 100 μg venom extract (II delta). In further analysis, with application of Mann–Whitney test both demographic and clinical data were regarded.

Patients: 37 children ($M = 29$, 78%) mean age 11.0 SD 3.4 (5–17) with systemic HVA history (Mueller grade: II° 10 (27%), III° 18 (49%), IV° 9 (24%)) were treated with 5-day rush-VIT (16 wasp venom, 43%). Seven subjects developed SSR following VIT (reactors with grade of reaction severity: III – 3, II –3, I – 1). No SSR during maintenance treatment were observed. None of patients experienced FIS during follow-up.

Results: Median change of serum tryptase concentration during rush-VIT (delta I) was significantly higher in reactors, equaling 33% (Q1 23%, Q3 121%), while in non-reactors respectively 10% (Q1 4%, Q3 29%; $P < 0.001$). After 1 year of VIT, median change of tryptase concentration (delta II) related to regular VIT was almost equal in both groups: in reactors Me −6% (Q1 −15%, Q3 −1%), while in non-reactors respectively Me -7% (Q1 −12%, Q3 −3%).

Conclusions: Serum tryptase values obtained during suspected hypersensitivity reaction should always be compared to baseline values. Contrary to results seen in adults, a RDB to ≥135% of tryptase concentration even below 11.4 μg/l during a SSR to incremental dose of VIT was not confirmed in children.

1814
Platelet-activating factor acetylhydrolase is a marker of severe hymenoptera venom anaphylaxis

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Background: The role of platelet-activating factor (PAF) in the pathogenesis of anaphylaxis has been demonstrated in murine models; the administration of platelet-activating factor acetylhydrolase (PAF-AH) or PAF-receptor antagonists prevents mice hypotension and anaphylaxis. Recently two studies on PAF-AH in humans found a correlation between high PAF and low PAF-AH levels and severe anaphylaxis. Interestingly, significantly lower PAF-AH levels were detected in nine children died for peanut anaphylaxis, in respect to patients with not fatal anaphylaxis or allergic reactions. This is the first study evaluating the role of PAF-AH in hymenoptera venom anaphylaxis.

Method: We selected 169 hymenoptera venom-allergic patients, classified according to the four Mueller grades of venom anaphylaxis. Sixty healthy subjects were enrolled as controls. Specific venom IgE and serum tryptase were measured by ImmunoCAP (Thermo Fisher Scientific, Milan, Italy) and basal PAF-AH activity was determined by a colorimetric kit (Cayman Chemical Company, Ann Arbor, MI, USA) with lower detection limit of 20 nmol/ml/min. Data were statistically analyzed by SPSS® program release 17.0 (SPSS Inc., Chicago, IL, USA).

Results: No significant differences between the controls and grade I, and between grade III and grade IV were found. PAF-AH activity was significantly different between grade I and II ($P < 0.001$), and between grade II and III–IV ($P < 0.001$). Low enzyme levels were detected only in patients with severe anaphylaxis (grade III–IV). 74% of grade III and 89% of grade IV patients presented enzyme activity lower than 20 nmol/ml/min. A correlation between age, serum specific IgE, tryptase and PAF-AH activity was significant only for age ($R = -0.184$, $P = 0.006$), being PAF-AH levels lower in elderly subjects. Finally, by means of ROC curve, we found that the best cut-off of PAF-AH activity (sensitivity 89.3%, specificity 81.7%) was 25 nmol/ml/min, instead of 20 nmol/ml/min.

Conclusion: In our hymenoptera venom allergic patients, low PAF-AH activity was significantly decreased in severe anaphylaxis. Differently from Vadas study, where low PAF-AH levels were detectable only in fatal anaphylaxis, in our hymenoptera allergic patients low PAF-AH levels correlate with severe but not fatal anaphylaxis. In hymenoptera venom allergic patients, enzyme levels lower than 25 nmol/ml/min could be considered a prognostic factor for venom severe anaphylaxis.

1815
Change in baseline serum tryptase level related to 1 year venom immunotherapy in children

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Background: Baseline serum tryptase (BST) is a useful molecular marker for mast cell burden and pathologies involving mast cells, being also helpful in the context of Hymenoptera venom allergy (HVA) and venom immunotherapy (VIT)[1,2,3]. Retrospective studies provide evidence for a decline of baseline serum tryptase (BST) concentration during long-term (2–12 years) VIT in adults[4]. There are no data on the dynamics of this marker in VIT-treated children.

Method: In a prospective study, tryptase levels were measured by ImmunoCAP system four times:

1. one hour just before,
2. one hour after the last dose of rush-VIT, or one hour after symptoms presentation in patients with SSR to rush-VIT,
3. after 1 year of maintenance treatment with a monthly administered dose of 100 μg of venom extract, just before the regular dose,
4. one hour after regular maintenance dose.

Both systemic and local reactions to venom extract were recorded. None of the patients experienced field sting during follow-up. Further analysis included both clinical and demographic characteristics. Linear regression with gamma distribution of dependent variable and identity linking function was estimated using Generalised Estimating Equations.

Patients: 39 children (31 boys, 80%) mean age 11.1 SD 3.4 (5–17) with history of IgE-mediated systemic reaction (Mueller's grades: II° 11 (28%), III° 18 (46%), IV° 10 (26%)) were treated with VIT (16 wasp venom, 41%). Seven of these developed SSR following venom injection during rush-VIT (SSR grades: III −3, II −3, I −1). No systemic reactions and field stings during maintenance treatment were observed.

Results: Mean value of BST before VIT was 3.93 μg/l (95%CI = 3.10, 4.76, and increased after VIT to 5.12, 95%CI = 3.53, 6.71, ns), while 1 year later it decreased from 4.44 μg/l (95%CI = 3.39, 5.49–4.17 μg/l, 95%CI = 3.11, 5.22), $P < 0.001$. Multivariate model showed that the change in tryptase level between those four time point measurements was significantly affected by time of measurement ($P < 0.001$) and SSR during incremental phase of rush-VIT ($P = 0.037$), interaction between SSR and measurement time ($P = 0.018$), as well as between measurement time and kind of culprit insect ($P = 0.004$).

Conclusions: In children, the level of BST decreases after 1-year maintenance dose VIT treatment.

1816
Basophil activation test in resolving the specific IgE double positivity in patients with unknown culprit insect

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Background: Double specific IgE positivity to honeybee and wasp venom is evident in up to 60% of Hymenoptera venom allergic patients. Distinguishing between true double sensitisation and cross-reactivity is crucial for the choice of proper allergen for specific immunotherapy, especially in patients with unknown culprit insect. In our study, we tried to evaluate the role of basophile activation test (BAT) in resolving this problem.
Method: 18 patients with specific IgE to both honeybee and wasp venom were included into the study. All patients experienced severe anaphylaxis of Muller grade III or IV and did not recognise the culprit insect. BAT was performed on whole blood with maximal 1 and sub-maximal 0.1 μg/ml of honeybee and wasp venom allergen concentrations.
Results: BAT was single positive in 4 (22%) and double positive in 14 (71%) patients. Of four single positive BAT patients three were positive for wasp venom and one for bee venom. In BAT double positive patients the response to sub-maximal 0.1 μg/ml of allergen concentration was at least 4-fold higher (median 14-fold) for one venom then for other venom in majority of cases (9 of 14 patients). In five patients the sub-maximal basophil response was markedly higher for honeybee and in four patients for wasp venom.
Conclusion: BAT is a helpful, but also limited diagnostic tool, which can directly resolve the problem of double positivity in about one fifth of patients. However, in case of BAT double positivity the apparent differences between sub-maximal responses suggest that additional whole dose response curve analysis might further elucidates the pattern of double positivity, possibly showing a clinical relevance for only single venom.

1817
Management of patients with repeated systemic anaphylactic reactions during Hymenoptera venom immunotherapy: treatment with anti-IgE-antibodies and elevated venom dose is safe and effective

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Background: Patients showing repeated systemic anaphylactic reactions (SAR) during venom immunotherapy (VIT) are a particular risk group. For these patients, it is of utmost importance that VIT can be continued and that tolerance to VIT and to subsequent stings is established.
Method: We retrospectively included consecutive patients who (i) had exhibited repeated moderate to severe SAR to VIT, (ii) in whom antihistamines (in some cases in combination with corticosteroids) were ineffective to prevent SAR to VIT, (iii) for whom we had managed to find a sponsor for an anti-IgE-antibody (omalizumab) treatment, and (iv) who had consented to an off-label therapy by this drug. After the first appearance of SAR VIT was either stopped or continued with the lowest tolerated venom dose every 2–4 weeks. Subsequent dosing of omalizumab was done according to the recommendations established for asthma treatment, and was guided by total IgE-levels and body weight. Omalizumab was injected 4 and 1 week before, and every 4 weeks after the new build-up phase of VIT. Simultaneously, patients received an elevated maintenance venom dose. After 4–6 months on maintenance VIT, omalizumab was stopped. Sting challenge was done at a time when at least 6 months had passed since the discontinuation of omalizumab.
Results: Nine patients (four males, mean age 40.9 years at the beginning of omalizumab therapy) could be analysed. Four patients had mastocytosis. Omalizumab was given to eight patients on bee VIT and to two patients on Vespula VIT; one patient received omalizumab for a bee and Vespula VIT. After pre-treatment with omalizumab VIT was tolerated by all patients. Maintenance venom dose was 200 μg in three patients with a bee VIT, and in two patients with a Vespula VIT. Five patients with a bee VIT received a 300 μg maintenance venom dose. Sting challenge was done in eight patients (six patients with a bee venom allergy, and two patients with a Vespula venom allergy) and was tolerated by all patients.
Conclusion: Patients showing repeated SAR during VIT may universally profit from an omalizumab pretreatment and from the application of an increased maintenance venom dose. However, prospective randomised studies are necessary to evaluate this treatment approach.

1818
Down-regulation of FcεRI-mediated basophil response during short-term venom immunotherapy determined non-specific allergen desensitisation

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Background: We recently showed a desensitisation of FcεRI-mediated basophil response after short-term VIT. Our aim was to evaluate if the observed basophil desensitisation is allergen specific.
Method: In ten *Hymenoptera* venom double sensitised and two mono sensitised subjects basophil threshold sensitivity (CD-sens) to anti-FcεRI, honeybee and *Vespula* venom was assessed at the beginning and just before the first maintenance dose (MD) of single ultra-rush VIT. Genuine double sensitisation to both venoms was confirmed in seven subjects with recombinant Api m 1 and Ves v 5 and/or Ves v 1.
Results: We demonstrated a marked reduction of CD-sens to anti-FcεRI and VIT-specific *Hymenoptera* venom before the first MD in all included subjects. Furthermore a significant and comparable decrease was evident both in VIT and non-VIT *Hymenoptera* venom before the first MD of single ultra-rush VIT in nine out of ten double sensitised subjects. Most evident decreases in CD63 basophil response were achieved at low submaximal concentrations of allergen stimulation.
Conclusion: Short-term VIT induced basophil desensitisation of VIT-specific as well as VIT-non-specific allergen. In genuinely double sensitised subjects to both venoms the decrease in basophil response was evident both in VIT and non-VIT *Hymenoptera* venom. As opposed to long-term VIT which induces allergen-specific basophil changes, the mechanisms of short-term VIT seem to be allergen non-specific.

1819
Changes of *in vitro* parameters in patients with honey bee and wasp venom allergy in the course of venom immunotherapy – 6 years study

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Background: Changes in allergen-specific IgE, IgG4 and basophile response have been reported during VIT, but the only available clinically relevant method for evaluation of the induction of tolerance is the sting challenge test. This test is poten-

tially risky procedure and searching for an *in vitro* method, which reflects the state of tolerance is required.

Methods: We follow a group of 117 patients with proven allergy to honey bee (58 patients) and to wasp venom (59 patients) treated with bee or wasp VIT. Specific IgE and IgG4 (UniCap Phadia) to venom extracts (I1, I3) and to available recombinant allergens (rApi m1, rVes v1, r Ves v5) as well as basophile activation test with venom extracts were performed before VIT and after each year of treatment (1st to 5th). We recorded information about field stings and consequent clinical reactions. For statistical evaluation of changes in followed parameters Wilcoxon paired test was used. Changes after each year of VIT were evaluated in relation to values before treatment. The number of patients declines each year of VIT.

Results: Bee VIT:We observed a significant decrease of basophile response after 1st, 2nd, 3rd, 4th and 5th year of VIT as well as significant decrease of IgE to I1 in each year of VIT. The trend to decrease of IgE to rApi m1 was not statistically significant. We noted significant increase of IgG4 to I1 after 1st, 2nd, 3rd, 4th and 5th year and of IgG4 to rApi m1 after 1st, 2nd, 3rd and 4th year of VIT.

Wasp VIT:We observed a significant decrease of basophile response after 1st, 2nd, 3rd, 4th and 5th year of VIT as well as significant decrease of IgE to I1 after 1st and 3rd year, of IgE to rVes v5 after 2nd, 3rd and 4th year and of IgE to rVes v1 after 3rd and 4th year of VIT. IgG4 to I3 and to rVes v1 significantly increased after each year of VIT. Increase of IgG4 to rVes v5 was significant after 1st, 2nd, 3rd and 5th year of VIT.

Conclusion: The decrease of basophile response and increase of IgG4 to venom extract were significant each year of VIT in both groups of patients. Changes in IgG4 to recombinant allergens were more expressed than changes in IgE to recombinant allergens in both groups. The lower significance of changes in last years of VIT is probably influenced by lower number of patients. Unfortunately we can not definitely confirm the relation of these changes to the clinical effectiveness of VIT because of low number of patients with field stings during VIT till now.

1820
Effectiveness of anti-allergic drugs used to treat anaphylactic reactions associated with sting challenge tests: a retrospective data-base analysis

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Background: Systemic anaphylactic reactions (SAR) are potentially life-threatening. Because of ethical reasons, drug therapy of SAR is not based on formal evidence (randomised studies). This observational study wants to explore potential benefits of individual drugs used for treating emergencies in patients who have a SAR at sting challenge while being on venom immunotherapy.

Method: We performed a retrospective search in our institutional data base looking for patients who had had an anaphylactic reaction during diagnostic sting challenge between 1999 and 2007. Sting challenge tests were routinely done in patients on maintenance venom immunotherapy (>100 μg venom every 4–8 weeks). Indications and contraindications of sting challenge tests followed the EAACI position paper. During sting challenge patients were kept under surveillance by two anesthesiologists and one allergologist. Details on how to treat anaphylactic reactions were left to the discretion of the stand-by anesthesiologist. Severity grade of allergic reactions before starting the emergency therapy was classified according to Ring (I, generalised skin reaction; II, moderate cardiovascular and/or pulmonary symptoms; III, anaphylactic shock; IV, near fatal reactions).

Results: Of 51 cases had mild (grade I), 41 moderate (II), and 7 severe (III) SAR. Most patients received an intravenous therapy including H1-blocking antihistamines ($n = 86$) and corticosteroids ($n = 67$), in part combined with H2-blocking antihistamines ($n = 36$). Only four patients (8.3% of patients with a grade II or III SAR) required an epinephrine therapy which was either provided intravenously (two cases) or via inhalation (two cases). In 90% of the patients systemic symptoms relieved shortly after medical interventions had been started; in 10% drug therapy had to be repeated or extended. Thirteen patients did not receive medical treatment. All patients recovered without sequelae.

Conclusion: More than 90% of patients who had developed a grade II or III SAR during sting challenge recovered although no epinephrine was given. Our findings do not support current guidelines recommending an epinephrine therapy for all SARs of a severity grade of II or higher. Prospective studies appear to be justified to further elucidate the importance of epinephrine as a first line drug therapy for severe SAR.

1821
Coexistence of autoimmunological diseases does not affect safety of immunotherapy in hymenoptera allergic patients

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Background: Coexisting autoimmunological diseases are believed to be associated with adverse course of immunotherapy in hymenoptera sting allergic patients. The objective of our analysis was to check if this kind of correlation is to be found in our group of patients.

Method: A retrospective, statistical analysis of our Department database, describing hymenoptera allergic patients treated with immunotherapy, was done.

Results: There were 282 patients allergic to hymenoptera venom treated with immunotherapy in the Department in the years 2002–2012. The data on 201 (109 women, 92 men in the age of 18–78 (mean 43)) were included in the further analysis due to the complete data on the follow up. Co existing diseases were found in 69 (34%) of them including asthma (27 cases), allergic rhinitis and conjunctivitis (36), psoriasis (3), autoimmunological thyroid diseases (25), mastocytosis (4), atopic skin diseases (13).

Adverse reactions (defined as local and systemic) during immunotherapy were found in 68 patients (34%) including initial phase (30 cases) and maintenance phase of immunotherapy (49 cases).

Systemic reactions were found in 43 cases, while large local side effects in 25.

We found no statistical correlation between side effects of immunotherapy and autoimmunological diseases coincidence, neither counting side effects as all ($r = 0.00089$) nor dividing them into occurring in the initial phase of therapy ($r = 0.00043$) and maintenance phase of therapy ($r = 0.00371$). There were also no correlation between thyroid diseases and side effects counted separately ($r = 0.00228$).

Conclusion: Coexistence of autoimmunological diseases doesn't affect safety of hymenoptera venom immunotherapy.

1822
AAAAI membership experience with venom immunotherapy use in specific chronic medical conditions

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Background: Little data exists regarding use of venom immunotherapy (VIT) in specific high-risk chronic medical conditions.
Method: A web-based survey (Surveymonkey®) was sent out to all AAAAI members to explore their experience with VIT regarding use in high-risk medical conditions. Minor problems were defined as… 'some dose-reduction or doses postponed, but no major problems. AIT could be continued.' Major problems were defined as 'activation of underlying disease and/or AIT not well tolerated (systemic adverse events) and/or AIT discontinued for medical reasons'. Results are expressed descriptively.
Results: Six hundred and ninty-seven of 5123 (14%) surveys were completed. Eighty-seven percent of respondents were US-based, with 28% working in an academic setting, and 41%, 54% and 5% working in urban, suburban and rural settings, respectively. Most respondents had worked as an Allergist for >15 years (62%). The following data represent the specific medical conditions with percentages of Allergists who have treated/would treat/contraindicates VIT in patients with the condition. This data is followed by number of Allergists who reported utilizing VIT in patients with this condition and the (%) that reported major problems: severe asthma: 29/43/28%, 212 (4.2%); hypertension 70/25/5%, 287 (1.1%); coronary artery disease 54/36/10%, 222 (3.6%); arrhythmias 37/49/14%, 136 (3.4%); cerebrovascular disease 28/57/15%, 104 (5.1%); cancer, in remission 41/51/8%, 166 (0%); cancer, stable, but still under treatment 19/59/22%, 44 (7.2%); history of bone marrow transplantation 9/70/21%, 15 (4.9%); history of solid organ transplantation 9/70/21%, 29 (3.6%); infected with human immune-deficiency virus, but not yet AIDS 11/70/19%, 53 (1.4%); AIDS 8/61/31%, 24 (6.2%); autoimmune disease in stable stage 31/57/12%, 164 (2.8%); mastocytosis 15/56/29%, 66 (18.4%); elevated serum tryptase 23/58/19%, 101 (10.8%); immunodeficiency 11/71/18%, 59 (2.5%).
Conclusion: VIT was commonly utilised in patients with hypertension, coronary artery disease, arrhythmias, cancer in remission and stable autoimmune disease. Conditions most frequently felt to be contraindicated by respondents were AIDS, mastocytosis, severe asthma, cancer under treatment, or patients with a history of bone marrow transplants. Major problems were most frequently reported in use with mastocytosis, elevated serum tryptase, and cancer still under treatment.

1823
AAAAI membership experience with venom immunotherapy regarding dosing, premedication, and use in pregnancy and young children

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Background: Little data exists regarding contraindications to VIT in children and pregnant women and current practice patterns among allergists.
Method: A web-based survey (Surveymonkey®) was sent out to all AAAAI members to explore their experience with VIT regarding dosing, pre-medication, and use in pregnancy and young children.
Results: Six hundred and ninty-seven of 5123 (14%) surveys were completed. Eighty-seven percent of respondents were US-based, with 28% working in an academic setting, and 41%, 54% and 5% working in urban, suburban and rural settings, respectively. Most respondents had worked as an Allergist for >15 years (62%). Most respondents had ≤10 patients (43%) or 10–50 patients (41%) on VIT, while 5.8% did not prescribe VIT (6%). For flying Hymenoptera, a maintenance dose of 100 μg (300 μg for mixed Vespid) is used by 92.5% of respondents. Only 38% of respondents prescribe imported fire ant(IFA) IT, utilizing a maintenance dose of 0.5 ml of a 1:100 wt/vol (63%), 0.5 ml of 1:10 wt/vol (29%) or 0.5 ml of 1:200 wt/vol (9%). Regarding pre-medication, 24% pre-medicate routinely, 10% only pre-medicate for accelerated schedules, and the remaining 65% do not pre-medicate routinely or pre-medicate only for high-risk patients: 46% use H1 antihistamines, 6% H2 antihistamines, and 9% leukotriene receptor antagonists. Of Allergists who treat children, many would give VIT down to as young as age 5 (42%), while some would give VIT down to 1 (8%), 2 (11%), 3 (8%) or 4 (8%) years old. Most respondents (71%) felt pregnancy was a contraindication for starting VIT. Of those who reported starting pregnant women, most had 1–4 patients on VIT and had experienced no problems (70%), while fewer had experienced minor (22%) or major (8%) problems. More respondents (51%) would continue VIT if the woman became pregnant after starting therapy. Most Allergists reported no problems (66%) or minor problems (18%) in this scenario with very few major problems (1.2%).
Conclusion: The most common maintenance dose was 100 μg for flying Hymenoptera and 0.5 ml of 1:100 wt/vol for IFA. Most Allergists do not pre-medicate routinely, but when doing so most commonly use H1 antihistamines. While many Allergists felt comfortable using VIT in young children, most felt pregnancy was a contraindication for starting VIT.

1824
Specific immunotherapy with Vespa crabro venom

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Background: The family *Vespidae* includes subfamilies *Vespinae* and *Polistinae*. Subfamily *Vespinae* is part of the *Vespula, Dolichovespula* and *Vespa* genera, and among the *Vespa* genus, it is the *Vespa crabro* (*VC* – European hornet) that predominates in Europe. A recent study conducted in the Mediterranean area showed that the relative risk of developing severe systemic reactions is three times higher from a hornet sting compared to the bee or wasp. In the case of sensitisation to *VC* venom, the European guidelines consider venom immunotherapy (VIT) using only *Vespula* venom sufficient for obtaining adequate protection against an allergic reaction. However, antigen 5 immunoblotting studies showed that there is a true allergic sensitisation to *VC* venom, thus this venom should be used in VIT. For the last few years, *VC* venom has been available for use in diagnosis and in VIT (Anallergo srl). We evaluated the efficacy and tolerability of VIT with *VC* venom in patients who have had a systemic reaction to the *VC* sting and who were eligible to be admitted to the VIT.
Method: VIT: a modified rush regimen was used; during the build-up period, *VC* venom in the aqueous phase was used, while *VC* venom adsorbed in tyrosine was used during the maintenance phase.
Results: Two hundred and five patients were admitted to the VIT program, of

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whom 93 had already completed a 5 year cycle. Safety: no patient showed adverse systemic reactions; 27 patients showed large local reactions only during the initial phase (13% per patient). Efficacy: 66 patients were field re-stung by *VC*, for a total of 117 stings; out of them 19 were large local reactions and 93 negative, while five patients showed a systemic reaction (generalised urticaria/erythema); efficacy was 95.7%. Following discontinuation of VIT, 15 patients were re-stung, for a total of 17 stings: 16 were negative and one patient presented large local reaction.

Conclusion: Our study demonstrates that VIT with *VC* is safe. With regard to efficacy, the results of re-stings confirm the data reported in the literature. Although at present the number of patients who were restung after discontinuing VIT is quite small, it should still be noted that no systemic reactions occurred.

1825
Venom immunotherapy in patients with clonal mast cell disorders: efficacy, safety and practical considerations

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Background: A preferential association between systemic mastocytosis (SM) and Hymenoptera allergy (HVA) has been observed. Patients with both diseases are at risk for more severe reactions and venom immunotherapy (VIT) may represent a life-saving treatment, but the use of VIT in such patients raised concerns about the safety.

Objective: We evaluated a large population of patients with SM and HVA receiving VIT.

Methods: This prospective study was performed in Italy and Spain. Diagnosis of SM and HVA and VIT prescription were made according to international recommendations. Patients were carefully followed-up during VIT, with a special attention to field-stings.

Results: Of 84 patients (70 male, mean age 52.1), were included, 81% with grade IV reaction, 91% with indolent SM. No difference was seen between the Italian and Spanish patients. There were ten adverse reactions during the induction phase: three with the conventional induction and seven with the rush-modified induction, none resulting in epinephrine administration/hospitalisation. Fifty patients had one or more field re-sting (95 episodes), none during build-up. The time elapsed from starting VIT and first re-sting was 2 months–7 years, and the number of re-stings per patient was 1–6. Of the 50 re-stung patients, 43 (86%) resulted to be fully protected. Seven patients had reactions, and the maintenance dose was safely increased to 200 μg. The maintenance dose interval was not different between patients with and without reactions at re-stings.

Conclusions: VIT is well tolerated, safe and effective in patients with SM.