Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

Poster Session TPS 19

Management and alternatives in drug allergy

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A single day desensitization protocol for iron salts: a case report

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Background: Hypersensitivity reaction to iron salts have not been occured commonly.

Immediate and late immunologic reactions or non-immunologic reactions by mast cell activation could be seen. There were limited number of case reports about desensitization with iron salts in literature. Our aima is to report a case who experienced anaphylactic reaction by using iron salts 2 and 3 were succesfully and rapidly desensitized to ferous glisin sulphate.

Method: Oral provocation test with ferrous II glisin sulphate was performed to the patient. When she had pruritus, erythema and dispnea on the third dose (50 mg elemantal iron), she was treated immediately. Rapid desensitization protocol was started at tenth day after the oral provocation test.

Results: The patient had severe anemia at the beginning (plasma Hb:7.7 g/dl, hematocrite value:24.1%, MCV:72 fl). After the premedication with Pheniramin maleat and prednisolone, the desensitization was started. The protocol was modified from the 2 days protocol of Demir and coll. Solution form of ferrous glisin sulphate was used in the protocol. First dose of desensitization was 1:10 000 dilution of daily dose of ferrous II glisin sulphate. Single day protocol was performed at 13 steps. Three seperate bottle were prepared and one of them contained the originale dose. Desensitization was started with 0.25 ml (0.01 mg elemantal iron) from the second bottle containing 1:100 dilution of the originale dose and dose was doubled in every 20 min. The patient was desensitized successfully at the end of the first day. At the second day the treatment have been continued with the original dose. There have been no problem on the second month of desensitization.

Conclusion: Single day rapid desensitization with iron salts has never been mentioned in literature. As being fast and helpful, this protocol would be useful in the patients who have hypersensitivity to iron salts and having no other alternative treatment.

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Successful desensitization protocol with Linezolid

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Background: The goal of the current study was to evaluate the tolerance and effectiveness of Linezolid challenge using a 300-min desensitizing oral regimen in a patient with clinically documented mild to moderate Linezolid hypersensitivity.

Introduction: Linezolid (Oxazolidinone) is an antibiotic used for the treatment of serious infections caused by gram-positive bacteria that are resistant to other antibiotics. Minimal data exist on linezolid desensitization protocols.

Method: A 70-year-old man with bilateral pleural effusion, community- acquired pneumonia and empiema secondary to *S. intermedius*, presented a mild-moderate hypersensitivity reaction to Linezolid during his stay at the hospital. Cutaneous tests confirmed hypersensitivity. Premedication was administered before the desentization procedure. A 15- step Linezolid oral desensitization protocol was developed and successfully implemented without adverse reactions.

We did not have to follow test doses of Tigecycline or Daptomycin.

LINEZOLID (ZYVUDIX) 100 mg/5 ml granules for oral suspension.

Table with: Time (min), Administered dose (mg) and Cumulative dose (mg).

Results: We report a successful desensitization protocol for a patient with a proven allergic reaction to Oxazolidinone by using an escalating 15- dose oral procedure.

Desensitization was successful, safe and convenient, offering an effective therapeutic strategy to our patient. He subsequently completed and tolerated a week course/ 12 h of Linezolid therapy upon finishing the desensitization protocol.

Conclusion: Linezolid desensitization can be a viable option in patients requiring antimicrobial therapy for complicated gram- positive bacteria- skin and soft tissue infections. With precautions, including premedication, a monitored nursing unit, and immediate availability of an emergency anaphylaxis kit, drug desensitizationallows patients the ability to safely use medications to which they may have hypersensitivity.

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Immediate reaction to omeprazole. Management in *Helicobacter pylori* gastritis

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Background: Proton pump inhibitors (PPIs) are widely used for the treatment of acid-related gastrointestinal diseases. Hypersensitivity reactions (DHRs) with PPIs are rare, but they are being more reported in recent years due increasing consume. Helicobacter pylori gastritis is increasing, and treatment with a PPI is essential, in addition with antibiotics.

Omeprazole was found to be the most common culprit PPI causing IgE-mediated reactions. Several cross-reactivity PPIs patterns were described: among all group; between some groups with tolerance to others (Omeprazole/Esomeprazole/Pantoprazole and Lansoprazole/ Rabeprazole); and no cross reactivity.

We presented an atopic 43-year-old woman who received omeprazole 40 mg/ day as treatment for Helicobacter pylori gastritis, 30 min after the first tablet, she developed generalized urticaria.

She was referred to our unit for evaluation of drug allergy.

Method: After written informed consent obtained, skin prick tests (SPTs) were performed with undiluted commercial

parenteral preparation PPIs (omeprazole, esomeprazole and pantoprazole at 40 mg/ml), and solutions (powder in saline) of lansoprazole at 30 mg/ml and rabeprazole at 20 mg/ml. Intradermal tests (IDTs) were performed with 1/10 dilution of initial concentration. Histamine and buffered saline were used as positive and negative controls, respectively. Basophil activation test (BAT) was performed: with omeprazole, esomeprazole, pantoprazole and lansoprazole at 3 different concentrations (2, 0.2 and 0.02 mg/ml) using CD193 (CCR3) and CD203c for basophil selection and CD63 as activation marker. Drug provocation test (DPT) was performed if skin tests and BAT were negative.

Results: SPT and IDT were positives with omeprazole and esomeprazole. BAT was positive with omeprazole and esomeprazole. DPT was negative with lansoprazole and pantoprazole.

Conclusion: We report a sensitized patient to omeprazole and esomeprazole with good tolerance to lansoprazole and pantoprazole.

Skin test, BAT and DPTs were useful for diagnosis and cross reactivity assessment

Our Algological work up allowed to perform a correct treatment of helicobacter pylori infection.

Similar chemical structure of Omeprazole and Esomeprazole (S-isomer of omeprazole) could explain the sensitization to both, although there are reports of patients sensitized to omeprazole who tolerated esomeprazole.

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Successful desensitization of a delayed type local hypersensitivity reaction due to anakinra

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Background: Anakinra is a recombinant IL-1 receptor antagonist which can be used in rheumatoid arthritis, gout and Familial Mediterranean Fever. The most common adverse reaction is reported as the local reactions seen in the injection site which may cause the cessation of the treatment. Here we present a patient who experienced a delayed type local hypersensitivity reaction to anakinra and was therefore successfully desensitized.

Case: A 32 year old woman was referred to us because of repeating delayed type hypersensitivity reactions on the injection sites of anakinra with a daily dose of 100 mg. On the 10th day of the treatment, erythematous, itchy swollen lesion with a diameter of 10 cm developed on the injection site and therefore anakinra was stopped. Two months later due to the lack of effective alternative treatment, desensitization was planned. The prick and intradermal tests were negative. A single blind placebo controlled provocation test with 100 mg anakinra was subcutaneously performed. The next day the same lesion developed on the injection site. The day after, we administered two separate doses of 50 mg and again the same reaction developed on both sites. We planned a desensitization protocol starting with 10 mg/day and following by 20, 40 and 50 mg anakinra which was administered on three consecutive days. On the 5th day, a total of 100 mg was injected on two different sites with equally divided doses. On the 6th day, a single dose of 100 mg was administered and an erythematous and itchy lesion with approximately one cm in diameter developed. Therefore, the daily 100 mg dose was considered to be applied in two 50 mg doses on two different sites in her follow up. She had no complaints during her 6 month of follow up.

Result: This presentation reports the first case who was successfully desensitized for a delayed type local hypersensitivity reaction induced by anakinra.

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Use of omalizumab as preventive treatment in a carboplatin's desensitization

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Background: Carboplatin is a chemotherapy drug used in the treatment of ovarian cancer. Hypersensitivity reactions occur in up to 20% of patients, most after the rechallenge of a second stage of treatment. To assess the efficacy and safety of the desensitization protocol with carboplatin in 12 steps, by using as preventive treatment with omalizumab, in an anaphylactic shock patient.

Method: A 52 year-old woman, with no previous history of atopy and suffering an ovarian serous papillary adenocarcinoma stage IV with peritoneal carcinomatosis.

February 2013: Hyperthermic intraperitoneal chemotherapy with Taxol is combined with cytoreductive surgery and adjuvant chemotherapy (5 cycles of Taxol and Carboplatin).

March 2014: Progression of the disease. A new line with Liposomal Doxorubicin and Trabectedin is started completing 3 cycles but recurrence of cancer is evidenced in CT and a new line of treatment with gemcitabine-carboplatin is chosen.

June 2014: The first cycle of gemcitabine and carboplatin is administered with good tolerance. In the second, third and fourth cycles, the patient had immediate reactions during infusion of Carboplatin, earlier and more severe each time. During the fourth cycle, within 10 min of starting the infusion, begins with itching, generalized erythema, labial-facial angioedema, generalized urticaria, dyspnea, low O_2 saturation, throat tightness and hypotension. Ought to the suspicious of carboplatin as a culprit for immediate hypersensitivity, skin tests with carboplatin at different concentrations were performed.

Results: Intradermal skin test with carboplatin was positive at 0.1 mg/ml. Because of the severity of the reaction, the baseline health of the patient and that carboplatin was the only possibility of treatment, Omalizumab was administered as preventive treatment and desensitization protocol in 12 steps, it was done successfully. The patient suffered only a mild skin reaction at the 11th step.

Conclusion: Omalizumab used as a preventive treatment, could be an option for patients diagnosed with immediate hypersensitivity reactions, with severe symptom and needed of the agent used in the desensitization.

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Successful desensitization to vitamin d in vitamin D deficiency

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Low levels of vitamin D are associated with asthma severity and exacerbation rates especially in nonatopic asthma. On the contrary, colecalciferol can rarely cause allergic reactions including anaphylaxis.

Case: A 52-year- old female who was diagnosed with vitamin D sufficiency, experienced itch and hives on the first dose of colecalciferol. Because of these complaints, she referred to our allergy clinic. To evaluate the patient for drug hypersensitivity, a skin test with the culprit drug was performed. This test was conducted 4 weeks after the last reaction to minimize the likelihood of a false-negative result. Due to negative skin test with the culprit drug, oral drug provocation test with colecalciferol was performed in 30 min intervals in

increasing doses starting with 1/10 of the total dose, following by 1/4, and the remaining dose. Ten minutes after taking the last dose, she experienced urticaria, dyspnea, palpitations and hypotension. Her clinical reaction was considered as anaphylaxis and 0.5 mg of epinephrine, 45 mg of pheniramine and 40 mg of methylprednisolone were administered immediately. The reaction resolved within 2 h. As an alternative treatment was not recommended for vitamin D deficiency, desensitization protocol with colecalciferol was planned. Desensitization was successfully completed and the patient could tolerate a total dose of 50 000 IU of colecalciferol (Table 1). In conclusion, this report describes the first successful desensitization protocol for a type 1 hypersensitivity reaction due to colecalciferol.

Table 1 Colecalciferol Desensitization Protocol

Hour	Dose
08:30	1 drop
09:00	2 drops
09:30	3 drops
10:00	5 drops
10:30	8 drops
11:00	12 drops
11:30	18 drops
12:00	27 drops
12:30	40 drops
13:00	60 drops
13:30	124 drops
Maintenance dose	6 drops daily

The total dose is 300 drops = 50 000 IU.

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Clinical features of ranitidine induced immediate hypersensitivity and their cross reactivity

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Background: Ranitidine, a competitive reversible H2 receptor antagonist, commonly used to treat gastric acid related disease. It is usually well-tolerated, and immediate severe hypersensitivity reactions to ranitidine are rare. In addition, little information is available on cross-reactivity with other H2-receptor antagonists. We aimed to investigate the clinical features of ranitidine induced immediate hypersensitivity and their cross reactivity.
Method: We recruited patients diagnosed as immediate hypersensitivity to ranitidine based on clinical history and immunologic test and/or provocation test from 4 University hospitals in Busan, Korea. Their medical record was retrospectively reviewed. To evaluate their cross-reactivity, skin test results performed with various H2 receptor antagonist were analyzed.
Results: A total of 10 patients were enrolled in this study. The mean age was 50.8 ± 13.7 years (range 26–68) and 6 patients were male. 3 patients had history of allergic rhinitis or drug allergy. 6 patients previously experienced allergic reaction to H2 antagonists, but they were not diagnosed before. All patients except one presented systemic symptoms by ranitidine. Anaphylaxis was the most common symptom ($N = 6$, 60%), followed by systemic urticaria ($N = 2$), local urticaria with rhinitis symptom ($N = 1$), and local urticaria ($N = 1$). The mean latent time was 24.3 ± 25.7 min (range, immediate~90). Although 6 Patients experienced these symptoms by taking oral table, 4 patients with intravenous injection all presented anaphylaxis. Skin test results showed positive response in both cimetidine and famotidine in 6 patients.
Conclusion: Ranitidine is widely used and generally tolerated. However, anaphylaxis was the most common symptom in ranitidine induced immediate hypersensitivity. In addition, our data showed significant cross reactivity between ranitidine and cimetidine, famotidine drugs.

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Shrimp and iodinated contrast media allergy: myth or reality?

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Background: Iodinated contrast media (ICM) is the most commonly used contrast media in radiology and increasingly used in medicine. However, misconceptions concerning reactions to ICM are still very prevalent, namely the association to shellfish allergy.
Objective: Evaluate the existence of an association between shrimp allergy and ICM allergy.
Methods: Observational retrospective study of adult patients with reactions to ICM followed at the authors' Immunoallergology Department. Analyses included demographic data, route of administration, characterization of the reaction, sensitization profile to ICM [by skin prick (SPT), intradermal and patch tests], sensitization to shrimp (by SPT with Der p 10 and shrimp extract) and clinical history of shrimp allergy. Patients were included if they had both ICM and shrimp data described above.
Results: 70 patients were included: 23 men, 47 women, averaging 59 ± 15 years. The most common administration route of the ICM was intravenous (65.7%). 55.4% of the ICM reactions were immediate (≤1 h) and 44.6% were late (>1 h);21 patients (30%) had positive skin tests do ICM: 15 (21%) intra-dermal and 7 (10%) patch tests. No SPT was positive. The most commonly identified agent in tests was iopromide in intradermal tests and iodixanol in patch tests.

2 patients had positive sensitization to shrimp: 1 (1.4%) had positive intradermal tests to ICM and SPT to shrimp and also had a clear history of allergic reaction to shrimp (but developed it years after the ICM reaction). The other, had positive SPT to shrimp and *Der p 10*. Of note, a third patient had had positive SPT to *Der p* 10 but not shrimp. Neither of these last two had history of allergic reaction to shrimp nor positive tests to ICM (but both had sensitization to mites and allergic rhinitis).
Conclusion: Only 1 in 70, had both shrimp and ICM allergy; but shrimp allergy developed years later and cannot be considered a risk factor for ICM reactions. One had an asymptomatic shrimp sensitization due to mite tropomyosin cross-reaction. Patients may be simultaneously allergic to shellfish and to ICM. However, these allergies are not related, nor is there any data to suggest that a history of allergy to shellfish is a risk factor to the development of ICM allergy.

Patients undergoing exams with ICM should not be specifically questioned about possible allergy to shellfish. If they are, neither prophylactic medication nor postponement of the exams should happen due to that fact.

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Is 'Iodine Allergy' a contraindication to iodinated contrast media? The spread of a myth

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Background: Before every contrast media (CM) exam, patients are asked about a possible 'iodine allergy', because people believe that there is a relation between iodinated contrast media (ICM) and others substances with iodine. This idea has been

spreaded for decades, even in medical community but it isn't more than a myth. Our objective was evaluate if patients with suggestive history of ICM allergy would have iodine allergy or iodine sensitization.
Method: Retrospective observational study between June 2006 to April 2015, with patients referred to our department with suggestive history of ICM allergy. Patients were characterized according to demographic data, way of ICM administration, time between administration of ICM until allergic reaction, type of allergic reaction to ICM, sensitization pattern to various ICM with skin prick tests (SPT), intradermic tests (IDT) and epicutaneous tests (EpiT) and pattern of sensitization to iodine, iodopovidone and povidone by EpiT. There were excluded all patients without concomitant study of sensitization to ICM, iodine, iodopovidone and povidone.
Results: From 109 patients observed, 101 were selected, which had had suggestive history of reaction to ICM (38% male, 62% female, Median Age 60 ± 15 years). The more frequent way of ICM administration was intravenous (62%). 52% of reactions occurred less than an hour after administration of ICM (immediate reactions) and the others 48% were late reactions. From 101 patients, 45% had ICM positive cutaneous tests: 24% IDT and 34% EpiT. Only 2 (2%) had positive EpiT with iodine, 19 (21%) with iodopovidone and 4 (4.5%) with povidone. From 19 patients with sensitization to iodine/iodopovidone, 9(47%) had positive cutaneous tests to ICM. Any patient had referred clinical issues with contact with iodine products.
Conclusion: Besides most of allergic reactions associated to administration of CM occurs with ICM, only 2% of patients seem to be sensitized to iodine and 21% to iodopovidone, without any clinic associated. Doesn't exist correlation ($P = 0.86$) between 'iodine allergy' and reaction after ICM administration, so mention to this allergy or reaction after contact with iodine products can't be contraindication to do exams with administration of ICM or indication to do prophylactic therapeutic.

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Risk factors associated with cardiac arrest and death in hospitalized patients due to anaphylaxis during the period 1998–2011

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Background: We have evaluated in the Spanish database of patients admitted, the risk factors related to cardiac arrest and to die during hospitalization due to anaphylaxis.
Method: The study was carried out using the basic Spanish minimum data set for 1998–2011 years. The system uses the codes of the Spanish version of the ICD-9-CM and covers 98% of public hospitals in Spain. Possible cases of anaphylaxis were obtained only in the principal diagnostic field. We use two strategies: First, we chose the codes ICD-9-CM specifically associated with anaphylaxis. Secondly, we used combined codes of causes of anaphylaxis and symptoms or signs of organ and systems in order to select episodes that met the criteria for the definition of anaphylaxis following an adapted Harduar-Murano′s strategy. A record of the database was considered fatal anaphylaxis if the type of discharge was death. Comorbidities ascertained as risk factors were selected from that used in the Elixhauser′s score. We build different logistic regression to estimate the various risks using all illnesses of Elixhauser′s score, age, sex and cause of anaphylaxis
Results: 5261 admissions whose main diagnosis was anaphylaxis were found. Out of them, there were 116 cases of deaths and 136 cases of cardiac arrest. Cardiac arrhythmias and aged over 50 years were common risk factors to suffer a cardiac arrest or death. In the case of cardiac arrest, other associated risk factors were chronic lung diseases, solid tumours without metastases and age group of 15–49 years. On the other hand, pulmonary circulatory disorders, coagulopathy and electrolyte disturbance was associated with an increased risk of death among anaphylaxis admissions. Similarly, the risk of death due to anaphylaxis echinococco was higher than all other causes of anaphylaxis. For both outcomes, C-statistics or discrimination was high (cardiac arrest 0.77; 95% CI 0.75–0.77, 0.82 deaths, 95% from 0.80 to 0.83). Good calibration was noted for cardiac arrest, but not for death ($P = 0.59$ and 0.03 respectively, Hosmer-Lemeshow test).
Conclusion: Respiratory, cardiovascular disorders and older ages, as classically described, were involved in patients who suffered a cardiac arrest or death. Echinococco anaphylaxis was the only great cause of anaphylaxis, which was a risk factor for deaths. Coagulopathy and electrolyte disturbances occurred frequently in cases of death and cardiac arrest. Finally, the chosen models had discrimination higher than 0.75.

Poster Session TPS 20

Delayed drug reactions

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Generalized fixed drug eruption induced by fluconazole: lymphocyte transformation test and measurement of intracellular cytokines secretion confirm the diagnosis

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Background: Fixed drug eruption (FDE) is a kind of drug hypersensitivity reaction characterized by skin lesions that recur on the same sites upon re-exposure to a drug. Although single lesion is usually seen, multiple eruptions can be developed. Fluconazole is frequently used for the treatment of oral, esophageal or vaginal candidiasis. Generalized form of FDE caused by fluconazole is rarely seen. Here we present a rare case of generalized FDE caused by fluconazole of whom diagnosis was confirmed by lymphocyte transformation test (LTT) and measurement of intracellular cytokines secretion.
Case: A 45 years old female patient was referred to us because of the lesions which were developed after the fluconazole ingestion due to vaginal candidiasis. Five months ago, after the forth dose of the drug erythematous, itchy oval multiple lesions over the body were developed. She stopped to use the drug and applied the topical steroid to the lesions and they were resolved with hyperpigmentation. The biopsy taken from hyperpigmented area only revealed increased melanocytes. Patch tests with the culprit drug on areas of clean skin and above the lesion were found negative. Since the patient did not want to be provocated with the culprit drug in order to clarify the reaction, LTT was performed and intracellular secreted IL-4 and IFN-γ levels were measured after the drug exposure. Significant proliferation of $CD4^+$ T cells in response to fluconazole was observed. After the drug exposure, IL-4 level was increased and IFN-γ level was decreased which can confirm the diagnosis. Since the patient needed a safe antifungal drug due to her recurrent vaginal candidiasis, and itraconazole was not suitable for *in vitro* tests, single blind placebo controlled drug provocation test was performed with itraconazole and it was found negative.
Conclusion: This is a rare case report of generalized FDE caused by fluconazole of whom diagnosis was confirmed by *in vitro* tests.

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Exanthema induced by cinitapride

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Background: Cinitapride is an orthopramide with prokinetic activity in the gastrointestinal tract with procholinergic and serotoninergic activity. Its main difference with other orthopramide like clebopride, domperidone and metoclopramide is the ausence of antidopaminergic activity.
Method: We present the case of a 72-year-old woman referred to our department with a diagnosis of gastroesophageal reflux disease, for which cinitapride 1 mg were prescribed. After 7 days taking drug, she developed a pruriginous maculopapular rash without other lesions, which spontaneously resolved untreated. She stopped using drug during 15 days and reintroduced them again; after 7 days of treatment, she developed generalized exanthema without other symptoms. Se was treated with Ebastine and her symptoms disappeared after a few days.
Results: Write informed consent was obtained from the patient for patch tests and drug provocation test. Patch test performed in10%, 20% and 30% pet with cinitapride gave negative results at 48 and 96 h. Then we performed a single-blind placebo-controlled drug provocation tests with Cinitapride 0.375 mg on first day and 1 mg after 4 days. Eight days later, patient came to our department complaining of itching and maculopapular rash distributed on back and legs, which dissapeared without treatment.
Conclusion: We present a case of nonimmediate reaction to cinitapride. There are few reports of hypersensitivity reactions to prokinetic drug, most related to metoclopramide. We have only found one report of delayed hypersensitivity to cinitapride in which patient can tolerate other orthopramides. The mechanism involved in these reactions is unknow. As in the previous case publicated, skin tests were negative, and oral challenge had to be performed to confirm the diagnosis.

903
Acute generalized exanthematous pustulosis: a purpose of 4 cases

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Background: Acute generalized exanthematous pustulosis (AGEP) is a rare, acute eruption characterized by the development of numerous nonfollicular sterile pustules on a background of edematous erythema. Fever and peripheral blood leukocytosis are usually present. In approximately 90 percent of cases, AGEP is caused by drugs. The eruption develops within hours or days of drug exposure and resolves spontaneously in 1–2 weeks after drug discontinuation. We report 4 cases of pacients which had compatible syndrome with AGEP.
Method:

Patient 1: A 32-year-old female presented pustules in trunk after taking 2 days Azithromycin 500 mg every 24 h due to respiratory infection.
Patient 2: A 41-year-old female presented pustules in face and neck after taking 3 days Amoxicillin 500 mg every 8 h due to pharyngitis.
Patient 3: A 36-year-old female presented pustules in chest and back, after taking 2 days Amoxicillin/clavulanic acid 500/125 mg every 8 h due to dental abscess.
Patient 4: A 26-year-old female presented pustules in arms and trunk after taking 5 days Doxycycline 50 mg every 8 h due to urinary infection.

None of them had relevant medical history or usual treatment. All patients referred dysthermia without measurable fever. No symptoms of organ involvement were reported. Eruptions resolved spontaneously in less than a week after leaving suspected drugs, no emergency health care was required and there weren't any

Patient	Elapsed time (in years)	Skin test (prick e intradermal)	Oral controlled challenge test
1	8	Azithromycin: Negative	Azithromycin: Positive at 2nd day
2	4	Beta-lactams (PPL, MDM, Penicillin G and Amoxicillin): Negative	Amoxicillin: Positive at 6th day
3	3	Beta-lactams (PPL, MDM, Penicillin G, Amoxicillin and Amoxicillin/ clavulanic acid): Negative	Amoxicillin/clavulanic acid: Positive at 3rd day Cefuroxime: Positive at 3rd day
4	1	Doxycycline: Negative	Doxycycline: Positive at 2nd day

[Allergologic study]

laboratory determination extracted when symptoms. The Primary Care doctor's monitored the clinical evolution of four patients which was favourable.

Results: Results are showed in the following table.

In pacient 4, pustular liquid smear was taken and his culture resulted negative for bacteria. No skin biopsy was done.

Conclusion: We report 4 cases of AGEP which were suspected clinically and confirmated after oral controlled challenge tests. The involved drugs were antibiotics (beta-lactam, tetracycline and macrolide). In all cases, patients have not relapse of episodes avoiding involved drugs with posterior tolerance to other antibiotics.

905
Exudative erythema multiforme caused by hidden drug

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Background: Exudative erythema multiforme is a self-limiting dermatosis with characteristic skin lesions and variable mucosal involvement. In almost 50% of cases, the trigger is unknown. This condition has been associated with viral infections (eg, herpes simplex infection), drugs, connective tissue disease, and tumors. Several drugs have been associated with this reaction, especially sulfonamides, penicillins and other antibiotics, NSAIDs (diclofenac, ibuprofen, naproxen) and allopurinol.

Method: 34-year-old women with a history of gestational DM, presented several episodes of demarcated violaceas-erythematous plaques located extremities with a blister, oral mucosal lesions. All episodes appeared after tooth extraction or manipulation and taking drugs. She has taken different drugs in different episodes (amoxicilin in 3 episodes, espiramicin/metronidazole in one episode) and in all of them ibuprofen. In all episodes the local anesthesic used was lidocain.

Following these episodes she tolerated ibuprofen, espiramicin/metronidazol, lidocain. She did not take amoxicillin again.

Subsequently during allergy study, after 4 h of administration a capsule of metamizol on his own presented the same clinic.

Remembering all the episodes of dental manipulation she has taken in every episode a capsule of metamizol.

Skin tests with beta-lactam antibiotics, metamizol, skin biopsy performed under informed consent. Oral challenge with amoxicillin, metamizol was carried out.

Results: Skin prick and intradermal tests with penicillin G, ampicillins, amoxicillins, cefuroxima and metamizol were negative. Delayed intradermal tests with metamizol were negative.

Oral challenge tests were negative for amoxicilin, but positive for metamizol.

Histopathology of a skin biopsy from the lesions on the hands revealed the lesions to be compatible with exudative erythema multiforme.

Conclusion: We present a case of erythema multiforme secondary to pyrazolones whose cause was difficult to diagnose because the offending drug was not specified.

A good medical history, skin biopsy and drug challenges are useful tools to detect the drug involved in reaction in pacients with histories of mild reactions including many drugs.

906
Generalized exanthematous pustulosis induced by ambroxol

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Background: Acute generalized exanthematous pustulosis is a rare manifestation of drug allergy. It is characterized by fever, exanthema and multiple small pustules. The most frequent cause is antibiotics. Drugs adverse reactions associated with an acute infection is one of the most difficult entity to manage and diagnose. We describe one case of generalized exanthematous pustulosis with an unusual drug implicated.

Case report: A 59-year-old man with cough because of a respiratory infection started treatment with Paracetamol and Ambroxol syrup every 8 h. After 2 days, he began with facial erythematous rash that generalized to the back, thorax, limbs, and associated generalized swelling. At this point, the patient was evaluated in Emergency and Dermatology Departments and he was hospitalized with antibiotic and high dose of corticoids treatment. In the following days he began with high fever and the rash became desquamative. During his hospitalization the biopsy was made with the diagnosis of 'toxicodermia - Acute generalized exanthematous pustulosis'

He had no problem with Ambroxol previously.

Method: Patch tests with 5%, 10% Paracetamol and 0.5% Ambroxol in petrolatum, with 48 and 96 h readings. Oral challenge test with Paracetamol 1 g Oral challenge test with Paracetamol 500 mg every 8 h during 2 days at home.

Results: Patch tests with 5% and 10% Paracetamol: negatives. Patch test with 0.5% Ambroxol: positive (++/+++) at 48 and 96 h readings. Oral challenge test with Paracetamol 1 g: negative. Oral challenge test with Paracetamol 500 mg every 8 h during 2 days at home: negative.

Conclusion: We have presented a case of acute generalized exanthematous pustulosis caused by hypersensitivity to Ambroxol after several days of treatment. We emphasize the importance in the management and the biopsy for a correct diagnosis.

To our knowledge, this is the first case reported in the literature.

907
Fixed drug eruption due to unrelated antibiotics

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Background: Fixed drug eruption (FDE) is a cutaneous adverse drug eruption characterized by skin lesions which recur in the same sites upon re-exposure to the drug. It may occur as single or multiple lesions affecting any part of the body. Cross-

reactivity between related drugs has been widely reported, but a few cases of FDE due to different drugs have been published.
Method: A non-atopic 52-year-old man, with a history of chronic liver disease and recurrent urinary tract infections was referred for evaluation of drug allergy two times. First: 2 years before, he had developed two episodes of itchy, erythematous, well-circumscribed plaques on his back, several hours after receiving ciprofloxacin for acute cellulitis. Hyperpigmented maculas persist in the affected skin. He avoided all quinolones and he tolerated during years several betalactamics (Amoxicillin, Bencilpenicilin, Imipenem and Cefalosporins). Second time, 7 years later, the patient received Amoxicillin 500 mg/day as a treatment for respiratory tract infection. Two hours after the first tablet, he developed an itching, erythematous plaque on his left gluteus.
Results: After obtaining an informed consent, patch test were performed with quinolones over pigmented residual lesions, obtaining a positive result to ciprofloxacin and levofloxacin; and negative results to norfloxacin and moxifloxacin. Skin prick tests (SPT) and intradermal test (IDT) with all quinolones were negative in immediate and delayed readings. We performed a single-blind placebo-controlled oral challenge to norfloxacine, con negative result. The patient refused oral challenges to other quinolones.

Second work-up: Epicutaneous test, SPT and IDT with benzylpenicilloyl polylysine, minor determinant mixture, benzylpenicillin y amoxicillin were negative in immediate and delayed readings. The patient consented to perform a single-blind placebo-controlled oral challenge to amoxicillin: 60 min after 250 mg, the patient developed one itchy erythematous plaque in the same location as previously.
Conclusion: We report an unusual case of FDE induced by two groups of antibiotics in the same patient, quinolones and amoxicillin, demonstrated by epicutaneous test and oral challenge, respectively. Epicutaneous test has been useful to study cross-reactivity to quinolones, obtaining norfloxacin as a therapeutic alternative in this patient. The later consume of betalactam antibiotics could provoque the second sensitization.

908
Oxcarbazepine-induced Stevens-Johnson syndrome: a pediatric case report

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Background: Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are two rare but life-threatening diseases characterized by detachment of epidermis, bullous skin lesions and mucous membrane erosions. Although carbamazepin is the most associated antiepileptic drug, oxcarbazepine-induces SJS is extremely rarein the literature.
Case report: A 6-year old boy, who had been followed with the diagnosis of benign rolandic epilepsy and was using levatiracetam for 10 months, was admitted to our hospital because of uncontrolled seizures. Oxcarpazepin was started with the dose of 12 mg/kg/day and 5 days later the dose was increased to 18 mg/kg/day. On the 10th day of the treatment our patient had rashes around the mouth and on the lips. The rashes spreaded towards his face, body, arms and legs within a few days. He admitted to our hospital 5 days after the rash had started.

On phisycal examination; his vital signs were within normal limits and physical examination revealed red maculopapular rash and flat atypical target lesions mostly on his face and less intensly on his trunk and extremities. There werre bullous lesions and hemoragic crusts on his lips. Fotosensitivity and erythema on the preputium penis were observed.

He was hospitalized and oxcarbazepine treatment was stopped. Topical corticosteroid (metylprednisolon aseponat) was aplied to the lesions on his mouth and skin. On the 7th day of his hospitalization significant improvement was observed and he was discharged.

Punch biopsy, taken from the lesions revealed focal full thickness epidermal necrosis, basal vacuolar changes, perivascular lymphocytic infiltrates in the papillary dermis.
Discussion: Hypersensitivity to antiepileptic drugs (AEDs) was first reported by Silber and Epstein as 'nirvanol sickness' in 1934. Carbamazepine is the primary antiepileptic drug associated with SJS/TEN, but oxcarbazepine-induced SJS/TEN is extremely rare with the incidence of 0.5–6/1 000 000 in 1 year in normal population according to the FDA. OXC is a 10-keto anologue of CBZ, however there is significant differences between the metabolism of the two drugs. Although OXC is thought to be a safe drug, recent studies demonstrated that cytotoxic T-cells are drug-specific and directed against the native form of the drug rather than against a reactive metabolite. Both drugs share the same molecular structure of dibenzazepine ring, so we speculate that this might explain why OXC can induce SJS as CBZ.

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Acute generalized exanthematous pustulosis associated to amoxicillin and clavulanate - a case report

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Background: Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous reaction, characterized by the abrupt development of numerous nonfollicular sterile pustules arising on a diffuse erythematous area; fever and peripheral blood leukocytosis are usually present. The majority of cases (approximately 90%) are secondary to drugs, most often antibiotics (B-lactams and macrolides). The Naranjo Scale classifies the probability of an adverse drug reaction.
Case report: A 76-years-old female patient, with several comorbidities, was admitted to the Nephrology Department because of an acute exacerbation of her end-stage kidney disease and a rash that had appeared 1 week earlier. The dermatosis was characterized by hundreds of nonfollicular pinhead-sized pustules, involving the trunk and limbs, with flexural accentuation and some areas with anular peripheral fine scale desquamation. Twelve days prior to the admission she had been prescribed a 7-day course of amoxicillin and clavulanate (A+C) for a gout tophus infection. There was no prior history of drug allergy. Naranjo Scale score was 7, suggesting a probable adverse drug reaction. Laboratory results revealed leukocytosis with a neutrophil count over 29×10^9/l. Punch biopsy from pustules was performed, showing perivascular infiltration in the dermis, with epidermal spongiosis and exocytosis, which are histopathological features typical of AGEP. Treatment with topical and oral corticosteroids was instituted, with complete resolution of the rash after 6 days and no residual lesions.
Discussion: Clinical and histopathological findings of this case were diagnostic of AGEP. Although this is a self-limiting condition, corticosteroids may have shortened the course of disease. The acute skin eruption after the intake of A+C together with clinical improvement after drug withdrawal

and a calculated Naranjo score of 7, allow us to presume an ethiological diagnosis. Patch testing and/or lymphocyte transformation test could be useful to ultimately confirm the diagnosis.

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Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome induced by rheumatological drugs

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Background: DRESS syndrome is a rare, potentially life-threatening idiosynchratic adverse reaction to a drug with a long latency period, severe cutaneous eruption with eosinophilia and systemic symptoms. Abnormal liver function tests are found in 70–90% of cases and liver failure is a major cause of fatalities as a result od DRESS syndrome. The most common causative drugs are anticonvulsants, sulfa derivates, anti-inflammatory and antimicrobials. DRESS syndrome must be recognized promptly due to its high mortality rate. We present the case of DRESS syndrome caused by rheumatological drugs.
Case presentation: A 52-year old female was hospitalized in Vilnius University Hospital Santariskiu Klinikos with following symptoms: a temperature of 38.8°C lasting for 1 week, facial angioedema and generalized maculopapular rash. The patient had a history of rheumatoid arthritis and specific treatment was needed. Treatment with hydroxychloroquine sulfate and sulfasalazine was introduced 8 and 4 weeks respectively before the aforementioned symptoms had developed. Laboratory tests revealed an elevation in liver enzymes, eosinophilia and an increase of inflammatory markers. Serological tests for hepatitis B and C were negative. Diagnosis of DRESS syndrome was made, with reference to RegiSCAR diagnostic criteria. The treatment with sulfasalazine and hydroxychloroquine sulfate was discontinued. The treatment with prednisone 60 mg/day and clemastine 1 mg/day was started with a good respone to it. The patient was discharged from hospital in a good condition: clinical symptoms improved and all laboratory markers returned to baseline.
Conclusion: In this case we illustrate the importance of an early recognition of DRESS syndrome and a good outcome achieved with an immediate withdrawal of the causative drugs.

911
Delayed reaction due to interferon-α 2b controlled by premedication with oral antihistamines

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Background: Interferon-α 2b is a glycoprotein mainly used for the treatment of chronic hepatitis, leukaemia, multiple myeloma, follicular lymphoma, carcinoid tumour and malignant melanoma. Hypersensitivity reactions related with this drug have been rarely reported.
Case report: A 59- year-old woman treated for melanoma since April 2015 with subcutaneous interferon-α 2b presented in October 2015, 8 h after the administration of the drug, with large pruriginous wheals in the inner thighs, small hives on the inside of the arms, morbilliform rash on her face and slight edema in the ear lobes. No other symptoms associated. The patient was treated in the Emergency Department with antihistamines and corticosteroids improving within 48 h. She had taken paracetamol prior to the administration of interferon α-2B, and perhaps also dexketoprofen some hours earlier. After the reaction, she has not taken any of these drugs.
Methods and Results: After written informed consent was obtained, we performed the allergologic study 4 weeks after the reaction. The oral controlled administration of paracetamol and dexketoprofen was well tolerated. Prick tests with interferon-α 2b proved negative. Reading intradermal tests at 8–10 h with the highest concentration of interferon-α 2b (6 MU/ml) showed local erythema, without induration or pruritus. This reaction was more attenuated with 1/10 dilution and was negative with 1/100 dilution. Both reactions disappeared after 48 h without treatment. We considered these reactions as negative, so subcutaneous administration of interferon-α 2b was carried out. Forty-eight hours later the patient suffered the reaction previously described, which was controlled with oral antihistamines within 48 h. No reaction was observed at the injection site of administration. Because interferon-α 2b was an irreplaceable drug for the patient and the reaction was mild, we prescribed loratadine (10 mg/12 h) as maintenance therapy and we indicated the patient to keep the usual dose of interferon-α 2b (3 days a week on alternate days). Since then, no further reactions have been observed.
Conclusion: We report the case of a patient with a delayed cutaneous reaction with interferon-α 2b controlled with premedication with oral antihistamines, an option to consider in similar cases.

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Contact dermatitis caused by a hair dye: a case report

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Background: Contact dermatitis is a skin disorder caused by the contact with an exogenous substance that is produce type IV hypersensitivity that is mediated by cells, lymphocytes, macrophages and the clinical appearance is eczema and skin edema almost immediately after the appliance of the substance.
Case presentation: A 70 year old male with history of intermittent rhinitis presented with eyelid edema and eczema on his face that appears 20 min after the use of hair dye (HD). Patch test was performed with positive results. He receive treatment with antihistamines and corticosteroids. The ingredients of hair dye were: Sodium perborate, p-phenylenediamine sulfate, Cellulose Gum, M-aminophenol, sodium carbonate, disodium lauryl sulfosuccinate, algin, Sapindus Mukurossi, magnesium stearate, p-aminophenol, and fragrance. Some of them report dangerous side effects such as the p-phenylenediamine sulfate, which is the most common cause of contact dermatitis in stylists and users.
Conclusion: Several hair dyes are freely available both OTC and online. Some may contain dangerous substances that can cause side effects. Given the widespread use of OTC HD allergologists and dermatologists should be able to recognize angioedema, which may be under reported.

913
Sneddon Wilkinson disease: differential diagnosis issues with acute generalized exanthematous pustulosis. A case report

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Background: Sneddon Wilkinson disease is a rare, chronic, recurrent disorder, of unknown etiology, characterized by the occurrence of erythematous patches with flaccid pustules distributed in the flexural areas and the trunk. Acute generalized exanthematous pustulosis is an uncommon skin reaction characterized by the sudden

appearance of a pustular eruption, usually triggered by drugs or infections.

Method: We report the case of a 46 year old male Caucasian patient who addressed the dermatology department for a skin eruption consisting in erythematous, scaly plaques with multiple flaccid pustules, distributed on the trunk, the axillary and inguinal regions and the arms, which had occurred 5 days beforehand. The patient had had a dental infection 2 weeks before and had been treated with amoxicillin, cephalexin and clarithromycin. The physical examination was within normal range. The patient was afebrile.

Results: A complete blood count was performed and showed mild leukocytosis, neutrophilia and thrombocytosis. The erythrocyte sedimentation rate and the C-reactive protein were within normal range. Serum protein electrophoresis showed no alterations. The lymphoblastic transformation test (LTT) was performed for amoxicillin, cephalexin and clarithromycin and was positive for amoxicillin. Two biopsies were taken, one from the axillary region and one from the trunk. The histopathological examination showed ortokeratosis, sub- corneal pustules with neutrophils and some eosinophils, acanthosis, papillomatosis, dermal oedema with dilated capillaries and inflammatory infiltrate with lymphocytes, monocytes and some eosinophils. Based on the clinical examination, the laboratory findings and the histopathological examination the patient was diagnosed with Sneddon-Wilkinson disease.

Conclusion: The differential diagnosis with acute generalized exanthematous pustulosis was difficult because the lymphoblastic transformation test was positive for ampicillin. However, the physical examination, clinical examination and laboratory testing pleaded for the diagnosis of Sneddon-Wilkinson disease. Multiple tests are often required to establish the diagnosis in rare cases, such as the one we are presenting, but the clinical examination still plays a central role in diagnosing dermatological disorders.

914
Rare case report of contact hypersensitivity to parabens and glucocorticoids

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Background: 60 years old, male, caucasian. Presented intense skin itching on arms and forearms that started 7 years ago, which progressed to skin lesions on the dorsum of the hands including fingers and interdigital surfaces, feet and genital area, characterized by eczematous-desquamative plaques, with the presence of fissures. These lesions were related with the local application of propionate clobetasol 0.05% cream self-prescribed. Each time he was treated with topical glucocorticoids, after every application he developed more severe skin lesions as previous described. Patient used to apply many self-prescribed topical drugs as glucocorticoids, local anesthetics, oat based creams and hemorrhoids over the counter ointments.

Results: On 2015, a biopsy sample was taken from the left forearm. The pathologist diagnosis was: Vacuolar interfase dermatitis, superficial perivascular lymphocytic infiltrate with keratinocyte necrosis, this suggested cutaneous drug adverse reaction. Laboratory results were normal. A Patch test Smart Practice TRUE battery was performed with positive for parabens mix 16% (++), Methylisothiazolinone (++). It was also performed a patch test with all the creams and ointments the patient already had used, the positive results were: nistatine (+++), propionate clobetasol 0.05% (+++), lidocaine gel 2% (+++), hydrocortisone 2.5% cream (+++), clobetasol propionate 0.05%/vitamin A/lactic acid cream (+++), oat based cream with parabens (+++). A new patch test was performed in order to discriminate between parabens hypersentivity reaction and glucocorticoid hypersensitivity reaction. This patch test was performed with propionate clobetasol 0.05% parabens free vehicle (+++), parabens free base cream vehicle (-) and base cream vehicle with parabens (+). It was concluded that the patient presented a cutaneous retarded hypersensitivity reaction to parabens and as well to clobetasol.

Conclusion: Parabens are a class of widely used preservatives in cosmetic and pharmaceutical industry. Most of the time sensitization occurs after the application of topical products. Glucocorticoids have potent anti-inflammatory and immunosuppressive effects. Type IV allergy, has a prevalence of 0.2–5% and is induced mainly by tixocortol pivalate and budesonide and represent 2% of positive results patch test. The patient was indicated to avoid parabens and clobetasol and he is being treated with pimecrolimus. Written Informed consent previous signed by patient.

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Acute generalized exantematous pustulosis: common features in two cases induced by different antibiotics

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Background: Acute Generalized exanthematous pustulosis (AGEP) is a rare delayed hypersensitivity reaction to drugs, characterized by the development of numerous non-follicular sterile pustules on a background of edematous erythema, associated with fever and peripheral blood leukocytosis. Antibiotics are the prevalent causative agents in approximately 90% of cases.

We hereby present 2 cases from the onset of symptoms till full recovery and the subsequent allergy diagnostic evaluation.

Case presentations: We retrospectively register the clinical characteristics, diagnostic evaluation and management of 2 patients who were admitted to our Clinic with diagnosis of AGEP.

The first patient, a 28-year old ♀ with a history of plaque psoriasis during childhood developed generalized maculopapular exanthema with hundreds of non-follicular pustules the third day of treatment with amoxicillin/clavulanic acid (1000 mg bid) for infectious cystitis. She also developed fever 38.7°C, neck and inguinal lymphadenopathy and peripheral blood leukocytosis (WBC = 40770 K/μl, NEU = 38970 K/μl). The second patient, a 45 years old ♂ with an unremarkable medical history, developed a confluent macular exanthema partly covered with pustules in his trunk and thighs accompanied by face edema, the fourth day of clindamycin intake (300 mg tid) for otitis media. He also had fever 38.3°C, neck lymphadenopathy and peripheral blood leukocytosis (WBC = 15000 K/μl, NEU = 13815 K/μl). A skin punch biopsy was performed in both patients. Histological examination confirmed the diagnoses of AGEP. Both cases were treated identically; upon clinical suspicion antibiotics were stopped and topical corticosteroids were applied until the rash gradually began to recede followed by excessive desquamation almost 2 weeks later in both patients. Six weeks after resolution of the reactions, patch tests with the culprit antibiotics (amoxicillin/clavulanic acid and clindamycin respectively at concentrations 5% and 10% w/v in petrolatum) were applied and evaluated in 30 min, 48 and 72 h. Both patients

produced positive reactions with reproduction of pustular exanthema on the sites of application, in late readings, most prominent at the 72 h reading.
Conclusion: AGEP is in most cases a self-limited disease with a favorable prognosis. Early recognition is crucial for management which mostly relies on prompt cessation of the culprit drug. Patch testing is a safe, non-invasive and accurate method to identify the offending drug.

916
Pityriasis lichenoides chronica after tetanus reimmunization

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Background: Pityriasis lichenoides chronica (PLC) is a relatively rare benign inflammatory skin condition. The pathophysiology is not clear. A cell-mediated mechanism has been proposed based on a T-lymphocytic infiltrate, diminished epidermal Langerhans cells, and a reduction of the CD4/CD8 ratio. Some authors refer PLC as a self-limited self-healing lymphoproliferative disease. The etiology remains unknown despite the common association with infections such as stretptococcal ones and Epstein-Barr virus (EBV).
Method & Results: Herein we present a 55-years-old Caucasian man with a generalized skin eruption since 4 weeks. The condition developed 10 days after tetanus reimmunization because of physical trauma.

Upon admission skin changes involved the trunk and the extremities and were presented by non-coalescent polymorphic, dome-shaped erythematous papules. Thick scales could be observed on the surface of some lesions. The patient was otherwise in good general health with no current of previous history of other disease and allergy. He did not take any medications.

Routine blood examination revealed no abnormalities with normal levels of ESR and CRP, excluding ongoing infectious process. EBV serology was negative. Histopathology examination of a skin biopsy was consistent with the diagnosis of PLC.

Treatment with Midecamycin 3 times daily 400 mg for 10 days and topical clobetasol propionate cream was administered. The patient was clear of lesions 1 month later. No recurrence was evidenced in the follow up period of 6 months.
Conclusion: In the presented case we suspect medicamentous etiology of the disease due to the almost concomitant onset of PLC after the vaccination. We were able to exclude infectious origin of the disease. As far as we are aware PLC after tetanus reimmunization has not been described in the literature.

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Codeine-induced acute generalized exanthematous pustulosis: an unusual case

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Background: Acute generalized exanthematous pustulosis (AGEP) is a rare and severe cutaneous adverse reaction characterized by the rapid development of non-follicular, sterile pustules on an erythematous base. Antibiotics are the most common implicated drugs. Only one case of AGEP induced by dihydrocodeine phosphate has been reported in the literature.
Aim: To report a rare case of AGEP induced by codeine and confirmed by a positive oral challenge.
Case report: A 21-year-old woman, with a history of psoriasis, had received Voltarene Retard® (diclofenac sodium), Co-Algesic® (paracetamol-codeine) and Lanzopral® (lansoprazole) for knee pain. Two weeks later, she developed fever and pruritic skin eruption on the neck, spreading over the next day to involve nearly his entire body surface. Physical examination showed a diffuse erythema marked in the intertriginous folds dotted with nonfollicular pustules. No mucosal involvement was noted. Laboratory findings showed neutrophils (7790/mm3) with normal hepatic and renal parameters. This clinical picture suggested an AGEP. Histopathological examination of skin lesions revealed intracorneal pustules, orthokeratosis and few necrotic keratinocytes in the epidermis, basal cell attack and perivascular lymphocytic infiltrate in the superficial dermis. Voltarene®, Co-Algesic® and Lanzopral® were withdrawn and gradual resolution of the skin eruption has been noted during the following 2 weeks. Six weeks after complete resolution, patch tests were separately performed with Voltarene®, Co-Algesic® and Lanzopral® (10% in water and in petrolatum according to the ENDA recommendations'). At 48-h reading, the patch tests were negative. The patient consented to perform a sequential oral challenge test with suspected drugs. After administration of one tablet of Co-Algesic®, the patient developed an identical skin rash within few hours. Oral challenge with paracetamol was well tolerated. According to Euro-SCAR algorithm, our case deserves a score of 8 determining the diagnosis to be definite.
Conclusion: To the best of our knowledge, this is the second reported case of AGEP caused by codeine and confirmed by oral challenge.

918
Stevens Johnson syndrome after cephalexin use: a case report

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Introduction: The Stevens-Johnson Syndrome (SJS) is a rare, acute and severe, adverse reaction to drugs, and its pathogenesis is still not fully understood. The disease is characterized by the presence of widespread maculopapulous and purpuric lesions mainly distributed over the face and trunk, as well as blisters, with positive Nikolsky sign and epidermal detachment less than 10% of body surface. It reaches the mucosa in approximately 90% of cases, with erythema and edema, and can progress to pseudomembranous formations in the eyes, mouth, genitals, throat and upper airways. There is systemic involvement in 30% of patients, with fever and lesions in the gastrointestinal and respiratory tracts. SJS is a condition that deserves attention due to its high morbidity and the need for hospitalization, sometimes in intensive care unit.
Case description: Brazilian female patient, 11 years old, black, presented on admission fever, diffuse purpuric and maculopapulous exanthema and blisters, widely distributed across the face, chest, back, limbs and oral cavity, with crusted lesions on the lips. The symptoms had acute onset, and there were no itching or pain. The patient had been taking cephalexin for 3 days as treatment for urinary tract infection.

As initial management, the drugs previously used were suspended and intravenous corticosteroids were initiated. For the injury, chlorhexidine and topical vaseline. Laboratory tests showed no significant changes.

The ophthalmology evaluation excluded ocular damage and suggested the use of ocular lubricants. Throughout the hospitalization period, the patient had her conduct similar to that established for burns, with vigorous hydration and high-protein and calorie diet. On the sixth day, the plastic surgery team performed surgical debridement of bullous lesions, followed by extensive dressing. On the thirteenth hospitalization day, the patient already had full re-epithelization and was discharged

with oral prednisolone, to be reduced weekly.

Conclusion: The therapeutic options for SJS are limited and controversial. Although the use of systemic corticosteroids did not show proven benefits in the literature, the patient presented a favorable outcome with its use.

We believe that further studies should be conducted to elucidate the pathogenesis, etiology and possible treatments, since there is difficulty in identifying and manage this disease, which has poor prognosis and high incidence of sequelae.

Poster Session TPS 21

Infections and microbiota

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Evaluation of level of total IgE in *Mycoplasma* infection in children with respiratory tract deseases

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Background: Aim of our study was to evaluate level of IgE in children during an episode of acute lower respiratory tract infection caused by *M. pneumonia*, *M. hominis*.
Method: 234 patients aged 5 months to 7 years old suffering from acute pneumonia concomitant with wheezing were included in our study. Levels of specific antibodies of *M. pneumoniae, M. hominis* (IgM, IgG) and the peripheral blood concentrations of IgE were determined by using *ELISA* in all 234 children.
Results: 234 children completed the study: 116 children composed study group with *Mycoplasma* infection (75 patients with *M. pneumoniae* infection and 41 patients with *M. hominis* infection) and 118 children without *Mycoplasma* infection (control group). The level of IgE in children with *Mycoplasma*-positive bronchopulmonary disease was two times higher in comparison with *Mycoplasma*-negative group [88.12 ± 16.53 UE/ml vs 43.9 ± 8.56 UE/ml, respectively, $F = 5.8$ ($P < 0.02$)]. In particulary groups in *M. pneumoniae* infection level of IgE was 102.6 ± 23.66 UE/ml and in *M. hominis* - 59.2 ± 14.85 UE/ml, $F = 4.1$ ($P < 0.02$). So, level of IgE in our study group it is increased in comparison with control group and in *M. pneumoniae* infection it is higher than in *M. hominis* infection and than in control group, $P < 0.02$.
Conclusion: The level of total IgE it is two times higher in *Mycoplasma*-positive infection in comparison with group of children with lower respiratory tract infection without *Mycoplasma* infection.

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Imunoglobulin levels of IgA, IgM, IgG in children with bronhopulmonary diseases caused by *Mycoplasma pneumonia* and *Mycoplasma hominis* infection

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Background: Aim of our study was to evaluate the levels of immunoglobulin A, M, G in children during an episode of acute lower respiratory tract infection caused by *M. pneumonia* and *M. hominis*.
Method: The study group included 115 children who had mycoplasma infection and the control group consisted of 112 children without mycoplasma infection. Determination of specific antibodies (IgM, IgG) for *M. pneumoniae* and *M. hominis* infection, levels of immunoglobulin A, M, G were determined in serum samples obtained from all 227 children and were tested by using *ELISA*.
Results: IgA levels in children with *Mycoplasma*-positive bronchopulmonary disease were 0.76 ± 0.042 g/l and did not differ from levels of IgA in control group (0.71 ± 0.034 g/l). In the group with *M. pneumoniae* infection the average level of IgA was 0.76 ± 0.06 g/l, and in *M. hominis* infection was 0.77 ± 0.05 g/l. Elevated serum levels of IgM were found in study group (1.67 ± 0.074 g/l), which is higher than in the control group (1.52 ± 0.07 g/l, $P < 0.05$). For *M. pneumoniae*-infection group the average level of IgM was 1.61 ± 0.082 g/l, and in *M. hominis*-infection group the level of IgM was 1.77 ± 0.15 g/l, and it is higher than in the control group ($F = 1$, $T = 1.04$). IgG-mediated immune responses in children with micoplasma-positive infection were 9.13 ± 0.3 g/l. In the micoplasma-negative group registered a less intensive synthesis - 8.69 ± 0.3 g/l. For *M. hominis*-infection group average level of IgG was 9.4 ± 0.45 g/l and for the group with *M. pneumoniae* infection group - 9.0 ± 0.40 g/l.
Conclusion: *Mycoplasma hominis* infection induces a more expressed humoral immune response in comparison with *Mycoplasma pneumoniae* infection in an acute bronhopulmonary affection in children.

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Corticosteroid use in the management of a pediatric erythema multiforme minor case related to mycoplasma pneumonia

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Background: Erythema multiforme (EM) is an acute onset immune mediated mucocutaneous disease. In EM minor, lesions are frequently present in papullary forms, which could then enlarge and eventually form the typical 'target' and/or 'atypical target like' lesion with erythema surrounding an area of central clearing. The rash in EM minor preferentially affects the limbs, particularly the extensor surfaces; however it can also be seen throughout the body, excluding mucous membranes. Herpes simplex type 1 and 2 are the most frequently encountered infectious agents in etiology of the disease.

Mycoplasma pneumonia is a very rare infectious agent as a cause of EM minor and usually leads to Steven-Johnson Syndrome (SJS) which has a different type of clinical spectrum. Although the initial treatment strategy must be made against the main cause, there are suggestions for the use of systemic and topical corticosteroids as an adjuvant therapy. The advantage of adjuvant therapy is reducing the duration and severity of symptoms. Therefore healing could be ensured before the occurance of any complication.
Case: A-four year old girl admitted to our out-patient unit with the complaints itchy skin eruptions of fadeless with pressing, fluffy from surface, centrally erythematous and slightly demarcated. Her symptoms were continuing for 12 days and unresponsive to antihistaminic therapy. Her history revealed a respiratory tract infection 1 week ago with the symptoms of fever, nasal discharge and cough. 1 mg/kg methyl prednisolone was initially administered until the laboratory tests completed. After 5 days of corticosteroid treatment, skin lesions were healed, leaving hyperpigmentation. Mycoplasma pneumonia Ig M and Ig G positivity was detected at laboratory and complete cure was achieved by adding

15 mg/kg clarithromycin and topical % 0.1'lik methylprednisolone aceponate to the treatment.

Conclusion: In the investigation of the etiology of EM minor, mycoplasma pneumonia should be kept in mind as a rare cause of the disease. Treatment of these patients with oral and/or topical corticosteroids would be helpful by decreasing the severity of lesions and shortening the recovery time.

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Humoral immunological reactions in cystic fibrosis patients with *Ps. aeruginosa* pulmonary chronic infection

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Aim: To study the IgA, IgM, IgG levels in serum in cystic fibrosis (CF) patients with *Ps. aeruginosa* chronic pulmonary infection.

Methods: In a study we have evaluated 58 patients with CF, of which 36 patients with chronic lung infection with *Ps. aeruginosa*. The IgA, IgM, IgG levels in serum was determined by turbidimetry method. The genetic research in CF children was effectuated by DNA examination of PCR reaction for CFTR gene mutation. The severity of pulmonary manifestations was confirmed by respiratory insufficiency with restrictive and obstructive disorders. Growth and development disorders were estimated in 41.4% of patients with CF.

Results: Immunologic researches in patients with CF determined higher ($P < 0.05$) serum level of the IgA - 1.22 ± 0.013 g/l (healthy children - 1.18 ± 0.05 g/l), IgM - 1.85 ± 0.016 g/l (healthy children - 1.26 ± 0.24 g/l), IgG - 13.85 ± 0.074 g/l (healthy children - 11.04 ± 0.74 g/l). The lung infection with *Ps. aeruginosa* in CF patients induced immunological humoral phenomena with a significant increase ($P < 0.05$) in the serum level of IgA (1.32 ± 0.022 g/l), IgM (1.99 ± 0.028 g/l) and IgG (14.41 ± 0.113 g/l) compared with CF patients, the bronhopulmonary system of which was not infected by *Ps. aeruginosa* (IgA - 0.94 ± 0.029 g/l, IgM 1.28 ± 0.028 g/l, IgG - 12.71 ± 0.21 g/l).

Conclusion: The chronic pulmonary infection with *Ps. aeruginosa* in CF patients induce efficient immunological humoral reaction with increasing of the level of immunoglobulins A, M, G in serum.

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Effect of fermented milk with *Lactobacillus paracasei* CBA L74 on gastrointestinal and respiratory infections in children: multicenter randomized controlled trial

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Background: Recently it has been demonstrated that cow's milk or rice fermented with *Lactobacillus paracasei* CBA L74 are able to prevent common infectious diseases (CIDs) in children. We aimed to confirm in a multicenter study the efficacy of cow's milk fermented with *L. paracasei* CBA L74 in reducing CIDs.

Method: Multicentre, randomized, double-blind, placebo-controlled trial on healthy children (aged 12–48 months) consuming daily 7 gr of cow's milk fermented with *L. paracasei* CBA L74(group A), or placebo (group B) attending daycare during the 3-month study course. Over this period, acute gastroenteritis (AGE) and upper respiratory tract infections (URTI) were recorded by family pediatricians. At enrollment and after 3 months a stool sample was obtained from all study subjects to determine the effects on α-and β-defensins, cathelicidin (LL-37), and secretory IgA production by ELISA.

Results: 126 children (71 males, 56.3%) with a mean (SD) age of 32.8 (9.2) months completed the study: 66 in group A and 60 in group B. ITT analysis showed that during the study 105 out of the 146 (72%) children experienced at least one episode of CID. The proportion of children presenting at least one episode of CID was significantly lower in group A compared with group B (60% vs 83%, $P < 0.05$). The absolute risk difference (ARD) for the occurrence of at least one CID was −23% (95% CI: −37% to −9%, $P < 0.01$, binomial regression) for group A vs group B. This correspond to a number of children needed to treat of 4 (95%CI 3–11) for group A vs group B. Per-protocol-analysis (PPA) showed that the proportion of children presenting at least one episode of AGE was significantly lower in group A vs group B (18% vs 40%, $P < 0.05$). The ARD for the occurrence of at least one episode of AGE was −22% (95% CI: −37% to −6%, $P < 0.01$) in group A compared to group B. Similar findings were obtained at PPA regarding the proportion of children presenting at least one episode of URTI, that was significantly lower in group A vs group B (51% vs 74%, $P < 0.05$). The ARD for the occurrence of at least one episode of URTI was −23% (95% CI: −40% to −7%, $P < 0.01$) in group A vs group B. Net changes in $\log_e$α-defensin ($P < 0.001$), $\log_e$β-defensin ($P < 0.001$), $\log_e$LL-37 ($P < 0.001$) and $\log_e$-sIgA ($P < 0.001$) were seen at 3 months vs baseline for group A vs group B.

Conclusion: Dietary supplementation with cow's milk with *L. paracasei* CBA L74 can be recommended as a valid strategy in preventing pediatric CIDs.

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Real life management of RSV bronchiolitis in polish children and comparison with existing practice guidelines

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Background: Despite the frequency of bronchiolitis, its diagnosis and management practices remain variable between countries. Few national societies publish their practice guidelines, that advocate supportive care for this self-limited disease. We sought to describe treatment patterns for inpatient RSV bronchiolitis in an academic medical center in Poland and to compare the findings to the existing national and international guidelines.

Methods: A retrospective chart review was performed in children <24 months of age, who were admitted to an academic hospital with a diagnosis of bronchiolitis and confirmed RSV etiology between 2012 and 2014. Care practices were compared to three existing guidelines in bronchiolitis: the American Academy of Pediatrics (AAP 2014), Polish National Recommendations (Rekomendacje 2010), and Scottish National Clinical Guideline (SIGN 2006).

Results: There was no major contradiction or disagreement among analyzed guidelines, and the three documents were used for subsequent analysis.

Ninety eight patients met inclusion criteria. The all patients fulfilled criteria for diagnosis and hospital admission.

Overall, the management of RSV bronchiolitis in Poland is in line with all three guidelines, including:

1 diagnostic criteria of bronchiolitis,
2 identification of high-risk patients, particularly those requiring monitoring (74.5% of all patients) and administering supplemental oxygen (55.1% of total),
3 administration of nebulized hypertonic saline (65.3% of patients), and
4 avoidance of corticosteroid administration (12.2% for nebulized CS and 6.1% for systemic CS).

Two procedures remained at odds:

1 albuterol administration was common and it was administered in 68.4% of all patients, and
2 the number of chest X-rays obtained remains relatively high (31.6% of patients) with subsequent excessive use of antibiotics (31.6%).

Conclusion: The inpatient management of RSV bronchiolitis oi Poland is in general in line with current guidelines, although rates of unnecessary medication (including albuterol and antibiotic administration) need to be improved. Additional health care provider training and education, based on existing guidelines is warranted to reduce unnecessary interventions and healthcare resources use.

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Mathematical modeling and image analysis: possible clinical application in practice as a predictor of fungal rhinosinusitis

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Background: CT analysis of sinuses is not precise for diagnosis of fungal rhinosinusitis (FRS). Further investigation (mathematical modelling and fractal analysis of CT image) could improve more precise diagnosis of FRS. The aim of the research is to quantify the area of mucosa of sinuses using texture analysis and to compare CT images based on fractal dimension with clinical parameters of FRS patients.
Method: The prospective study included 37 patients (male:female = 25:12) with chronic rhinosinustis/CRS from the Clinic of Allergology, Clinical Centre of Serbia. The observation unit was the sinus with any content ($n = 63$), fungi were isolated in 21 (33.3%) of them. Study design included: history data; total IgE Ab, absolute eosinophile count (Eo), skin prick test; rhinologic and CT observation; mycological finding, mathematic modelling. We used Gray Level Co-Ocurrence Matrix algorithm for assessing the characteristics of text images: uniformity, contrast, homogeneity and entropy. The fractal dimension was obtained by the Box-counting method, consists of covering the image infected mucosa with sets of squares as a measure of occupied area of the sinus cavity (space filling).
Results: Fractal image analysis demonstrated that clinical parameters (length of the CRS, CRS severity scored by SNOT-22, total IgE Ab, Eo, poor response to topical corticosteroid Th) correlated with the parameters of image analysis - contrast, homogeneity and entropy ($P = 0.042$, $P = 0.008$, $P = 0.022$; respectively) in patients with FRS. High statistical correlation was found between total IgE Ab and contrasts and homogeneity of CT images ($P = 0.001$, $P = 0.000$; respectively), patients with higher amount of total IgE Ab exhibited less homogeneity and higher contrast. Statistically significant difference ($P < 0.001$) was found between the mean value of the parameter 'homogeneity' of CT image in patients with and without FRS (498 ± 16, 216 ± 7, respectively). Patients with FRS had less homogeneity of CT image.
Conclusion: Texture analyzes of CT scans is highly sensitive tool in diagnosing of FRS by detecting difference in parameters of image in patients with or without FRS. Results indicate that it is not possible to find an universal trans-sectional thickness of mucosa of the sinuses, which would serve as an indicator for the diagnosis of FRS. Low homogeneity and higher contrast CT image are important image parameters that potentially indicate the presence of FRS and can improve radiological diagnosis of FRS.

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Urticaria: the first manifestation of ocular filariasis

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Background: Intraocular filariasis is rare in humans but frequent in animals. Zoonotic filariases are nematodes belonging to the Filarioidea superfamily. Filarial infestation usually manifests as larva migrans or subcutaneous nodules and only rarely affects the eye. The aim of the paper is to present a rare case of ocular filariasis manifesting as urticaria and acute uveitis.
Method: We report the case of a 54 year old female, Caucasian patient from the urban area who addressed our clinic for blurred vision and conjunctival hyperemia. Her family history was unremarkable. The disease had occurred a few years before when the patient presented urticarial lesions with intensely positive patch tests for all tested antigens. After several months she presented with blurred vision, conjunctival hyperemia and pain in her right eye and was diagnosed with acute anterior uveitis and treated with antibiotics, anti-inflammatories and mydriatic agents. She presented recurrent episodes of uveitis in both eyes and chronic urticaria ever since.
Results: Peripheral blood smear examination was performed and was positive for Dirofilaria, Strongiloides stercoralis and Toxocara canis. Ocular examination of the right eye showed pupillary seclusion occlusion and keratic precipitates. Visual acuity was hand movement perception for the right eye and 60/60 for the left eye. Ocular ultrasound revealed no involvement of the posterior pole. She was treated with diethylcarbamazine, ivermectin and albendazole as well as corticosteroids. Despite the treatment, the patient presented yearly reoccurrences of acute uveitis, most of them associated with urticarial lesions, and required high doses of prednisolone and anti-parasitic agents.
Conclusion: We report a very rare case of acute anterior uveitis and urticaria due to ocular filariasis. While very few cases of filariasis were documented in our country so far, the incidence of the disease is increasing in other European countries. We therefore suggest that ocular filariasis should be suspected in cases of recurrent anterior uveitis of unknown etiology.

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Differences in airway microbiome between eosinophilic asthma and chinosinusitis with nasal polyposis

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Background: The airway has a diverse microbiome and the microbial colonization might have a role in the pathogenesis of chronic airway diseases. Compiling evidence supports the relationship of chronic

rhinosinusitis (CRS) and asthma and one potential link is eosinophilic and Th2 immune responses in patients with eosinophilic phenotype. However, the relationship of the microbiome and eosinophilic asthma and CRS with nasal polyposis (wNPs) is not yet well known. We sought to characterize and compare the microbiome of the induced sputum in patients with eosinophilic asthma and nasal lavage fluids (NLFs) in patients with CRSwNPs.

Method: Induced sputum samples were obtained from 5 patients with eosinophilic asthma and NLFs from 3 patients with CRSwNPs. Total DNA was extracted from sputum supernatants and NLFs and amplified by using primers specific for the V3-V5 region of the bacterial 16S rRNA gene.

Results: All sputum samples contained 5 major bacterial phyla: Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, and Fusobacterium. Nasal fluids contained 3 major bacterial phyla: Proteobacteria, Actinobacteria, and Firmicutes. Firmicutes and Bacteroidetes were more prevalent in asthma than in CRSwNPs (31.3% vs 5.6% and 34.8% vs 0.2%, $P < 0.0001$, respectively). Proteobacteria were more predominant in patients with CRSwNP not asthmatics, meanwhile Fusobacteria were found only in samples from asthmatics. Samples from asthmatic patients had greater bacterial diversity compared with samples from the patients with CRSwNP and without asthma.

Conclusion: There were significant differences in bacterial communities between the patients with eosinophilic asthma with RS and CRSwNPs without asthma.

*Funding source; this research was supported by Hallym University Research Fund 2014(HURF-2014-58).

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Developing a multi-species probiotic platform for food intolerance

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Background: Probiotics are defined as 'live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.' Probiotic microorganisms are often consumed as part of fermented food products or as food supplements and typically consist of strains from the genera *Lactobacillus* and *Bifidobacterium*. Although the beneficial effects of commensal gut microbiota and potential probiotic effects have been considered already by Metchnikoff more than 100 years ago, over the past decades research has been more focused on investigating aspects of interplay between our innate microbiome, gut permeability and immunological pathways. The aim of this research was to specifically design a new multi-species probiotic formulation for supplementation in people suffering from food intolerance.

Methods: The selection of probiotic strains was focussed on the capacity to influence mechanisms of action that are important in development of food intolerance with the following parameters measure: *in vitro* capacity to produce β-galactosidase, *in vitro* strengthening of the epithelial barrier function, *in vitro* stimulation of cytokines produced by regulatory T cells, in addition to assessing fundamental quality criteria (stability, gastrointestinal (GI)-survival, multispecies concept, allergen-free).

Results: *Bifidobacterium lactis* W51, *Lactobacillus acidophilus* W22, *Lactobacillus plantarum* W21 and *Lactococcus lactis* W19 strains demonstrated ability to survive the GI-tract and strain specific effects in producing β-galactosidase, strengthening the gut barrier function after immunological-induced stress and inhibiting Th2 cytokines [IL-4, IL-5 and IL-13 (≥50%)], in addition to stimulating Th1 IL-10 levels.

Conclusions: *In vitro* evidence for the efficacy of the selected strains warranted the development of a multi-species probiotic supplement consisting of the aforementioned species, to provide beneficial effects in patients suffering from food intolerance.

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Correlations between patients with allergic diseases and indoor microorganisms

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Background: Considerable studies have indicated that mould concentration is significantly related to allergic diseases, long-term exposure to and inhalation of mould can cause allergic diseases and symptoms of the whole body, the skin or the respiratory system. This study was performed to explore the correlations of the concentration of indoor microorganisms with the symptoms of allergic diseases and the effects of indoor environment on mould concentration.

Method:

1 Patients with clinically diagnosed allergic diseases ($n = 26$) and normal controls ($n = 10$) were recruited. The concentration of mould and bacteria in indoor air was measured by air deposition method. All subjects were required to fill in the International Study of Asthma and Allergies in Childhood (ISSAC) questionnaire.
2 Twenty patients were selected from the case group to use air cleaner for 2 months, after which, microorganism sample was collected from the home of patients every month.
3 SPSS21.0 statistical software was utilized for data entry and analysis, descriptive statistics for measurement data, and spearman correlation analysis for the correlations between symptoms and microbial concentration. $P < 0.05$ was considered as a statistically significant difference.

Results:

1 The concentration of bacteria and mould in the case group was 1107.65 ± 1112.37 cfu/m^3 and 19.2 ± 15.43 cfu/m^3, in the control group was 997.65 ± 832.21 cfu/m^3 and 19.2 ± 15.43 cfu/m^3, respectively, and comparisons of the concentration of bacteria and mould between two groups showed no statistical significance.
2 Indoor mould concentration presented a positive correlation with allergic diseases caused respiratory and gastrointestinal symptoms. In addition, indoor mould concentration was higher in families with long-term smokers, and obvious damp and damage by water in indoor ceiling and floor was also a cause of mould concentration increase.
3 One month after using air cleaner, bacterial concentration reduced, showing statistical significance, after 2 months, mould concentration presented statistical significance as compared with before.

Conclusion: Mould concentration correlated with indoor inviromental factors and may affect allergic diseases, therefore, indoor microbial concentration control should be considered to reduce the effects on allergic diseases. In addition, the application of air cleaner can be a means to control indoor microbial concentration.

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Adenoid hypertrophy and its influence on immunity and microbiome of upper airways in children undergoing adenoidectomy

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Background: Adenoid hypertrophy (AH) represents a common condition associated with childhood and can lead to various complications (e.g. recurrent infections, chronic sinusitis, sleep apnoea). Adenoids are active lymphoid organs and should participate on the upper airway protection. On the other hand, they can have negative influence on the immune system and microbiome of the airways.
Aim: We aim to examine the influence of AH and adenoidectomy on immune parameters and microbiome of upper airways.
Method: In our prospective study, we enrolled 72 children (48 boys, 66.7%; aged 4.5 ± 2.2 years) with AH treated with adenoidectomy in general anaesthesia. All the subjects underwent the panel of laboratory and clinical tests (humoral and cellular immunity, complement analysis, cultivation studies, nasal nitric oxide measurement) before and 6 months after adenoidectomy. Atopy was evaluated by skin prick tests with the panel of common inhalant allergens.
Results: In general, we were not able to detect any significant changes in the cellular immune parameters comparing the results before and 6 months after adenoidectomy. However, we found a significant increase of IgG1, IgG2, total IgE and complement components (C3, C4) after adenoidectomy On the other hand, the serum concentration of mannose binding lectin (MBL) and lymphocytes percentage declined significantly after surgery. Interestingly, in 14 children (19%) we detected the complete deficiency of MBL. Atopy was detected in 83% of children and the most common allergens were house dust mites and cat dander. The values of nasal nitric oxide (nNO) were significantly associated with the presence of pathogenic microorganisms in nasopharynx. nNO significantly declined after adenoidectomy ($P = 0.036$). Moreover, we observed the correlation between nNO and age. Exposure to tobacco smoke was associated with Streptococcus pneumoniae carriage in nasopharynx ($P = 0.004$) and increase of IgG a IgA in serum.
Conclusion: Adenoid hypertrophy negatively influences the upper airways microbiome and immune system defence mechanisms. Atopy and passive smoking could contribute to the AH development. Adenoidectomy leads to the compensatory changes especially in humoral and complement part of immunity, decreases mucosal inflammation and corrects the upper airways microbiome composition. This work was supported by VEGA 1/0252/14.

Poster Session TPS 22

Functional genomics and immunogenomics

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Lipopeptides as a vehicle for gene silencing

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Background: RNA interference is a natural mechanism of regulation of gene expression in the cells. The main advantages of immunotherapeutic drugs based on siRNA are high specificity and high efficiency, but their wide use is limited by their relatively weak delivery into target cells. This problem can be solved by using synthetic cationic amphiphiles. So it's very important to examine the properties of the lipopeptide/siRNA complexes.
Methods: Photonic correlation spectroscopy, *in vitro* gene silencing experiments, MTT-test, electron microscopy, confocal microscopy with different dyes and trackers.
Results: Luciferase assay demonstrated that treatment of Huh-7 cells with luciferase-specific siRNA combined with lipotripeptides has the most luminescent intensities in comparison with lipodi- and lipotetrapeptides. But the whole physical-chemical properties (the size of liposome and lipoplex, the structure of lipoplex) had the linear dependence. We analyzed the mechanism of lipoplex penetration in to the cells by confocal microscopy. It was shown that the rate of penetration into the cells is similar for all lipoplex. But in case of lipotetrapeptides the signal of peptide dye and LysoTracke (Molecular Probes) had more colocalization in comparison with lipodi- and liportipeptides. The cytotoxicity increased slightly from the lipodi to lipotetrapeptide, and IC50 varies from 70 to 333 μg/ml depend on cell line (it is higher than effective concentration).

Based on obtained data we choose lipotripeptides for siRNA silencing therapy as the most promising (they have the highest transfection efficiency and low toxicity).

Conclusion: We examined different properties of lipopeptide/siRNA complex and could choose the best one for using in gene silencing therapy.

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Gene expression profile in patients with NSAIDs-exacerbated cutaneous disease

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are the main triggers of drug hypersensitivity reactions (DHRs). In some individuals with a history of chronic spontaneous urticaria aspirin and other NSAIDs induce an exacerbation of this pathology, a condition known as NSAIDs-exacerbated cutaneous disease (NECD). Although COX-1 inhibition is thought to play a role and the influence of the genetic background may be suspected, the mechanism underlying NECD remains unknown. To identify genetic mechanisms potentially involved we analysed gene expression patterns in patients with NECD using microarrays technology.
Method: Total RNA was obtained from skin biopsies during the acute phase in 3 patients with NECD, and 14 heathy controls. After quality control procedures, gene expression patterns were compared using the GeneChip Human Gene 2.0 ST microarrays system (Affymetrix).
Results: From a total of 48227 transcripts analysed, 163 were differentially expressed in NECD (FDR P value < 0.05, and a log fold change >1 or <1). A number of upregulated transcripts were related to structural integrity of epithelial cells (*KRT16, KRT17*), HLA system (*HLA-DQB1*) and microRNAs (*MIR4427*). Some downregulated transcripts were also related to microRNAs (*MIR3127*) and microRNA-mediated gene repression (*DND1*), adhesion and migration of epithelial cells (*POSTN*), transcription factors (*ZNF667*), and collagen integrity (*COL6A5*).

Conclusion: The differential expression patterns described suggest a complex interaction between gene regulation mechanisms affecting skin structural integrity, cell adhesion and migration, and the HLA system. Our results open up new potential pathways for understanding the mechanisms underlying NECD.

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Lack of association between *PDCD-1* single nucleotide polymorphisms and susceptibility to juvenile idiopathic arthritis

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Background: Juvenile idiopathic arthritis (JIA) is a clinically heterogeneous cluster of complex diseases, in which both the genetic and environmental factors seem to play role in the development of the disease. The current study aims to assess of the association of programmed cell death 1 (PDCD1, also called PD-1) gene variants with JIA vulnerability in Iranian population.
Method: In this case-control association study, we investigated a group of 50 Iranian patients with JIA in comparison with 202 healthy controls and evaluated the frequency of alleles, genotypes, and haplotypes of *PDCD1* single-nucleotide polymorphisms (SNPs), comprising *PD-1.1* G/A, *PD-1.3* G/A and *PD-1.9* C/T, using PCR-RFLP method.
Results: Both the allelic and genotype frequencies of *PD-1.1*, *PD-1.3* and *PD-1.9* were similar in two groups of patients and controls. Moreover, no significant difference was observed between the two groups of patients and controls for GGC (*PD-1.1* G, *PD-1.3* G, *PD-1.9* C), GAC (*PD-1.1* G, *PD-1.3* A, *PD-1.9* C), and AGT (*PD-1.1* A, *PD-1.3* G, *PD-1.9* T) haplotypes.
Conclusion: Our results did not show any associations between *PDCD1* SNPs and

the development of JIA in Iranian population.

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Polymorphisms of genes encoding interleukin-4 and its receptor in Iranian patients with juvenile idiopathic arthritis

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Background: As cytokines, including interleukin-4 (IL-4), seem to have a pivotal role in the pathogenesis of juvenile idiopathic arthritis (JIA), this study is aimed at investigating of association of polymorphisms in *IL-4* and IL-4 receptor α (IL-4RA) genes with susceptibility to JIA.
Method: A case-control study was conducted on 55 patients with JIA and 140 healthy unrelated controls. Single nucleotide polymorphisms of *IL-4* gene at positions −1098, −590 and −33, as well as *IL-4RA* gene at position +1902 were genotyped using polymerase chain reaction with sequence-specific primers method, and compared between patients and healthy individuals.
Results: At the allelic level, C allele at *IL-4* −33 was found to be more frequent in patients compared to control (P value < 0.01). At the genotypic level, CC genotype at *IL-4* −590 (P value < 0.01), together with CC and TT genotypes at *IL-4* −33 (P values < 0.01), were significantly higher in patients with JIA, while TC genotypes at *IL-4* −590 and −33 positions were found to be lower in case group (P values < 0.01). At the haplotypic level, *IL-4* (positions −1098, −509, −33) TTC, GCC and TTT haplotypes were significantly lower than controls (P value < 0.01, P value = 0.03 and P value = 0.04, respectively). Although, TCC haplotype at the same positions was found to be higher in patients (P value < 0.01). Polymorphic site of +1902 *IL-4RA* gene did not differ between cases and controls.
Conclusion: Polymorphisms in promoter region of *IL-4* but not *IL-4RA* genes confer susceptibility to JIA and may predispose individuals to adaptive immune responses.

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Association of tumor necrosis factor-alpha G/A −238 and G/A −308 single nucleotide polymorphisms with juvenile idiopathic arthritis

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Background: Juvenile isiopathic arthritis (JIA) is a heterogeneous autoimmune disorder of unknown origin. As proinflammatory cytokines are known to contribute towards the pathogenesis of JIA, this case control study was performed to examine the associations of certain single nucleotide polymorphisms (SNPs) of tumor necrosis factor-α (TNF-α) gene.
Method: Fifty-five patients with JIA participated in this study as patients group and compared with 140 healthy unrelated controls. Genotyping was performed for *TNF*-α gene at positions −308 and −238, using polymerase chain reaction with sequence-specific primers method.
Results: Results of the analyzed data revealed a significant positive association for *TNF*-α gene at positions −308 and −238 for A allele in patients group compared with controls (P values < 0.01). At the genotypic level, the frequency of *TNF*-α gene at positions −308 and −238 for GG genotype was discovered to be higher in the patients with JIA compared to the healthy controls (P values < 0.01), while GA genotype at the same positions was observed to be less frequent in the case group than the controls (P values < 0.01). At the haplotypic level, a significant positive association for *TNF*-α GG haplotype (positions −308, −238) together with a notable negative association for *TNF*-α AG and GA haplotypes at the same positions were detected in the patients group in comparison with the healthy individuals (P values < 0.01).
Conclusion: Cytokine gene polymorphisms might affect the development of JIA. Particular *TNF*-α gene variants could render individuals more susceptible to JIA.

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Association study of childhood food allergy in the Japanese population with GWAS-discovered loci of atopic dermatitis

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Background: The prevalence of food allergy (FA) has increased over the past two decades, particularly in industrialized countries including Japan. There appear to be both environmental and genetic predisposing factors for FA development, but the genetic components of FA in children remain largely unexplored. Epidemiologic studies have revealed that most patients with FA have a concurrent history of atopic dermatitis (AD). Genome-wide association studies (GWAS) for AD have found a number of susceptibility loci with genome-wide significance; however, influences of GWAS-discovered loci of AD on susceptibility to FA are unclear.
Method: To examine whether genetic variants in GWAS-identified loci of AD could affect the susceptibility to childhood FA, we assessed 19 susceptibility variants previously reported in GWAS for AD. We performed an association study using a primary set of 593 FA cases and 985 controls, followed by validation of the results in an independent set of 279 cases and 886 controls. We combined the primary and validation data by the Mantel-Haenszel method, and conducted the Breslow-Day test to assess heterogeneity across the studies. We further stratified the case subjects by comorbidity of AD or asthma to investigate clinical heterogeneity of FA.
Results: In combined analysis using the primary and validation data sets, we found significant associations between FA and five loci: *C11orf30*, *KIF3A*/*IL13*, *GLB1*, *CCDC80*, and *ZNF365*. The most significant association was observed at rs1295686, which is in absolute linkage disequilibrium with the functional SNP rs20541, a non-synonymous coding genetic variant (Arg130Gln) in *IL13*. A total of three variants at *KIF3A*/*IL13*, *CCDC80* and *CLEC16A*/*DEX1* loci showed stronger associations with FA after stratification by comorbidity of AD compared to the whole FA group.
Conclusion: We identified significant associations between childhood FA and five GWAS-discovered loci of AD. Although further investigations with a larger sample size and in multiple ethnic populations are needed, these findings improve our understanding of the genetic basis of FA.

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Genome-wide association study unravels genetic determinants of the atopic march

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Background: The atopic march describes disease progression from infantile eczema to allergic airway disease in childhood. About 20–30% of infants with eczema undergo this unfavorable disease course which is associated with severe and persistent allergic disease manifestations. We aimed to identify the genetic determinants underlying this characteristic pattern of allergic disease by performing a genome-wide association study (GWAS) on individuals with early eczema plus childhood asthma.

Method: In the discovery phase, GWAS results of 6 study populations were meta-analyzed. Candidate single nucleotide polymorphisms (SNPs) were subsequently replicated in another 6 study populations. In total, our meta-analysis included 2428 cases and 17 034 controls of European descent. Association was calculated by logistic regression using an additive allele-dosage model. Meta-analyses were carried out with METAL using the inverse variance fixed effects model.

Results: We identified 7 susceptibility loci associated with the atopic march at genome-wide significance. Two SNPs, in *EFHC1* on chromosome 6p12.3 (OR, 1.27; 95% confidence interval (CI), 1.17–1.38) and between *TMTC2* and *SLC6A15* on chromosome 12q21.3 (OR, 1.58; 95% CI, 1.35–1.84), were specific for the combined eczema plus asthma phenotype and associated with allergic disease for the first time. Four additional loci, *FLG* (1q21.3), *IL4*/*KIF3A* (5q31.1), *AP5B1*/*OVOL1* (11q13.1), and *C11orf30*/*LRRC32* (11q13.5), were previously identified in GWASs on eczema whereas with *IKZF3* (17q21) a single asthma-specific locus was detected. We found that eczema loci were significantly more likely to be associated with the atopic march than asthma loci.

Conclusion: The two novel loci provide genetic support for a specific atopic march phenotype. In addition, we demonstrate that eczema loci were the main genetic determinants of the atopic march which may point to the development of eczema as a key event initiating this unfavorable disease course. We suggest that the prevention or early treatment of infantile eczema could be a promising approach in order to reduce the burden of allergic diseases associated with the atopic march.

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Vitamin D receptor taqi gene variant in exon 9 and asthma risk

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Background: Asthma is a chronic heterogeneous respiratory disease with a strong genetic and immunological component and is the most common chronic disease in Ireland, affecting around one out of every five children. The results of recent studies implied that vitamin D receptor (VDR) genetic variants may impact lung function and allergic or systemic inflammation in asthma. In this study we aimed

1 to determine the VDR TaqI gene variant in exon 9 (T/C) (rs731236) in paediatric patients with uncontrolled asthma and in healthy volunteers in Ireland and
2 to investigate the impact of this polymorphism in asthma susceptibility in relation to vitamin D status.

Method: In this study, carried out in Ireland (at high latitude and during the winter season), 44 urban, Caucasian children with uncontrolled asthma participated. 29 healthy volunteers were used as a normal control group. Outcome measured lung function and biochemical parameters of total 25-hydroxyvitamin D (25OHD), allergy, immunity, airway inflammation and systemic inflammation. Genotypes of VDR TaqI in exon 9 (T/C) (rs731236) were performed using TaqMan® SNP Genotyping Assay.

Results: The frequencies of VDR TaqI T and C alleles were 0.63 and 0.37 in cases and 0.91 and 0.09 in controls. Also, the genotypic frequencies of VDR TaqI were 40%, 47% and 13% in cases, and 83%, 17% and 0% in controls for TT, TC and CC genotypes respectively. The distribution of T and C alleles and genotype frequencies differed significantly between asthmatics and controls (P value < 0.05). No association was found between genotypes and serum 25OHD levels and other biomarkers including IgE, Eosinophil Cationic Protein (ECP), Cathelicidin antimicrobial peptide (CAMP) and high sensitivity CRP, with the exception of IL-10. IL-10 levels were significantly low in asthmatics with TC genotype (P value < 0.003).

Conclusion: This report, a first of its kind in Irish paediatric patients, suggests that the CC genotype and presence of C allele of VDR TaqI in exon 9 (rs731236) is associated with uncontrolled asthma in children.

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A polymorphism in the CRHR1 gene is associated with the response to asthma treatment in children

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Background: Inhaled corticosteroids (ICS) are the most widely prescribed medications for controlling asthma. Levels of endogenous glucocorticoids are heritable and vary significantly, both at baseline and in response to environmental perturbation. The level of response to treatment with ICS is characterized by high intra-individual repeatability and high inter-individual variability with up to 50% of asthmatic patients having poor or even no response to treatment. Polymorphisms in *CRHR1*, a gene important for the biological action of corticosteroids, have previously been associated with treatment response in asthmatics.

Aims and objectives: To determine treatment outcomes in children with asthma in association with *CRHR1* (rs242941 and rs1876828) genotypes.
Methods: We recruited 365 children with asthma and clinically assessed their health status and treatment outcome over 4 years at 3 time points: at the point of diagnosis, and after 3 and 4 years. Genetic material was extracted from whole blood samples and these were then genotyped for rs242941 and rs1876828 polymorphisms in the *CRHR1* gene.
Results: 281 children were treated with ICS (alone or in combination) continuously for at least 4 years. When treatment success was assessed by relative changes in lung function parameters (Forced vital capacity in 1 s, FEV1) both after 3 and 4 years, the frequency of CC genotype was significantly higher in good responders compared to the AA genotype (rs242941). Moreover, the frequency of the C allele was significantly higher in good vs bad responders. This genotype related response was even more evident when comparing patients with moderate and bad response to treatment with patients with good response: the frequency of AA genotype was also significantly higher in moderate and bad (inadequate) responders, compared to children with good response to treatment.
Conclusion: Our results demonstrate that both good and inadequate levels of response to treatment with ICS in children with asthma, assessed as changes in lung function parameters (FEV1), are associated with a polymorphism in the *CRHR1* gene.

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Relation of human microRNA in sputum with influenza A/B virus infection in exacerbated asthmatics

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Background: Exacerbations of asthma frequently occur due to upper and lower airway infections by respiratory viruses. MicroRNA (miRNA)s act as a key regulatory molecules between viruses and hosts. We aimed to search for candidate miRNAs of host and to validate the relation of the miRNAs in sputum with viral infection in exacerbated asthmatics.
Method: Information on sequences of mature human miRNAs was obtained using miRBase and applied to the whole genome sequence of influenza viruses A/B by searching complementarity. Viral RNAs and miRNAs were extracted from sputums of exacerbated asthmatics ($n = 41$) using Viral Gene-spin™ kit and miRNeasy kits. RT-PCR and Real-time PCR were used to detection of 7 respiratory viruses and the measurement of miRNAs in sputums of 41 exacerbated asthmatics.
Results: MiR-23b-3p was predicted among known 2578 human miRNAs using *in-silico*-analysis. It analyzed that MiR-23b-3p was matched with 7 nucleotides in four location of influenza A virus mRNA and three location of influenza B virus mRNA. It analyzed that MiR-23b-3p was matched with 7 nucleotides in one location of polymerase basic protein 2 mRNA, three locations of haemagglutinin RNA of influenza A virus and one location of polymerase each polymerase basic protein 2 mRNA, haemagglutinin and neuraminidase RNA of influenza B virus. Respiratory viruses were identified in sputums of 25 patients. The levels of miR-23-3p were significantly lower in patients infected with influenza A/B virus ($n = 7$, P-value = 0.001) and rhinovirus ($n = 9$, P-value = 0.017) compared to uninfected patients ($n = 16$) but had no significant relation between other viral infected patients ($n = 12$) with uninfected patients ($n = 16$).
Conclusion: Down regulation of miR-23b-3p expression might be associated with infection of influenza A/B virus in exacerbated asthmatics.

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Haplotypic similarity in immunogenes of Turkish population with Europeans and Central Asians

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Background: Immunogenes (i.e., genes involved in immune system functions) play a pivotal role in numerous traits related to human health. Variations in these genes are responsible for phenotypic variability, observed among human populations. Turkish population presents particular genetic features since its genetic pool is an admixture of European, Middle-Eastern, and Central Asian populations. Here, we investigated the haplotypic structure of well-known immunogenes in comparison with other worldwide populations.
Method: We analyzed the haplotypic structure of 4 genomic regions containing immunogenes (i.e., 1. *IL13* and *IL4*; 2. *MS4A2*; 3. *IL4R*; 4. *ADAM33*) in 422 apparently healthy and unrelated subjects. These data were compared with the haplotypic information of 1871 unrelated subjects belonging to 26 human populations from 5 ancestry group available through the 1000 Genomes Project Phase 3. Maximum-likelihood haplotype frequencies was estimated using the Expectation-Maximization algorithm.
Results: Considering an ancestry-level, we observed haplotypic similarity of Turkish subjects with European populations in *IL13-IL4*, *IL4R*, and *ADAM33* regions; and with central Asians in *MS4A2* region. Within Turkish-European haplotypic similarity, we observed differences between Turkish subjects and northern Europeans in all three genomic regions investigated (i.e., *IL13-IL4*, *IL4R*, and *ADAM33*). Conversely, no significant difference was observed in *MS4A2* region between Turkish populations and central Asians.
Conclusion: Our results demonstrated that Turkish immunogenic variations are shared with both European and central Asian populations. However, Turkish populations seem to have consistent differences with northern Europeans and no relevant diversity with central Asians. This study was supported by TUBITAK.

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Asthma-specific phenome-wide association study for immunogenes in Turkish asthmatic children

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Background: Many immunogenes (i.e., genes involved in immune system functions) have been associated with asthma and allergy. In the present study, we investigated well-known immunogenes with respect to 108 clinical and physiological traits (i.e., asthma and allergy clinical features, lung function measurement, allergy tests, and blood parameters) in 477 asthmatic children and 495 controls from Turkey.
Method: Using International Study of Asthma and Allergies in Children (ISAAC) Phase II tools, elementary schoolchildren aged 9–11 years were surveyed in 5 city

centers in different regions of Turkey. Risk alleles in 8 immunogenes [*ADAM33* (rs2280091, rs2787094, rs511898, rs612709, rs3918396, rs2280090, and rs543749), *ADRB2* (rs1042714 and rs1042713), *CD14* (rs2569190), *IL13* (rs20541, rs1800925, and rs1295686), *IL4* (rs2070874 and rs2243250), *IL4R* (rs1805015 and rs1801275), *MS4A2* (rs569108 and rs1441586), and *TNF* (rs1800629)] were genotyped by KASP, fluorescent based endpoint technology. Linear and logistic regressions were applied for the association analysis. Matrix spectral decomposition was considered to calculate the significance threshold after multiple testing correction.

Results: We observed significant association with ADAM33 risk alleles (rs2280090, $P = 2.29*10^{-4}$; rs2280091, $P = 6.07*10^{-4}$) and baseline lung function measurement (MEF), and with eczema-wheezing phenotype (rs3918396, $P = 5*10^{-4}$). Additional suggestive findings were observed for: IL4 rs2243250 with absolute FEV ($P = 9.56*10^{-3}$), ADRB2 rs1042713 with platelet count ($P = 1.71*10^{-3}$), and ADAM33 rs2280090 with positivity to dust mite skin test ($P = 2.95*10^{-3}$).

Conclusion: This is the first phenome-wide analysis for asthma in Turkish patients. Our data indicated that variation in immunogenes play an important role in determining clinical features, respiratory volumes, and blood parameters of asthmatic children.This study was supported by TUBITAK.

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The A896G polymorphism of TLR-4 gene in adults asthma patients with different sputum cellular phenotypes in Crimea

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Background: The TLR4 single nucleotide polymorphism A896G (ramino acid substitution Asp299Gly) impacts the extracellular domain of the TLR4 receptor. This polymorphism can modify the receptor's response to endotoxin, which is an important trigger of neutrophilic or eosinophilic asthma.

Methods: The Asp299Gly polymorphism of TLR-4 gene was studied in 331 patients with bronchial asthma. The control group included 285 non-atopic volunteers. The single nucleotide polymorphism of Asp299Gly was detected by PCR. Eosinophilic phenotype was defined as ≥3% sputum eosinophil count while neutrophilic phenotype consisted of ≥76% sputum neutrophil count. Paucigranulocytic phenotype was defined as sputum eosinophil count <3% and sputum neutrophil count <76%. Patients and volunteers provided written informed consent for the genetic study.

Results: In the control group, the frequency distribution of genotypes [AA - 242 (85%), AG - 40 (14%), GG - 3 (1%)] did not significantly differ from that with neutrophilic (AA - 51 (85%), AG - 9 (15%), GG - 0, $\chi2 = 0.66$, $P = 0.72$), eosinophilic (AA - 108 (76%), AG - 32 (22%), GG - 3 (2%), $\chi2 = 5.70$, $P = 0.06$) and paucigranulocytic asthma (AA - 102 (80%), AG - 25 (19%), GG - 1 (1%), $\chi2 = 2.05$, $P = 0.36$). The analysis risk of allele G revealed that the frequency of AG + GG genotype in patients with eosinophilic asthma (24%) is significantly greater (odds ratio = 1.82 [1.11–3.01], $P = 0.02$) compared to control (15%).

Conclusion: The risk of eosinophilic asthma in the population of Crimea is associated with the prevalence of AG and GG genotypes of Asp299Gly polymorphism of the TLR-4 gene.

Poster Session TPS 23

Hymenoptera venom allergy and anaphylaxis

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Which is the most significant for the diagnose of hymenoptera venom allergy; history, skin tests or serum specific immunoglobulin (Ig) E?

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Background: Aim of this study is to evaluate the significance of serum allergen specific Ig E level and skin tests in the diagnosis of hymenoptera venom anaphylaxis.
Method: Retrospectively, the data were obtained from 77 patients who had venom immunotherapy in our clinic between 2000–2014 years. Data were included as patient's detailed sting histories, skin tests and venom specific Ig E to honey bee venom (HBV), yellow jacket venom (YJV) and polistes paper wasp venom (PWV). Positive specific Ig E levels were defined as an IgE level > 0.35 kU(A)/l (ImmunoCAP Thermo Fisher Scientific Inc©.). Skin prick and intradermal tests were performed by using ALK © solutions.
Results: 43 of patients were male and 34 were female. Mean age was 44. Double positive serum specific Ig E was determined in 25/77 (32%) patients, triple positivity was determined in 17/77 (22%) patients. Double positive skin tests were determined in 16/77 (20%) patients whose history were definitely with only one bee type. Skin tests were helped us in 80% of cases and serum specific Ig E levels were helped us in 40–50% of cases to determine the responsible venom definitely. Immunotherapy was decided for the patients who had double positivity both in skin tests and serum specific Ig E levels according to their description of bee spices definitely. After the evaluation of these parameters, venom immunotherapy was decided in 30 patients with HBV, 42 patients with YJV and 1 patient with PWV. Four patients had immunotherapy with both HBV and YJV because they had double positivity both with skin tests and serum specific Ig E levels and with no clear history about bee species.
Conclusion: Description of the bee spices by the patient is important for immunotherapy decision but its reliability is extremely suspicious. Our data indicate that in cases of double positivity to both venoms, supplementary screening tests with at least one CCD (cross-reactive carbohydrate determinant) or component resolved diagnosis (CRD) should be performed to find out whether it's true double positivity or cross reactivity. N-glycans (CCDs) may induce double or triple Ig E reactivity to HBV, YJV and PWV in patients who are monosensitized to either of these venoms. These results cause diagnostic difficulties concerning therapeutical strategies. If the patient couldn't describe bee type clearly, CCDs are of vital importance to decide about venom immunotherapy.

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Usefulness of available recombinant molecules for the diagnosis of bee venom allergy

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Background: The rApi m 1 was the first molecule available for diagnosing of bee venom allergy. The rApi m 1 sensitivity was first reported 97% by Müller using the Advia system in 2009; several groups later registered unfortunately lower sensitivity using ImmunoCap ranging from 56 to 82%. Recently additional molecules for ImmunoCAP solid-phase system and Immulite liquid-phase system have become available. The aim of our study was to assess the usefulness of these new molecules.
Method: 39 bee venom allergic patients with clear history of bee anaphylactic sting-reaction and positivity of skin tests and/or bee venom extract IgE were included in our analysis. Specific IgE to rApi m 1 and rApi 10 were measured by the ImmunoCAP and specific IgE to rApi m 1 and rApi m 2 by the Immulite system in all patients. Sensitivity of all tests was calculated. Then sensitivity of CAP rApi m 1 and Immulite rApi m1 was compared and finally optimal molecule combination was found.
Results: Sensitivity of CAP rApi m 1 was 66.6%; Immulite rApi m1 93.3%; rApi m 10 46.6%; and rApi m 2 60%. Sensitivity of combination of CAP rApi m 1+ rApi m 10 was 73.3%; Immulite rApi m 1+ rApi m 10 93.3%; CAP or Immulite rApi m 1+ rApi m 2 reached 100%; as well as CAP or Immulite rApi m 1+ rApi m 2+ rApi m 10 100%.
Conclusion: Sensitivity of Immulite rApi m 1 is higher than sensitivity of CAP rApi m 1. The rApi m 1+ rApi m 2 represent the optimal molecule combination for the diagnosis of bee venom allergy.

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Levels of serum tryptase and prevalence of mastocytosis in Hymenoptera venom allergy

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Background: A severe systemic reaction to Hymenoptera venom can be the first clinical sign of mastocytosis. The prevalence of increased serum tryptase levels and mastocytosis among patients who have an indication of Hymenoptera venom immunotherapy is a matter of debate. We sought to evaluate serum tryptase levels before starting Hymenoptera venom immunotherapy in order to identify the patients in need of further testing to confirm or exclude mastocytosis.
Method: During two consecutive years, 47 patients (in 2014 $n = 23$; in 2015 $n = 24$) referred to our clinic, were diagnosed to have suffered a severe systemic reaction to Hymenoptera venom of such a degree that Hymenoptera venom immunotherapy was indicated. Serum samples for tryptase measurement were taken in 37 cases. If serum tryptase levels were >11.4 ng/ml, the patient was referred to bone marrow biopsy.
Results: Four of 37 samples (10.8%) had serum tryptase levels higher than 11.4 ng/ml. In one of these patients (baseline tryptase 15 ng/ml), bone marrow analyses revealed newly diagnosed systemic mastocytosis. In the second case (baseline tryptase 22 ng/ml), a patient with previously known urticaria pigmentosa was diagnosed with systemic mastocytosis following bone marrow analysis. In the third case (baseline

tryptase 22 ng/ml), bone marrow analyses did not reveal any clonal mast cell disorder. In the fourth case (baseline tryptase 89 ng/ml), the patient had previously undergone Hymenoptera venom immunotherapy and after being diagnosed with systemic mastocytosis the immunotherapy was reinitialised for lifelong treatment.

Conclusion: In patients who have suffered a severe systemic reaction to Hymenoptera venom, the measurement of baseline tryptase levels is strongly indicated.

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Bee allergy in Portuguese bee keepers: how do they react, what do they do and what do they know?

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Objectives: To describe Portuguese beekeepers' conduct and treatments after being stung. The secondary objective was to evaluate their knowledge on adrenaline auto-injectors (AAI), bee venom immunotherapy (VIT), and the medical specialty of Immunoallergology.

Method: Cross-sectional study using a questionnaire filled out by beekeepers during an apiculture meeting. Data on demographic characteristics, number of stings, reaction description and admissions to ER were collected. Awareness of AAI, VIT and the medical specialty of Immunoallergology was also questioned.

Results: Twenty-six beekeepers were included, 21 (81%) male with a median (interquartile range, IQR) age of 37 (10) years. The median (IQR) time of beekeeping was 3 (5) years. Twenty-four (92%) were amateur beekeepers. All had been stung in the last 12 months; 13 had systemic reactions, 13 had local reactions and, of these, 6 were large local reactions. Three reported respiratory or cardiovascular symptoms in association with cutaneous symptoms. Only 5 (39%) of the 13 with systemic reactions went to the ER. Only one stated that adrenaline was administered in the ER and only another one had an AAI. Five used alternative treatments on the sting site, namely, metal, ammonia, vinegar and urine. Five were aware of the existence of AAI, 8 of VIT and 7 of the medical specialty of Immunoallergology.

Conclusion: This group of Portuguese beekeepers showed insufficient knowledge on what to do in case of a sting reaction. Half of the beekeepers in this sample had systemic reactions and less than half of them went to an ER. There is a growing interest and consequent increase in beekeeping in Portugal. In order to prevent potentially fatal reactions, it is imperative to promote education on the risks, sting prevention measures and proper treatment of stings.

The increasing awareness of the medical specialty of Immunoallergology and the existence of bee venom immunotherapy should assure an early referral in case of systemic reactions, which could be crucial in this population.

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Usefulness of component-resolved analysis in the diagnosis of Hymenoptera venom allergy

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Background: Determination of serum specific IgE (sIgE) to Hymenoptera venoms is a very sensitive diagnostic test for venom allergy (VA). However, a large proportion of patients with allergic reactions to bee or wasp stings have also specific IgE to other venoms. Such double positivity causes significant problems in the selection of venoms for immunotherapy. Double positivity in diagnostic tests may be due to double sensitization (DS) to both venoms or to cross-reactions. IgE inhibition studies can help to distinguish DS from cross-reactivity, however they are expensive, often not easy to interpret and not suitable for routine purposes. Component-resolved analysis with recombinant species-specific major allergens may help to distinguish true double sensitization from cross-reactivity.

Methods: In this retrospective study, we included 18 patients (33% female), with a mean age of 43.6 years old, with Hymenoptera VA documented by a history of systemic allergic reactions to Hymenoptera stings and positive sIgE to whole bee and/or wasp venom, who also had determinations of venom recombinant allergens, namely Api m 1, Ves v 1, Ves v 5 and Pol d 5 (ImmunoCAP, Phadia, Thermo Fisher Scientific).

Results: In 61% of the patients the suspected insect was the bee and in 36% the wasp, being unknown in 17%. When the suspicion was the bee ($N = 11$), all the patients had sIgE to whole bee venom, but only 72% of those had positive sIgE to Api m 1. 27% had positive sIgE to Polistes and Vespula venom, but they all had negative sIgE to Ves v 1, Ves v 5 and Pol d 5. When the suspicion was the wasp ($N = 4$), all the patients had sIgE to whole Polistes venom, as well as sIgE to Pol d 5; 3 patients had sIgE to whole Vespula venom, and the same patients had positive sIgE to Ves v 1; one patient had positive sIgE to whole bee venom, but not to Api m 1. Four patients showed double positivity (bee/Vespula) when regarding only sIgE to whole venom; in all these cases the component-resolved analysis allowed the exclusion of true double sensitization. These patients were prescribed immunotherapy to the venom to which they were allergic.

Conclusion: In our study recombinant bee and Vespula venom allergens were able to distinguish true DS from cross-reactivity, which allowed an accurate prescription of venom immunotherapy. Only 72% of the patients with positive sIgE to whole bee venom had positive sIgE to Api m 1, suggesting that other molecular allergens may have an important role in bee VA.

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First aid management in insect venom anaphylactic patients in Silesia. A review from 1992 to 2015

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Background: Anaphylaxis is a serious systemic allergic reaction. It is thought to have affected between 1% and 2% of the general population Hymenoptera stings can cause systemic allergic reactions (SR) with estimated prevalence 0.15% to 0.8% in children and 0.3% to 8.9% in adults and occasionally fatal outcome, which may significantly contribute to morbidity and deterioration of quality if life after a sting. Most of anaphylactic reactions are the first time the patient has reacted It is very important to give all anaphylactic patients an appropriate first aid. This retrospective survey has examined patients with a history of anaphylaxis. We aimed to analyze and characterize medical care given to the patients with systemic reaction after insect sting.

Method: The subject of the retrospective analysis was a total of 2954 patients of allergy clinic, all of them allergic to Hymenoptera venom treated in the years 1992–2015. To the final analysis we selected 361 patients (196 women, 165 men) with complete questionnaire and medical documentation. Severity of anaphylactic reactions was estimated according to Mueller's scale). Time to the first medical intervention, the administered treatment, and follow up measures were registered.

Results: In this retrospective study most of patients were after severe anaphylactic reaction: 141 (41%) Muller IV°, 112 (31%) Muller III°. In these cases first professional medical help got 312 patients. Mainly delivered be personnel of emergency ambulance 152 (42%) and emergency 72 (20%). Primary care physicians helped 79 (22%) patients, no qualified medical intervention reported 49 (14%) subjects. The most common medications used were corticosteroids administered intramuscularly or intravenously (78%), antihistamines (54%), a combination of corticosteroids and antihistamines (48%), adrenaline was used only in 18% of patients. Analyzing medical intervention in the last 5 years (cut off 2010) adrenaline were administered in 36% patients. (statistically significant change $P < 0.05$). Not all patients were contacted with specialist, 274 patients (76%) were consulted by an allergist within 1 year after the sting.

Conclusion: This retrospective study has documented that insect venom anaphylactic reactions are insufficient effectively managed.

The use of adrenaline in observed therapeutic interventions was insufficient.

There is an educational need in real life regarding first aid anaphylaxis management.

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Patient knowledge of correct self-administration of adrenalin auto-injector after hymenoptera venom anaphylaxis

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Background: Correct self-administration of adrenalin is crucial in the management of possible repeated anaphylaxis. Several reports have shown the lack of patient's knowledge about the use of auto-injectors. With this study we wanted to assess the influence of education by different health care workers on the knowledge of self-administration and proper performance of self-administration of auto-injectors.

Methods: 63 patients with a history of anaphylaxis after hymenoptera sting were included in the study. In the first group 32 patients had regular contact with health care workers at specialized allergy canter because they were receiving venom immunotherapy. In the second group 31 patients that were not treated with immunotherapy were included. Questionnaire to assess patients' knowledge of correct administration of auto injectors was used. Correct administration was checked with supervised self-administration of placebo auto-injector. Checklist was used to rate the self-administration.

Results: Patients that were treated with immunotherapy had better knowledge of correct indications for auto injector use ($P < 0.01$) but there were no significant difference in knowledge of correct site of administration. Patients trained by specialized allergy nurse or doctor also had better knowledge of correct indication for auto injector use, compared to patients trained in the pharmacy ($P < 0.01$). But supervised self-administrations of placebo auto-injectors weren't more accurate in patients with frequent contact with healthcare workers compared with the control group ($P = 0.124$).

Conclusions: Although patients that were educated about adrenalin auto injector use by specialised allergy nurse or doctor and had frequent contact with health care workers at specialized allergy centre had better knowledge of correct place and timing of auto injector use, the demonstration of use with placebo auto injector was not better. Further studies are needed to increase the correct use of adrenalin auto-injectors.

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Optimism and emotional control in the group of people allergic to Hymenoptera venom

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Background: Optimism is a protective factor and is associated with the ability to express emotions. Ability to express emotions prevents emotional tension, which is particularly important among people with the diagnosed allergy to Hymenoptera venom and subjected to immunotherapy.

Method: A group of 110 people allergic to wasp and bee venom and subjected to immunotherapy was examined The patients were treated in the Clinic of Allergology, Immunology and Internal Diseases in Jan Biziel University Hospital No.2 in Bydgoszcz. The respondents had been subjected to the therapy from 1 to 5 years. Life Orientation Test (LOT-R) and the Emotional Control Scale (CECS) were used in the study. Satisfactory reliability of the used tools was obtained in the examined group. For LOT-R Cronbach's alpha in the examined group was 0.71 (while the authors of the tool obtained 0.78). Cronbach's alpha in the examined group for the whole emotional control scale CECS was 0.85 (the authors obtained: for the whole scale 0.87).

Results: The level of optimism and level of emotional control in the examined group. The average level of optimism obtained in the group was 16.15. In accordance with the standards specified by the authors, it was determined that among the respondents 49.53% showed an optimistic attitude, 34.58% obtained an average result and 15.89% had a pessimistic attitude. The emotional control scale consists of 3 subscales, in every of the subscales the maximum attainable score is 28 and the overall score of the emotional control scale is the total of 3 subscales, that is: maximum 84 points can be achieved. The higher the score, the higher the suppression of negative emotions, which is the people's belief in the ability to control their own emotions. Among the respondents the average score for the entire scale was 50.19, the highest score achieved for the anxiety subscale 17.91 and the lowest one for the anger subscale 15.33, while in the depression subscale 16.91 was obtained.

Statistically significant correlations between the level of optimism and the general emotional control rate were found ($R = -0.229$, $P < 0.05$) and the subscales of anger ($R = -0.237$, $P < 0.05$) and depression ($R = -0.274$, $P < 0.05$) in the examined group. There is no statistically significant relationship between the level of optimism and the anxiety subscale.

Conclusion: People with a higher level of optimism have greater emotional control, lower severity of anger and lower level of depression.

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Influencing factors on the severity of systemic sting reactions: the Austrian experience

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Background: Severe systemic reactions to Hymenoptera stings are associated with a variety of risk factors. While some are confirmed by several studies, data about other risk factors, like sting localization, sex or type of venom, differ from study to study. We therefore aimed to clarify this

discrepancy in a large study cohort and hypothesized that stings in skin areas, which are well supplied with blood, lead to more severe reactions.
Method: 644 patients with confirmed Hymenoptera venom allergy were included. Patients were asked about sting localization and symptoms using standard questionnaire. In order to determine stinger's depth of penetration, we used excess skin after excision of skin tumors in two patients and performed sting challenges.
Results: The stinger's depth of penetration depends on the part of the body: the stinger in the back got stuck in the reticular dermis, whereas the stinger in the face reached the deep arteriovenous plexus of the subcutis. We therefore expected more frequent severe reactions to stings in areas with thin reticular dermis. However, symptom severity was independent from skin thickness: only 15.2% of patients with severe reactions were stung on the head, compared to 84.8% stung on other parts of the body ($P = 0.007$). Interestingly, men were more likely stung on the head than women ($P < 0.001$). While sex and type of venom had no influence on symptom severity, we confirmed that age > 40 years is a risk factor ($P = 0.001$) as well as an elevated basal tryptase level: only 29.3% of patients with normal basal tryptase level had a severe reaction compared to 58.3% with elevated basal tryptase level ($P < 0.001$). Furthermore we detected a highly significant correlation between the severity of the reaction and the absence of cutaneous signs: in about 75% of patients with severe reactions, urticaria or angioedema were absent ($P < 0.001$ and $P = 0.004$, respectively).
Conclusion: We could not confirm that stings on the head or neck more frequently result in more severe reactions. However, we were able to confirm other risk factors: age > 40 years, elevated basal tryptase levels, and absence of urticaria/angioedema indicated a higher risk for severe systemic sting reactions.

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Honeybee immunotherapy in a patient with systemic mastocytosis

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Background: Mastocytosis is a significant co-morbidity in patients with allergic reactions to Hymenoptera. It is associated with an increased risk of more severe reactions following field stings or sting challenges, increased side effects and reduced efficacy to venom immunotherapy (VIT).
Method: We report a successful case of honeybee immunotherapy in a patient with Systemic Mastocytosis (SM).
Results: A 37 year old caucasian male beekeeper, previously healthy, was referred to our outpatient clinic for suspected Hymenoptera venom allergy. He presented with rapid onset of abdominal pain, nausea, diarrhea, vomiting, headache, paresthesia of the hands, dyspnea and syncope after 2 bee stings in the back. Physical examination revealed reddish-brown macules in the chest without any other abnormalities. Laboratory evaluation showed elevated serum basal tryptase [34.9 μg/l (1–15)] and specific serum IgE to honeybee venom of 1.24 UK/l. Skin prick tests to honeybee, wasp and polistes were negative. Intradermal skin tests were positive to honeybee at the concentration of 0.1 μg/ml and negative for the other venoms. SM was considered and the patient was referred to the Hematology outpatient department. Bone marrow biopsy confirmed the diagnosis. Since this patient has a history of a grade IV reaction of Mueller Classification to honeybee, positive skin tests and serum results, he started VIT with a conventional protocol. Premedication with ebastine was used and no adverse reactions occurred. The maintenance dose of 100 μg every 4 weeks is well tolerated and he was already re-stung without any reactions.
Conclusion: As described in literature, VIT is effective to treat IgE-mediated Hymenoptera anaphylaxis in patients with Mastocytosis. Its use is recommended despite a relatively high risk of adverse reactions, and provides protection from anaphylaxis in 75% of patients.

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Immunotherapy with bee venom successful in spite of persistence of specific IgE

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Background: Immunotherapy may be successful although skin test to allergen and specific IgE persist.
Method: We present a case of 52 year old beekeeper who had repeated systemic reactions to bee sting. Skin prick test with bee venom was positive and specific IgE to bee venom was detected in serum.
Results: Imunotherapy with bee venom was started and after 1 year both skin test and specific IgE became negative. Two years later prick test became positive and specific IgE in serum was detectable again. However, the patient was exposed to bee stings many times but he had no reaction after first year, and after second year of immunotherapy. We conclude that although both skin prick test and specific IgE are used not only before but also during the course of immunotherapy, reactions to bee sting can not be predicted on the basis of these tests.
Conclusion: More expensive test as measurement of specific IgE in serum is often needed before immunotherapy is started but its value during the course of immunotherapy is limited.

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Systemic mastocytosis after anaphylactic reactions to hymenoptera venom immunotherapy:two cases

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Background: Severe systemic reactions to hymenoptera venom is the most common type of anaphylaxis in patients with systemic mastocytosis.
Method: Severe systemic reactions to hymenoptera venom is the most common type of anaphylaxis in patients with systemic mastocytosis. Anaphylaxis is characterized by hypotension and syncope in the absence of urticaria and angioedema.
Results: Case1: A 40-year-old man had an anaphylactic reaction in 5 min after being stung by a honeybee while working in his farm. Because of deep hypotension he was treated with epinephrine and intravenous fluids in emergency room. Skin prick test and specific IgE were positive for honeybee venom. After starting to venom immunotherapy, he had two severe anaphylactic reactions during buildup period of immunotherapy requiring epinephrine administration and fluid replasement. Serum tryptase level after 1 and 3 h from episode was 156 ng/ml and 56 ng/ml respectively, with a baseline level of 24 ng/ml, also c-kit was negative in peripheral blood. A bone marrow biopsy was performed, which revealed multifocal dense infiltrates of mast cells. The patient was diagnosed as indolent systemic mastocytosis. Although, venom immunoteraphy was restarted with omalizumab concurrently, we just reached to half of the maintenance dose because of the systemic reaction.

Case2: A 48-year-old woman had an anaphylactic reaction in 5 min after being stung by a yellow jacket in picnic and was treated in emergency room. Skin prick test and specific IgE were positive for yellow jacket venom. He had systemic reactions during buildup period of venom

immunotherapy requiring epinephrine administration and fluid replasement. Serum tryptase level after 1 h from the episode was 38 ng/ml, with a baseline level of 26 ng/ml, also c-kit was positive in peripheral blood. A bone marrow biopsy was performed, which revealed multifocal dense infiltrates of mast cells. The patient was diagnosed as indolent systemic mastocytosis. Immunotherapy was continued without problems reaching to maintenance doses.

Conclusion: Patients with anaphylactic reactions to hymenoptera venom immunotherapy may have an increased risk of having systemic mastocytosis. Tryptase levels should be measured in all patients with a history of a systemic reactions to hymenoptera venom immunotherapy and further evaluation for the systemic mastocytosis may be needed.

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Care of Hymenoptera venom allergy: 10 years experience of a specialized department of Algiers

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Background: The Hymenoptera venom allergy is an important cause of anaphylaxis. The prevalence of systemic reactions is 0.7–8% in the general population, from 0.34 to 8% in children, 14–32% among beekeepers. The risk populations are beekeepers and their families, pastry cook, people exercising outdoors. Prevalence is totally unknown and the treatment remains inadequate in our countries. The creation since December 2006 of a specialized center at the University Hospital Beni Messous (Algiers) for the diagnosis, treatment and prevention of Hymenoptera venom allergies. Risk factors are the severity of the initial reaction, age (adult), the type of insect (bee, wasp, hornet, bumblebee), the degree of exposure, the interval between injections and presence of cardio-respiratory diseases.

Method: This is a national prospective survey which took place from December 2006 to October 2015, on a sample of 424 patients (256 male and 168 female) with 80 children from 17 departments from Algeria. It took place at the hospital the day of the Pneumo -Allergologie Service (CHU Blessed Messous, Algiers).

The average age of patients was 23 years, ranging from 06–62 years the examinations are conducted skin tests (bee and wasp) and IgE assay (bee and wasp).

Results: The concept of atopy was found in 46% of patients, 27% in those exercising exposed profession. We note a predominance of Stage III (43%) followed by Stages IV (31%) as classified by Muller, the tests are positive almost exclusively for bees (47%), it is the same for specific IgE.

Treatment decisions: From the 168 patients who were put under desensitization 32 are children, 165 are allergic to bee venom and 03 to wasp venom, 42 according to the rush protocol and 122 according to ultra-rush protocol with systematic health education for the sick ones.

Conclusion: Allergic reactions after Hymenoptera stings are potentially serious with a risk of death by anaphylactic shock. An emergency kit containing adrenaline must be prescribed to patients at risk.

The desensitization has an efficiency superior to 90% to prevent the risk of second recurrence of a general reaction during later.

There is a need for more specialized centers in the Maghreb and African countries to improve the diagnosis, treatment and prevention of allergies to Hymenoptera venom.

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The sting challenge test (SCT): our experience

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Background: SCT in hymenoptera venom allergy is a widely accepted and highly recommended provocative testing that we use to value how successful immunotherapy (IT) with pure venom is, as well as to learn the degree of protection that the patient presents once suspended.

We present a series of 50 patients, of whom 3 with systemic mastocytosis, that suffered an anaphylactic reaction after an insect bite, diagnosed of hypersensivity to hymenoptera venom allergy and treated with IT.

Method: We performed *70 RIH*: 26 with apis, 39 with polistes and 5 with vespula.

33 patients were men and 17 women.

Average age 46, 4 years old, of which: 23 were atopic, 5 with beekeepers family and 5 farmers.

We determined the plasmatic concentrations of tryptase, total IgE and basal specific, before (pre-SCT) and after (post-SCT) provocative testing.

Results of the testing were considered *positive* only if they presented systemic reaction.

Results:

POSITIVE RIH: Of all 70 RIH performed 7 were positive (10%): 5 with apis, 1 with vespula y 1 with polistes.

In total 4 patients: 1 man, 3 women, of whom 1 beekeepers family, 2 atopic, 1 with mastocytosis.

Average age of 34, 57 years.

Seric levels of tryptase were duplicate, while seric levels of IgE total and specific pre-SCT and post-SCT did not show significative changes.

No patient under treatment with antihypersensitive medication had positive RIH.

Conclusion: SCT shows to be a useful test in the valuation of IT in hymenoptera venom allergy effectiveness.

All patients being treated with antihypertensive presented negative RIH.

Seric tryptase levels are useful as a meter towards the positivity of the test, but not in all cases.

No significative variations in IgE specific levels to hymenoptera venom allergy were noticed, unlike with tryptase.

We find a higher proportion of systemic reaction to SCT in women and by bee bite.

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Re-sting reactions in real-life of patients receiving hymenoptera venom immunotherapy

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Background: Systemic allergic reactions (SAR) in patients with Hymenoptera venom allergy are prevented by venom immunotherapy (VIT) in most patients. The efficacy of VIT can be determined by the outcome of sting challenge test or field re-sting reaction. In this study, we addressed the outcome of field stings occurring in patients who completed VIT and who are still under VIT.

Method: A total of 125 patients receiving VIT between 1995–2015 were included in the study. The medical records of patients were evaluated, and all patients were called by telephone to ask about possible re-stings. The patients who could be contacted, were invited for an interview in the clinic. A questionnaire about re-sting and reaction history (time, type of insect, severity) was filled out at this follow-up visit. Severity of SAR was graded according to Ring and Messmer classification. Characteristics of patients, diagnostic tests, allergen extract, schedule and duration of VIT were analyzed.

Results: The mean age of 125 cases (F/M:46/79) was 38.3 ± 12 years (min–max; 17–70). We could not reach 43 (34%) patients by telephone call whereas 82 (66%) patients who could be contacted,

were interviewed face-to-face. Sixty-six patients (52.8%) were treated with *Apis mellifera* venom, 58 (46.4%) with *Vespula vulgaris* venom and one patient (0.8%) with both venoms. The schedule of VIT were cluster in 54 cases (43.2%), rush in 50 (40%) and conventional in 21 (16.8%). The mean duration of VIT was 31.9 months. There was 88 (70.4%) patients who completed or prematurely ended VIT while 37 (29.6%) patients were still ongoing VIT. Thirty-five patients were re-stung 52 times (*Apis*: 33, *Vespula*: 19) during the treatment or after completion of VIT. Most frequent re-stings were occurred in the first year of VIT. Twenty-two (25%) patients who completed VIT were re-stung, SAR was observed in eight patients. Thirteen (35%) patients who were still under VIT were re-stung, SAR were detected in two cases. Of the 52 re-stings, 14 (27%) were Grade 2–3 SAR. Seven patients used ACE inhibitor or beta-blocker drugs. In one patient who had asthma and were on ACEI treatment developed Grade 3 SAR after injection during updosing and maintenance phase. In the same patient, two Grade 2 SAR were occurred due to sting re-exposure during first year of VIT.

Conclusion: Our findings demonstrate that vast majority of patients tolerated field re-stings indicating effectiveness in protecting from SAR despite short-term of VIT.

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The anaphylactic shock risk grading to Hymenoptera stings allergy with basophilic activation and serum tryptase testing

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The basophilic activation with bees, wasps, hornets venom allergens using (BUEHLMANN, Flou-CAST-Allergens, Switzerland) and serum tryptase level («UniCAP 100» (Phadia, Sweden) were examined among the 102 patients with systemic allergic reactions to Hymenoptera stings with the help of the diagnostic kit BASOTEST ™ (Glicotope Biotechnology, Germany). The research was carried out in 2 weeks after the systemic allergic reactions to Hymenoptera stings (the range from 2 to 364 weeks).

The research results showed that the group of patients with anaphylactic shock (Ash) (Me = 19.5[15.77;30.4]) had sensitization to bee venom BASOTEST (BAT) higher in comparison with the values of the patients group with systemic allergic reactions I, II, III (H.L. Mueller,1966) with the degrees (Me = 10.35 [7.33; 15.64]) ($P = 0.001$). The basal tryptase level was also significantly higher in the patients group with Ash (Me = 8.7 [5.85; 9.0]) compared to the group systemic allergic reactions I, II, III with the degrees (Me = 5.9 [4.8; 6.9]) ($P = 0.05$).

Among the patients with wasps venom sensitization the BAT values tended to be significantly higher within the patients group with Ash (Me = 11.9 [8.29; 18.35]) in comparison with the patients with systemic allergic reactions I, II, III with the degrees (Me = 10.07 [7.12; 12.54]) ($P = 0.054$). The basal tryptase levels of the patients with Ash (Me = 8.6 [6.85, 9.1]) were also significantly higher compared to the patients with systemic allergic reactions I, II, III with the degrees (Me = 6.8 [4.3, 7, 9]) ($P = 0.001$).

The BAT values tended to be increasing in the patients group with hornet sensitization having Ash (Me = 17.45 [13.49; 21.4]), but no significant difference with the patients group systemic allergic reactions I, II, III with the degrees (Me = 10.8 [7.4; 15.25]) was found ($P = 0.018$). The basal tryptase level was significantly higher in the patients group with Ash (Me = 7.6 [6.9; 9.0]), compared with the group systemic allergic reactions I, II, III with the degree (Me = 6.2 [4.8; 7.5]) ($P = 0.031$).

The basal tryptase level was significantly higher within the patients with Ash, regardless of the identified insect, which gives us the reason to use this indicator to predict a severe anaphylactic reaction risk.

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Epidemiology of doctor diagnosed anaphylaxis in Korea; using big data of 48.1 million South Korean health-care records

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Background: Anaphylaxis is a rare allergic disease. However, it is potentially life-threatening even if immediate treatment is given and the rates of unexpected late response and recurrence can be high. The incidence of anaphylaxis has been increasing worldwide for the past few decades. The aim of this study was to estimate the incidence of anaphylaxis in Korea.

Method: To investigate the incidence of anaphylaxis (T78.0, T78.2, T88.6), we analyzed the nationwide database (National Health Insurance Corporation) which included the health-care records of 48.1 million individuals between January 1, 2009, and December 31, 2014.

Results: There has been a pattern of increasing number of anaphylaxis patients in Korea; 6841 (2009), 7243 (2010), 8074 (2011), 10 125 (2012), 10 859 (2013), and 14 387 (2014). Moreover, there was a tendency of increasing incidence of anaphylaxis: 0.014% (2009), 0.015% (2010), 0.016% (2011), 0.020% (2012), 0.022% (2013), and 0.029% (2014). In 2014, there were 8039 male and 6348 female patients of which; 321 were under 2 years old, 372 were aged 3–6, 432 were aged 7–12, 747 were aged 13–19, 1242 were aged 20–29, 1768 were aged 30–39, 2675 were aged 40–49, 3488 were aged 50–59, 2074 were aged 60–69, and 1032 patients were over 70 years old.

Conclusion: Incidence of anaphylaxis in Korea tended to show an increase in all age groups. Etiologic analysis was limited as the study was carried out using the ICD-10 code. So, further study is needed.

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Anaphylaxis and cardiovascular event: a case report of Kounis syndrome

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Background: Kounis Syndrome (KS), the occurrence of acute coronary events as consequence of allergic or hypersensitivity reactions has been described for years. It is still relatively unknown and consequently underdiagnosed, leading to inadequate treatment and subsequent morbidity. There are three subtypes of KS: type I which occurs in patients without predisposing cardiovascular factors; type II which occurs in patients with cardiovascular risk factors; and type III by stent thrombosis.

Case description: A 66 year old housewife on bee venom immunotherapy for the past 4 years with type 2 Diabetes, hypertension and rheumatoid arthritis, was stung in October by a wasp. She immediately felt unwell, with lipothymia, angioedema of the tongue, dyspnea, retrosternal chest pain with radiation to the left arm and nausea. She self-administered her adrenaline 0.3 mg autoinjector and took ebastine 40 mg. She was assessed by the mobile medical team on site as being hemodynamically stable, with dyspnea, and SpO2 was 88% (FiO_2 21%). She improved on route to the ER and became symptom free. No further medication was administered and she was discharged after 2 h. Serum tryptase was not measured. One hour later she returned to the ER with chest pain

radiating to her back, sweating and nausea. ECG confirmed NSTEMI with an elevated troponin I (0.364 ng/ml). She was admitted to the Coronary ICU and cardiac catheterization showed severe triple vessel disease. Subsequent to this she had revascularization with drug-eluting stents.

Conclusion: This is a typical case of Kounis Syndrome. The WAO Anaphylaxis guidelines recommend a minimum 4 h of observation after anaphylaxis, 8–10 h if respiratory or cardiovascular compromise; not only for detection and treatment of biphasic reactions, but also to investigate for cardiovascular events especially in patients with risk factors. We stress the importance of adequate observation as in this case, the mininum 4 h observation period and continuous electronic monitoring would have allowed for early detection and treatment of her MI.

Poster Session TPS 24

Epidemiological and clinical studies on occupational allergy

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Work - related asthma: an 5-year retrospective review

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Background: Work-related asthma (WRA) is a major health challenge, with significant potential for acute morbidity, long-term disability and socio-economic consequences for both the patient and the society and is probably underdiagnosed. As much as 25% of adult asthmatic patients are estimated to have WRA. The aim of our study was to characterize the cases with suspected WRA referred to our out-patient Occupational Unit during a 5 years period.
Methods: We retrospectively analysed the patients with suspected WRA followed up between 2010 and 2014. Data regarding: gender, age, industry, suspected causal agents, latency period, individual risk factors and short/long-term disability were collected. Objective diagnostic tests were conducted in periods at and away from work (peak expiratory flow recordings (PEFRs), spirometry, bronchodilation test, and methacoline responsiveness). Skin prick test (SPT) and specific IgE (sIgE) were also performed when reliable and available. T-Student test for paired samples was used for comparisons (significance if $P < 0.05$).
Results: A total of 130 adult patients [65M/65F, mean age 46 ± 11 years(y)] were studied. Twenty-six (20%) were smokers and 66 (51%) were atopic. The highest incidence were observed in the baking industry (19%), followed by footwear (12%), cork (10%), textile (8%), and furniture (7%) industries. The most common causal agents were isocyanates (23%), flour/grain (20%), wood dust (7%), cork (6%), chemical disinfectants (5%) and hair dyes (5%). Latency period: mean 11 ± 9 years: epoxy resins (3y), isocyanates (4y), flour/grain and chemical disinfectants (9y); cork and wood dust (≥10y). In 79% of patients symptoms improve on weekends or on holiday. There was statistically significant differences, between the PEFRs and the FEV1 mean values in working days compared to days away from work (389 vs 429 l/min; $P = 0.002$; 80 vs 93%; $P < 0.05$, respectively). In 35 patients (27%) an individual diagnosis of WRA was made. Of these, 26 (74%) were reported to the National Centre for the Protection against Occupational Risks (CNPRP), of which 16(62%) had been recognised as an occupational disease. We found a significant association between atopy and the outcome of WRA ($P < 0.05$).
Conclusion: The majority of reported WRA cases were found in baking, footwear, cork and textile industries. The diagnosis of WRA was made in 27% of patients. A correct diagnosis is extremely important to reduce or limit the consequences of the disease.

974
Coexistence of allergic conjunctivitis symptoms in subjects with work-related rhinitis exposed to high and low molecular weight allergens

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Background: Ocular symptoms may occur due to exposure to allergens among patients with allergic rhinitis. Recognition of occupational allergic conjunctivitis (OAC) and rhinitis requires to demonstrate the relationship between exposure to workplace allergens and allergic eye and nasal symptoms. The study aim was to evaluate relationship between the presence and severity of nasal and eye symptoms and the type of allergen [high (HMW) and low (LMW) molecular weight allergens].
Method: The study group included 153 subjects reporting nasal symptoms at the workplace. In all subjects questionnaire study, as well as allergologic diagnostic tests like skin prick tests, evaluation of specific IgE level (if available) were performed. Moreover, the specific inhalative challenge tests (SICT) with evaluation of conjunctival tear fluid and nasal lavage fluid (NLF) were performed.
Results: 134 subjects (87.6%) reported nasal symptoms whereas 126 (82.4%) conjunctival symptoms. In NLF increase in the percentage of eosinophils was found in 51 (46.4%) and 9 (20.9%) patients, while in conjunctival tear fluid in 52 (47.3%) and 11 (25.6%) subjects exposed to HMW and LMW agents respectively. Concomitant increase in the percentage of eosinophils in both NLF and tears was found in 41 (37.3%) and 6 (13.9%) subjects exposed to HMW and LMW agents respectively. Moreover, in patients occupationally exposed to HMW allergens a significant increase in the percentage of eosinophils in NLF both in 4 and 24 h after the SICT and a significant increase in eosinophils in tears cytology at 6 and 24 h after SICT among patients with OAC as well as in those with occupational rhinitis, also in the isolated form were documented.
Conclusion: Cytological evaluation of tears in 1 h after SICT yet shows no significant changes despite the subsequent increase in the number of eosinophils in allergic individuals with occupational allergy thus it is not proper time interval to perform evaluation.

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Risk factors for work-related asthma in health care workers with exposure to diverse cleaning agents

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Background: The role of exposure to cleaning products and disinfectants in work-related asthma is increasingly recognised in health care settings, although the specific substances that increase asthma risk are not well identified. This study investigated risk factors associated with various asthma phenotypes in health care workers with widespread use of cleaning agents for high-level disinfection of medical instruments, routine daily surface cleaning, wound care and hand cleaning.

Method: A cross-sectional study of 346 health care workers used a modified ECRHS questionnaire, immunological tests [Phadiatop; ImmunoCAP specific IgE to chlorhexidine, ortho-phthalaldehyde (OPA), NRL (Hev b5, Hev b6.02)], fractional exhaled nitric oxide (FeNO), spirometry and methacholine challenge test.
Results: The median age of this population was 46 years, 84% were female, 12% current smokers and 47% were atopic. The prevalence of current asthma was 22% (atopic asthma = 12%, non-atopic asthma = 10%) with 4% having work-related asthma and 1% probable occupational asthma. Among the 6% with allergic sensitisation to occupational allergens, 4% were sensitised to OPA, 2% to NRL allergen components and 1% to chlorhexidine. In multivariate statistical models, floor finishing tasks (stripping/buffing/waxing) (OR = 2.6; 95% CI: 1.0–6.5) and the use of floor waxes (OR = 3.3; 95% CI: 1.4–7.7) was strongly associated with non-atopic asthma. Furthermore, the use of enzymatic cleaning agents (containing proteases, lipases, amylases, cellulases, ureases) on fixed surfaces/equipment/instruments was strongly associated with probable occupational asthma (OR = 9.6; 95% CI: 1.2–75.3).
Conclusion: Routine daily cleaning of fixed ward surfaces/equipment/instruments using enzymatic cleaning agents was associated with an increased risk of probable occupational asthma predominantly due to ortho-phthalaldehyde sensitisation.

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New short-duration method of performing specific inhalation challenge with persulfate salts

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Background: Persulfate salts from hair bleaching products are considered the major cause of occupational asthma (OA) and occupational rhinitis (OR) in hairdressers. The specific inhalation challenges (SIC) is considered 'reference standard' for diagnosing OA and OR. In this work, we describe the results from a new short-duration SIC with persulfate salt designed to test for both rhinitis and asthma simultaneously in 1 day. In addition, the value of skin prick tests (SPTs) with high concentrations of persulfate salts and histamine release-tests (HRTs) with persulfate salts is assessed.
Methods: The study population included 19 symptomatic hairdressers and 12 asthmatic controls. The SIC was performed potassium persulfate (PP) in a provocation chamber for 3 × 5 min in 1 day, and participants were monitored with FEV_1, acoustic rhinometry, subjective symptoms scores and scoring by anterior rhinoscopy. In addition, SPTs with persulfates (concentration: 2–20% w/v) and HRTs with persulfates (concentration 0.031–1% w/v) were performed.
Results: During SIC with PP, six hairdressers (31.6%) had a nasal response and two (10.5%) had a bronchial response. None of the asthmatic controls reacted to the test. No positive SPTs were recorded. Both hairdressers and asthmatic controls showed unspecific non-IgE mediated histamine release.
Conclusion: The new short-duration SIC with potassium persulfate proved useful for diagnosing occupational rhinitis, however, its sensitivity in diagnosing occupational asthma might be too low. We suggest that the proposed procedure is extended to several days of exposure if patients with a history suggestive of OA do not react during the test.

SPTs with persulfates in high concentrations do not produce false-positive toxic reactions. The HRT with persulfates is of no use to document asthma or rhinitis caused by persulfates.

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Skin sensitization model based by qualitative structure-activity relationships (QSAR) approach based on EC3 of LLNA

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Background: Contact dermatitis is by far the most common form of occupational skin illness. *In silico* assessment of skin sensitization is increasingly needed owing to the problems concerning animal welfare, as well as excessive time consumed and cost involved in the development and testing of new chemicals. We previously made skin sensitization model from human and animal data and reported. Its accuracy was 61.2% (sensitivity 60.7%, specificity 62.8%) by external validation. This time we made skin sensitization QSTR model from only animal data (LLNA, 471 chemicals,) by using K-step Yard sampling (KY) methods (U.S. Patent No. 7725413, 2010) and 1 model KY method (US Patent Application).
Methods: This time we made QSAR model based on EC3 value of LLNA to discriminate between strong and weak sensitizers by using ordinary discriminant function. A total of 203 skin sensitizers (183 learning sets for generating model and 20 for external validation) were used in this study. Multiple Linear Regression (MLR), Support Vector Machine (SVM) and Logistic Regression (LOGR) were applied to generate model. Less than 9.4% of EC3 was judged as strong sensitizer. All data analyses were performed using ADMEWORKS/ModelBuider software (Fujitsu Kyushu Systems Limited, Japan).
Results: Correlation coefficient between predicted values and measured values of EC3 were 70.34% in MLR, 68.78% in LOGR, and 60.02% in SVM. Correct classification of sensitizers (strong and weak) were 67–76% in internal validation and 55–5% in external validation.
Conclusions: The concordance in strong ensitizers were better than that in weak sensitizers. This would be because 183 learning sets were composed by 117 strong and 66 weak sensitizers.
Acknowledgment: This work was supported by JSPS KAKENHI Grant Number 25293148.

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A specific immunoassay for Guinea pig urinary protein

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Background: Laboratory animal allergens (LAA) are a common source of occupational exposure (asthma) for laboratory personnel in biomedical research worldwide. In recent years, mouse urinary protein and rat urinary protein have been the focus of extensive monitoring in animal lab facilities. Although guinea pig allergy is prevalent among lab workers, limited exposure data has been collected. Our aim was to develop a sensitive ELISA that could be used to measure guinea pig urinary protein (GPUP) for both exposure assessment and allergen standardization.
Method: A two-site ELISA was developed using affinity purified polyclonal antibody raised against GPUP for capture, and biotinylated polyclonal anti-GPUP for detection. The assay was calibrated using purified GPUP, with total protein content determined by Advanced Protein Assay.
Results: The ELISA standard curve ranged from 1000–2 ng/ml, with a limit of quantitation of 20 ng/ml. The assay readily detected GPUP in guinea pig urine,

epithelial and hair preparations as well as air samples collected in animal labs (n = 10, < DL-60 ng/filter). Various urine, epithelial, hair and purified natural allergen samples of mouse, rat, hamster or rabbit did not react in the assay (<0.02 μg/ml).
Conclusion: A sensitive ELISA with defined specificity for guinea pig urinary proteins has been developed. This assay will allow occupational exposure monitoring programs to develop preventative processes in animal facilities handling guinea pigs. In addition, this assay will provide a method for measuring guinea pig allergen exposure in the environment.

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Evolution of occupational asthma: does cessation of exposure really improve prognosis?

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Background: To assess the evolution of occupational asthma (OA) depending on whether the patient avoids or continues with exposure to the suspected offending agent.
Method: A follow-up study of 41 subjects with occupational asthma was carried out. Clinical interview and physical examination both at diagnosis and re-examination were performed. Functional spirometric test was carried out, during both examinations. Clinical improvement, deterioration or no change were defined according to the changes seen on the GINA severity scale at the time of diagnosis.
Results: Of the 41 patients finally included, 28 had totally ended exposure and 13 continued to be exposed at work. Clinical improvement was observed in 46.3% of those who had terminated exposure and in 22% of those who remained exposed. Logistical regression analysis, including the type of agent and the persistence or avoidance of exposure among the variables, did not show any predictive factors of clinical evolution. Similarly, the change in FEV1 was not associated with the avoidance or continuation of exposure to the causative agent.
Conclusion: Avoiding exposure to the causative agent in patients with OA does not seem to improve prognosis in this disease. Despite these findings, there is insufficient evidence to recommend a change in current management guidelines.

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A 3 -year follow-up study of sublingual specific immunotherapy with wheat flour in Italian occupational baker's asthma and rhinitis

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Background: Allergy to wheat flour is the main cause of occupational rhinitis and asthma of bakers, pastry and pizza makers. It is consider a socio-economic burden too.
Methods: 9 patients suffering from allergic rhinitis and/or asthma to wheat flour were diagnosed through specific respiratory challenges. They were treated for 3 years with sublingual specific immunotherapy (SLIT) with the same scheduled flour extract (Anallergo, Firenze). A quality of life questionnaire (SF12 standard V1) and an asthma control test (ACT AIFA 2005) were recorded.

Some markers were dosed before and after the treatment: total IgE, wheat flour specific IgE, recombinant proteins (Tri a 14 and Tri a 19 ω gliadin) and exhaled nitric oxide levels (FeNO). Alongside dosages we carried on skin prick tests (SPTs) to wheat flour, occupational and common aeroallergens, respiratory function test and metacholine challenge test.
Results: 6 out of 9 patients continued to carry out their work: 3 with good control of asthma (ACT >20/25) and 3 with acceptable control of asthma (ACT 18/25). 3 out of these 6 patients reduced their environmental exposure. 3 patients stopped SLIT: 2 because of adverse reactions, while one changed work because of inefficacy of therapy (persistent respiratory and skin symptoms). After 3 years total IgE levels and FeNO levels were statistically reduced. No correlation was found between specific IgE, SPTs and the other clinical data. No significant variations of respiratory function parameters were evidenced, but 2 workers exposed to wheat flour showed higher methacholine threshold values. 2 out of 6 patients responding to immunotherapy had recurrence of nasal respiratory symptoms after few months from the end of 3-year SLIT.
Conclusions: Immunotherapy for occupational wheat flour allergy seems to be feasible and efficient, avoiding job loss. SLIT, instead of subcutaneous immunotherapy, is likely to have more compliance because of less risks, more convenience, easier use, and independence. The most effective method to evaluate efficaciousness of the therapy is based on symptoms: the reduction of pharmacological therapy and the ability to keep up with the specific job task should be take into account. Total IgE and FeNO may be also appropriate markers in order to assess both the success of the immunotherapy and the exposure of workers. It is difficult to evaluate compliance and effectiveness of SLIT due to the low number of workers approaching this therapy.

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Clinical application of EAACI position papers on occupational rhinitis and work related asthma

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Background: In past years a number of Position Papers on occupational allergy have been published by *ad hoc* task forces with the endorsement of the European Academy of Allergy and Clinical Immunology. The main goals of the papers were to issue key messages and consensus recommendations and to provide operative protocols for disease assessment in the daily practice. The aim of our work is to evaluate the actual clinical application of the operative protocols provided by the 'EAACI position paper on occupational rhinitis'[1,2] and by the 'EAACI consensus statement for investigation of work-related asthma in non-specialized centres'[3].
Method: We reviewed the available published literature from PubMed, using the following key words search strategy: 'occupational rhinitis' and/or 'work-related rhinitis' and 'occupational asthma' and/or 'work-related asthma'. The date range was from the publication date of the two Position Papers to the end of 2015. Further restrictions were 'humans' and 'adult: 19+ years'. Selected papers were then independently reviewed by the two authors.
Results: 248 articles at all has been found for occupational rhinitis in the range between March 2009 to December 2015. The EAACI Position Paper published on Allergy[1] has been cited in 6 works, while the one published in Respiratory Research[2] (open access journal) in 50 papers. For occupational asthma 512 articles has been found in the range between January 2012 to December 2015. The EAACI Position Paper published on Allergy[3] was cited in 15 papers. Most papers that refer to the Position Papers were review, and only few

studies used the proposed protocols for the diagnosis of occupational rhinitis and asthma.

Conclusion: Despite the aim of both position papers was to provide and spread operative protocols for disease assessment, years after publication only few researchers refer to these in their daily practice. The reasons for a such result will be discussed and should be explored for planning future task forces strategies.

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Chironomidae allergy

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Background: Bloodworms are larvas of chironomes, insects of the Diptera chironomids family, very popular source of food for many fish species both in the wild and in captivity. They also are used in the aquarium fish food in frozen form, paste or live food.

Method: Patient aged 28 years, with history of family atopy, non-smoking, professional aquarist that consult for an embarrassing rhino-conjunctivitis, cough, dyspnea, wheezing, fissural pulpite aggravated at his workplace and with remission of symptoms during the day rest.

Results: The objective physical examination enlarged middle nasal concha. Negative Prick-test to pneumallergens.

Skin tests to bloodworm with a dilution of 1/1000: Papule 12 mm, erythema 35 mm.

Positive specific IgE to chironomides with 7, 17 Ku/ml: Class IV.

Discussion: Chironomid allergy is manifested by clinical of asthma, rhinoconjunctivitis and urticarial type of skin reactions.

the global distribution of this allergy is mostly described in some countries (Japan, UK, Sudan).

The allergenic fraction of Chironomidae is located in the larval hemoglobin of the animal.

Conclusion: Respiratory allergies to food particles to domestic ornamental fish (aquarium) are a known phenomenon, its importance is difficult to quantify. It is necessary to think of it when the interrogation finds the notion of Fishkeeping. Skin tests and specific IgE (RAST with chironomids) a major allergens in fish food are part of diagnostic investigations.

It is interesting to look for a aeroallergen in some asthmas, conjunctivitis, even urticaria, with the subjects at risk

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Fatal anaphylaxis after insect sting during work

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Background: Hypersensitivity reactions due to insect stings may include large local or systemic allergic reactions (SAR). The life-time-prevalence of systemic sting reactions in the general population is reported to vary between 0.3 and 7.5%. Out-door-workers have an increased risk for SAR upon insect stings. E.g., bee-keepers suffer from bee venom allergy in more than 30% of the cases. Forest workers, gardeners, or farmers also have a higher risk to be stung and to develop subsequent SAR.

Case report: We report a 49-year-old forest worker, who had been stung from wasps during his work. Within minutes he developed a SAR rapidly turning into a cardiac arrest. Bystanders called the ambulance; resuscitation, however, was not successful. An inquiry at the family doctor revealed no history of an insect venom allergy.

At autopsy a small puncture corresponding to an insect sting was demonstrable. Other findings were very well compatible with an anaphylactic reaction being the cause of death. At the 4th day post mortem blood was taken from the inguinal vein. Serum was tested positive for Vespula-venom-specific IgE-antibodies (0.6 kU/l, CAP class 1). Serum tryptase concentration was 89.2 µg/l (95th percentile of living persons 11.4 µg/l). This tryptase level was compared to levels in the sera of 9 other corpses, in which autopsy had not revealed an anaphylactic reaction in context with the fatality. In these corpses, serum tryptase concentration on the fourth postmortal day was 22.8 ± 17.5 µg/l (mean, range 3.9–58.3, median 15.7 µg/l).

Conclusion: After a fatal SAR, the post mortem serum tryptase concentration may be significantly elevated. Together with history and other findings a fatal anaphylactic shock due to an insect sting was diagnosed in the forest worker. Even without a history of previous hypersensitivity reactions to insect stings, an insect sting may be fatal. Work safety for outdoor workers should raise the awareness for potential hazards from insect stings and promote the use of protection clothes for occupations with very high sting risk. First-aid-training of out-door-workers should include the management of anaphylactic sting reactions.

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Massive facial angioedema after occupational exposure to fish of the Scombroidae family - clinical case

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Background: Angoneurotic oedema is a common problem in occupational pathology and it's characterized with various etiology. Pathogenic mechanism that cause the disease are also various and they can be divided into two groups - allergic and non-allergic. The colourful palette of etiologic causes and pathogenic factors is often a reason for difficulties in quick diagnosis. This on its turn hinders the administration of adequate therapy. Some of the cases require exclusion of Hereditary angioedema as a rare and specific form of the disease.

This is why the choice of diagnostic and therapeutic algorithm should be individual for each patient and in accordance with the etiology and pathogenesis of angioedema.

Method: Clinical case. Patient 30 years old, hospitalized for treatment of angioedema and clarify its etiology. The incident is the first of its kind.

Results: The presented by us case supports and depicts the approach mentioned above. Hereby we present a patient with massive facial angioedema accompanied by itchiness. The thorough allergy and occupational history, the precisely registered allergologic status and the results of immunology testing that did not show any deviation from the referent levels let us accept the occupational etiology of angioedema. According to our literature research we concluded that allergic reactions to fish and fish products, including the ones to fish of the Scombroidae family are not isolated cases. What makes the presented by us case interesting is the occupational

contact with fish that provoked massive angioedema. Immunological and serological tests:lg E-70.0 IU/ml negative /-/, lg G-13.700 g/l, lg M-0.937 g/l, lg A-1.159 g/l, C3 serum level-1.2 g/l, C4 serum level-0.32 g/l, C1 INH leve-l201 g/l, C1 INH activity-90%, C1q serum level-170 mg/l, ANA (Antinuclear antibody)- 0.8 IU/ml, CRP-0.6 mg/l, RF (Rheumatoid factor)-5 U/ml, Specific IgE to mackerel/ Mackerel IgE- 0.05 kU/l.

Conclusion: Angioedema is a common disease whose etiology and pathogenesis is not always determined by allergic factors and mechanisms. Presented our case shows that any patient with angioedema should be considered and treated individually according to the specifics regarding the etiology, pathogenesis and clinical picture. Among the many unlockable manifestation of angioedema reasons should be given to the factors of the working environment.

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Occupational asthma caused by Krill allergy

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Background: IgE- mediated allergy to crustaceans is well known. Although the symptoms usually occur after ingestion, asthma and occupational asthma (OA) have been reported after exposure to steams or aerosols generated through the fish processing. We report the allergological study of two OA cases caused by krill powder inhalation.

Antartic Krill (Euphausiacea superba) represents small shrimp-like oceans crustaceans that are currently harvested for the production of omega-3 rich oils. Recently, cross-reactivity between krill tropomyosin and other tropomyosins has been referred.

Methods: Two patients (28 and 26 years) who worked at the same food-processing factory for several years, reported asthma symptoms related to the beginning of krill powder handling and were referred for study. Both of them had personal history of childhood dust mite allergy and had been successfully treated with specific immunoteraphy remained them nearly asymptomatics for asthma. Only patient one referred mild oral symptoms with shrimps.

We performed a respiratory study (spirometry and peak-flow registers) while working and after 4–6 weeks without krill exposure. Skin prick tests with common aeroallergens, sea foods and home-made krill powder extract (10% w/v) were carried out. We analyzed the protein composition of the krill extract by SDS-PAGE and the immune response of the patients was explored by means of:

1 specific IgE (sIgE) detected by immunoblotting and
2 basophil activation test (BAT).

Total IgE and sIgE were determined using CAP system (Thermo Fisher).

Results: Clinical features and respiratory study confirmed the diagnosis of OA. Skin prick tests with krill extract were positive in both patients as well as the BAT. The immunodetection with both sera confirmed IgE sensitization to several proteins of krill, one of them with a molecular weight (37 kDa) similar to tropomyosin. Skin prick test and sIgE showed sensitization to house dust mites, anisakis and shrimp (sIgE: 2.49 Ku/l). Serum sIgE against shrimp tropomyosin was negative (0.15 Ku/l).

Conclusion: This is, to our knowledge, the first report of OA caused by inhalation of krill powder. The immunological study confirmed IgE sensitization to several krill proteins, one of them with a molecular weight similar to tropomyosin molecular weight, the major allergen in crustaceans and probably the cross-reacting allergen in our patients (with previous house dust mite allergy).

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Occupational contact urticaria to cow's milk in the absence of cow's milk allergy in a cheesemaker

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Background: Cow's milk allergy (CMA) is the most frequent food allergy in infancy. Most cases of CMA in adults have persisted from childhood. In the literature, contact urticaria to cow's milk is mostly associated with CMA. Here, we describe a case of isolated contact urticaria to cow's milk.

Method: Skin prick tests (SPTs) were performed with fresh cow's milk, whey, butter and cream. Specific IgE (sIgE) assays were performed using the ImmunoCAP system (Thermofisher Scientific).

Results: A 35-year-old patient with a history of atopy had worked as a cheesemaker (using cow's milk) for 5 years. He first developed immediate erythema on the skin following contact with milk or the cheese-derived products that he handled at work. Thereafter, he developed severe urticaria on the arms and neck following direct or indirect contact with dairy products at work. Most recently, he had developed eczema on the back of the forearms at the end of a working week. These skin disorders always resolved during vacations. SPTs with fresh cow's milk, whey, butter and cream were all positive. SIgE assays were positive for c cow's milk (56.70 kUA/l) and its components alphalactalbumin (1.35 kUA/l), betalactoglobulin (36.40 kUA/l) and casein (23.40 kUA/l). The patient reported that his consumption of dairy products never triggered the symptoms of food allergy. This was confirmed by a negative oral challenge test with 298 ml of fresh cow's milk. Although the patient never experienced life-threatening reactions at work, it was subsequently decided to make him quit his job.

Conclusion: To the best of our knowledge, this is the first ever report of occupational contact urticaria to cow's milk in the absence of CMA and including component-resolved exploration. The present case demonstrates that food allergy and sIgE-positive skin allergy operate through different pathways.

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Occupational asthma due to ferrimanitol ovalbumin mediated by IgE

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Background: Ferrimannitol ovalbumin also known as profer (molecular weight 200KD) is an iron supplement used for the treatment of ferropenic anemia and other iron deficiencies. It is the result of trivalent iron mannitol coupled with ovalbumin (OA).

We present a 34 year old male employed by a pharmaceutical company who works providing technical support in several departments for 6 years. For over 5 years, he noticed symptoms of rhinitis immediately after being exposed to ferrimanitol ovalbumin (KILOR®). During the last year of symptoms, he also complaint of eczema on hands when handling this product.

Method: Skin prick tests with common aeroallergens, egg and fractions (OA, ovomucoid, yolk, white, lysozyme) and a prick-prick test with KILOR® were performed.

Respiratory workout included baseline spirometry, exhaled fraction of nitric oxide (FeNO) and methacholine test. While working, a specific inhalation challenge test (SIC) with ferrimanitol ovalbumin (KILOR®) tipped repeatedly was also

performed in a dynamic 7 m^3 challenge chamber with an accumulated time of 3 min. During and after SIC, respiratory symptoms and FEV1 were monitored every 10 min during the first hour and later hourly up to bed time. Previously informed consent was obtained. An IgE western blot analysis with KILOR® was performed.

Results: Skin prick tests were positive to cypress, grasses and olive pollen and ferrimanitol ovalbumin KILOR®. Negative with all egg components.

At baseline, spirometry was normal but with a bronchodilator response in FEV1 of +15% and +700 ml, FeNO of 105 ppb and a PC20 methacholine of 0.31 mg/ml. SIC with KILOR® elicited an immediate asthmatic response (30% fall of FEV1) at 3 min at mean concentration of 0.123 mg/m^3. No late asthmatic response was obtained. PC20 methacholine 24 h after SIC was of 0.125 mg/ml and FeNO of 145 ppb. In the IgE western blot analysis, a unique binding band molecular weight of approximate 200KD was identified. A control serum gave no binding bands.

Conclusion: We are presenting the first case of a patient with occupational allergic asthma due to the ferrimannitol ovalbumin mediated by IgE and demonstrated by SIC.

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Occupational asthma due to paprika powder

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Background: A 49-year old ex-smoker (25 pack years) was referred to our clinic for specific bronchial challenge (SBC) testing with paprika powder. He had been working in a potato chips factory since 15 years (the first year as a salter, then 3 years as a seasoning operator and then 10 years as a dough maker). 8 years ago he developed rhinitis, dry cough, wheezing and dyspnea, when working close to the seasoning hopper (the machine that sprays spices on the chips). His symptoms improved during weekends and holidays and worsened when paprika powder was used. After being transferred to the packaging department 10 months ago his symptoms gradually disappeared, as he was no longer directly exposed to spices. He had no history of allergies or other respiratory disease.

Specific bronchial challenge (SBC): A 3-day in-hospital work-up was performed. Inhaled corticosteroids and long-acting beta-agonist were stopped 48 h prior to the test. Baseline lung function was normal.

On day 1 peak expiratory flow (PEF) within-day variability did not exceed 3.1% and the lactose powder 'sham' bronchial challenge test did not show a drop in FEV_1 after 35 min cumulative exposure time. Delayed bronchoconstriction did not occur and the histamine bronchial challenge test revealed no aspecific bronchial hyperresponsiveness (BHR): $PC_{20}FEV_1 > 8$ mg/ml.

On day 2 SBC with paprika powder revealed a 20% drop in FEV_1 after 16 min cumulative exposure time. PEF variability that day increased to 45.3% and at the end of the day the histamine $PC_{20}FEV_1$ had dropped to 1.6 mg/ml, demonstrating non-specific BHR.

On day 3 PEF variability returned to baseline values and the histamine PC_{20} almost normalized (8 mg/ml). In this case we also measured FE_{NO} at baseline, as well as 1, 4 and 24 h after the SBC: FE_{NO} = 43, 22, 32 and 90 ppb respectively.

Conclusion: in this case report the SBC test confirmed occupational asthma due to paprika powder. The novelty of this case is the measurement of FE_{NO}, demonstrating the induction of airway inflammation after a single re-exposure with paprika powder.

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Rhinoconjunctivitis and occupational asthma due to poultry feed

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Background: Poultry farmers are exposed to various allergens being frequent the occurrence of respiratory allergic processes of the immediate type, IgE dependent as well as hypersensitivity pneumonitis (allergic alveolitis). Following we are presenting a case of occupational allergy due to exposure to poultry feed.

Method: A 28 year old man with no relevant medical history, since childhood has presented constant rhinorrhea, nasal obstruction, and watery itching eyes. In addition, occassional episodes of dyspnea (one to three per month), wheezing and coughing. He has been examined by a specialist and diagnosed with allergic rhinoconjunctivitis and asthma due to sensitisation to common dust mites parasites. For the past 3 years, he has been working as a canary breeder and showing exacerbation of his symptoms when feeding the animals.

Prick tests with common aeroallergens, storage mites (*Acarus siro, Tyrophagus and Lepidoglyphus*), canary feathers and feces were performed. Besides skin tests were performed with food for canaries that the patient uses such as: negrillo (*Guizotia abyssinica*), Perilla (*ocymoides linn*), hemp (*Cannabis sativa*), flax (*Linum usitatissium*), canary seed (*Phalaris canariensis*) and red radish (*Raphanus sativus*). Levels of specific IgE to these allergens were quantified. Precipitins detection was also performed to canary feces.

Finally imaging scans (X-ray CT and CAT scan) were performed.

Results: Prick tests were positive for *D. pteronyssinus*, *D. farinae* and negrillo, hemp and perilla seeds. Specific IgE to *Dermatophagoides pteronyssinus* 1.41 kU/l, Dermatophagoides farinae 0.76 kU/l, canary feathers 0.01 kU/l. Precipitins to canary feces were negative.

X-ray CT and CAT scan within normality.

Conclusion: Sensitisation, IgE mediated by mite Dermatophagoides and elm, hemp and perilla seeds, together with data from medical records confirmed the diagnosis of rhinoconjunctivitis and asthma due to sensitisation to Dermatophagoides mites and rhinoconjunctivitis and occupational asthma due to sensitisation to elm seeds, perilla and hemp seed used as food for poultry.

Clinical characteristics in our case, the normality of the CAT scan, and the absence of precipitins rule out the existence of a hypersensitivity pneumonitis (allergic alveolitis).

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Asthma associated with occupational exposure to mushrooms

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Case report: The authors report the case of a 32-year-old woman from Jaén (Andaluzia, Spain) residing in Portugal since 2006 when she started working in a greenhouse and packing warehouse of mushrooms. The patient was diagnosed with grass-pollen allergic rhinitis in the childhood and underwent specific immunotherapy. She was referred to an Allergology Department for worsening of nasal symptoms and recurrent episodes of dyspnoea and wheezing since 2012, particularly aggravated in the workplace. Initial spirometry assessment revealed normal lung-function parameters on baseline but a positive bronchodilation test. The skin prick tests (SPT) with common inhalant allergens were positive for house dust mites and grass pollens (*C. herbarium* and *A.*

fumigatus were tested and negative); SPT with Alt a 1 extract was also positive (4 × 4 mm). Subsequently, we performed skin prick-prick tests with white mushroom (*Agaricus bisporus*) using a sample collected from the patients' workplace, with a positive result. Serum specific IgE for *C. herbarium*, *A. Fumigatus* and *P. notatum* was below the significance level but high for *Alternaria alternata* (3.69 kU/l). These results were confirmed by ImmunoCAP ISAC® with a positive identification for Alt a 1 (17.9 ISU). The diagnostic hypothesis was of an occupational asthma and serial FEV_1 and PEF monitoring at work (mean FEV_1 = 1.47 l; mean PEF = 201 l/min) and away from work (mean FEV_1 = 3.39 l; mean PEF = 517 l/min) confirmed the diagnosis. Additional SPT were then performed with allergen extracts (Diater®) of 6 mushroom species sampled from the patients' workplace, confirming sensitization to *Agaricus bisporus* (10 mg/ml) e *Agaricus brunnescens*

(10 mg/ml). *Immunoblotting* identified only one high intensity band corresponding to an IgE-binding protein with a molecular weight of 12 KDa from the specie *Lyophyllum shimeji,* and other lower intensity bands correspondent to proteins of the specie *Flammulina velutipes*. These proteins have not been previously documented as fungal allergens.

Discussion: The diagnostic workup in the reported case confirmed the hypothesis of an asthma associated with professional exposure to a specific biologic agent. There are few reports in the literature of occupational sensitization to mushrooms, and the sensitizing proteins identified in this case has not been previously reported as allergenic.

Poster Session TPS 25

Primary immunodeficiency

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Expression pattern of bradykinin receptors on lymphocytes and monocytes in hereditary angioedema type I

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Background: Bradykinin - mediated mechanism of hereditary angioedema is well-established. Nonetheless, little is known about the role of bradykinin receptors type I (B1) and II (B2) on the functioning of the immune cells in the development of hereditary angioedema type I. The goal of our study is finding a distribution pattern of the both bradykinin receptors on monocytes and lymphocytes CD4+ and CD8+ in attack of angioedema and remission of the disease.
Method: Peripheral blood mononuclear cells (PBMC) collected from 5 adult patients in the age 24–70 with hereditary angioedema type I in attack and remission of the disease were isolated. Subsequently, PBMC were stained to distinguish: lymphocytes (anti- CD3, anti - CD4, anti-CD8), monocytes (anti -CD14, anti-CD16, anti HLA-DR) and their expression of B1 (anti-B1) and B2 (anti-B2) receptors by flow cytometry was performed.
Results: In our pre-eliminary data we found expression of B2 eceptor mainly on monocytes and lymphocytes CD4+ and CD8+ during attack of angioedema. Expression of B1 receptor was residual on monocytes and both types of lymphocytes. The expression of B2 receptor in attack was high in monocytes and highly variable in lymphocytes CD4+ and CD8+.
Conclusion: As it was expected, expression of B1 receptor was low and expression of B2 was high in attack of angioedema. In patients with hereditary angioedema type I during remission the expression of B2 was observed on monocytes and lymphocytes CD4+ and CD8+. During an attack of angioedema the expression of B2 increased high mainly on monocytes and was highly variable increased in lymphocytes CD4+ and CD8+. The expression of B1 in studied patients was residual on monocytes and both types of lymphocytes in attack of angioedema as well as remission.

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The features of the intestine microbiota in patients with a-and hypogammaglobulinemia

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Background: The purpose - study of the immune status and intestine microbiota condition at the patients with autoimmune and infectious phenotypes of the primary immunodeficiency by their humoral type.
Method: The study included patients with CVID (5 patients) and XLA (6 patients), 4 - with autoimmune phenotype (AP), 7 - with an infectious phenotype (IP). Phenotypic analysis was performed on lymphocytes cytometry 'FC' 500. The intestine microbiota condition was estimated by the excrement bacteriological inoculation (EBI), the respiratory hydrogen test (RHT) with lactulose (GastrcH - Gastrolyzer, Bedfont, UK), by the maintenance definition of the short chain fat acids and anaerobic index (AI) in excrements using gas-liquid chromatography (GLC).
Results: It was revealed more significant increase of opportunistic pathogenic water producing microflorae at the patients with AP: 143.8 + 53.4 ppt, at the patients with IP - 131.8 + 46.5 ppt. During bacteriological research more significant decrease in quantity of bifido - and lacto bacterium was established at the patients with IP on the average group. During GLC in the group with autoimmune variant AI was lowered in the area of distinctly negative values (at patients with IP it was lowered to the direction of weakly negative ones). Significant distinctions were noted in subpopulation structure of T-lymphocytes, and at the AP case the increase of cytotoxic cells number was not accompanied by the reduction CD+4-lymphocytes: IRI-1.2 $\pm$ 0.1, unlike the patients with infectious manifestations (IRI-0.6 $\pm$ 0.1). The differences in functional cell potential of congenital immunity were shown by TLR4 expression strengthening at the patients with AP (63 $\pm$ 8%) in comparison with the norm (20 $\pm$ 4%) and the patients with IP (21 $\pm$ 3%).
Conclusion: The noted distinctive features in patients with AP and IP phenotypes can become the basis for the forecast of a course and the differentiated introduction of additional therapeutic means of treatment.

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Polychromatic flow cytometry in immunophenotyping of primary immunodeficiencies: hidden phenotypes revealed

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Background: Research and clinical laboratories addressing investigation and diagnostics of primary immunodeficiencies (PID) use flow cytometry for phenotypic and functional measurements of the immune cells. Modern flow cytometers with multiple lasers and fluorescence detectors as well as the development of novel flurochromes conjugated to specific antibodies are used in various combinations. Simultaneous measurement of numerous parameters gives an insight into many phenotypically and functionally distinct subsets of leukocytes, any of which might be clinically relevant. The aim of this study was to establish a reliable and robust polychromatic flow cytometry assay for the daily routine analysis of the phenotype of human peripheral blood lymphocyte subsets in order to improve diagnostics and monitoring of PID in children.
Method: Peripheral whole blood samples were stained with antibodies for the cell surface markers: CD45, CD3, CD4, CD8, CD19, CD56 and CD16 as well as for the two activation markers: HLA-DR and CD27. Samples were lysed and fixed with 1× FACSLysing™ solution (BD Biosciences, USA). Upon centrifugation, leukocyte pellets were resuspended in 1% paraformaldehyde/PBS. Acquisition of the samples was performed using the Navios™ flow cytometer (Beckman Coulter, USA). The data were analyzed using FlowLogic™

software package (Inivai Technologies, Australia).
Results: Peripheral blood from more than 200 patients aged from 2 to 18 years was analysed in the same manner. A dual-panel platform involving two six color antibody combinations and extensive analysis of the FCS data files resulted in the finding of an increased number of cells with several interesting immunophenotypes: $CD19^{low+}CD27^{high+}$ B cells, $CD3^{+}CD8^{+}$ $CD16^{high+}$T cells, $CD3^{-}CD16^{-}CD56^{+}$ $CD27^{+}$ cells and $CD3^{-}CD4^{+}$ lymphocytes.
Conclusion: Polychromatic flow cytometry implementing an expanded immune monitoring panel in routine immunophenotyping enabled the detection of mononuclear subsets that could not be resolved in protocols where typical four-color immunophenotyping assays were used. In the studies of immune disorders, such as PID, a polychromatic approach using even six colors may allow a deeper insight and understanding of the complex interplay between immune cells and improve diagnostic procedures.

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Frequency of low serum immunoglobulin levels in children with allergic diseases

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Background: Antibody deficiencies are the most common type of primary immunodeficiency diseases. In this study we aimed to determine the frequency of low immunoglobulin levels in children with allergic diseases.
Method: The study was conducted at the outpatient Department of Pediatric Allergy and Immunology at Kirikkale University Faculty of Medicine between September 2014 and September 2015. Patients followed with a diagnosis of asthma, wheezy infant, allergic rhinitis, atopic dermatitis, food allergies and chronic urticaria were included study. Medical records and laboratory investigations of the patients were evaluated retrospectively.
Results: Of the 1245 children enrolled in this study, 149 (11.9%) were had a decrease at least one immunoglobulin levels. Of these, 92 (61.7%) were male, with a mean age of 6.6 ± 4.7 years. The allergic diseases of these patients were as follows: asthma (n = 69, 46.3%), wheezy child (n = 25, 16.7%), allergic rhinitis (n = 92, 61.7%), atopic dermatitis (n = 17, 11.4%), food allergy (n = 4, 2.7%) and chronic urticaria (n = 4, 2.7%). Decreased level of IgG, IgA, and IgM was detected in 101 (67.8%), 60 (40.3%), 42 (28.2%) out of 149 patients, respectively. One hundred and four (69.8%) patients had one subtype of immunoglobulin decrease, 35 (23.5%) had two subtype of immunoglobulin decrease and 10 (6.7%) had all subtype of immunoglobulin decrease.
Conclusion: In our study we determined high frequency antibody deficiency children with allergic diseases. Immunologically evaluation of these patients provides early diagnosis and it is important in order to prevent possible complications.

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Isoprinosine in long-term treatment in patients with PID

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Background: In 60% of patients with primary immunodeficiency (PID) are observed prolonged recurrent infections in the lower respiratory tract, non-infectious changes of the airways, chronic lung disease (with emphysematous and fibrotic areas), benign or malignant tumors. Chronic changes and recurrent respiratory tract infections are the most common cause of morbidity and mortality.
Material: We present 3 cases of PID patients treated with isoprinosine for more than a year. The first two cases were two brothers, 8 and 7 years old who almost every month suffered from infections (pneumonia, scarlet fever, gastroenteritis, tonsillitis, adenoidit). They had established general T-lymphocytes in the normal range with impaired immune biological balance at the expense of T heper- inducer cells with reduced subpopulation of T-cytotoxic-suppressors. The third case is a girl of 11 years with corrected in neonatal period transposition of the great vessels defect and coarctation of the aorta. On the occasion of frequent viral infections in 2014 PID was established - lymphopenia with reduced T-lymphocytes at the expense of supressor-cytotoxic subpopulation and reduced level of IgG1.
Results: We initiated treatment with isoprinosine 0.5 g/kg by regular scheme with excellent effect. For period of 12 months the three children have not suffered from any infectious diseases.
Conclusion: Isoprinosine is safe and reliable medication in some cases with PID.

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Epidermodysplasia verruciformis in a patient with common variable immunodeficiency (CVID)

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Background: Epidermodysplasia verruciformis (EV) is a rare skin disorder, caused by papilloma virus infection (in particular, subtype 5 and 8-HPV), a virus normally found in 80% of population as asymptomatic. Epidermodysplasia verruciformis can be recessive autosomal or X-linked in 20% of cases, caused by inherited T-cell-immunodeficiency, in the remaining cases is secondary to systemic lupus erythematous (SLE), HIV infection, transplantation. EV is responsible for an increased risk in early age of non-melanocytic skin cancer (NMSC).
Case report: We report the case of a 30-year-old man suffering from common variable immunodeficiency (CVID), treated with intravenous immunoglobulin (IVIg) at a dose of 20 g every 4 weeks, who came to our attention for the presence of generalized circular (diameter 3–8 mm), erythematous, papular and desquamative, not itchy, skin lesions. These ones appeared in adolescence with progressive and continuous worsening. Lesion biopsy confirmed the diagnosis of epidermodysplasia verruciformis. The molecular analysis and polymerase chain reaction (PCR) revealed the presence of the HPV 25 subtype in 98% of skin cells. Fortunately, this is a subtype not responsible for an increased risk of skin cancer. The treatment was based on Ig replacement (20 g each 3 weeks with last serum trough IgG levels = 744 mg/dl), oral supplementation with retinoids and avoiding risk factors, such as sun exposure.
Conclusion: In conclusion, although epidermodysplasia verruciformis is a rare disorder, physicians must always look for an underlying cause of immunosuppression, such as HIV or CVID.

Treatment of acute hereditary angioedema attacks during pregnancy

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Background: Hereditary angioedema (HAE) is a rare, autosomal dominant disorder characterized by recurrent attacks of subcutaneous or sub-mucosal oedema. Symptoms are extremely variable in frequency, localization and severity. The management of pregnant HAE patients is problematic, since there are only limited data on safety and efficacy of various therapeutic approaches.
Method: We present our clinical experience with repeated treatment of acute attacks of 3 HAE patients during pregnancy.
Results: Before the pregnancy all 3 patients were treated with tranexamic acid prophylaxis, which had to be discontinued resulting in increase of the attack frequency. During the pregnancies 55 attacks of HAE occurred. The most frequent were abdominal 42 (76.4%) followed by laryngeal 8 (14.5%), facial 7 (12.7%) and peripheral 7 (12.7%) oedema; 16.4% attacks were combined. 50 of attacks were treated with recombinant C1-INH, 6 with icatibant and 1 with plasma derived nanofiltered C1-INH. Treatment had to be repeated in 5 attacks (9.1%). Prophylactic plasma derivated C1-INH concentrate (500 IU) was administered before the delivery. All three deliveries (cesarean section and two spontaneous vaginal deliveries) were without complications. No congenital abnormalities were detected in the neonates. The newborns were healthy with birth weight 3370, 3690 and 2850 g respectively.
Conclusion: Our results show good efficacy of C1-INH or Icatibant treatment of HAE attacks in pregnancy. The therapy was effective in all attacks; no adverse effects were observed.

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Stiff-person syndrome and hypogammaglobulinaemia: an unusual combination

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Background: Stiff-person syndrome (SPS) is characterized by progressive rigidity and muscle spasms. SPS is supposed to be an autoimmune disorder as most patients have antibodies directed against glutamic acid decarboxylase (GAD65), the rate-limiting enzyme for the production of the inhibitory neurotransmitter γ-aminobutyric acid (GABA). Immunodeficiency has never been reported as a feature of SPS.
Method: We present a 73 year old female suspected SPS with a history of recurrent infections and hypogammaglobulinaemia. Flow cytometry of lymphocyte subpopulations and genetic analysis were performed.
Results: She is a 73 year old patient whom the diagnosis SPS was made at the age of 56 based on typical clinical features including muscle spasms and fasciculation, typical electromyography pattern and cardiac arrhythmias. Serum analysis revealed typically anti-GAD65 antibodies and a negative test for voltage-gated potassium channel and GABA-receptor antibodies. She also developed recurrent skin malignancies. She had a history of liver hamartomas and a congenital gastro-intestinal malrotation. Her recurrent infections started at the age of 56 with a systemic toxoplasmosis and recurrent respiratory infections. At the age of 66 the diagnosis of Common variable immunodeficiency was made. Rituximab was started later as a treatment for SPS. Laboratory investigations revealed undetectable B lymphocytes and plasma cells in both peripheral blood and bone marrow 4 years after rituximab therapy. T cell counts were 0.5×10^9/l ($0.7–2.1 \times 10^9$/l), CD8+ T cells were 0.3×10^9/l ($0.2–1.2 \times 10^9$/l). Naive, memory and effector CD8+ cells were 69%, 23%, 8% of CD8+ T cell subset respectively. CD4+ T cells were 0.2×10^9/l ($0.3–1.4 \times 10^9$/l). Naive, memory and effector CD4+ cells were 50, 38, 12% of CD4+ T cell subset respectively. CD16 + 56 + CD3- NK cells were 0.21×10^9/l ($0.1–0.5 \times 10^9$/l). Functional immunological analysis and exome sequencing are ongoing. Genetic analysis showed a 704 kb duplication in band 7q31.32, this duplication includes TAS2R16, SLC13A1 and exomes of CADPS2. The role of this duplication is unclear. Because of the combination hamartoma and hypogammaglobulinaemia PTEN was sequenced, however no variants were found. The PI3 kinase gene revealed no variants as well.
Conclusion: We describe for the first time a patient with Stiff person syndrome and immunodeficiency, combined with gastro-intestinal malrotation and hamartomas suggesting a yet non-detected gene variant.

1002
Hyper IGE syndrome - an undetected mutation?

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HIES is a rare primary immunodeficiency characterized by recurrent eczema, skin abscesses, lung infections, eosinophilia and high serum levels of IgE.

This is the story of an 8 year 10 month old girl, who presented to the Red Cross War Memorial Childrens Hospital, with a history of eczema since birth, recurrent superficial and deep seated infections, and multiple severe viral and bacterial pneumonias. Laboratory analysis displayed a persistent eosinophilia, elevated serum total IGE, sensitization to multiple aeroallergens, and evidence of food specific IGE mediated sensitizations, but no food allergy. Genetic studies for mutations and deletions in the STAT3, DOCK8 and Tyk2 gene for Hyper IGE syndrome were negative. Currently, she has interstitial lung disease with features of reversible lower airway obstruction, primary immunodeficiency, with abnormal immunoglobulin levels, low vaccine responses, and recurrent infections. She first presented with a severe lower respiratory tract infection, but has had a history of lower airway obstruction treated at primary facilities since the age of 7 months. She is currently on maximal bronchodilator and corticosetroid therapy, but still presents with frequent exacerbations. The patient is (HIV) exposed, but confirmed negative, with a normal birth history, normal family history and no history of consanguinity. Clinically, she is a well grown girl, is cushingoid, with coarse facial features, normal dentition, and no high arched palate or increased nasal width. Skin manifestations include well controlled eczema and persistent molluscum contagiosum. There are no significant skeletal or connective tissue affectation, and she has never suffered bone fractures. There is normal neurology. She has chronic hyperinflation and digital clubbing.
Discussion: 8 year old Miss LN with structural lung disease with reversible lower airway obstruction, immune dysfunction with significantly elevated serum total IGE, multiple aeroallergen sensitizations, and steroid dependence. She remains a frequent visitor to the emergency unit, often requiring ventilatory support, and has displayed worsening lung function despite optimal therapy. Currently, she is on monthly intravenous immunoglobulin therapy and receiving omalizumab injections fortnightly.

The literature on Hyper IGE syndrome recognizes two major subtypes, however

our patient demonstrates textbook clinical presentation. Does she have an undescribed subtype, and how do we diagnose it?

1003
Facilitated subcutaneous immunoglobulin in common variable immunodeficiency associated hemolitic anemia

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Background: Common variable immunodeficiency (CVID) is a highly heterogeneous immunodeficiency with varying complexity. Besides infections, CVID is associated with a variety of non-infectious complications including autoimmune hemolytic anemia (AIHA), in 7% of cases. Facilitated subcutaneous immunoglobulin (fSCIg), a new therapeutic option in primary immunodeficiencies, constitutes a potential effective treatment also in autoimmune disorders such as AIHA.

Case report: A 51-year-old woman came to our attention for weakness and pain of the legs arising from few weeks. Past medical history was free of major diseases. Clinical assessment revealed jaundice, spleen enlargement (16 cm) and mild fever. Lab tests showed a macrocytic anemia(Hb 7.1 g/dl, MCV 101 fl) with normal count of platelets and white cells, high levels of lactate dehydrogenase (360 U/l), low levels of aptoglobin (8 mg/dl), positive antinuclear antibodies (ANA, 1:160, nucleolar), negative antibodies to extractable nuclear antigen (anti-ENA) and a positive direct Coombs test. The diagnosis of AIHA was made. To rule out lymphoproliferative disorders, a bone marrow biopsy with cytogenetic and a thorax-abdomen CT scan showed no relevant clinical findings. The patient started therapy with high dose prednisone (120 mg/day with tapering) with partial improvement of Hb levels (Hb 10.5), and reduction, without normalization, of markers of hemolysis. After 2 months the patient developed a symptomatic hypogammaglobulinemia for which she came to our attention. Due to low serum IgG and IgA levels (IgG 376 IgA 7 IgM 67 8.7%) and low response to tetanus vaccination, diagnosis of CVID was made. We decided to start immunoglobulin replacement treatment. We used 10% subcutaneous facilitated immunoglobulin (fSCIg) with progressive ramp up, up to a dosage of 20 g every 15 day. After 1 month we obtained an improvement of serum IgG levels. Moreover, the patient reached normal Hb levels with normalization of laboratory parameters and she able to reduce prednisone. After 3 month of fSCIg therapy, she still maintained stable normal levels of Hb without signs of hemolysis with a low dose prednisone (2.5 mg/day).

Conclusion: Hematologic autoimmune diseases, such as AIHA, are the most frequent autoimmune disorder associated with CVID. fSCIg constitute an effective and safe alternative therapeutic option in patients with CVID and associated autoimmune disorders.

1004
Successfull rescue with Privigen® of three patients with common variable immunodeficiency and previous reactions to intravenous immunoglobulin

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Background: Common variable immunodeficiency (CVID) is the most common symptomatic primary antibody immunodeficiency in the adulthood. Treatment is based on intravenous (IVIg) or subcutaneous (SCIg) immunoglobulin administration. We here report three patients with CVID with adverse reaction to IVIg administration, successfully rescued with Privigen® (human intravenous immunoglobulin 10% liquid preparation; CSL Behring).

Methods and Results: The first case was a 42-years-old woman with a history of recurrent upper respiratory infections, autoimmune thyroid disease and a previous miscarriage. Despite the use of premedication, she had a systemic reaction to IVIg. IVIg treatment was withdrawn for 3 months, when she got pregnant. Thus we decided to adopt Privigen ® at the dose of 10 g/weekly during pregnancy and after every 3 weeks. Treatment was well tolerated and she gave birth a normal healthy male.

The second patient was a 65-years-old female with a diagnostic delay of CVID of about 20 years, despite recurrent pneumonia with frequent hospitalizations. Two years after the beginning of treatment, she had a systemic reaction to IVIg. She refused the switch to subcutaneous administration, so we decided to use Privigen ® (10 g every 3 weeks). The drug was well tolerated and effective, with a significant reduction of infections.

The third case was a 69-years-old female with an history of recurrent fever treated with antibiotic therapy, splenomegaly, mediastinal lymphadenopathy and lymphoproliferation. During the first infusion of IVIg, she had a systemic reaction. Thus, she started Privigen ® (10 g every 3 weeks) with benefit. No adverse reactions were reported.

In all patients protective levels of IgG were achieved.

Conclusions: Our cases demonstrate that treatment with IVIg should be tailored to patients characteristics. Privigen® is safe, well tolerated and effective, and can be used to rescue patients with adverse reactions to other IVIg products.

Poster Session TPS 26

Immunotherapy

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Effects of birch pollen AIT on antibody profiles of Bet v 1 and cross-reactive food allergens

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Background: 100 million people worldwide suffer from adverse reactions to the major birch pollen allergen Bet v 1. 70% of them develop birch pollen-related food allergies. Allergen immunotherapy (AIT) is currently the only effective strategy to cure allergic diseases. Thereby, the induction of blocking antibodies is pivotal for the progress of therapy. Whether pollen-specific immunotherapy can be used to treat associated food allergies is controversially discussed. Therefore, we aimed to fully characterize antibody profiles during birch pollen AIT and investigated whether therapy-induced blocking antibodies can inhibit IgE binding to Bet v 1-related food allergens.
Method: Five birch pollen-allergic patients were treated with SCIT using conventional birch pollen extracts. Serum samples were taken before therapy, after reaching the maintenance dose, and after 1 year. Bet v 1 and the related food allergens from hazelnut Cor a 1 and apple Mal d 1 were produced as recombinants, purified and characterized physico-chemically. The humoral immune response towards these allergens was monitored by nasal provocation tests, ELISA, ImmunoCAP, immunoblots, facilitated antigen binding (FAB) and rat basophil leukemia cell degranulation (RBL) assays.
Results: All 5 patients showed reduced nasal provocation scores during AIT. ELISA and ImmunoCAP data revealed a decline of allergen-specific IgE levels after 1 year. This was accompanied by the induction of IgG, especially IgG4. Interestingly, high levels of IgA were detected, which were boosted after 6 weeks; however, declined after 52 weeks. Antibody levels were generally not comparable between patients and did not match with provocation scores. Bet v 1-specific blocking antibodies were detected in all donors by FAB assays. In 4 out of 5 patients, birch pollen AIT induced blocking antibodies to Bet v 1 related food allergens. RBL data indicated a link between mediator release and IgE levels.
Conclusion: Neither ELISA nor RBL results revealed a correlation with clinical data, which could be found for FAB assays. Therefore, we speculate that not only the quantity but rather the quality of the IgG response is decisive for successful AIT. This hypothesis will be further tested by NMR-based antibody epitope mapping using antibodies isolated from patient sera.

This research was supported by the Austrian Science Fund (FWF) project P26125 and the University of Salzburg's priority program 'Allergy-Cancer-BioNano Research Center'.

1006
Clinical evolution of patient treated with a *precoseasonal* sublingual immunotherapy with a mix extract of *grass pollen and Olea europaea*

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Background: Allergic rhinitis is a major public health concern in many countries, particularly in the case of developed countries, where up to 30% of adults are affected and up to 40% of children. Sublingual route is an effective alternative to subcutaneous and enables improved acceptance of immunotherapy by the patient.

The analytical objective of this systematic data collection was to determine the clinical course of patients allergic with coexisting allergy to grass and *O. europaea* pollen, treated with sublingual immunotherapy (SLIT) following standard clinical practice.
Method: The information recorded for 85 patients (adult and paediatric) with grass and olive pollen allergy who received IT in a precoseasonal regimen for at least one pollen season was analysed retrospectively.

All patients (100%) had been diagnosed with allergic rhinitis/rhinoconjunctivitis and 75.3% also had associated bronchial asthma, in all cases controlled. All received SLIT with an aqueous allergen mix extract of grass and *O. europaea* between 2003 and 2013.

To assess the efficacy of treatment the following aspects were analysed:

1 Evolution of drug treatment over the previous year
2 Evolution of rhinitis/rhinoconjunctivitis during the last year of treatment
3 Evolution of asthma, during the last year of treatment

Safety of treatment was assessed by recording local and systemic adverse reactions (EAACI 2006).
Results: This percentage (82.4%) was statistically significant ($P < 0.001$) compared to the percentage of patients that remained the same or required further treatment (16.5% and 1.2% respectively). Regarding the evolution of the symptoms of rhinitis/rhinoconjunctivitis, 15.3% were asymptomatic and 71.8% of patients showed improvement over the previous year. For asthma, 46.8% were asymptomatic and 45.2% were better than the previous year. About a total of 27.300 doses were administered and no adverse reactions were registered.
Conclusion: Treatment with SLIT in patients allergic to both grass and *O. europaea* pollen was safe and effective, improving the situation of patients with the disease in relation to the three parameters analysed.

1007
Treatment benefit of sublingual immunotherapy with the 5-grass pollen tablet - an assessment from the patient's point of view

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Background: The evaluation of treatment benefit from the patient's point of view is becoming increasingly important. A validated instrument for the assessment of patient-relevant benefit in the treatment of allergic rhinitis (AR) is the Patient Benefit Index (PBI-AR). In our study we

investigated the treatment benefit of a sublingual allergen immunotherapy (AIT) in patients with grass pollen-induced AR using the PBI-AR.

Methods: The open, prospective, multicenter, non-interventional observational study with the 5-grass pollen tablet (Stallergenes, France) was conducted in 145 study centers in Germany. Patients were observed during their 1st treatment year. Besides treatment needs and treatment benefit, demographic data, medical history and clinical parameters, e.g. impairment due to AR symptoms, were documented. The Patient Benefit Index was computed based on the assessment of treatment needs and benefits (0 = not at all important/did not help at all to 4 = very important/helped a lot) (global PBI and subscales for different dimensions of benefit).

Results: Data of 600 patients were analyzed (56.8% f; mean age 36.6 ± 12.6 years); for 417 of these patients a global PBI score could be computed. Patients achieved a mean PBI of 2.4 ± 1.0 (0 = no benefit to 4 = maximum benefit). Of the 4 PBI-AR dimensions (reduction of treatment-related burden, clinical symptoms, performance/activities and psychological burden) the first showed the highest benefit for the patients (2.5 ± 1.1). In total, 89.2% of the patients achieved relevant benefit from treatment with the 5-grass pollen tablet (PBI≥1).

The patients' impairment by AR symptoms decreased during the treatment. The global PBI significantly correlated with a change in the impairment by AR symptoms ($r = -0.3$).

Conclusion: In the first year of treatment, the 5-grass pollen tablet already attained patient-relevant benefit, especially due to the easiness of treatment and the reduction of symptoms.

1008

SQ® HDM SLIT-tablets in addition to pharmacotherapy are cost-effective compared to pharmacotherapy only in treating patients with allergic rhinitis

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Background: Patients with persistent moderate to severe allergic rhinitis despite use of allergy pharmacotherapy constitute a significant cost to society while having reduced quality of life. Allergy immunotherapy tablets for sublingual administration (SLIT-tablets) have been developed as an effective, well tolerated and convenient treatment modality, suitable for home administration. The purpose of this analysis was to model cost-effectiveness of the SQ® house dust mite (HDM) SLIT-tablet in a population having persistent moderate to severe allergic rhinitis despite use of allergy pharmacotherapy.

Method: A cost-utility analysis was performed using a decision tree structure comparing the SQ® HDM SLIT-tablet in addition to pharmacotherapy vs pharmacotherapy only. Health care utilisation and quality of life data measured by EQ-5D were taken from a multicentre, double-blind, randomised, placebo-controlled clinical trial with the SQ® HDM SLIT-tablet (Demoly et al 2015). The trial showed statistically significant improvement for quality of life, the primary endpoint (total combined rhinitis score) and all key secondary endpoints in allergic rhinitis. Where data from the clinical trial was limited, conservative assumptions were defined by experts. As basis for the analysis, German preference weights and costs were applied and a 9-year time horizon adopted. Uncertainty around efficacy assumptions was explored by sensitivity analyses.

Results: The SQ® HDM SLIT-tablet in addition to pharmacotherapy was cost-effective compared with allergy pharmacotherapy only in treatment of allergic rhinitis (ICER < 15 000 €/QALY). The results of the sensitivity analysis indicate that the results are sensitive to changes in input parameter values, highlighting the importance of establishing long term outcomes with the SQ® HDM SLIT-tablet.

Conclusion: The SQ® HDM SLIT-tablet in addition to pharmacotherapy proved to be cost-effective in the treatment of allergic rhinitis, compared to pharmacotherapy only in the applied model. Conservative assumptions regarding efficacy assumptions were adopted, suggesting the benefits of the SQ® HDM SLIT-tablet may have been underestimated.

1009

Phase III trial with allergen specific sublingual immunotherapy in birch allergic patients: significant improvements in quality of life scores and significant changes in immunoglobulins with acceptable safety

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Background: A clinical development program was started for a sublingual immunotherapy (SLIT) product to treat birch pollen allergy, to obtain full marketing authorization. This abstract describes the pivotal short-term efficacy phase III study results of this birch SLIT product in patients with birch pollen induced allergic rhinitis/rhinoconjunctivitis (AR).

Method: A randomized, double-blind, placebo-controlled, parallel-group study was conducted in 406 adult patients with moderate to severe birch pollen induced AR with or without mild to moderate persistent asthma (ClinicalTrials.gov NCT02231307). Treatment was started 3–6 months pre-season (pre-specified definitions: birch pollen season: 3 out of 5 consecutive days birch pollen counts with ≥80 grains/m^3 per 24 h; birch peak pollen season: all days with birch pollen counts ≥500 grains/m^3 per 24 h). The EAACI recommended combined symptom and medication score during the pollen season was used as primary endpoint (data not shown). Quality of Life has been assessed using the disease specific Rhinoconjunctivitis Quality of Life Questionnaire [RQLQ (S)], the general quality of life questionnaire (EQ-5D) and the Asthma Control Questionnaire (ACQ). The specific immune response was determined by the measurement of birch pollen and Bet v1 specific immunoglobulin levels (IgE, IgG and IgG_4). For safety, AEs were monitored throughout the study.

Results: RQLQ(S) ($P < 0.0001$) and EQ-5D ($P = 0.004$) showed statistically significant improvement in the active treatment compared to placebo. The ACQ (restricted to the 27% patients with asthma) showed a similar trend of improvement after active treatment without reaching statistical significance. The Birch pollen and Bet v 1 specific serum IgG and IgG_4 levels were significantly increased after 12 weeks and at the end of trial (EOT) in active treated patients, while the IgE levels were

increased after 12 weeks and similar to placebo at EOT. Although active treatment resulted in more local and systemic adverse reactions compared to placebo, the occurring adverse reactions were mainly of mild intensity and well controlled.
Conclusion: After at least 3 months of SLIT for the treatment of birch pollen allergy, this pivotal phase III study showed significant improvement in quality of life and significant changes in specific immunoglobulins in combination with an acceptable safety profile. The results of these secondary endpoints confirm the efficacy and safety of this birch SLIT product.

1010
Detection of panallergens in commercial pollen extracts for allergen immunotherapy

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Background: Up to 50% of pollen-allergic patients are sensitized to at least one pollen panallergen, profilin and polcalcin. These allergens may have clinical relevance but the content in profilin and polcalcin of commercial extracts for allergen immunotherapy (AIT) is unknown. We detected both panallergens in commercial pollen extracts for AIT of various sources.
Method: The IgE reactivity to Phl p 7 and Bet v 2 of sera from 18 adults hypersensitive to profilin and/or polcalcin was investigated by ELISA before and after absorption with grass, birch, ragweed, pellitory, and olive pollen extracts for AIT from different producers. Immunoblot inhibition experiments were carried out as well using the same allergens.
Results: Birch, Grass, Ragweed, and Olive pollen extracts for AIT contained large amounts of profilin inducing a 80–90% inhibition in most cases; Parietaria AIT extract appeared to contain little profilin. On immunoblot, both grass and birch pollen extracts for sublingual AIT were able to absorb completely IgE specific for rBet v 2. Interestingly, only grass pollen extracts induced a significant inhibition of IgE binding to rPhl p 7 both on ELISA and immunoblot. A grass pollen allergoid lost most of the inhibitory potency suggesting a much weakened affinity for specific IgE.
Conclusion: With the exception of Parietaria, commercial extracts for AIT of most pollens are rich in profilin, and hence potentially able to desensitize to this allergen; in contrast, only grass pollen extracts seem rich in polcalcin. These are the pollens to go for in case of severe symptoms induced by pollen panallergens.

1011
Acute and subacute systemic toxicity studies *in vivo* of mannan-conjugated polymerized mite extract

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Background: Hypoallergenic allergens (allergoids) polymerized with glutaraldehyde are commonly used in immunotherapy. Targeting allergoids to dendritic cells to enhance cell uptake may result in a more effective immunotherapy. Allergoids coupled to yeast mannan, as source of polymannoses, would be suitable for this purpose, since mannose-binding receptors are expressed on these cells.

The aim of this study was to establish the toxicity of mannan-conjugated polymerized mite extract (*Dermatophagoides pteronyssinus* and *D. farinae*) in an animal model.
Material and Methods: The toxicity experiments were carried out with 5 albino mice (acute systemic toxicity) and 10 albino mice for the problem and 5 albino mice for the blank control (subacute systemic toxicity), respectively. Mannan-conjugated polymerized extract of *Dermatophagoides* was administered with a single dose level of 50 ml/kg it in a single application in acute test and in repeated doses (5 days of administration + 2 days off) for 28 days in subacute test. The administration was subcutaneously of 1 ml per 20 g mouse (25 000 TU/ml). In both studies, the animals were observed daily to detect symptoms of toxicity, abnormal behaviour or death. The weight had been monitored previously to start the test, twice a week during the experimental period and weekly during the observation period. The study were made according to the specifications of rules UNE-EN-ISO 10993-11 and OECD Guideline 420 that have been developed in the internal procedure LTAN-019-2 and under GLP conditions.
Results: In acute and subacute systemic toxicity test, animals did not show symptoms of toxicity, abnormal behavior or death. The weight did not change during the observation period and in subacute systemic toxicity test. No macroscopic alterations were observed in any organ and no symptoms of toxicity and no changes in in skin, eyes, or changes in activity or posture were observed.
Conclusion: Mannan-conjugated polymerized mite extract has not toxicity symptoms in acute and subacute systemic toxicity studies *in vivo*.

1012
Sublingual immunotherapy with house dust mites and 5 grasses/4 cereals extracts: the effectiveness on allergic rhinitis control

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Background: Allergic rhinitis is the most common allergic disease and among the most common diseases globally. The management of allergic rhinitis (AR) is well established. Although the majority of patients present with controlled symptoms during pharmacologic treatment, 20% are still uncontrolled, suffering from severe chronic upper airway disease (SCUAD). Symptoms of AR are results of the allergic inflammation and their control could be achieved by treatment which could manage the inflammation such as immunotherapy. However there are no data concerning control of the disease after sublingual immunotherapy. The aim of the study was to assess control of allergic rhinitis in adults on the third year of sublingual immunotherapy with house dust mites and 5grasses/4cereals extracts.
Method: In the prospective study 149 patients with allergic rhinitis [men 53.69%; mean age 25.92, SD6.14] were included. 76 (51%) were treated with house dust mites sublingual immunotherapy (SLIT) and 73 (48.99%) - with 5grasses/4cereals SLIT. The level of allergic rhinitis control was assessed by the Rhinitis Control Assessment Test (RCAT) on the third year of treatment.
Results: When assessed on the third year, 67(88.16%) patients, treated with SLIT for house dust mites were with controlled rhinitis. In the group of patients, treated with SLIT for 5 grasses/4 cereals, 63 (86.30%) of them were with controlled allergic rhinitis.
Conclusion: The results from our study established that sublingual immunotherapy with house dust mites and 5 grasses/4 cereals extracts is effective in control allergic rhinitis. It could decrease the number of patients suffering from severe chronic upper airway disease (SCUAD).

1013
Semi-depot house dust mite allergen extract for Chinese with allergic rhinitis and asthma

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Background: Real-world data of the subcutaneous immunotherapy with Semi-Depot House Dust Mite Allergen Extract (HDM-SCIT) (a house dust mite allergen extract containing a 50%/50% mixture of D. pteronyssinus and D. farina) for allergic rhinitis and asthma is unavailable in China until recently. This study aims to investigate the effectiveness and safety of a HDM-SCIT for allergic rhinitis and asthma in Chinese patients.
Method: This was a multi-center, single-arm, open-label, self-controlled study. Chinese patients with allergic rhinitis or allergic asthma and history of symptoms at house dust mite exposure were included, and received allergen-specific immunotherapy for 1 year by subcutaneous injection of HDM-SCIT. The primary outcome measure was the percentage of patients with an improvement in symptom severity assessed at 12 months after initiation of the treatment. Occurrence of adverse events (AEs) and compliance of treatment were also evaluated.
Results: 272 outpatients were included for effectiveness analysis. Subject-evaluated improvement rate in VAS was 76.1% and 71.3% at 6 and 12 months, respectively; corresponding values for investigator-evaluated VAS were 77.9% and 71.7% ($P < 0.0001$). Symptom score changes were −2.43 and −3.79 at 6 and 12 months, respectively (both $P < 0.0001$); VAS improvement rate and symptom score change did not differ significantly between children and adolescents/adults. 98.8% of patients had good injection schedule adherence. No study drug-related serious AEs or serious systemic allergic reactions occurred.
Conclusion: HDM-SCIT is safety and effectiveness in the treatment of allergic rhinitis and asthma in a Chinese population with a good compliance.

1014
The analysis of curative effect of allergic rhinitis patients with subcutaneous immunotherapy (SCIT)

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Background: Allergic Rhinitis (AR) affects approximately 20% of the population of developed countries. Allergen immunotherapy is currently the only disease-modifying treatment available for allergic rhinitis.
Method: Using self-control methods, a total of 89 patients with allergic rhinitis were recruited into the study. These patients were treated with dust mite subctutaneous immunotherapay for 2 years. Symptom score and visual analogue scale (VAS) score were observed before treatment and 1 year, 2 years after treatment respectively. The therapeutic evaluation index included: rhinitis symptoms score, drug score, skin prick test, serum specific IgE (sIgE).
Results: The symptoms VAS score and drug scores of the 89 patients who were treated with specific subctutaneous immunotherapy (SCIT) after 1 year were significantly reduced than that before treatment ($P < 0.05$), the same result of the patients who were treated with specific subctutaneous immunotherapy (SCIT) after 2 years were significantly reduced, the differences were statistically significant ($P < 0.05$). The skin test result were no change after 2 years of SCIT ($P > 0.05$). No severe adverse events occurred.
Conclusion: SCIT for dust mite is a safe and an effective method for patients with perennial allergic rhinitis, which can be used as a routine treatment for allergic rhinitis. The symptoms of patients with allergic rhinitis were obviously improved by SCIT and a long term curative effect. To further improve the therapeutic effect, SCIT should be continued for at least 2 years.

1015
Evaluation of novel and current biomarkers for monitoring clinical efficacy of allergen immunotherapy for allergic rhinoconjunctivitis and allergic asthma

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Background: Allergen immunotherapy (AIT) is an effective treatment for allergic rhinoconjunctivitis (AR) with or without asthma. However, it is important to note that due to the complex interaction between patient, allergy, symptomatology and vaccines used for AIT, some patients do not respond optimally to the treatment. Furthermore, there are no validated or generally accepted candidate biomarkers that are predictive of the clinical response to AIT. Clinical management of patients receiving AIT and efficacy in randomised controlled trials for drug development could be significantly enhanced if there were means to identify those who are most likely to respond, when to stop treatment and how to predict relapse.
Method: The EAACI taskforce reviewed all candidate biomarkers used in clinical trials of AR patients with/without asthma. A literature review was performed and the following levels of evidence was assigned; (randomized) double blinded placebo control (level A), placebo control (level B), untreated control, cross sectional (level C), retrospective, responders vs non-responders (level D). Biomarkers were devided in seven domains: (i) IgE (total IgE, specific IgE and sIgE/Total IgE ratio), (ii) IgG (sIgG1, sIgG4 including SIgE/IgG4 ratio, (iii) IgE-FAB and IgE-BF, (iv) Basophil activation, (v) Cytokines and Chemokines, (vi) Cellular markers (T regulatory cells, B regulatory cells and dendritic cells) and (vii) *In vivo* biomarkers (including nasal and chamber provocations tests).
Results: All biomarkers were reviewed in the light of their potential advantages as well as their respective drawbacks. Unmet needs and specific recommendations on all seven domains were addressed. It is recommended by the task force to explore the use of sIgG4 as a potential biomarker for compliance of treatment. Candidate biomarkers that were associated with clinical outcome at the population level were IgE-FAB, IgE- blocking factor and IgE-ratio. Cytokine/chemokines and cellular reponses provided insight into the mechanisms of AIT.
Conclusions: The EAACI Task Force successfully evaluated surrogate immunologic and clinical biomarker data on the effects of AIT for AR with and without Asthma and have proposed a consensus position on candidate biomarkers for monitoring AIT and how these biomarkers could be used and implemented in future clinical trials of AIT and daily practice.

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Subcutaneous allergen specific immunotherapy in South Korea: efficacy, safety and predictors for clinical response

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Background: Allergen specific immunotherapy is the only treatment known to alter the clinical course of allergic diseases. However, the efficacy of immunotherapy may vary around the world due to differences in climate, the nature of aero-allergens and their distribution.
Methods: We reviewed medical records of 1113 adult respiratory allergy patients who were sensitized to house dust mite (HDM) and/or pollens and have taken subcutaneous immunotherapy (SCIT) with Novo-Helision Depot® from 2000 to 2012(49 with allergic asthma (AA), 578 with AA and allergic rhinitis (AR), 486 with AR). Variables including demographics, past and family histories of allergic diseases, mode of build-up phase (rush or conventional), target allergens (HDM, pollens, mixed), duration of immunotherapy, severity of AA and AR, control status, medication requirements, and adverse events (AEs) were collected.
Results: Of 627 patients with AA (mean age 35.6 ± 13.5, 49.8% male, 39.7% mild AA, 45.3% HDM, 30.1% Rush), 407 (64.9%) achieved AA remission. Mean time to get remission was 4.68 ± 0.19 years. Cox regression analysis revealed that mild asthma (OR 1.95, 95% CI 1.56–2.43, $P < 0.001$) and higher baseline FEV1% (1.02, 1.01–1.03, $P < 0.001$) were significant predictors for AA remission during SCIT, whereas age, gender, disease duration, mode of build-up phase, target allergens, and the occurrence of AEs had no significant influence on AA remission. Of 1064 patients with AR (mean age 33.8 ± 13.5, 49.5% male, 48.9% severe AR, 49.1% HDM, 29.7% Rush), 374 (35.2%) achieved the remission of AR. Mean duration for achieving remission was 7.56 ± 0.17 years. Cox regression analysis showed that old age (0.99, 0.98–0.99, $P = 0.001$), severe AR (0.68, 0.54–0.85, $P = 0.001$), and accompanied AA (0.74, 0.60–0.91, $P = 0.005$) were the significant factors of poor response to SCIT regardless of gender, disease duration, mode of build-up phase, target allergens, and the occurrence of AEs. In total 238 (21.4%) patients experienced AEs during build-up phase, and particularly in patients starting SCIT with rush mode, AEs were found more frequently compared to those with conventional mode (39.3% vs 14.0%, $P < 0.001$).
Conclusions: A retrospective cohort study demonstrated that 64.9% of AA patients and 35.2% of AR patients arrived at the remission with low occurrence of severe AEs with SCIT. Initial symptom severity, FEV1%, age and comorbid AA can impact on the clinical response to SCIT in patients with AA and/or AR.

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A multicentre randomised placebo-controlled double-blindclinical trial for evaluation of the dose-dependent effect of a hypoallergenic house dust mite preparation (*Dermatophagoides pteronyssinus*) for subcutaneous immunotherapy (SCIT)

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Background: House dust mite allergy is a major cause of respiratory allergic diseases worldwide with a high risk for developing asthma. This study was conducted to investigate the dose-dependent safety and efficacy profile of a house dust mite allergoid from Allergopharma GmbH & Co. KG, Reinbek, Germany.
Method: The dose-dependent safety and efficacy profile of a house dust mite (*D. pteronyssinus*) allergoid for SCIT was analyzed in a multi-center, randomized, double-blind, placebo-controlled, dose-response study with 5 treatment arms. 146 adults (Safety Set; SAF) from 18 to 40 years of age with controlled allergic asthma and rhinitis/rhinoconjunctivitis caused by house dust mites, were treated with placebo ($n = 32$) or one of the following doses of the allergoid preparation, 600 PNU ($n = 24$), 1800 PNU ($n = 31$), 3000 PNU ($n = 28$) as well as 5400 PNU ($n = 31$). On average, patients received 15 injections over half a year.

The primary endpoint for efficacy was the change in late phase response (swelling in cm^2 after 6 h) to intracutaneous testing from before to after SCIT. As secondary efficacy variable, the change of the minimal asthma control dose before and after treatment was assessed. The safety profile of all applied doses was evaluated through adverse events as well as vital signs and laboratory values.
Results: All 4 active groups showed a statistically significant reduction of the late phase response after intracutaneous testing in comparison to placebo ($P < 0.001$). The number of patients without need for ICS after treatment was between 75% and 85% for the doses 1800 PNU, 3000 PNU, and 5400 PNU with statistical significance for the highest dose ($P = 0.0238$) compared to placebo. Treatment was shown to be safe at all doses tested, with an increase in local reactions observed at the dose of 5400 PNU.
Conclusion: Based on the data of the primary and secondary efficacy endpoints the three higher doses showed good results with slight differences only. Taking the safety profile into consideration further investigations are warranted to establish the optimal risk benefit ratio.

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Patterns of allergen recognition by *Dermatophagoides*-allergic patients: implications for allergen immunotherapy

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Purpose: The aim of this study was to analyze the patterns of allergens recognized by *Dermatophagoides*-allergic patients living in various areas of the world, in order to design an allergen immunotherapy (AIT) product suitable for worldwide treatment of house dust mite (HDM)-allergy.
Methods: Using a customized microarray assay, IgE specific for 12 purified allergens from *Dermatophagoides pteronyssinus* or *D. farinae* were assessed in sera from 1302 *Dermatophagoides*-allergic patients, including adults and 5- to 17-year-old children from America, Canada, Europe and/or Japan. Comprehensive proteomic analyses were performed by mass spectrometric (MS) and two-dimensional difference gel electrophoresis (2D-DIGE) in order to characterize *D. pteronyssinus* and *D. farinae* extracts, as well as purified bodies and feces.
Results: Patterns of allergen recognition by the IgE from *Dermatophagoides*-allergic patients were comparable in all cohorts patients analyzed. Overall, more than 70% and 80% of tested allergic patients were sensitized, respectively, to group 1 and group 2 allergens from *D. pteronyssinus* and/or *D. farinae*. Furthermore, 20–50% of patients also had IgE to allergens from groups 4, 5, 7, 13, 15, 21, and 23. All patients have IgE to allergens present in mite bodies and feces. MS-based analyses confirmed the presence of mite allergens recorded by IUIS in *D. pteronyssinus* and *D. farinae* extracts, with groups 2, 8, 10, 11, 14, and 20 prominent in bodies and groups 1, 6, 18, and 23 well represented in feces.

Conclusions: Based on patterns of IgE reactivity in *Dermatophagoides*-allergic patients, HDM-specific AIT should rely upon a mixture of *D. pteronyssinus* and *D. farinae* extracts, manufactured from both feces and bodies. Such a combination product is appropriate to treat children and adult *Dermatophagoides*-allergic patients from Asia, Europe, and North America.

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Allergy immunotherapy cost-benefit, overall satisfaction and quality of life perceived by patients in real life: the ESPIA questionnaire

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Background: The ESPIA questionnaire (ESPIA) is the first Spanish satisfaction questionnaire for adult patients receiving allergy immunotherapy (AIT). The aim is to assess the cost-benefit balance (CB) and to describe the clinical features of patients with allergic rhinitis (AR) who perceive an improvement in their overall satisfaction (OS) and quality of life (QoL) after being treated with AIT.
Methods: ESPIA consists of 16 items with a total score 0–100. A longitudinal multicenter cross-sectional study with 1302 patients divided into two groups: patients with ≤12 or >12 months undergoing AIT, who completed ESPIA was conducted. Multivariate analyses of the results of the validation process were performed. Perceived CB, OS and QoL were analyzed according to the following variables: Type of AR, AR severity according to the modified ARIA classification and use of symptomatic medication in the last 7 days.
Results: The maximum score for perceived CB was 83.2, OS 89.3 and QoL 82.7, in patients with >12 months of treatment with AIT, mild intermittent rhinitis without symptomatic treatment in the last 7 days. These scores gradually decreases with severity and persistence of AR to 55, 59.8 and 52 respectively, in patients with severe persistent AR treated for ≤12 months with AIT using symptomatic treatment in the previous 7 days.
Conclusion: Differences obtained between groups (up to 28.2, 29.5 and 30.7 points respectively) confirm the discriminative ability of ESPIA to assess CB, OS and QoL perceived by patients with AR treated with AIT. Maximums score were in patients with >12 months of treatment with AIT, with mild intermittent rhinitis without symptomatic treatment in the last 7 days.

Poster Session TPS 27

Allergens

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Specificity of non specific lipid transfer proteins and influence of the ligands on their three dimensional structure

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Background: Plant non-specific lipid transfer proteins (nsLTPs) are relevant food allergens e.g. from peach (Pru p 3), hazelnut (Cor a 8) or walnut (Jug r 3). They share a conserved fold with an internal cavity. Different lipid-protein complexes showed that the tunnel adapts its volume while binding a broad range of hydrophobic molecules.
Method: The binding of lipids to Pru p 3, Cor a 8, and Jug r 3 was monitored by adding 10 μM 1,8-ANS and measuring the decrease of 1,8-ANS fluorescence. Furthermore, molecular dynamic analysis (MD) was applied to explore the nature of interaction between nsLTPs and tested ligands. Saturation transfer difference (STD) spectroscopy and W-LOGSY (Water-Ligand Observed via Gradient Spectroscopy) technique were applied to confirm results obtained *in silico*.
Results: Due to pre-incubation of Pru p 3 with lipids a concentration dependent reduction of ANS binding was observed. Pru p 3 incubated (1:1; 1:10) with lauric acid showed 19% and 66% of ANS fluorescence reduction respectively, compared with Pru p 3 without lipids. For oleic acid (1:1; 1:10) reduction was 7% and 77%, respectively. Molecular dynamic analysis suggests changes in protein structure due to binding to certain ligands. Interaction between oleic acid and Pru p 3, moved the C-terminal loop out towards the surface of the molecule. NMR based experiments confirmed binding capacity observed in MD analysis.
Conclusion: In this study, we observed differences in binding capacity of Pru p 3. Molecular dynamic simulation has shown that interaction between Pru p 3 and tested ligands can lead to conformational changes. The allergen-lipid interaction may act as a potential danger signal during the allergic sensitization phase or increase allergenicity during the effector phase.

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Molecular, structural and immunological characterization of Der p 18, a chitinase-like house dust mite allergen

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Background: The house dust mite (HDM) allergen Der p 18 belongs to the glycoside hydrolase family 18 chitinases. The relevance of Der p 18 for house dust mite allergic patients has only been partly investigated.
Objective: To perform a detailed characterization of Der p 18 on a molecular, structural and immunological level.
Methods: Der p 18 was expressed in *E. coli*, purified to homogeneity and its secondary structure was analyzed by circular dichroism. Der p 18-specific IgG antibodies were produced in rabbits to localize the allergen in mites using immunogold electron microscopy and to search for cross-reactive allergens in other allergen sources (i.e. mites, crustacea, mollusca and insects). IgE reactivity of rDer p 18 was tested with sera from clinically well characterized HDM-allergic patients ($n = 98$) and its allergenic activity was analyzed in basophil activation experiments.
Results: Recombinant Der p 18 was expressed and purified as a folded protein. Despite considerable sequence identities with Der f 18 from *Dermatophagoides farinae* and proteins from the other tested allergen sources, no relevant cross-reactivities were found. The allergen was mainly localized in the peritrophic matrix of the HDM gut and to a lower extent in fecal pellets. Der p 18 reacted with IgE from 10% of mite allergic patients from Austria and showed allergenic activity when tested for basophil activation in Der p 18-sensitized patients.
Conclusion: Der p 18 seems to be a species-specific minor allergen but exhibits allergenic activity and therefore should be included in diagnostic test panels for HDM allergy.

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Amb a 1 isoforms show distinct IgE-binding properties

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Background: Ragweed pollen allergies represent a serious health problem throughout vast regions of North America as well as Europe, and are an emerging risk factor for respiratory allergies in Asia. The major allergen of short ragweed, Amb a 1, has been identified as member of the pectate lyase allergen family. To date five different Amb a 1 isoforms have been acknowledged by the WHO/IUIS allergen nomenclature subcommittee.
Methods: Thus, we performed mass spectrometry analyses of aqueous ragweed pollen extracts to quantify the isoform composition of Amb a 1. Based on our data, three highly abundant Amb a 1 isoforms were purified from natural extracts. Moreover, one oft these isoforms was produced as recombinant protein in P. pastoris. The allergens were fully characterized and their IgE-binding properties were compared by immunoblot, ELISA and mediator release assays.
Results: Amb a 1 isoforms show a considerable degree of sequence heterogeneity. The predicted structure of Amb a 1 is characterized by a central parallel-beta-helix surrounded by alpha helical fold motives. Our investigations of secondary structure elements by CD and FTIR spectroscopy revealed slight differences between the

Amb a 1 isoforms. This translated into different IgE-binding properties of Amb a 1 isoforms in mediator release assays.
Conclusion: Analyses of pollen extracts demonstrated that several Amb a 1 isoforms are present in rather similar quantities in ragweed pollen. Therefore, the differences of IgE-binding to Amb a 1 isoforms could be a result of different sensitizing properties. This should be taken into consideration when selecting particular ragweed pollen isoforms for allergy diagnosis as well as therapy.
Acknowledgments: This work was supported by FWF project L688, CK-CARE AG Individual Project 2009-02, Biomay AG, the Christian Doppler Research Association, and Sparkling Science SPA 05-193.

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Update on AllergenOnline.org: a comprehensive, searchable database for risk assessment

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Background: Food safety regulators in many countries are demanding evaluation of the potential allergenicity of genetically engineered food crops and processed foods containing novel proteins. Currently no single or combinations of laboratory tests are highly predictive at gauging the potential allergenicity of individual proteins. However, practical clinical experience has demonstrated the common, serious risk of food allergy (anaphylaxis) are due to the unexpected consumption of proteins from known allergenic sources by consumers who have been diagnosed and told to avoid their allergens. In some cases cross-reactive IgE binding to homologous proteins causes severe reactions. The AllergenOnline database, established in 2005 is updated annually and curated by our expert panel to provide a sequence-searchable bioinformatics tool to identify potentially risky proteins before they are transferred to new food sources.
Method: Each year the NCBI Protein database and the WHO/IUIS Allergen database are searched for newly identified candidate allergens. Published scientific literature is searched using PubMed for data demonstrating protein-specific IgE binding from donors allergic to the source of the protein. Evidence of IgE binding to cross-reactive carbohydrate determinants is evaluated along with characterization of the protein (expression in the source material and amino acid sequence or expected translation product). Additionally evidence of biological activity related to specific IgE binding is sought (basophil activation, skin prick tests or challenges) to support the designation as an allergen. The amino acid sequences are compiled and relevant references are listed for each taxonomic protein group.
Results: Version 16 will be released 26 January, 2016. It includes 1956 sequences from 778 taxonomic protein groups. Version 15 included 1897 proteins in 744 groups. Use of the database is free to the public. We do not collect user or query sequence information. Users enter the amino acid sequence of their protein of interest to search for alignments with identities that might conservatively predict potential cross-reactivity as described online with alignment identity and *E* scores.
Conclusion: Search results should guide developers and regulators to accept the protein as unlikely to present a known risk of immediate allergic elicitation or alternatively identifies the protein as an allergen or one that should require specific serum tests.

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Bet v 1-homologous proteins from chickpea show IgE cross reactivity in patients with birch pollen allergy

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Background: Homologues of Bet v 1, the major birch pollen allergen, from legume foods are mainly involved in allergic reactions caused by IgE cross-reactivity. Chickpeas have been reported to cause IgE-mediated hypersensitivity reactions in patients from Spain & India, particularly in pediatric patients. So far no chickpea allergens are listed in the official IUIS allergen database. The objective of the present study was the cDNA cloning, recombinant expression and immunological characterization of Bet v 1 homologous PR10-proteins from chickpea.
Method: Two Bet v 1 homologous PR10 proteins from chickpea which were predicted by an *in silico* analysis to be potential allergens. The pre synthesized cDNA sequences, designated as Cic a 1.01 (Q9SMK8) and Cic a 1.02 (Q39450), were expressed in E. coli. Cic a 1.01 was purified under native conditions by DEAE & size exclusion chromatography (SEC) whereas Cic a 1.02 was purified under denaturing conditions by MonoQ & SEC. Purity & secondary structure of the proteins were analyzed by SDS-PAGE, CD spectroscopy, DLS and LC-MS. Serum samples of 9 birch allergic patients who were sensitized to Bet v 1 along with 26 sera samples of chickpea allergic patients from Spain were investigated for IgE reactivity with raw & boiled chickpea extract, purified Cic a 1.01 & Cic a 1.02.
Results: Cic a 1.01 (AJ275304) & Cic a 1.02 (X79706) showed 64% amino acid identity (aa-id) to one another and 49% and 44% aa-id to Bet v 1 (X15877), respectively. Both recombinant proteins displayed secondary structures similar to those of Bet v 1. IgE detection of raw chickpea extract with Spanish chickpea allergic patient's serum samples resulted in multiple bands. 2 out of 26 Spanish sera showed IgE reactivity with these proteins. IgE detection of raw & boiled extract with Bet v 1 cross reactive sera resulted in multiple bands and few of these sera also showed reactivity with purified proteins. IgE binding with raw chickpea extract was inhibited at a single band using recombinant purified Bet v 1 homologous chickpea proteins, confirming the presence of these proteins in chickpea.
Conclusion: Chickpea allergy might be mediated by means of cross-reaction with the Bet v 1 homologue from chickpea in a subgroup of patients allergic to Birch, Bet v 1. These proteins were not seen to be so relevant for Spanish chickpea allergic patients. The allergenic potency for these proteins needs to be further evaluated to determine its clinical relevance.

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Supporting diagnostic test allergens used for *in vivo* diagnosis of allergic disease: a case study

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Background: It remains of paramount importance for the clinician to have available a comprehensive range of high-quality diagnostic tests for *in vivo* diagnosis of IgE-mediated allergies. However, the regulatory demands and associated costs for manufacturers in maintaining a comprehensive 'gold-standard' skin-prick test

portfolio has become increasingly challenging, and as such, is driving manufacturers to significantly limit their test allergen (TA) portfolio. In a recent review of the situation, Klimek and colleagues, 2015, presented a number of regulatory considerations that might help facilitate the maintenance of TAs in Europe. Of note, was to promote the concept of homologous groups. The work presented herein provides a route to assess inclusion criteria for new Tree and Epithelial allergens within their respective homologous groups, in line with EMA guidance, providing scope for manufacturers to extrapolate quality data where appropriate, thus facilitating TA maintenance.

Methods: Structural homology was assessed for epithelial allergens (Lipocalins) from cat, dog, guinea pig, hamster and horse. In addition to this, their biological cross-reactivity was compared using diagnostic formulations in separate ELISA experiments using cat IgG rabbit sera and IgE human sera.

Identical assessments for Plane and Lime Tree allergens with the 'Birch' group were also made. The comparability of biochemical stability of different allergen sources was assessed through statistical methods for the aforementioned tree and epithelial species.

Results: Allergen cross-reactivity and/or structural homology have been described providing justification for inclusion of Epithelial and Tree allergens within homologous group formations. Statistical physicochemical/biological similarities among mammalian epithelial species provided for further justification in accordance with EMA guidance. An example of how stability data of TAs may be extrapolated within the same homologous group was further assessed.

Conclusions: The concept of homologous groups is dynamic allowing the flexibility and potential in streamlining quality parameters, such as stability profiles, due to extrapolation of exemplar data to a wider range of allergens. The work presented herein pays tribute to the concept of homologous groups providing an assessment of the current literature and supporting data for establishing a homologous group for Epithelials and extending the 'Birch' tree group.

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First case series: exotic pets allergy among Chilean patients

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Background: The most frequent pet allergy is allergy to cats and dogs, but exposure to other nontraditional pets, such as rodents (eg, mice, hamsters, guinea pigs), other mammals (eg, ferrets, hedgehogs, pigs, monkeys), spiders (eg, tarantulas), reptiles (eg, snakes), and exotic birds has increased in recent years inducing new allergic sensitization, frequently manifested by respiratory or cutaneous symptoms.

Objective: To characterize the first cases series of chilean patients with exotic pet allergy.

Results: In this report we describe five patients allergic to exotic pets, four women and one man (median age 30 years old). Pets included three hedgehogs, one ferret and one guinea pig. The clinical symptoms included rhinoconjunctivitis, contact dermatitis, urticaria, angioedema and bronchial obstruction. All patients were tested with common aeroallergens, a battery of animal epithelium commercial extracts (cat and dog), and extracts prepared with dander and spine (hedgehogs) or dander and hair (ferret and guinea pig) (unavailability of commercial extract). All patients allergic to hedgehog showed allergic rhinoconjunctivitis and two of them also had bronchial hyperreactivity. All of them had positive skin prick test (SPT) to spines and dander extract. One of these patients tested positive also to SPT with dust mite. The only patient with contact dermatitis owned a ferret, and had negative SPT to his pet, but a positive patch test at 72 h to the dander and hair ferret extract. One patient presented severe persistent rhinoconjunctivitis with the exposure to guinea pig, she had positive IgE levels for guinea pig (0.7 UI/ml) and tested positive to SPT with dust mite and grass polen commercial extracts. Only two patients of this report were atopic and had other sensibilizations. All patients improved their symptoms when their pets were removed or not had direct contact with them, except for one patient who showed no response despite she was sensitized only to her pet (hedgehog) and not to any other inhalant.

Conclusion: The allergy to exotic pets like hedgehog, ferret and guinea pig occur in our country, so it is necessary to be aware that some symptoms may not be caused by common inhalants. It is important to study this allergy, so recommendations like pet removal can help to improve symptoms.

1028
Hedgehog allergy

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Background: Hedgehogs are any of the spiny mammals of the subfamily Erinaceinae whose most distinctive trait are his quills, not poisonous sharp hollow hairs made with keratin that are used as a defense. When threatened, a hedgehog is able to curl up into a ball with its quills extended.

The long-eared hedgehog, known as African pygmy, is the most common type sold as pets.

Although two cases of adverse reactions after exposure to hedgehog have been reported, no cases of IgE-mediated allergy to hedgehog have been described in the literature.

The aim of this study was to present a case of IgE-mediated allergy and to identify two relevant allergens.

A 23-year-old woman with a previous diagnosis of seasonal rhino-conjunctivitis presented with shortness of breath, ocular and nasal itching, runny nose and contact urticaria after exposure to hedgehog. She had an African pygmy hedgehog at home as a pet, and presented perennial symptoms coinciding with the introduction of the animal at home.

Method: Skin prick tests (SPT) was performed with the most common aeroallergens in our environment.

Hedgehog extract was performed with small, round balls of hedgehog feces with urine obtained from the bedding material.

Protein bands were separated by SDS-PAGE and immunoblotting was performed to detect IgE binding bands from hedgehog extract. IgE binding bands were identified by mass spectrometry using liquid chromatography-tandem mass spectrometry.

Results: SPT was positive (wheal $\geq$ 3 mm) to pollen - Phleum pratense, Olea europaea, Platanus acerifolia, Cupressus arizonica -, cat and dog epithelium and moulds (Alternaria, Aspegillus fumigatus and Cladosporium).

SDS-PAGE revealed bands between 97 and 9 kDa. The immunoblotting showed IgE- binding bands of 42, 40, 32 and 29 kDa identified by mass-spectrometry as acidic mammalian chitinase-like for the

40 kDa, carboxypeptidase A1 for the 32 kDa and chymotrypsin-like elastase family member (CELA) for the 29 kDa. The 42 kDa IgE-binding band was not visualized in the SDS-PAGE and, thus, could not be analyzed.
Conclusion: We present a case of IgE-mediated to Hedgehog and we identify chitinase-like, carboxypeptidase A1 and chymotrypsin-like elastase as relevant allergens.

1029
Allergy to Marijuana: a case report

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Background: The increasing consumption of Mariajuana drug has resulted in a higher prevalence of sensitization. This drug is a preparation of the *Cannabis sativa*plant, and contains a lipid transfer protein (LTP), which is considered a pan-allergen in plant food allergies. However, both allergenic profile and cross-reactivity should be further analyzed.
Method: We present a 25 years man living in the south of Spain with chronic diarrhea syndrome with suspect of food allergy. The patient was allergic to olive pollen with symptoms of rhinoconjunctivitis and asthma. He referred asthma after smoking marijuana and urticaria after skin contact with it. He also presented OAS after the ingestion of some fruits like apple and gastrointestinal disorders after beer intake. We performed skin prick test with common inhalant allergens (pollens, moulds and epithelia), latex, and a standard battery of food allergens as egg, milk, nuts, fish, flours and anisakis. We also performed prick-pirck test to apple and cannabis. Specific IgE to a battery of single allergens was analyzed by the ADVIA-Centaur platform. An immunoblotting against a Cannabis extract was also carried out.
Results: Skin prick tests were positive for Olive (12 mm), Artemisia (6 mm), Alternaria (9 mm) and Cat (12 mm). Prick-prick tests were positive, with apple (8 mm) and Cannabis (12 mm). Specific IgE were positive to Pru p 3 (12.5 kUA/l), Ole e 1 (28.8 kUA/l) and Ole e 7 (1.9 kUA/l) and negative to Ole e 9 and Ole e 2 (profilin). Immunoblotting with the cannabis extract showed different bands with molecular weight ranging between 10 and 75 kDa. The most important bands had a molecular weight around 10 kDa (which might correspond to Can s 3, ansLTP), 20 kDa (which might corresponds to Can s OEP, an Oxygen-evolving Enhancer Protein), 37 kDa (which might corresponds to Can s TLP, a Thaumatin-like Protein) and 75 kDa.
Conclusion: We reported a patient with sIgE to *Cannabis sativa*, with asthma and urticaria after inhalation and contact with this drug. The sensitization profile to Cannabis together with the presence of sIgE to *Rosacea* fruits and Ole e 7 points to a possible cross-reactivity mediated by LTPs.

1031
pH dependence of oligomerization states and ligand binding in Alt a 1

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Background: Alt a 1 is the major allergen of *A. alternata*. It's a highly allergenic protein responsible for chronic asthma in childrens and in Southern Europe, over 20% of the patients with a history of respiratory allergy are sensitized to this mold.

Its crystal structure revealed a unique β-barrel fold with four linear epitopes and the position of two of them led the interaction with the IgE only in the dimeric form.

In this work we study the oligomerization state of this protein and, consequently, in the allergy sensitization process.
Method: Absorbance measurements were employed to measure the ability of Alt a 1 to bind Quercetin, and size exclusion chromatography were used to demonstrate the effect in the presence of this ligand and also differents pHs in the oligomerization state of the protein.

Moreover the results were supported by *in silico* studies using Docking and Poisson-Boltzmann electrostatic potentials calculations, and we explored the system with Molecular Dynamics calculations.
Results: Docking calculations predict a high-affinity tetrameric Alt a 1-quercetin complex and the Poisson-Boltzmann electrostatic potential show pH- dependent differences for the electrostatic energy. Experimental procedures using a size exclusion chromatography revealed the ability of Alt a 1 to tetramerizes when the quercetin is present, and the pH dependence is show like a highly increase in the monomeric form at pH5.
Conclusion: The oligomerization state of Alt a 1 is highly dependent on the presence of the ligand molecules, such as quercetin, and the pH of the medium. As the tetrameric form don't have the epitopes in the correct position to interact with the Ig E, the study of the oligomerization state of this protein is highly relevant to understand the sensitization process.

1032
Seafood proteases present in workplace bioaerosols - effects on inflammatory pathways in skin and airway cell models

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Background: Workers in seafood industry are exposed to seafood enzymes as part of the bioaerosol generated during seafood processing. Proteases in the bioaerosol are inhaled together with seafood allergens, microorganisms, endotoxins and other bioactive agents. The skin is exposed through squirts and direct contact. Trypsin is a serine protease shown to be present in bioaerosols and liquid samples from seafood industry. This presentation will focus on trypsin from different seafood species as activators of inflammatory signaling pathways in skin and airway cell models. Combined effects of seafood trypsins with bacterial lipopolysaccharide (LPS) will be presented.
Method: Human keratinocytic (HaCaT) and pulmonary epithelial (A549) cell lines were exposed to various concentrations of trypsin isolated from salmon (*Salmo salar*) and king crab (*Paralithodes camtschaticus*) as single agents or in mixture with LPS. The stimulation of interleukin (IL-) 8, NF-ℓB, matrix metalloproteinase (MMP) 2 and 9, and the role of protease-activated receptor (PAR) 2 in the inflammatory signal mediation were investigated. IL-8 levels, NF-ℓB binding and matrix metalloproteinases were measured using enzyme linked immunosorbent assay (ELISA), a luciferase reporter gen assay and gelatin zymography respectively. Involvement of PAR-2 was investigated using specific siRNA against hPAR-2.
Results: Purified salmon and king crab trypsin generated secretion of IL-8 and binding of NF-ℓB in a concentration-dependent manner in skin and airway cell models. Mixed exposure to LPS and seafood proteases augmented the inflammatory signalling. We also showed a concentration dependent increase in MMP-2 and MMP-9 following trypsin exposure of HaCaT cells. By the use of specific siRNA we demonstrated that the effects of seafood trypsin were mediated through activation of PAR 2.

Conclusion: The results suggest that exposure to proteases present in seafood industry bioaerosols may add to work-related airway and skin symptoms by activating well known inflammatory pathways. Mixtures of bioactive agents, as relevant in workplace bioaerosols, may augment the inflammatory responses. Protease activated receptor-2 seem to play an important role in mediating these effects.

Poster Session TPS 28

Component resolved diagnosis: Inhaled allergens

1033
Mannan-conjugated polymerized allergens of *Dermatophagoides pteronyssinus* are more hypoallergenic than the corresponding native and polymerized preparations

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Background: Glutaraldehyde polymerized allergens (allergoids) are hypoallergenic preparations commonly used in immunotherapy. These allergoids are more hypoallergenic *in vitro* (specific IgE binding) and are better uptaken by dendritic cells when they are mannosilated. They have demonstrated clinical effectiveness in dogs suffering of canine atopic dermatitis. The aim of this study was to compare the *in vivo* skin prick test allergenic response of native allergens (N), polymerized allergoids (POL) and polymerized allergoids conjugated to mannan (PM) of *Dermatophagoides pteronyssinus*.
Method: Twenty-two patients (14 men and 8 women, median age 31, age range 23–37 years), with the diagnosis of rhinoconjunctivitis ($n = 15$) or rhinconjunctivitis and asthma ($n = 7$), due to hypersensitivity to *Dermatophagoides pteronyssinus*, were skin-prick tested with N, POL and PM at a concentration of 150 μg of protein/ml. The area of the wheal size induced by each preparation was measured using PrickFilm and expressed in mm^2. Descriptive results were expressed as the median with the first and third quartiles. Friedman′s test was used to compare the results between the 3 preparations and the Nemenyi procedure was used for pairwise comparisons.
Results: The median value of the wheal size obtained was 64.2 (54.2–72.3) for N, 40.1 (20.9–48.0) for POL and 24.1 (16.3–33.8) for PM. The comparison between the 3 preparations was highly significant ($P < 0.0001$). The pairwise comparisons showed that there were significant differences between PM and N ($P < 0.0001$), PM and POL ($P = 0.028$) and POL and N ($P < 0.007$).
Conclusion: Mannan-conjugated polymerized allergens of *Dermatophagoides pteronyssinus* have a significant reduction of *in vivo* allergenicity, as measured *in vivo* with SPT, compared to their respective native and polymerized preparations. This fact and their improved dendritic cell allergen uptake may provide a more effective immunotherapy with a high degree of safety.

1034
Development of sandwich ELISAs for the quantification of clinically relevant house dust mite allergens

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Background: House dust mite (HDM) allergy affects more than 10% of the population in industrialized countries. Beside Der p 1 and Der p 2, the HDM allergens Der p 5, Der p 7, Der p 21 and Der p 23 have been identified as the clinically most important allergens with high allergenic activity. Assays for measuring allergen concentrations in environmental samples, diagnostic and therapeutic allergen extracts are available only for Der p 1 and Der p 2.
Method: Allergen-specific antibodies with defined specificities were obtained by immunizing rabbits with synthetic peptides derived from different portions of the allergens and with the complete recombinant allergens. The rabbit antisera were tested for allergen reactivity towards immobilized allergens and allergens in solution and used to build sandwich ELISAs based on capturing and detecting antisera with defined specificity.
Conclusion: Using purified allergens for standardization will allow to quantify the natural allergens in biological samples. The sandwich ELISAs will be useful to measure and quantify the HDM allergens Der p 5, Der p 7, Der p 21 and Der p 23 in environmental samples, in allergen extracts used for challenge tests as well as in diagnostic and therapeutic allergen extracts

Supported by the FWF-funded PhD program MCCA, by the FWF projects F4605, F4602 and by a research grant from Biomay AG, Vienna, Austria.

1035
Clinicical impacts of dust mite allergy: sensitization to Der p1 and Der p2

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Background: Dust mites are frequent allergen sources in Central Europe and often lead to rhinits and conjunctivitis followed by asthma in long-term course. Cross reactions from the European dust mite Dermatophagoides pteronyssinus (D. pter.) to the American dust mite D. farinae were often described, whereas the distribution of different allergen components in clinical context did not find larger regard so far. D. pter. contains two major allergens, Der p1 is significantly associated with dust mite faeces, Der p2 with dust mite body surface.
Method: On a continuing group of 86 patients allergic to dust mites we screened the distribution of sensitization rates to Der p1 and Der p2 to correlate these with their clinical course (affected organs by allergy and severeness of allergy).
Results: 45 out of 86 patients (52%) showed sensitizations to both major allergen components, whereas 8 (9%) were only sensitized to Der p1, 21 (24%) only to Der p2, and 12 to none of both (14%). Patients sensitized to Der p1 and p2 showed a slightly higher number of affected organs than those sensitized to Der p1 alone, but significantly higher rates and higher severity of allergy symptoms than those sensitized to Der p2 alone or none of these components.
Conclusion: The results lead to the conclusion that Der p1 has a higher allergen potency than Der p2. One explanation might be the multiple larger amounts of faeces in comparison to mite bodies, one other the particle size carrying the allergens, which is smaller of faeces (10–20 μm) than of mite bodies (250–400 μm) and is predestined to move deeper into the smaller airways.

1036
Cross-reactive molecules of animal lipocalin allergens

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Background: Lipocalins are a widespread family of animal derived allergens. Nowadays there are several lipocalins commercially available, for example Fel d 4 (cat), Can f 1 and Can f 2 (dog), Equ c 1 (horse). Fel d 4 has a high amino acid sequence identity with the major horse allergen Equ c 1.
Method: 9 horse allergic patients, age 18–65 (av. 33.5), were included into the study. We collected detailed medical history of all patients, performed skin prick test with cat, dog and horse allergen extract and established the concentration of allergen specific IgE (asIgE) directed against cat, dog and horse allergen extract and allergen components from the lipocalin family: Can f 1, Can f 2, Fel d 4 and Equ c 1.
Results: All patients had positive skin prick test with horse, cat and dog allergen extract. Concentration of IgE against horse allergen extract was elevated in 8 cases.

Results of component resolved diagnosis are displayed in Table 1.

In 6 patients the concentration of IgE against Equ c 1 was elevated. In the group of 9 patients only 1 had elevated IgE concentration against only 1 lipocalin (patient 9, Can f 1). 3 patients were sensitized by 2 examined lipocalins, 1 by 3. 4 patients were allergic to all four lipocalins from 3 independent allergen sources.
Conclusion: Most of the patients (8 from 9 in the study group) had elevated level of IgE against at least 2 different lipocalins, probably because of high amino acid sequence homology between lipocalins from different mammals.

Horse allergic patients are more prone to allergy to other fur animals.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Can f 1	86.7	0.22	>100	84.6	0.35	77.5	1	57.3	7.9
Can f 2	60.5	0.28	>100	86.8	0.01	37.7	0	15	0
Fel d 4	11.5	37.2	8.61	22.1	0.98	8.69	0.88	1.64	0
Equ c 1	29.1	17.6	14.4	5.19	3.57	2.94	0.05	0.01	0

[Results of component resolved diagnosis in IU/ml]

1037
Analysis of the sensitization profile in 57 dog allergic patients

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Background: The aim of this study was to analyze the frequency of hypersensitivity to allergen components (Can f 1, Can f 2, Can f 3 and Can f 5) in dog allergic patients. Can f 1 is a lipocalin and a major dog allergen. Can f 2 is also a lipocalin, a minor allergen, and shares epitopes with Can f 1. Can f 3 is dog serum albumin and Can f 5 is prostatic kallikrein, similar to p*rostate-specific antigen* (PSA) in human.
Method: In the studied group there were 57 patients aged 18–68 (av. 35.83) allergic to dog, what was confirmed by positive skin prick tests (SPTs) with dog allergen extract. 10 patients with negative history of dog allergy and negative SPTs with dog allergen extract were included into control group. We collected detailed medical history of all patients and established the concentration of allergen specific IgE (asIgE) directed against dog allergen extract and allergen components Can f 1, Can f 2, Can f 3 and Can f 5.
Results: In the studied group we found elevated concentration of asIgE (greater than 0.7 IU/ml) against dog allergen extract in 44 cases (88%). Results of component resolved diagnosis are displayed in Table 1. Only 18 patients (31.58%) had elevated level of IgE against Can f 1, which is the major dog allergen. Correlation between concentration of IgE against Can f 1 and dog allergen extract is 0.8. 19 patients were allergic only to 1 dog allergen component. In control group the level of IgE against dog allergen extract and dog allergen components was not elevated.

Dog allergen components	rCan f 1	rCan f 2	nCan f 3	rCan f 5
Patients (%)	18 (31.58%)	4 (7.02%)	11 (19.3%)	15 (26.32%)
Concentration of IgE (IU/ml)	0.72–77.5 (av. 18.7, median 4.79)	9.21–37.7 (av. 22.58, median 21.7)	0.88- >100 (av. 26.82, median 15.3)	0.78–75.7 (av. 13.47, median 2.03)

Dog allergen components	Can f 1 and Can f 2	Can f 1 and Can f 3	Can f 1 and Can f 5	Can f 2 and Can f 3	Can f 2 and Can f 5	Can f 3 and Can f 5
Patients (%)	4 (7.02%)	6 (10.53%)	5 (8.77%)	2 (3.51%)	2 (3.51%)	5 (8.77%)

Dog allergen components	Can f 1, Can f 2 and Can f 3	Can f 2, Can f 3 and Can f 5	Can f 1, Can f 2 and Can f 5	Can f 1, Can f 2, Can f 3 and Can f 5
Patients (%)	2 (3.51%)	2 (3.51%)	0 (0%)	1 (1.75%)

[Results of component resolved diagnosis]

Conclusion: Can f 1, although it is the main dog allergen, was sensitizing only 31.58% of dog allergic patients. Most of the patients were monosensitized to only 1 of dog allergen components.

1038
Changes in molecular structure of silver birch pollen allergen in different climatic areas of Ukraine

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Background: Ukraine is the country in Europe which due to the ongoing changes in the climate has 7 climatic zones (De Martonne classes). The major and minor molecular structure of the pollen of the trees growing in different zones can vary. Extracts of the allergens made of raw materials from different regions can differ on component structure that can frame difficulties in diagnostics by a prik-test method. Researches of many European authors showed that diagnostic solutions of allergens for unification of skin testing results have to be standardized, first of all, on the level of major molecular components. This research was the first stage of standardization of diagnostic preparations of extracts of allergens in Ukraine.
Method: In total, 6 samples of Betula verrucosa Ehrh. pollen has been prepared in Vinnitsa, Kyiv, Kharkiv, Lviv, Odessa and Zaporizhzhya regions of Ukraine. Presence of major and minor components was analyzed by electrophoresis (PAGE) method. Expression level of Betv1 gene was analyzed by using of the quantitative real-time PCR.
Results: Six molecular components were found in birch pollens, existence of minor molecular components, as well as quantity of major components, was various in all tested samples.

Regions	Components
Lviv	Bet v1, Bet v2, Bet v3, Bet v6
Odessa	Bet v1, Bet v2, Bet v3, Bet v5
Kyiv	Bet v1, Bet v3, Bet v4, Bet v6
Vinnitsa	Bet v1, Bet v2, Bet v3, Bet v5, Bet v6
Kharkiv	Bet v1, Bet v3, Bet v4, Bet v6
Zaporizhzhya	Bet v1, Bet v2, Bet v3, Bet v6

[Betula allergens mollecular structure]

By results of PAGE analysis sample from Lviv region was chosen as a calibrator for expression analyses. The analysis showed that the levels of Bet v1 expression differ in the samples from different areas. In samples from Kiev and Odessa was the expression of Betv1 allergen in average 1.2 × higher when comparing to the calibrator. In samples from Vinnitsa and Kharkiv area was the expression of Betv1 allergen only 0.60× higher when comparing to the calibrator.
Conclusion: Skin prik test is the 'gold standard' for IgE-mediated reactions. However, differences in an expression of major components in allergenic extracts can be the cause of incomparability of testing results. The various ratios of minor components can lead to two-dimensional reactions. Further researches are necessary for gradual standardization of extracts of allergens for the countries with various climatic conditions as Ukraine.

1039
Test BAT in diagnosis of allergy to hazelnut in patients with birch pollen allergy

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Introduction: Basophiles and mastocites are main effectors cells of allergic reactions. In scientific research and diagnostic the BAT (basophile activation test) is frequently applied. In patients with atopic allergy contact with specific allergen leads to activation of basophiles and the increase of expression on the surface of certain activation markers. Markers can be assessed by flow cytometry method with the monoclonal antibodies linked with fluorochromes.
Aim of the study: The aim of our study was to prove the usefulness of BAT test in diagnostic and assessment of hypersensitivity to hazelnut in patients with primary allergy to birch pollen.
Material and Methods: 15 patients with allergy to birch pollen and cross reactivity to hazelnut took part in the study on the base of medical history, positive skin prick tests SPT with birch extract and the presence of as IgE confirmed in a multiplex allergen test and/or FEIA test. The most frequent symptoms were typical OAS symptoms, nettle rash and dyspnoea. The control group consists of 8 healthy volunteers without atopy with negative SPT test and without asIgE in serum. The measurement of basophiles' activation was conducted using the Flow CAST certified CEIVD according to the producer's instruction. Assessed was the percentage of basophiles with marker expression CD63 on the surface after stimulation with hazelnut allergen from the BAT supplier. Simultaneously, as the positive control the specific monoclonal antibody anti FcεRI and unspecific activator fMLP were used. As negative control we used wash buffer. Analysis was conducted in flow cytometer. The positive results of BAT test was confirmed when the applied allergen had caused the expression on the surface of more than 15% analyzed Ba defined as cells SSC-low CCR3+.
Results: Among the 15 patients examined, positive results of BAT test were confirmed in 11 of them (73.3%) and in one person (12.5% - out of 8 person) in control group.
Conclusions: BAT test is a valuable diagnostic tool for hypersensitivity to hazelnut in patients with cross-reactivity to birch pollen.

1040
The IgE antibody profile patient's with birch pollen allergy

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Background: Birch pollen allergens are in Poland, the second most common cause of symptoms of allergic rhinitis, periodic conjunctivitis and atopic asthma. Serious problems in patients allergic to birch pollen are cross-reactions with foods. So far, basic research in the daily diagnosis of food allergy were skin prick tests and determining the level of allergen-specific IgE. New opportunities assessment for food hypersensitivity, including cross-reactions, provides a molecular diagnostics.
Method: The aim of the study conducted at the Department of Allergology, Clinical Immunology and Internal Medicine in Bydgoszcz was to obtain an IgE antibody profile patient's with birch pollen allergy. The study has enrolled 40 adult patients allergic to birch who showed manifestation of the cross reaction with food. Each of the patients had positive skin tests for birch pollen. The blood of patients was tested by ImmunoCAP ISAC test.
Results: All patients were detected antibodies against Bet v1, the major white birch pollen antigen. Six patients were detected antibodies against Bet v2, and three patients against Bet v4. Also were detected antibodies against proteins PR-10 that could give the symptoms of cross-reactivity: Cor a1.04- 85% of patients, Cor a1.01- 80%, Aln g1- 77%, Mal d 1- 75%,

Pru p1- 63%, Ara h8- 53%, Gly m4- 35%, Act d8- 33%, Api g1- 30%.
Conclusion: All patients participating in the study were detected antibodies against Bet v1, the major white birch pollen antigen. The most common foods that may give cross-reactions are: hazelnut, apple, peach and peanut.

1041
In vivo standardization of *Platanus acerifolia* allergen extract to determine its biological activity in HEP units

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Background: *Platanus acerifolia* was widely planted in European cities because of its tolerance for urban pollution, being now a common ornamental tree in parks and streets in most European and US cities. It is an important source of airborne allergens during the flowering season (peak in early spring), particularly in the Mediterranean area, and its pollen grains have been described as a trigger of seasonal asthma. Since avoidance is often not possible because of natural exposure, a more effective treatment such as immunotherapy could be used to treat this pollen allergy. *P. acerifolia* allergy has evolved dramatically since its first *in vivo* standardization conducted in 1997. *P. acerifolia* allergic patients have increased exponentially, with patients reacting in a different manner and showing *in vivo* values also different compared to that date.
Objectives: The main objective of this study was to perform a new *in vivo* standardization based on the current pathology of allergic patients in order to have a product adapted to their necessities. The secondary objective is Adverse Drug Reactions (ADR) assessment.
Method: *In vivo* standardization of the extract was carried out following a slight modification of the Guidelines by the Nordic Council on Medicines (1989). Concentrations 0.01, 0.1, 1 and 10 mg/ml as well as a positive and negative control were tested simultaneously in the forearm of the 36 enrolled patients. Wheal sizes were measured during the immediate phase. The median of the concentrations of a native *P. acerifolia* allergen extract that elicit by Titrated Skin Prick Test (SPT) a wheal size equivalent to that provoked by10 mg/ml histamine dihydrochloride in the valid patients, corresponds to 10 HEP/ml. This value indicates the *in vivo* biological activity of the *P. acerifolia* allergen extract.
Results: The wheal data of 22 patients (Per Protocol population) were analyzed obtaining that 2.98 mg/ml is the median of the concentration of *P. acerifolia* allergen extract necessary to elicit a wheal size equivalent to that of histamine 10 mg/ml. No ADRs were observed in the 36 patients tested with the SPT.
Conclusion: The biological activity of *Platanus acerifolia* allergen extract equivalent to 10 HEP/ml is obtained using 2.98 mg/ml of this extract. The administration of the study medication by SPT was well tolerated and safe.

1043
Monoclonal antibodies to recombinant Fag e 3 buckwheat allergen and development of a two-site ELISA for its quantification

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Background: Buckwheat has been known as an important cause of anaphylaxis, and Fag e 3 has been known as the key major allergen of buckwheat. However, immunoassay system for the quantification of Fag e 3 has not been developed.
Method: A two-site ELISA was developed using monoclonal antibodies which were produced against recombinant Fag e 3, and applied for the quantification of native Fag e 3 in the total extract of buckwheat.
Results: Four clones of monoclonal antibodies were produced, and all were shown to recognize vicilin allergens not only from buckwheat but also from peanut and walnut. However, ELISA using the antibodies was able to quantify Fag e 3 in the total extract after addition of 1% SDS and heating to facilitate the dissociation of the allergen. The detection limit of the developed two-site ELSIA was determined to be 0.8 μg/ml. Approximately, 12% of buckwheat total extract is estimated to be Fag e 3.
Conclusion: An ELISA system for the quantification of group 3 buckwheat allergen, Fag e 3, was successfully developed. This assay should be useful for standardization of buckwheat allergen standardization and monitoring buckwheat contamination in the foods.

1044
The optimization of diagnosis of allergy to grass pollen in children

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Background: The wide expansion of atopic diseases among children, the importance of high pollen grasses as a sensitizing agent led to necessity for studies of diagnostic examination systems for appointment of adequate therapy. The research of the most relevant allergens for patients to exclude of duplicating and uninformative tests became urgent with the development of a new type of diagnostic tests that does not require high costs equipment. The objective of this research was to evaluate the results of '*in vitro*' - and '*in vivo*' diagnostic examinations of children with various forms of allergic diseases caused by pollen of meadow grasses, and to choose the most important prognostic parameters for the diagnosis.
Method: 277 children aged 4–16 years with various allergic diseases were included in the study. There were performed skin prick tests in patients and determination of levels of specific IgE antibodies to allergen extracts cocksfoot (g3), meadow fescue (g4), timothy grass (g6).
Results: In the study 32–50% of children had sIgE antibodies to grass allergens. There was a close correlation of antibody response on the investigated allergens; quantitative coincidence of sIgE to g3 and g4 allergens levels. sIgE (g6) concentration was close to the sIgE(g3) and sIgE(g4) levels (85.0 ± 21.6%). The analysis of the skin tests results showed that 44% of patients had a positive response to grass allergens, and '*in vivo*'-tests results coincided with serological tests results, but only in a quantitative sense. There was noted the most significant relationship between *in vivo* and *in vitro*-tests in the results of testing with pollen allergen extracts.
Conclusion: Based on these data there was concluded the possibility of using the concentration of sIgE-antibodies to meadow fescue allergens as a predictor of patients sensitization caused by pollen from grasses and to improve allergic diagnostic.

1045
Hypoallergenic skin prick test response of mannan-conjugated polymerized allergens of *Phleum pratense* compared to corresponding native and polymerized preparations

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Background: Allergens polymerized with glutaraldehyde (allergoids) show reduced allergenicity when compared to their corresponding native unmodified allergens. The polymerization process does not affect the immunogenicity of the allergoids. As a result, these hypoallergenic preparations are commonly used in immunotherapy. The conjugation of these allergoids with mannan enhances their uptake by dendritic cells and shows a high degree of *in vitro* hypoallergenicity (specific IgE binding). The aim of this study was to compare the *in vivo* skin prick test (SPT) allergenic response of native allergens (N), polymerized allergoids (POL) and polymerized allergoids conjugated to mannan (PM) of *Phleum pretense*.
Method: The study included 12 patients (5 men and 7 women, median age 34, age range 27–56 years), with rhinoconjunctivitis ($n = 8$) or with rhinconjunctivitis and asthma ($n = 4$) due to hypersensitivity to *P. pratense*. Patients were skin-prick tested with N, POL and PM at a concentration of 35 μg of protein/ml. The area of the wheal size induced by each preparation was measured using PrickFilm and expressed in mm^2. Descriptive results were expressed as the median with the first and third quartiles. Friedman′s test was used to compare the results between the 3 preparations and the Nemenyi procedure was used for pairwise comparisons.
Results: The median value of the wheal size obtained was 44.8 (34.2–67.3) for N, 12.6 (8.0–19.7) for POL and 0.0 (0.0–5.4) for PM. The comparison between the 3 preparations was highly significant ($P < 0.0001$). The pairwise comparisons showed that there were significant differences between PM and N ($P < 0.0001$), PM and POL ($P = 0.038$) and POL and N ($P < 0.038$).
Conclusion: Mannan-conjugated polymerized allergens of *P. pratense* are significantly more hypoallergenic *in vivo*, as measured *in vivo* with SPT, than their respective native allergens and glutaraldehyde polymerized preparations. These results combined with the enhanced uptake of mannan-conjugated allergens by dendritic cells may provide an effective and safe novel immunotherapy.

1046
In vivo standardization of *Artemisia vulgaris* allergen extract to determine its biological activity in HEP units

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Background: *Artemisia vulgaris* (mugwort) is native to temperate Europe, Asia and northern Africa, but it is also present in North America where it is an invasive weed. It is a very common plant growing on nitrogenous soils, like weedy and uncultivated areas such as waste places and roadsides. Its pollination takes place from late July to late August in North-Western Europe and up to 3–4 weeks later in Mediterranean areas. Mugwort pollen is one of main sources of hay fever and allergic asthma in Northern Europe, North America and in parts of Asia. This pollen generally travels only short distance (less than 2 km), therefore tearing this weed is known to lessen the effect of the allergy. As avoidance is often not possible, a more effective treatment such as immunotherapy, could be used to treat this pollen allergy.

Mugwort allergy has evolved since its first *in vivo* standardization conducted in 2001. The main *objective* of this study is to perform a new *in vivo* standardization based on the current pathology and *in vivo* values of allergic patients in order to have a product adapted to their necessities. The secondary objective is Adverse Drug Reactions (ADR) assessment.
Method: *In vivo* standardization of the extract was carried out following the Guidelines by the Nordic Council on Medicines (1989). Concentrations 0.01, 0.1, 1 and 10 mg/ml as well as a positive and negative control were tested simultaneously in the forearm of the 30 enrolled patients. Wheal sizes were measured during the immediate phase.

The median of the concentrations of a native *A. vulgaris* allergen extract that elicit by Titrated Skin Prick Test (SPT) a wheal size equivalent to that provoked by 10 mg/ml histamine dihydrochloride in the valid patients, corresponds to 10 HEP/ml. This value indicates the *in vivo* biological activity of the *A. vulgaris* allergen extract.
Results: The wheal data of 27 patients (Per Protocol population) were analyzed, obtaining that 1.63 mg/ml is the median of the concentration of *A. vulgaris* allergen extract necessary to elicit a wheal size equivalent to that of histamine 10 mg/ml. No ADRs observed in the 30 patients tested with the SPT.
Conclusion: The biological activity of *Artemisia vulgaris* allergen extract equivalent to 10 HEP/ml is obtained using 1.63 mg/ml of this allergen. The administration of the study medication by SPT was well tolerated and safe.

1047
Optimization of determining the cause-significant allergens of weeds in patients with hay fever

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Method: The study involved 316 people aged 18- 54 with complaints of seasonal symptoms of allergic rhinitis (AR), conjunctivitis (AC) and bronchial asthma (BA) in the period of August-September (the period of weed flowering in Odessa region, Ukraine) with the help of *in vitro* IgE diagnostics. There were determined specific IgE to ragweed pollen, mugwort, quinoa, sunflower, the major component of ragweed (w230 - nAmb a1), mugwort (w231- nArt v1), to the major (g213 - rPhlp 1, rPhlp 5b) and minor (g214 - rPhlp 7, rPhlp 12) component of herbs. In addition 126 patients were made skin prick tests with allergens of ragweed and mugwort.
Results: The most important allergen is ragweed and mugwort, sensitization to which have identified in 282 (89.2%) and 89 (28.2%) patients respectively. The reactions are much less frequently observed to quinoa - 39 (12.3%) and sunflower - 28 people (8.9%). The results of the skin prick test completely correlate with the data of laboratory studies. Sensitization to the major component of ragweed was detected in 281 patients (88.9%), to the major component of mugwort - in 88 (27.8%) patients. Combined sensitization to the major components of both allergens was observed in 76 (24.1%) subjects. This sensitization to the major component of the herbs was only found in 5 patients (1.6%), and sensitization to the minor components of herbs only in 6 patients (1.9%).
Conclusion: The most significant allergen in the period of weed flowering in the steppe zone of Odessa region is ragweed and mugwort is significantly less. Almost in all patients sensitization is marked to the major components of these allergens, which allows to use as an optimal diagnostic unit all three indicators during examination: the major component of ragweed (w230), mugwort (w231) and minor component of herbs (g214). Using this diagnostic unit allows to administer allergen - specific immunotherapy with a high efficacy.

Poster Session TPS 29

Air pollution and environmental allergies

1049
The impact of the Medical Indoor Environment Counselors (MIEC) in the management of allergic diseases. A retrospective study of 100 patients

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Background: Medical Indoor Environment Counselors (MIEC) is implemented at the request of the general practitioner or specialist, who believes that his patient's state of health is affected by their home environment. The main objective of this study was to estimate the contribution of MIEC on the care and quality of life of 100 allergic patients, advised and visited at home between 1 January 2013 until 31 December 2013 in the district of St Etienne, France.
Method: During the year 2013, one hundred allergic patients were visited at home by the MIEC. For this study, different data were recorded: data on each home environment, data on each counseling, the medical records of each patient, respiratory functional tests for the group of allergic asthma (35 patients), A rigorous medico-economic analysis was performed to know the impact of the counseling on anti-allergic/ anti-asthmatic drug cost. At the end of the study, a survey by questionnaire was done to appreciate the impact of the MIEC on patient quality of life (QOL).
Results: Functionally, we observed no significant changes in FEV1 caused by the MIEC action in the Asthma groupHowever, questionnaire analysis reported the positive impact of the MIEC counseling on QOL and the cost studies showed a highly significant reduction of anti-allergic/ anti-asthmatic drug cost during the year following the MIEC action. ($P \ll 0.00001$). The study we conducted confirms its positive impact on the quality of life of allergic patients whose triggering allergen was found at the indoor environment.
Conclusion: Medical Indoor Environment Counselors (MIEC): helps to highlight a large number of pollutants and allergens that can have a negative impact on the allergic patient. Further studies will be helpful to confirm the benefit in terms of health but also in economic terms, in order to reinforce the sustainability of the financing of that service.

1050
Outdoor aeroallergens in Georgia: comparative analysis of pollen counts in Tbilisi and Kutaisi

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Background: The number of people allergic to plant aeroallergens has substantially increased in big cities and industrial areas. Thus, monitoring of the pollen counts in the atmosphere of cities is of relevant medical importance. The aim of presented study was to profile the outdoor aeroallergens in Georgia and compare the character of pollen counts in two major cities of Georgia.
Methods: Two Burkard 7-day samplers were located in a two cities: Tbilisi, with climate transitional from humid subtropical to relatively mild continental and Kutaisi, with humid subtropical with a well-defined on-shore/monsoonal flow. Pollen and spores counts were expressed as a daily mean value in number of pollen grains/spores per m^3 of air. Data was obtained in the period of December 2014 - November 2015.
Results: The main tree pollen types for both centers were: *Corylus, Alnus, Acer, Quercus, Fraxinus, Castanae, Carpinus, Pinus, Tilia, Populus, Platanus, Fagus, Ulmus, Juglans, Salix, Cupressaceae* and *Morus*. Comparison analysis had shown that the pollination season of the most trees began earlier in Kutaisi. As an example, the beginning of pollination was 2 weeks earlier for *Corylus* (middle of December in Kutaisi vs beginning of January in Tbilisi) and Alnus (beginning of January in Kutaisi vs middle of January in Tbilisi). The difference in pollen count of particular taxa was observed as well. It was 2–3 times higher in Kutaisi for *Corylus* and *Alnus*, and significantly higher in Tbilisi for *Cupressaceae*, *Platanus and Pinus*. The highest account of tree pollen about 3884 *Cupressaceae* grains in m^3 per 24 h was observed in Tbilisi at the middle of March. Main grass pollen was *Gramineae:* the pollination started a little bit earlier in Kutaisi, but the pollen count was generally higher in Tbilisi. The features of pollen seasonal distribution and amount were revealed also for the weeds (mainly *Ambrosia, Artemiasia, Rumex, Chenopodium)*. Pollen season was similar in both cities; however, the pollen count value was higher for *Ambrosia* in Kutaisi and for *Artemisia* in Tbilisi.
Conclusion: The differences noted in pollen count between two major cities of Georgia may be due to a different composition of local flora and the influence of weather.

1051
A method to evaluate allergenic potential of bee pollen among airborne pollen allergic patients without having to extract allergenic proteins contained in bee pollen

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Background: Bee pollen (BP) is widely consumed but is a dangerous food for allergic patients because of allergenic pollens (AP). Aim is evaluate the allergenic potential of BP using skin testing method.
Method: It is first experimentally characterized relationship between mass of an AP ($Mass_{AP}$) content in BP and the allergenic potential of said AP measured by skin reactivity testing:

$Mass_{AP}$ is identified in BP mass after having calculated the proportion of AP using the BP pollinic spectrum. Spectrum analysis is based on the European standard as recommended by the International Commission for Bee Botany.

Skin reactivity to AP is assessed by measuring wheal diameters (W) from skin prick tests using three serial dilutions of BP on allergic patients to AP, in order to calculate equations of the relationship between $Mass_{AP}$ and skin reactivity.

Then, allergenic potentials of AP (W_{AP}) of a stated dose of BP having several AP, are assessed by:

BP spectrum analysis and AP identifications for $Mass_{AP}$ calculations,

W_{AP} calculations using equations.

Results: Linear functions $Log(W_{AP}) = A\ Log(Mass_{AP}) + B$ ($R^2 > 0.99$) were established using BP samples rich in only one AP. Eg, for Artemisia (A), forage-grasses

(FG), Zea (Z) and Fraxinus (F), functions are respectively: $Log(W_A) = 0.30\ Log(Mass_A) + 0.52$, $Log(W_{FG}) = 0.24\ Log(Mass_{FG}) + 0.33$, $Log(W_Z) = 0.23\ Log(Mass_Z) + 0.14$ and $Log(W_F) = 0.21\ Log(Mass_F) + 0.39$.

Artemisia and FG are the two AP of a polyfloral BP. BP spectrum includes: 34.9% Mercurialis, 18.4% Trifolium, 17.2% forage grasses, 15.9% Matricaria, 4.3% Artemisia, 3.9% Hypericum and 3.6% Melilotus (<1.8% undetermined). Calculated $Mass_A$ and $Mass_{FG}$ are 0.017 and 0.367 mg per mg respectively.

For an 1 g stated dose of said polyfloral BP, calculated W_A and W_{FG} are 7.7 and 8.9 mm respectively.

For a 5 g stated dose, calculated W_A and W_{FG} are 12.5 and 13.1 mm respectively.

Conclusion: The allergenicity of AP of a BP may be deduced of its mass, easily calculated with the pollinic spectrum analysis, and because its allergenic potential measured by skin reactivity is proportional to its mass.

This method makes it easy to evaluate the allergenicity of AP in a stated dose of BP.

1052
Annual incidence and immuno-biochemical study of airborne fungal spores in urban and rural areas of West Bengal, India with special reference to *Aspergillus terreus*

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Background: Airborne fungal spores represent one of the significant components of total airborne species to cause respiratory allergy, asthma etc. Prevalence rate for fungal allergy in local people of up to 30% have been reported from West Bengal, India. The present study aimed to investigate the quantitative and qualitative variations among airborne fungal spores found in indoor and outdoor environments of urban and rural areas of West Bengal and to determine allergenic potency of *Aspergillus terreus* through immuno-biochemical methods.

Method: Aerobiological monitoring was performed using Andersen and Burkard Personal sampler for trapping viable and non-viable spores from the air of Kolkata (Urban) and Habra (Rural), West Bengal. A questionnaire survey and hospitalization data were collected from the local hospitals. Protein from *A. terreus*, dominant aero-spore in the study area was extracted and its allergenecity was determined by SPT, ELISA and histamine release assay. Extract was profiled on SDS PAGE and immuno-blotted using 15 individual sera from *A. terreus* sensitized patients.

Results: Total fungal spore load in the rural area showed higher spore concentrations as compared to the urban area. Indoor air showed lesser spore concentration. The viable spore concentrations were found to be maximum during summer and monsoon season, whereas the non-viable spore concentrations were found to be highest during summer and post-monsoon. Out of eight viable spores, recognised at the time of sampling, *Aspergillus, Curvularia, Rhizopus* were the most dominant species. A total of twenty seven non-viable spores were detected of which ascospores, basidiospores, aspergili/penicilli, *Cladosporium, Curvularia, Drechslera* contributes the maximum concentrations. Nonviable spores like *Aspergilli/Penicilli* and *Cladosporium* were mainly noticed in indoor environments. The survey and hospitalization records were found to be positively correlated with spore load. Histamine release, specific IgE and SPT were also found in higher amount in susceptible patients. SDS PAGE, showed eighteen bands of which seven were found to be IgE reactive. Two dimensional blots revealed six spots as immuno-reactive.

Conclusion: This study will help to determine the presence of the diversified viable as well as non-viable fungal species and their total concentrations in the air of two sampling sites. *A. terreus* is found to be an important aeroallergen.

1053
Effect of benzopyren, polychlorobiphenyl, and toluene diisocyanate to IL-4 production in PBMC sampled in house dust mite sensitized human

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Background: Most epidemiological studies show a significant association between air pollutants and symptoms or exacerbations of allergic diseases. The role of outdoor air pollution in causing asthma remains controversial. This study aim to find out the effect of IL-4 cytokine production to air pollutants in PBMC (peripheral blood mononuclear cell) sensitized with house dust mites.

Method: PBMCs were sampled in 16 asthmatics who sensitized with *D. pteronyssinus* and D. farinae and 12 healthy controls. PBMCs were cultured in RPMI1640 media and centrifuged. 1 × 106 PBMCs were distributed in each wells mixed with autologous patients and healthy control serums incubated for 72 h with PBS (phosphate buffered saline), 2 μl extracts of mixture with *D. pteronyssinus* and *D. farinae* (Allergopharma, Germany), 2 μl benzopyren (BP, 100 pg/ml), 1 μl polychlorobiphenyl (PCB, 10 nM), 1 μl toluene diisocyanate (TDI, 10 mM). IL-4 was estimated by ELISA in each 50 μl supernatants.

Results: IL-4 production was increased significantly in asthmatic PBMC incubated with autologous serum and stimulated with house dust mites and benzopyren, was not in PCB and TDI.

Conclusion: The allergic cytokine response in autologous serum is different to kinds of pollutants. The allergic cytokine reaction direct to PBMC is very trivial. We need more *in vivo* study, especially in Th2 transgenic mouse.

1054
Environmental factor and allergic disease

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Background: Oxidative stress has been increasingly recognized as an important component of allergic disease pathogenesis. The correlation between environmental factors and allergic diseases has been generally accepted, but it has not been well understood how much environmental factors contribute to development and progression of allergic diseases. This study seeks to investigate it by observing the environmental factors around people with allergic diseases and determining MDA content in their urine sample.

Method: 32 cases of clinically confirmed allergic rhinitis (26 children and 6 adults), 17 cases of asthma (6 children and 11 adults), 32 cases of rhinitis combining asthma (8 children and 24 adults, and 34 healthy people as control (19 children and 15 adults) were selected. Lung function and exhaled nitric oxide were recorded; ISAAC questionnaire was filled by all subjects; and urine MDA level was determined. SPSS21.0 was used for data entry and analysis. Measurement data was descriptively analyzed, nonparametric test was used for comparison between groups, and the correlation between environmental factors and disease was analyzed by spearman correlation analysis, $P < 0.05$ was considered statistically significant.

Results: Among the adults, MDA level was 3.62 (0.83, 15.97) in the normal control group, 5.69 (0.14, 11.36) in the rhinitis group, 2.965 (1.18, 8.94) in the asthma group, and 4.79 (3.75, 12.58) in the rhinitis combining asthma group, MDA level was significantly higher in the allergic disease groups than normal; while among the children, no such significant difference was detected: 3.89 (0.83, 9.55) in the rhinitis group, 2.78 (0.42, 8.03) in the asthma group, 5.83 (0.56, 10.45) in the asthma with rhinitis group, and 3.62 (0.83, 15.97) in the normal control group ($P > 0.05$). In addition, MDA level in adult patients with asthma combining rhinitis was significantly higher than those with only asthma.

2. Certain environmental factors, such as living or working near the road where car exhaust is heavy, going to school or work on foot or by bus, are significantly correlated with MDA level .

Conclusion: Polyunsaturated lipids can be easily oxidized in the presence of reactive oxygen species to generate MDA and other end products, This work indicate that MDA can be used as an indicator for peroxidation of lipids in the body and an effective marker of oxidative stress, revealing some correlation between environmental factors and allergic diseases.

1055
Anaphylaxis on skin exposure to grass pollen in an adolescent boy

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Introduction: Anaphylaxis is an acute severe systemic hypersensitivity reaction with symptoms of an immediate allergic reaction and is potentially life threatening. We present a case of anaphylaxis following direct abraded skin exposure to grass pollen during the pollen season in an adolescent boy.

Case report: A 16-year old boy presented with generalized urticaria, hypotension, tachycardia and wheezing in emergency department after a basketball game. Laceration and abrasions were seen on his hands, feet and face. He had not bitten or stung by an insect, and had no unusual ingestions or exposures. The patient had a history of moderate allergic rhinitis during the grass pollen season but not taken a drug. He has no symptoms of asthma, atopic dermatitis, food allergy or exercise-induced anaphylaxis. Successful treatment consisted of ıntravenous saline infusion, oxygen, anthistamine, adrenaline with remission within 1 h. Skin prick test with inhalant and food allergens were negatif but grass specific Immunoglobuline E was 92 Kua/l (Class 5) at follow-up 8 weeks later. Based on the strongly positive clinical history and results of specific Immunoglobuline E tests, it was concluded that the boy had anaphylactic reactions to grass pollen. This patient was gıven an epinephrine autoinjector and avoidance of skin contact wih grass during the summer season was advised.

Discussion: We aimed to emphasize that life-threatening anaphylaxis can be caused by direct exposure of abraded skin to grass in grass pollen-allergic patient with a previous history of allergic rhinits.

1056
Study of the allergenic profile of pollen from *Platanus hybrida* in the city of Evora, Portugal

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Background and aim: Although grasses and olive are the most relevant allergenic species in the Alentejo region, aggravation of allergic symptoms in the early spring, unrelated with those species pollen seasons, has been reported, particularly in urban environment. Plane trees, hence pollen, are highly abundant in the city of Évora, nonetheless allergen pollen profile has not yet been evaluated. The aim of this work was to characterize the allergen profile of pollen from *Platanus hybrida,* one of the most representative species in Evora showing pollination prior to the main pollen season in Alentejo.

Methods: Pollen from *Platanus hybrida* and *Dactylis glomerata* was extracted with ammonium bicarbonate buffer, lyophilized and stored at −80°C until analysis. Protein content was determined by the Bradford method. SDS-PAGE followed by western blot, using allergic patient sera (obtained from the Hospital do Espírito Santo de Evora - HESE), were performed to evaluate the allergen profile of the pollen. Sensitization and cross-reactivity was assessed by solid phase immunoblot.

Results: Half of the patient exhibited sensitization to pollen extracts of *P. hybrida.* Western blot have shown several immunoreactive bands in the Mr 10–90 kDa range. Immunoreactive bands were also observed in the protein profile according to the pI in the pI range 4.0–6.1. Cross-reactivity of *P. hybrida* with *D. glomerata* was found. Although several bands are common to *D. glomerata*, a band with ~50 kDa was observed in *P. hybrida* but not in *D. glometata.*

Conclusion: These results evidenced allergens found in *P. hybrida* pollen. Moreover, cross-reactivity between *P. hybrida* and highly allergenic species such as *D. glomerata* was found which probably contributes for aggravation of pollinosis in the early spring.

Acknowledgments: This work was supported by FEDER through the 'Programa Operacional Fatores de Competitividade – COMPETE' (Strategic projects of ICAAM and ICT 2013–2015).

1057
Correlation between PM2.5 and quality of life of patients with allergic rhinitis

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Background: Allergic Rhinitis (AR) impairs the patients' quality of life and brings heavy economic burden on society. Growing evidences suggest that air pollution is correlated with occurrence of allergy symptoms. Air pollutants, mostly suspended factors including PM2.5, ozone, and nitrogen oxides, may facilitate allergens assessing the immunoregulatory cells, and promote development of allergic symptoms. However, whether PM2.5 level is directly correlated with symptoms of AR patients is unclear. This study aims to investigate the correlation between quality of life of AR patients and PM2.5 level in their surrounding environment.

Method: 1) 37 clinically confirmed AR patients were enrolled in this study, including 24 males and 13 females, aging 20 ± 6.5 years. The subjects were asked to fill in a Rhinitis Quality of Life Questionnaire (RQLQ) every day for a month (31 days), and corresponding PM2.5 levels in their living environment were recorded. Data collection and analysis were performed using the SPSS19.0 software, and the results were statistically described. Correlation between PM2.5 level and severity of AR symptoms was assessed by spearman correlation analysis, $P < 0.05$ was considered statistically significant.

Results: Among the sub scores of RQLQ, eye symptoms [1 (0, 5)] and PM2.5 concentrations (31 (24, 41) $\mu g/m^3$) showed no significant correlation ($r_s = 0.087$, $P = 0.274$); while activity limitation [3(0.6)] ($r_s = 0.236$, $P < 0.001$), sleep problems [1(0.3)] ($r_s = 0.126$, $P = 0.001$), nasal symptoms [4 (2.7)] [$r_s = 0.191$, $P < 0.001$), other

symptoms (3(0.7)] ($r_s = 0.095$, $P = 0.01$), practical problems (3 (0.5.5) ($r_s = 0.151$, $P < 0.001$), emotional problems [0(0.3)] ($r_s = 0.106$, $P = 0.004$) were significantly correlated with PM2.5 level.

Conclusion: PM2.5 level can affect the AR patients' quality of life.

1059
Airborne concentrations of Cladosporium spores in central Spain

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Background: *Cladosporium* is a cosmopolitan genus of fungi that includes species inhabiting in a wide variety of substrates including plants, soils and animals. *Cladosporium* infection can cause considerable economic losses in crops acting as plant pathogens and its spores provoke respiratory diseases and allergenic processes. The aim of this work is to report the dynamic and behaviour of the airborne concentrations of *Cladosporium* spores as well as to study the relation between these concentrations and the meteorological variables in central Spain.

Method: Sampling was carried out in the atmosphere of the city of Ciudad Real (central Spain) during the years 2009 and 2010 using a Hirst volumetric spore trap, following the methodology established by the Spanish Aerobiology Network. Slides analysis were carried out under a light microscope (1000× magnification), with two longitudinal sweeps per slide. Two statistical approach were performed: correlation and regression analysis between concentration spores and meteorological variables such as temperature and relative humidity. It has been considered risk of allergy when the spore concentration exceeds determinate thresholds taking into account the number of days on which this happens.

Results: *Cladosporium* spores constitute one of the most abundant spores in the atmosphere of Ciudad Real. A total of 335 873 spores have been recorded in the period of the 2 years studied representing the 47.74% of the total spores. The presence of spores of *Cladosporium* is constant throughout the year, although they have a seasonal pattern. The highest concentrations were obtained during the spring (June) and autumn (September-October). The correlation analysis show a significant positive relationship between the concentration of spores and temperature and a significant negative relationship with relative humidity. The model obtained to predict the daily concentration of *Cladosporium* spores includes as independent meteorological variables, the relative humidity and the mean temperature of 2 days earlier. The number of days when risk allergy thresholds exceeded 1000 spores/m^3, was 95.

Conclusion: *Cladosporium* spores produce aeroallergens which means a health problem at least during a part of the year. The knowledge of the dynamic of airborne *Cladosporium* spores provides information that can be used to know the periods when the concentrations of spores are higher and to assess the allergy risk.

1060
Smog might exacerbate the severity of persistent allergic rhinitis

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Background: Air pollution was the worldwide problem, and smog was getting worse by worse in china. PM 2.5 might destroy the structure of mucosa of airway to increase the symptoms of the diseases such as asthma. Our aim of the study is to investigate the effect of air pollution such as smog on allergic rhinitis

Method: 65 cases of persistent allergic rhinitis finished the VAS evaluation of nasal symptoms such as nasal blockage, sneezing, secretion and itchy when onset of allergic rhinitis in smog day and the next sunny day. The severity of smog was defined as PM2.5 level which was obtained from the weather report.

Results: the total VAS of symptoms of nasal allergic rhinitis was statically increased with the PM2.5. ($P < 0.05$). The VAS of nasal blockage and sneezing (both $P < 0.05$) were found higher in which smog was much more severe. The OR for the disease severity by PM2.5 was 2.250 (CI 1.1490–4.407).

Conclusion: Smog might exacerbate the severity of seasonal allergic rhinitis.

1061
Change of poaceae pollination season related to climactic factors in the 2 last decades in Vinnitsa, Ukraine

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Background: Grasses are the most important cause of seasonal allergy in central Ukraine. Poaceae pollination has changed over the last decades due to climate modification.

Method: Pollen counts in the years 1999 and 2000 were obtained by gravimetric sampling on three monitoring stations located in Vinnitsa. Pollen collection from 2009 to 2014 used volumetric methods employing a Burkard trap placed at a height of 25 meters above the ground on the roof of a Vinnitsa Medical University building. Samples were taken from March 1 until October 31. In order to establish the main climatic parameters affecting the pollen counts Statistica was used. Correlation between the Poacea pollen count and mean air temperature, dew point, relative humidity, in the years 2012–2014 were analyzed.

Results: Grass pollens include up to 20 genera in Ukraine. Poaceae pollens currently begin and end earlier compared with 1999 and 2000; Poaceae pollen counts for August are very low recently. Grass pollen counts were close to the peak in August 1999 and 2000. Intense grass pollination starts at mid May and ends mid July currently whereas it occurred at the beginning of June 1999 and 2000, 2 weeks later and finished at the end of June, 2 weeks earlier than at present. Poaceae season onset is now the beginning of May, while it was mid May in 1999 and 2000.

Mean air temperature (+ correlation) and relative humidity (- correlation) were the only two parameters impacting Poaceae pollen counts for all 3 years of interest. Dew point positively correlated with the grass pollen count in the year 2013. All reliable Spearman correlation coefficients were at a low level.

Conclusions: The members of the Poaceae Family demonstrate the tendency for early start and end of the season recently compared with 1999 and 2000. The most active grass pollination starts mid May and ends mid July currently, the onset being 2 weeks early than in 1999 and 2000. Mean air temperature (positively) and relative humidity (negatively) correlated with Poaceae pollen counts.

1062
Antihistamines sales correspond to grass pollination in Ukraine

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Background: Tree, grass and weed pollens cause seasonal allergy in Ukraine. Pollen season patterns in Vinnitsa, Ukraine were compared with antihistamine sales seeking a seasonal pattern to antihistamine use.
Method: The database of histamine sales of the largest regional wholesale company was analyzed including sales of tablets, injections, and syrups in 2015. The medications were manufactured in Ukraine, in Europe (Germany, Austria, Belgium, Hungary, Spain, Slovenia, Italy, Latvia) and India.
Results: 56 antihistamines products sold included 34 tablets, 10 syrups, 5 injections, and 7 other preparations. 57% of all sold antihistamines were tablets, 21% - injections, and 9% syrups. Other items constituted less than 1% each. Tablets made in Ukraine were represented in the TOP-10 while 3 of the TOP-10 tablets list were manufactured in Hungary and India. Syrups sold in Vinnitsa region were made in Ukraine and Belgium, injections made in Ukraine, Hungary and Austria, oral drops made in Hungary, oral solutions in Spain, and gels in Germany. Greatest antihistamines sales were in May (13%) and June (14%). The lowest number of antihistamines (3%) were sold in September with 10% sold in March and April. Oral drops were bought in April, May through July, oral solutions in March, May and June and gels in June. This sales mode can be explained by the 2015 intense grass pollen season in Ukraine and low *Ambrosia* pollen counts in 2015 caused by droughts.
Conclusions: Antihistamines sales corresponded with the grass pollen counts in Vinnitsa. Maximal sales occurred in the summer months during the grass season.

1063
Passive smoking is important risk factor of allergic diseases in Korean adolescents

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Background: Smoging and driking are hazard behaviors threaten health in adolescents and influenced to develop allergic diseases. We souight to study the relationship between smoking, drinking and allergic diseases in Korean adolescents.
Method: We uased the data of 2014 Korea Youth Risk Behavior Web-based Survey that 74167 Korean middle and high school students particitipated in. Dependendant variables were bronchial asthma, allergic rhinitis, and atopic dermatitis diagnosed within a year. Independent variables were current cigarett smoking, passive smoking, current drinking and dangerous level of drinking. Multivariate analysis was done to investigate the relationship between smoking, drinking and allergic diseases.
Results: Current smoking was a risk factor of bronchial asthma (BA) (OR 1.4, $P = 0.000$). Passive smoing was a risk factor in BA (OR 1.12 $P = 0.00$), BA treatment (OR = 1.2 $P = 0.00$), allergic rhinitis (OR 1.05 $P = 0.01$) and its treatement (OR1.1 $P = 0.00$). Current drinking was related to only atopic dermatitis diagnosis (OR1.18 $P = 0.00$).
Conclusion: Smoking was a significant risk factor of allergic diseases compared to drinking. The rate of passive smoking was higher than current smoking and was revealed a risk factor of allergic diseases' development. The strategy to prevent passive smoking should be improved and implemented to prevent allergic diseases in Korean alolescents.

Poster Session TPS 30

Learning from the case reports

1064
Venison demonstrated to cause anaphylaxis in a galactose-1,3 alpha galactose-sensitized patient

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In 2009 Platts-Mills and associates reported[1] that some patients presenting with anaphylaxis or urticaria were sensitized to galactose-1,3 alpha-galactose determinant, and they reported that these patients experienced anaphylaxis 2–8 h after ingestion of mammalian meat, including beef, pork, and lamb. Furthermore, they demonstrated that skin tests to these meats were positive in these patients. They also noted that the geographic distribution of this problem suggested the possibility that bites from certain ticks might be the sensitizing event for this rather unique food allergen. Since that initial report, they and others have collected additional data cementing these relationships, both in America and Europe. Spiro reported finding the galactose-1,3 alpha galactose determinant on the thyroglobulins of several species, including calf, sheep, pig, dog, rat, rabbit, guinea pig, and man, but no one has specifically investigated venison. We here report a case who presented to our facility with multiple episodes of anaphylaxis [some sufficiently severe as to lead to loss of consciousness and intensive care unit admission] occurring hours after meals that included venison [the patient was a hunter, processed his own deer, preserving the meat by freezing]. The problem started in mid-summer, at a time when the patient spent the majority of days outdoors in northern Wisconsin, hunting, fishing, and hiking. The total serum IgE immunoglobulin level was normal at 53 kU/l, but his allergen-specific IgE to galactose 1,3 alpha-galactose gave a strong positive response at 7.9 kU/l [performed at Viracor IBT Laboratories, USA]. Skin tests were positive to beef, pork, lamb, and milk, [using commercially available extracts] as well as to venison [done by prick-prick using a sample brought in by the patient from his own stores], but were negative to all other foods tested. Similarly, allergen-specific IgE assays of blood probing 27 condiments, 11 grains, 17 fish, 4 vegetable gums, 9 tree nuts plus the legume peanut, and a panel of inhalant allergens [12 molds, 4 animal danders, both species of house dust mite, and the pollens of 7 trees, 3 northern grasses, and 5 weeds] all gave uniformly negative results. Since avoiding ingestion of beef, pork, lamb, and venison, the patient has experienced no further anaphylaxis or urticarial outbreaks. The patient has always tolerated cow milk, as did half of the patients showing positive skin tests to it in Platts-Mills' report.

1065
Successful desensitization to red meat in an adult patient with alpha-gal anaphylaxis

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Background: Delayed anaphylaxis related to alpha-gal (galactose-alpha-1,3-galactose) found in red meat has recently been demonstrated. We describe the first successful desensitization for beef meat anaphylaxis due to alpha-gal sensitization which may take our current management approach further.

Case: A 21-year-old female patient was referred to our allergy outpatient clinic because of repeating delayed anaphylaxis episodes after eating beef meat. Itchy urticarial lesions 4 h after eating beef meat started when she was 7-years-old. Her allergic reaction to beef meat had a delayed onset of 4–5 h. Her complaints occurred with every beef exposure. Since she was afraid of contamination with beef, she gave up eating all kinds of red meat for 4 years. She and her parents didn't remember any history of tick bites in childhood but she used to play in natural hayfields and may possibly be exposed to tick bites. Her skin prick test with cooked beef revealed positive result. Alpha-gal specific IgE in the serum was 1.5 kU/l. Intradermal test with cetuximab of 1/1000 dilution was found positive (Figure 1). Two days before the challenge test, she had anaphylaxis 5 h after eating chicken which had been cooked in a pan contaminated with beef in a restaurant. Due to this reaction, she was no longer challenged with red meat.

A beef desensitization protocol with 27 consecutive steps, outlined in Table 1, was prepared. The protocol started with beef extract of 10 drops twice daily for two days. On the first day, the patient's arm began to itch 4 h after the first consumption, but she recovered without treatment. No further reactions occurred for the remainder of the procedure. The final amount of 60 g red meat was successfully administered. Skin prick tests with cooked beef repeated 6 months after the treatment was found negative. sIgE to alpha-gal displayed a 7-fold increase (10 kU/l) in 2 months, which is expected in oral immunotherapy.

Table 1 Red Meat Desensitization Protocol

Days Day1 Day2	First dose 10drops*, 10drops	Second dose 10drops, 10drops	Daily cumulative (mg) 20 drops, 20d rops
Day3 Day4	20 drops, 40 drops	20 drops, 40 drops	40 drops, 80 drops
Day5 Days6 to 8 Day9	0.5 mg, 1 mg, 2 mg	o.5 mg, 1 mg, 2 mg	1 mg, 2 mg, 4 mg
Day10 Day11 Day12	4 mg, 8 mg, 16 mg	4 mg, 8 mg, 16 mg	8 mg, 16 mg, 32 mg
Days13 to 15 Day16 Day17	32 mg, 64 mg, 128 mg	32 mg, 64 mg, 128 mg	64 mg, 128 mg, 256 mg
Day18 Day19 Days20 to 22	256 mg, 500 mg, 1 g	256 mg, 500 mg, 1 g	512 mg, 1 g, 2 g
Day23 Day24 Day25	2 g, 4 g, 8 g	2 g, 4 g, 8 g	4 g, 8 g, 16 g
Day26 Day27	16 g, 32 g	16 g, 32 g	32 g, 64 g

*Solution 1: 600 mg meat cooked in 600 ml water (%1) Solution 2: 10 ml solution 1 + 90 ml water (%0.1) 1 ml: 20drops.

Conclusion: To our knowledge, this case is the first example of red meat desensitization in a patient with delayed-onset anaphylaxis to beef.

1066
Thirty years of red meat allergy - a case report

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Background: Delayed anaphylaxis to mammalian meat is caused by IgE to alpha-gal and is often induced by tick bite. It was discovered recently, first description in the literature came 10 years ago, even though the disease existed before. We describe a case of a 55-year-old women who has been suffering from it for 30 years.
Case report: First anaphylaxis with dyspnoe and urticaria occurred after eating meat at the age of 25. Repeated reactions with angioedema, urticaria and diarrhea followed after eating pork kidney and soon after every piece of pork and beef too. She avoided red meat completely for 10 years and then could eat it again safely. After another 10 years it started anew. Symptoms were delayed 5 to 6 h, started with pain behind the breastbone and coughing, followed by itching, urticaria, tachycardia, anxiety, stomach ache, vomiting and diarrhea. Since then she is largely on a red meat free diet. However the red meat does not lead to symptoms regularly. There is strong association with augmenting factors like exercise and NSAID. A severe episode appeared 3 weeks after several simultaneous tick bites by *Ixodes ricinus*.
Method and Results: Specific IgE to alpha-gal (ImmunoCAP, Phadia, Sweden) is very high and shows dynamics with an increase after a tick bite. Some samples had to be diluted for full quantification: 88.4 … (tick bite)… > 100 … 456 … 144 … 209 kUA/l. Specific IgE to pork and beef is currently negative.
Conclusion: We present a case of alpha-gal allergy with 30 years history manifesting as delayed mammalian meat anaphylaxis, with irregular occurrence and strong influence of augmenting factors (exercise, NSAID). This newly discovered type of allergy should be searched for in patients with anaphylaxis appearing without any obvious cause, often during the night, even when association with red meat may not be regular.

1067
The first reported case of meat allergy following a tick bite in the UK

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There is marked interest in the role of Tick bites inducing Lyme's Disease and subsequently Chronic Fatigue Syndrome but they have also been shown to cause allergy to red meat in the USA and Europe. We report the first such case from the UK.

We present the case of a 51 year old man who suffered several tick bites 3 years ago while walking in Richmond Park in Surrey, UK. The patient subsequently complained of a 2 year history of episodes of a widespread urticarial rash which developed 4 to 6 h after he consumed lamb, pork or beef. There was no reaction when consuming chicken, fish or other foods. None of his reactions were accompanied by cardiorespiratory distress. The patient found antihistamines to be helpful in improving his symptoms. There was no previous history of asthma or eczema and the patient was otherwise in good health. The patients' blood tests confirmed a total IgE 132 kU/l and he had positive specific IgE to beef (1.30 kUA/l), and pork (0.55 kUA/l). The result was negative to lamb and gelatine (<0.35 kUA/l) but was significantly positive to alpha gal on pork thyroglobulin (9.44 kUA/l). His tryptase was normal at 1.46 μg/l. Complement C3 and C4 proteins and serum immunoglobulins were also normal.

The patient was been advised to avoid red meat and gelatine derived from pork despite the negative tests from the latter. To our knowledge our patient represents the first case of alpha gal allergy emanating from tick bites unequivocally acquired in the UK.

IgE mediated reactions are nearly always directed at protein antigens. However reactions to carbohydrate moieties are increasingly being discovered. An association between tick bites and red meat allergy has been described over the last several years. It is thought that Tick bites induce an IgE mediated response to the galactose-α-1,3-galactose (alpha-gal) moiety on tick salivary proteins. These IgE antibodies are known to cross react with alpha-gal found on proteins in red meat and resulting in delayed reactions of varying severity; urticarial rashes in some cases and anaphylaxis in others. Alpha-gal reactions are also implicated in allergies to the monoclonal antibody Cetuximab, and it is thought their full role in allergy is not fully understood. Certainly the mechanism for the delay in allergic reactivity after the consumption of meat has not been fully explained.

1068
A case of anaphylaxis to cow′s milk protein after gastrostomy in 22 months-aged child

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Background: Cow′s milk protein (CMP) is one of the most common food allergens in infancy. Allergic symptoms to CMP such as eczema, urticaria, vomiting, diarrhea, or gastrointestinal bleeding usually occur in early childhood, especially in infancy. Anaphylaxis to CMP after gastrointestinal surgery has been rarely reported.
Method: Review of medical records.
Results: Twenty two months-old female admitted for gastrostomy. She was born at 34 + 3 weeks of gestational age with 1.600 g of birth weight. Shortly after birth, she was taken small bowel segmental resection and anastomosis due to meconium plug syndrome. She had been followed-up in pediatric gastroenterology and neurology due to failure to thrive, gastroesophageal reflux, and developmental delay. Previous 24-h pH monitoring showed severe gastroesophageal reflux (GER) and hydrolysed formula could not improve the regurgitation and vomiting and aspiration pneumonia. At the day of admission for fundoplication with gastrostomy, she had had the high-caloric nutrient formula containing CMP for 4–5 times per day via nasogastric tube since 4 months ago. At post-operation day 4, tube feeding was started with same formula she had had. After 2 h from the initial feeding, she suddenly had respiratory distress, desaturation, cyanosis and hypotension. She was thought to have airway obstruction due to mucus secretion and recovered after hydration and respiratory care. The patient was transferred to the department of pediatrics, and we restarted to feed the same formula at post- operation day 5 after confirming recovery from the event. She had urticarias, respiratory distress with stridor and wheezing, and hypotension. On the suspect of anaphylaxis, intramuscular epinephrine, intravenous corticosteroid, hydration, and anti-histamines were administrated. All symptoms disappeared after 30 min. The level of specific IgE (ImmunoCAP) to cow′s milk, α-lactalbumin, β-lactoglobulin, and casein were 3.96, 1.24, 1.16, and 1.62 IU/ml, respectively. The level of serum tryptase was 13.5 ng/ml. We started hypoallergenic milk formula via gastrostomy and there was no symptom.
Conclusion: We reported a case of anaphylaxis to CMP after gastrostomy in 22-months old female.

1069
Anaphylactic reaction after inhalation of Inavir® (Laminamivir Octanoate Hydrate), lactose-containing dry powder inhaler in milk-allergic children

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Background: Lactose is widely used as an inactive ingredient in dry powder inhalers (DPIs) including influenza medications. Although some reports described contamination of lactose with milk proteins in DPIs products, no case reports exist in the literature which report a pediatric patient who developed anaphylaxis after treatment with a lactose-containing anti-influenza DPIs. We describe an anaphylactic reaction following the administration of Inavir® (lactose-containing anti-influenza DPIs) in a pediatric patient with severe milk protein allergy.
Case: A 9 years old boy with severe milk allergy and persistent asthma was maintained on Adoair® Diskus, a single DPI containing both salmeterol and fluticasone. He had continued to receive Adoair® Diskus for several months without any adverse reactions and with good asthma control. He had several anaphylactic reactions from ingestion with a small amount of milk in the past.

He was diagnosed as influenza A and prescribed Inavir® by primary care physician. Immediately after inhalation of Inavir®, he complained of chest tightness, short of breath, cough, and wheezing. Although blood pressure was within normal range, his consciousness was decreased and oxygen saturation was 82% on room air. He recovered with intramuscular epinephrine, corticosteroid, and inhalation of bronchodilator. Skin prick testing was done with the following Results

Inavir® positive, Lactose positive, Laninamivir Octanoate Hydrate negative. Milk specific IgE was 39.6 kU/l. Those results indicated that milk protein contaminated in Inavir® caused his anaphylactic reaction. After this anaphylactic episode, his Adoair® prescription was changed from DPI products to metered dose inhaler products.
Conclusion: Pharmaceutical grade lactose may cause anaphylactic reaction in patients with severe milk protein allergy. Lactose is widely used as drug additives, physicians should take special care not to prescribe lactose-containing drugs in patients with severe milk protein allergy.

1070
Over-the-counter products and food allergy in children

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Background: Food allergy (FA) is an important health problem with high prevalence resulting in considerable morbidity, specially affecting quality of life being usually neglected. Moreover it has high costs in terms of medical care. It is more frequent in the paediatric population, having practical implications on daily routine of children and their caregivers.
Case report: We report a case of an 18 months-old boy referred to our department due to cow's milk allergy (CMA). With reported history of atopic dermatitis since 2 months old, apart from CMA he also had episodes of urticaria after potato soup ingestion. Skin prick test and serum specific IgE were positive to milk (0.99 kUA/l), α-lactalbumin (0.93 kUA/l) and potato (0.39 kUA/l) and negative to β-lactoglobulin and casein. From 5 to 7 months old, parents reported the occurrence of four episodes of facial urticaria and one episode of urticaria of face and trunk accompanied by cough not related to potato or milk accidental ingestion. Extensive daytime routine register was made. At 7 months old, the father only reported the use of an over-the-counter (OTC) gingival gel for tooth eruption pain in all episodes. The gel was brought to analysis to our outpatient clinic (Mitosyl gingival gel®), and it was proven to contain lactoserum proteins. After strict eviction of milk and OTC products with milk proteins no more symptoms occurred. An oral food challenge (OFC) to milk has been made at 18 months and it was negative. Recently an episode of urticarial with angioedema occurred after incidental ingestion of potatoe.
Discussion: This is to our knowledge the first report of a child with episodes of allergic symptoms, one of them moderate to severe, due to exposure of hidden milk proteins in gingival formulas that are commonly used to ameliorate local pain due to teeth eruption in children. We aim to alert for the threat OTC in children with food allergy and the importance of its label reading.

1071
Flaxseed allergy: two case reports

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Background: Flaxseeds or Linseed (*Linum usitatissimum*) is a member of the genus Linum in the family Linaceae. Nowadays it is consumed in several foods for its laxative and cardiovascular properties. Two patients with symptoms by ingestion and inhalation of flaxseed are described.
Method: First case: a 52 year old woman with persistent moderate asthma by allergy to pollen and respiratory infections. She presented two episodes of anaphylaxis after eating muesli and salad which contained flaxseeds and another episode with dyspnea and general malaise when she opened animal food containing seeds (linseed, birdseed, millet and rapeseed).
Second case: A 47 year old woman who presented four episodes of angioedema and facial itching and one of anaphylaxis with the intake of pastries and yoghurt both containing seeds.

Prick and prick-prick test with the implicated seeds in each case, specific IgE (Thermofisher) and *in vitro* study were carried out (Diater laboratory) in both patients. Bronchial challenge test with flaxseed extract was performed in the first case.
Results: In the first case prick-prick and specific IgE were positive for flaxseed and negative for the remainder of the seeds. Bronchial challenge test with flaxseed extract was positive. Prick-prick with flaxseed, sesame, poppy, and pumpkin were positive in the second case and positive specific IgE was detected exclusively for linseed in this patient.

Immunoblotting: a band of 20 kDA in the hydrosoluble fraction (HSF) and bands between 20–18 kDA in the liposoluble fraction (LSF) of the linum extract were recognized in the serum of the first patient.

Bands of 20 and 35 kDA were only recognized in the HSF of the linum extract in the second case.

In addition, bands of 18 and 30 kDA were recognized in the LSF of the sesame extract in the second patient. The oral challenge test with the other seeds remains to be done in this case.
Conclusion: Nowadays it is essential to consider flaxseed as a food allergen. They can cause allergic reactions either by ingestion and inhalation.

1072
A rare food allergy case: anaphylaxis related pomegranate

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Background: The pomegranate is the fruit of *Punica Granatum* tree and belonging to Rosaceae family. LTPs (lipid transfer proteins) have been identified as major allergens in fruits of Rosaceae family. Immediate hypersensitivity reactions to pomegranate have been reported and two different LTPs have been described, (29-kDa and 9–12-kDa allergens).
Case report: A 28 years old female patient developed rhinorrhea, nasal pruritus, facial angioedema, shortness of breath 5 min after ingestion of pomegranate fruit. Physical examination revealed that TA: 100/70 mm Hg, pulse: 150/min, uvula edema, swelling of the tongue, wheezing. Adrenaline (1/1000) 0.5 mg (IM) was administered and allergic symptoms have been regressed in 30 min. Her personal history included seasonal allergic rhinitis for 8 years. Skin prick tests (SPTs) were positive to plantago, olive tree, corn and peanut. Also SPT with fresh pomegranate was positive (6/30 mm, histamin was 6/20 mm). Serum specific IgE levels were measured by EAST technique. The specific IgE value against pomegranate pulp extract was <0.35 kU/l, however we considered the IgE value higher than 0 kU/l as the absorbance detected with the patient serum was higher than the one detected with the control serum (pool of sera from non-atopic subjects), so class 0–1 (between 0–0.35 kU/l). The pomegranate extract was incubated with the patient serum and with an anti-Pru p 3 rabbit serum to assess the pomegranate LTP moleculer weight on the electrophoretic gel. At the rabbit serum which was sensitized to LTP with anti-Pru p3, 28, 19, 14.5, 13 kDa bands were obtained. Also a 14.5 kDa band and a15 kDa band were detected in patient serum. The 15 and 14.5 kDa IgE binding bands detected by the patient serum in non-reducing electrophoretic conditions as well as those detected by the rabbit serum, did not appeared when the pomegranate pulp extract was electrophoresed in reducing conditions (with 2-mercaptoethanol).
Conclusion: All these results together with those published about pomegranate allergens, we think that detected serum specific IgEs against pomegranate LTP 28, 19, 14.5, 13 kDa may be the cause of the clinical allergy symptoms. So, this case might one of the pomegranate allergy caused by LTPs.

1073
Anaphylaxis to honey

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Background: Anaphylaxis caused by honey is a very rare condition but can be serious health problem Usually it is due to cross reactivity with pollen allergy. There are only 4 cases described in the literature with only allergy to honey.
Case-report: We report a case of a 40-year-old female referred to our clinic with suspected allergy to honey. At the age of 36 she had 2 episodes of generalized urticaria 20 min after ingestion of honey (honey cake and a banana with honey) and 1 year after 1 episode of lips and tongue angioedema after an inadvertent contact with one teaspoon that was used to put honey in pancakes. The symptoms resolved after administration of oral corticosteroids and antihistamines. Her physical examination and routine laboratory analyses were normal at admission.

She hadn't a relevant personal history of atopy and neither referred *Hymenoptera* sting hypersensitivity. The patient reported prior ingestion and application of honey for cosmetic purposes with no complaints.

Skin prick tests (SPT) with inhalant and common food allergens were negative. Skin prick-prick tests (SPPT) where performed with one honey that she was eaten and 8 other varieties which are frequently consumed in our country. The results were positive for all. Thirty minutes after carrying out the SPPT, the patient presented with anaphylaxis: generalized urticaria, swollen of lips-tongue-uvula and an hypotension. Adrenaline was administered with sussess and she remained was on surveillance for 24 h.

SPT and intradermic tests with bee venom were negative. Serum total IgE-98 kU/l; specific IgE to honey 1.1 kU/l. Specific IgE to *Apis mellifera, Vespula* species were negative.

SDS- Immunoblotting assay using honey, bee venom and various pollen extracts with as solid phase was carried out. The only positive inhibition was with the honey (66 kDa).

The patient was informed about honey allergy and the importance of honey avoidance. Adrenaline autoinjection kit 0.3 mg was prescribed and the patient was educated for its usage. Until now, she has been asymptomatic.
Discussion and conclusions: Only a few adult cases have been reported about anaphylaxis occurred by honey. We could not find any sensitivity to pollens and bee venoms in our patient. To the best of our knowledge this is the first adult who had anaphylaxis caused by honey in the SPPT and confirmed by immunoblotting.

1074
Allergy to oregano in children

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Background: Food allergy (FA) is defined as the occurrence of a reproducibly adverse reaction up on exposure to food due to an underlying specific immune response. It affects up to 8% of children. Moreover it has been proven that food allergy negatively impairs quality of life.
Case report: We present a case report of a 10 years old boy with asthma and allergic rhinoconjunctivitis since 6 years old, sensitized to house dust mites. At 9 years old, he had 3 episodes of generalized pruritus, stridor and peripheral cyanosis after meals, months apart from each other. In all episodes spontaneous recovery occurred. The mother reports that in two meals he had french fries and hamburger with tomato and cheese and on the third he ate snails. Afterwards he had eaten all referred foods, except snail, without any reaction. There was no previous history of food allergies. After extensive and detailed inquiry about other possible food ingestion that were common in all episodes, and after questioned about eventual use of spices or seasonings, the mother figure out that in all episodes, oregano has been used as condiment or seasoning that he usually didn't ate. Skin prick tests (SPT) (Bial-Aristegui, Bilbao, Spain) were positive to house dust mites and to snail and negative to oregano. Prick by prick test with fresh oregano was positive (wheal size: 6 × 4 mm). Prick tests with fresh oregano have been performed in 10 healthy adult controls, being negative. Specific IgE (UniCAP®, Thermo Fisher Scientific, Uppsala, Sweden) were negative to snail, oregano, grass and Derp 10. Oral challenge test to snail was scheduled.
Discussion: FA could be sometimes challenging because in some cases reactions may occur without an immediate identification of the associated culprit. Moreover,

we should bear in mind that in western countries there are several processed foods that have spices and seasonings in their composition, such as sesame seeds, nuts and aromatic spices, and in Mediterranean countries it is very common to use some condiments such as oregano.

Conclusion: With this case report we aim to describe the first report on allergic reaction to oregano (*Origanum vulgare*) in children pointing the importance of a proper inquiry and clinical suspicion.

1075
Should we fear food?

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Background: Anaphylaxis is defined as a severe systemic, life- threatening reaction, produced as a result of mediators released from the mast cells and basophils. Degranulation occurs following exposure to an allergen to which the patient is already sensitized.

Anaphylaxis usually affects simultaneous the cutaneous, respiratory, cardiovascular and gastrointestinal systems. The skin or mucous membranes are involved in almost all cases.

Case presentation: We present the case of a male patient, 44 years old, who comes to allergy service for a reaction of anaphylaxis with shock and cardio-respiratory arrest, which required cardiopulmonary resuscitation, 2 weeks prior to the presentation. The reaction occurred in the morning, after eating watermelon, white sesame′s seeds sticks and honey, within half an hour.

The patient has no personal or family history of atopy, no associated pathology. At the time of the presentation, he already consumed again sesame's seeds, but a small amount, mixed with other foods without any allergic reactions.

Patient history ruled out other possible causes: other foods, alcohol, drugs, insect bites, exercise, occupational allergens, exposure to latex. Mastocytosis was excluded, serum tryptase was within normal limits; clinical examination was normal, and common laboratory investigations were also normal.

Specific IgE for sesame, honey and watermelon were negative, but the patient had received the recommendation to avoid them. The specific IgE to pollens, possible to contaminate honey, were negative. No sensitization to tree nuts or peanuts was detected. The patient received emergency kit recommendation with self-injectable epinephrine, antihistamines and oral corticosteroid.

Within 2 months the patient presents to declare that he consumed again sesame sticks, this time as a single food, and within minutes he experienced generalized urticaria with angioedema.

Conclusion: The culprit may be an allergen that is the core of sesame's seed, and when chewing was better because of greater quantity, the allergen was exposed to the mucosa, developing anaphylaxis. This case shows the limitations of laboratory investigations, the complexity of food allergy and the increased incidence of severe food allergies, even in adults.

1076
Allergy reactions caused by cherry ingestion

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Background: Cherry (*Prunus avium*) is a fruit belonging to *Rosaceae* family. *Rosaceae* fruits may cause two allergic clinical patterns: oral allergy syndrome and systemic reactions habitually caused by lipid transfer protein (LTP) or thaumatin-like proteins. Clinical manifestations due to sensitization to cherry are rarely described, and most described cases corresponded to the oral allergy syndrome.

Patient and methods: Case 1: A 37 year-old male patient experienced generalized pruritus, erythema and hives and edema in the face, lips and tongue with difficulty in speaking 3 h after eating some cherries. He progressively improved after treatment with adrenaline and corticosteroids. He had been previously diagnosed with rhino-conjunctivitis and oral allergy syndrome caused by peach.

Case 2: A 15 year-old woman experienced pruritic hives of widespread distribution 30 min after eating some cherries. Lesions improved within a week without treatment. She has also been diagnosed with rhino-conjunctivitis and asthma and oral allergy syndrome caused by nuts.

Skin prick test (SPT) were performed with common allergens (mites, pollens, moulds and epithelia), profilin, LTP and different foods. Immunoblotting under reducing conditions (with 2-mercaptoethanol) with cherries were realized with both patient sera. Total IgE and specific IgE against *prunus avium* were determined in one of the patient.

Results: Case 1: SPT were positive with *grass* pollen, LTP, peach and cherry and negative for the rest of neumoallergens, profilin and other fruits. SDS-PAGE immunoblotting showed weak recognition IgE binding bands about 25 kDa similar to thaumatin, previously described as Pru av 2.

Case 2: SPT were positive with *salsola, olea, chenopodium, fraxinus* and *betula* pollen and with almond and hazelnut and negative with cherry. Total IgE was elevated (1124 IU/ml). Specific IgE to cherry (*prunus avium)* was positive (26.2 kU/l). SDS-PAGE immunoblotting showed various IgE binding bands. One 12 kDa could correspond to LTP, that in the case of cherry was described as Pru av 3. Another band of 25 kDa could correspond, as previously mentioned, to thaumatin-like. Two bands about 55 and 70 kDa may be due to cross-reactivity with carbohydrate determinants.

Conclusion: We report two infrequently cases of IgE-mediated hypersensitivity due to cherry ingestion, confirmed by skin test and *in vitro* test. By immunoblotting we identify various IgE binding proteins with different molecular mass.

1077
Recurrent anaphylaxis in LTP allergy patient - a case report

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Background: Lipid transfer proteins (LTPs) are plant panallergens, clinically relevant mainly as food allergens. The contents of LTP depends on the maturity, storage conditions and cultivation of fruits and vegetables.

Methods: Patient, 39 year old female, was admitted, in December 2014, to the Department of Allergology, Clinical Immunology and Internal Diseases due to recurrent anaphylactic reactions gathered with food allergy. First symptoms of allergy appeared in patient in 2003 during pregnancy, when she experienced topic dermatitis. In April and June 2014 she experienced 4 prophylactic reactions in the form of swelling of the upper and lower extremities, eyelid and lips edema, Disney and increased heart rate. Symptoms occurred probably after eating peach, sunflower seed and poppy seed.

During diagnostics patient had skin prick tests (SPT) with food and inhalatory allergens and spirometry. We also established the concentration of IgE against peach, apple, rye and wheat flour and the level of IgE against allergen components using microarray technique ImmunoCap ISAC.

Results: SPT were positive to weeds allergen extract, birch, cat dander, strawberry, rye and wheat flour. The concentration of asIgE was elevated against peach (2.02 IU/ml) and wheat flour (1.38 IU/ml).

In ImmunoCap ISAC we found elevated levels of asIgE against rAra h 9 (peanut, 7 ISU-E), rCor a 8 (hazelnut, 2 ISU-E), nJug r 3 (walnut, 4.7 ISU-E), rPru p 3 (peach, 6.3 ISU-E), nArt v 3 (mugwort, 1.4 ISU-E), nOle e 7 (olive, 1.4 ISU-E), rPla a 3 (plane tree, 3.4 ISU-E). All of the above allergen components belong to the LTP protein family.

Conclusion: Results of component resolved diagnosis, with elevated level of IgE against multiple LTPs from independent allergen sources enables to diagnose LTP syndrome. Pru p 3 is considered a marker of LTP syndrome. Knowledge of clinical pattern of allergy may help our patients understand their disease and prevent life-threatening anaphylactic reactions.

1078
Oat-induced anaphylaxis

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Introduction: Cereals are seeds obtained from grasses such as wheat, rice, barley, oat, rye, and maize. They are commonly consumed as part of the daily diet. Common oat (*Avena sativa*) has been reported to cause non-immunoglobulin E (IgE)-mediated reactions, namely food protein-induced enterocolitis syndrome. Percutaneous sensitization to oat used in emollients/moisturizers has also already been reported, both in the form of allergic contact dermatitis or urticaria. To our knowledge, only two reports of anaphylaxis were published, none of them in the elderly.

Case report: A 73 year-old male with a history of arterial hypertension, type 2 diabetes, dyslipidemia and benign prostatic hyperplasia was referred to our outpatient clinic. He had had one episode of anaphylaxis (generalized urticaria, angioedema, dyspnea, nausea and hypotension without loss of consciousness) seconds after the ingestion of four breakfast biscuits. Until this episode he regularly ate bread and biscuits containing several types of cereals, as well as peanut and tree nuts, without any reaction. He called the emergency telephone number and was assisted minutes later, having been medicated with systemic cortisteroid and antihistamine and taken to the Emergency Department, where he was further given adrenaline, with good response. We performed skin prick tests, which were positive to oats (12 mm), wheat (9 mm), rye (7 mm), maize (7 mm), hazelnut

(7 mm), sunflower seeds (6 mm), walnut (5 mm), barley (4 mm) and peanut (3 mm). Serum specific IgE (ImmunoCAP, Phadia, Thermo Fisher Scientific) was strongly positive to oats (25.2 kUA/l), but also positive to wheat, hazelnut, rye, barley, walnut, maize, sunflower seed and peanut (all inferior to 5 kUA/l). Since the episode he had already eaten bread and biscuits containing several types of cereals except oat, as well as peanut and tree nuts, without any reaction. Food challenge test to oat carried a risk of anaphylaxis for the patient, so it was not performed.

Conclusion: The clinical history as well as the strong positivity of the skin prick tests and serum specific IgE to oat led us to the diagnosis of oat-induced anaphylaxis. The patient was advised to use the adrenaline auto-injector and go to the Emergency Department in case of accidental ingestion. To date no oat allergens have been sequenced and characterized for the International Union of Immunological Societies (IUIS) allergen database.

1079
Anaphylaxis to soy protein isolates present in hyperproteinated dietary supplements

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Background: Soy protein isolates can be found in various foods such as protein bars, meal replacement shakes, dietary supplements, among others. Hyperproteinated dietary supplements are increasingly being consumed either for weight-loss programs or in athlete's diet.

Method: Two case-reports of severe allergic reactions after intake of dietary powder supplements are described.

Results: The two patients were consuming hyperproteinated dietary supplements in the setting of weight-loss diets. The powders were labelled as containing respectively 40% and 41.2% soy protein isolates. Both patients had known rhinitis and asthma related to birch-pollen allergy. One had oral allergy syndrome to apple and soy milk. They both reacted immediately and severely (urticaria, angioedema and asthma) after the first intake of the powder, leading them to seek medical care at emergency room. Intravenous corticosteroids and bronchodilator were administered without need for adrenaline injection. The reactions occurred beyond the birch pollen season.

Conclusion:

1 Birch sensitized patients can be affected by severe cross-reactions to soy protein isolates present in dietary powders rich in proteins, via Gly m 4 sensitization. This information could be important in case of unexplained reactions in birch allergic patients but also for food allergy education in birch allergic patients sensitized to Gly m 4.
2 Those dietary supplements contain more Gly m 4 than soy milk or tofu.

1080
Severe food allergy to water chestnut - water caltrop (Singoda flour): a case report

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Background: We report a rare case of a 37-year-old man with oral allergy symptoms, the feeling of a lump in the throat, nausea, abdominal cramps, vomiting and urticaria. The symptoms started minutes after intake of legumes battered in water chestnut (Singoda) flour and evolved over the next 1–2 h. The subject had experienced two severe reactions after eating water chestnut products as described and probably more with abdominal pain only. He suffered from birch, grass, cat, dog and house dust mite allergy with positive skin prick and Specific ImmunoCAP IgE tests with seasonal rhinitis and mild perennial exercised induced asthma but no other medical history of allergic reaction to other foods.

Method: Food challenge, skin prick test, ImmunoCap and ISAC tests, Histamine Release test, SDS-page and Immunoblot.

Results: Open titrated food challenge was positive after ingestion of 1.5 g of a Singoda flour-water-salt pancake. We obtained a positive prick-by-prick test (22 × 11 mm), a positive Histamine Release test (>20 ng/ml) and a specific IgE ImmunoCAP test (14.8 kU_A/l) with Singoda flour. SDS-Page followed by immunoblotting revealed specific IgE antibodies against a 26 and 28 kD antigenic band. Specific ImmunoCAP IgE and ISAC tests were positive to birch and hazelnut with related PR-10 proteins, to grass (21 kU_A/l, rPhl-p-5 = 20 ISU-E) and to house dust and storage mites (*Der. f.* 10.8, *acarus siro* 0.6, *lepidoglyphus destructor* 0.7 kU_A/l, rDef-1,2 and rDer-p-1,2 = 7–11 ISU-E). Negative ImmunoCAP ISAC tests to tropomycin-, LTP-, traumatine-

like-, profillin-, CCD- and polcalcin proteins. Skin prick tests and/or Specific ImmunoCAP IgE tests to common food allergens, several seeds, cereal products, glass wort, tiger nut and grain Weevil was negative. Histamine Release urticaria test was negative and total IgE was 173. Serum-tryptase was normal (2.8 μg/l) before and after provocation.

Conclusion: To our knowledge this is the first case presented with food allergy to water chestnut also called water caltrop (*Trapa natans, T. bicornis* or *T. rossica*). Water chestnut is widely used as a raw food, boiled or dried and ground to flour in Asia, Australia, tropical Africa and islands of the Pacific and Indian Oceans. It is rich in carbohydrates, gluten free and considered as a 'safe' food for allergic subjects. Allergy to water chestnut may be under diagnosed. Water chestnut should not be confused with the unrelated Chinese water chestnut from the sedge *Eleocharis dulcis*.

1081
Allergic reaction to tower cress (*Arabis turrita*), a wild plant

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Background: Allergic reaction after ingestion of wild plants are anecdotally reported. However, in some specific areas, culinary uses of some wild plant species is the traditional and still widespread. Here we report the clinical case of a patient who had an allergic reaction after having eaten Tower Cress (*Arabis turrita*), a wild plant used for some traditional sicilian dishes.

Case report: A 18 yo. man without any known suspect allergy apart from labial pruritus after ingestion of peach (fruit that has been excluded by his diet some years ago) refers to our Allergy Outpatients′ Clinic for an acute episode of diffused urticaria, eyelid angioedema and dyspnoea after about 20 min from having eaten a pasta with *ricotta* cheese and Tower Cress. Skin prick tests with common food allergens were positive for walnut, hazelnut, peanuts, almond, soybean, maize, wheat, peach, kiwi and beans. Prick-by-prick with a Tower Cress′ leaf and with broccoli (food of the same botanical family of *Arabis turrita*, the *Brassicaceae*) resulted both strongly positive. Specific IgE dosage for recombinant plant foods allergens showed a strong positivity for the Lipid Transfer Proteins (LTPs) Pru p3 and Cor a8.

Conclusion: To our knowledge, this is the first reported case of allergic reaction due to Tower Cress (*Arabis turrita*), a wild plant frequently used for culinary purposes in the central areas of Sicily. The finding of sensitization to LTPs may lead to speculate that a variant of this allergen may be involved in the described reaction.

1082
Reactions to shrimp including severe anaphylaxis upon oral food challenge in patients with asthma who have never eaten shrimp: clinical relevance of cross-reactivity among invertebrate tropomyosins

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Background: Immunologic cross-reactivity among shrimp, mites and cockroach has been demonstrated, and it is thought to be due to IgE responses to shared allergens, particularly tropomyosin. However, the clinical implications of this immunological cross-reactivity are largely unknown. Our aim was to study IgE responses to tropomyosin and to perform oral shrimp challenges in mite and cockroach allergic patients who had never eaten shrimp.

Method: Four patients with well-controlled asthma (35–58 years-old, one female), allergic to mites and cockroach, who had never eaten shrimp, other crustacean and mollusk, underwent double-blind, placebo controlled food challenge (DBPCFC) with shrimp to a cumulative dose of 5.1 g, followed by an open challenge with a cumulative dose of 20 g of shrimp after 1 week. For DBPCFC, shrimp was given in a mixture of hazelnut cream, oat flakes, milk ice cream, chocolate and vanilla. Total IgE and IgE to shrimp and Pen m1 allergen tropomyosin were measured by ImmunoCAP, and IgE antibodies to shrimp tropomyosin, sarcoplasmic calcium binding protein and arginine kinase (Pen m4 and Pen m2 allergens, respectively) were investigated by ImmunoCAP ISAC.

Results: All patients had positive skin tests to shrimp, and 3/4 were strongly positive for IgE to shrimp and to shrimp tropomyosin (IgE to Pen m1 ranging from 31.7 to 64.7 kU/l). None presented symptoms upon DBPCFC with shrimp. However all three patients with IgE to shrimp tropomyosin presented reactions on the open challenge. One patient had mild oral allergy syndrome requiring no treatment; one patient had mild urticaria which resolved with IV antihistamine and corticosteroid. The third patient, a 58 year-old woman, presented with severe life-threatening anaphylaxis, 10 min after ingestion of the cumulative dose of 20 g of shrimp on the open challenge. She presented with urticaria, abdominal pain, nausea, vomiting, severe dyspnea with generalized wheezing, and progressed rapidly to respiratory failure, despite prompt treatment including epinephrine, requiring endotraqueal intubation and ICU admission. She evolved to a favorable outcome, with discharge from ICU within 48 h.

Conclusion: Our results suggest that IgE sensitization to mites and cockroach primarily through the respiratory tract, leading to allergic inflammation and asthma, could induce cross-sensitization to shrimp, in a way that ingestion of shrimp could potentially lead to life threatening systemic allergic reactions.

1083
Anaphylaxis caused by Anisakis

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Background: Anaphylaxis is a rapid-onset severe allergic reaction that can be potentially fatal, and can worsen by a series of well-defined risk factors as well as re-exposure to allergens involved in previous anaphylaxis episodes.

Anisakis is a genus of parasitic nematodes, which have life cycles involving fish. Their larvae pose a health risk to human. They are infective and can cause allergic reactions, including anaphylaxis, after eating fish that have been infected with Anisakis species.

Method: Desing: Case series of 2 patients with recurrent anaphylaxis Ages: 25 and 56 years both females.

Scope: Allergy service, Hospital Central de la Defensa, Madrid.

Period: December 2015.

Main variables assessed: demographic and allergologic workup (clinical variables, diagnostic criteria, treatment, evolution).

The patients have given written informed consent for the publication research.

Results: Both patients were attended the emergency service with hives (urticaria)-angioedema, nausea and abdominal pain, hypoxia and hypotension after handling and eating raw fish. They were treated with corticosteroids and antihistamines, being necessary the use of fluids and oxygen therapy. They were hospitalized in the Allergology Service. Over the past year, both had experienced several mild anaphylaxis

episodes (3 and 5 respectly) After one patient was admitted she had a neurological deterioration and recived adrenaline im. three times. The allergologic study in both cases reveals sensitization to Anisakis by skin-prick test and detection of specific antibodies against 20–40 ku/l ImmunoCAP. The serum showed tryptase 35–45 μg/l.

Conclusion: Anisakis simplex should be taken into account in sensitized patients with a high risk of recurrence. Allergen avoidance is the main treatment. However, sometimes patients eat non infected fish, thus reducing their awareness about the risk of anaphylaxis in subsequent fish ingestions. It should be considered an individual emergency action plan with indications for self-injectable epinephrine identification and avoidance of allergens like Anisakis.

1084
Food allergy vs Wilkie syndrome

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Background: Clinical manifestations of food allergies can vary widely, which can complicate early diagnosis and present a problem when making a specific diagnosis with regard to other illnesses with similar symptoms.

Method: A 14-year-old girl, with no prior relevant medical conditions, presented with epigastric pain radiating towards the upper right quadrant, nausea and postprandial emesis episodes. No fever. Asthenia and weight loss of 2 kg in 1 month. The patient was admitted several times to the accident and emergency department where no notable physical symptoms were determined except pain on palpation of the abdomen, with no muscular defence, with preserved peristalsis, Blumberg's and negative percussion. Test readings were normal at all times (CRP, ESR, hemogram, liver enzymes, urea, creatinine, amylase), as were the x-ray and abdominal echography. There was no clinical analysis with the ingestion of any specific food. Treatment with proton pump inhibitors and antacids was prescribed, with no response.

Given the persistence of the symptoms and the family history of atopy (the mother suffers from asthma and the sister from hay fever), the patient was referred to the allergy department to rule out food allergies. Skin tests were carried out for different foods (eggs, milk, fruits, nuts, meat, fish, flours, spices, anisakis, LTP, profilin), and analyses were requested (total IgE and allergen-specific IgE).

The results showed a digestive problem, for which specialists requested anti-transglutaminase antibodies, anti-endomysium, anti IgA anti-gliadin, upper GI endoscopy, and abdominal CT scan with contrast.

Results: Total IgE 106 IU/ml. Allergen-specific IgE: undetectable. The CT scan showed a decrease in the aortic-mesenteric distance and a < 25° reduction of the angle between the vessels, which radiology points to Wilkie syndrome. Endoscopy: No findings. Celiac disease and lactose intolerance were ruled out.

Conclusion: Although rare, when these symptoms of unspecific abdominal symptoms and weight loss present in young females of low weight, this syndrome should be considered, even when patients are referred in order to rule our food allergies. Diagnosis is usually by exclusion, especially in cases of chronic symptoms. In this particular patient weight gain improved the symptoms (avoiding the need for surger).

1085
Pine mouth syndrome

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Background: Pine nuts can trigger dangerous allergic reactions. Of all reported cases, severe anaphylactic reactions account for the majority of the described reactions. Pine nuts allergy appears to be characterized by low cross-reactivity with other nuts and by a high proportion of monosensitization. However, there is a non-IgE mediated syndrome associated with pine nut intake: ¨Pine Mouth Syndrome¨, described as a food adverse reaction, different from a classic allergy. One of the abnormalities is a remarkable decreased appetite and enjoyment with food, not causing itching, dizziness or hives. Patients with this syndrome describe a persistent metallic or bitter taste within 48 h of eating pine nuts that can last for up to 2 weeks. Symptoms are self-limiting, with no adverse health effects. Both raw and processed pine nuts have been implicated in the syndrome. No mechanism has been described for pine mouth syndrome, and no pine nut compounds have been considered the cause of the disturbance.

Method: A 35 year-old female patient, previously diagnosed with non-allergic asthma and rhinoconjunctivitis, presented a burning sensation of the tongue that disappeared without medication some hours after eating cod, raisins and pine nuts. Two days later she ate again the same foods presenting a burning mouth sensation and bitter taste that persisted for several hours without any other associated respiratory, digestive or cardiovascular symptoms. Days later she again ate cod without presenting any symptom. Skin prick test (SPT) were performed with profilin and LTP and different foods, including white fish, nuts and fruits. Prick-prick was realized with pine nuts and raisins. Specific IgE against pine nut and raisin was determined. The patient refused to perform oral challenge test with involved food.

Results: SPT were negative for all the allergens tested. Prick-prick with raisin and pine nut were also negative. Specific IgE against pine nut and grape was negative.

Conclusion: We report a probable case of ¨pine mouth syndrome¨ caused by pine nuts ingestion in a patient with a negative food allergy study. This diagnosis has been realized by a suggestive clinical pattern. The etiology of this syndrome is unknown but it has been suggested that decomposing lipids from the seed can cause symptoms, although the role of seed contaminants in the syndrome has not yet been investigated.

1086
Is it really Eosinophilic esophagitis? - a reflection over 3 pediatric cases

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Introduction: Eosinophilic esophagitis (EoE) is an antigen-mediated disease of the esophagus frequently diagnosed in childhood. The diagnosis of EoE depends on the exclusion of other causes of esophageal eosinophillia, namely gastroesophageal reflux disease (GERD) and the most recently described PPI-responsive esophageal eosinophillia (PPI-REE). We present 3 pediatric cases of EoE diagnosed (with normal 24 h esophageal pHmetry) according to the 2007 consensus, before PPI-REE had been recognized as a new differential diagnosis.

Case 1: An 18 months old infant was referred to our hospital with failure to thrive. As well as EoE, he also presented IgE sensitization to egg. Egg avoidance and PPI were started with clinical and histological remission. At 3 years old, while on an egg-free diet, EoE relapsed, ensuing therapeutic switch to topical fluticasone (500 μg bid), achieving remission. At

6 years old, after a new relapse, treatment with lansoprazole 30 mg bid was started, achieving clinical and histological resolution.

Case 2: A 2 year old boy was referred due to recurrent vomiting. Diagnosis of EoE was made and remission was achieved with topical fluticasone, after combined egg avoidance and standard PPI had failed. A new relapse was diagnosed at 8 years old. Treatment with esomeprazole 20 mg bid was initiated, achieving remission.

Case 3: A 15 month old boy with a past history of corrected esophageal atresia was referred with diagnosis of EoE after complaints of food impaction. Skin prick tests were positive for egg white and yolk. Inital treatment with egg avoidance and PPI was initiated without improvement. Topical fluticasone achieved clinical and histological resolution. Relapsing disease was diagnosed at 5. Clinical and histological remission was achieved after a trial with esomeprazole 20 mg bid.

The three patients still remain asymptomatic under PPI treatment.

Discussion: PPI-REE is an emerging cause of esophageal eosinophilia. A treatment regimen with a high dose PPI, despite normal pHmetry, is mandatory to confirm this diagnosis and rule out EoE. As described recently in adults, in this small pediatric series clinical and histological remission of esophageal eosinophilia was achieved in the same patient, whether with high dose PPI or the usual treatment for EoE (diet or fluticasone). It sounds plausible we may be not talking about different diseases, but only different manifestations of a pathology with a wide spectrum of presentation range.

1087
Was bee venom immunotherapy a trigger for eosinophilic esophagitis?

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Background: Venom-specific immunotherapy (VIT) is the treatment of choice for patients with IgE-mediated systemic allergic reactions (SARs) after developing Hymenoptera venom allergy. Pre-treatment with humanized anti-IgE antibodies (omalizumab) is effective in patients with repeated SARs to VIT. Previous case reports suggested that eosinophilic esophagitis (EoE) might develop as a long-term complication in children after completion of oral immunotherapy.

Method: A 31-year-old female social worker with a history of anaphylaxis, grade 4 (Mueller), to bee stings since 2011; positive bee skin prick tests [SPT] (10 μg/ml) and positive intradermal tests (0.001 μg/ml) and sIgE *apis mellifera* >100 KU/l; had several SARs during the maintenance phase of bee VIT. In March 2013, she underwent VIT with pre-treatment with omalizumab for 6 months and since then she has tolerated VIT with occasional local reactions (especially during the premenstrual phase). One year later, she complained of recurrent episodes of retrosternal pain and dysphagia for solid foods requiring her to drink abundant liquids during meals. She had no previous history of gastrointestinal symptoms.

Results: Upper endoscopy showed rings and longitudinal red furrows and confluent whitish exsudates in the proximal and the distal esophagus. Biopsies from these lesions revealed a predominantly eosinophilic inflammation with a peak infiltration of >15 eosinophils per high power field, which confirmed the diagnosis of EoE. SPT to milk, egg, soy, wheat, peanut and nuts, fish, crustaceans and cephalopods were all negative. Due to the risk of SARs with bee stings and the fact that her husband is a beekeeper, we decided not to discontinue VIT. She initiated the six-food elimination diet (SFED), which led to complete resolution of the dysphagia within 2 weeks, without any other medical intervention. A follow-up endoscopy 6 weeks after the SFED demonstrated macroscopic improvement. Biopsies from the proximal and distal esophagus revealed mucosa with rare inflammatory cells without any eosinophilic inflammation. She was still undergoing VIT during the SFED, so this improvement may be a confounding factor.

Conclusion: This is the first case report demonstrating venom immunotherapy as a possible trigger for eosinophilic esophagitis in an adult patient.

1088
A case of eosinophilic esophagitis with allergic rhinitis

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Background: Eosinophilic esophagitis (EoE) is a chronic, immun mediated disease, characterized by eosinophilic infiltration into the mucosa of esophagus. Symptoms of esophageal dysfunction include dysphagia, food impaction, regurgitation, vomiting and chest pain in adults. The other common causes of esophageal eosinophilia including gastroesophageal reflux disease (GERD) may present similar histological and clinical findings with EoE.

Case report: 23 years old male patient, diagnosed as seasonal allergic rhinitis for thirteen years. Also within 2–3 years, he had disphagia, regurgitation and vomiting, which increased the last 3 months. He used various antihistamines for about 3 months, but his symptoms not resolved. On physical examination, all system findigs were normal; serum eosinophil count was 470/μl. Skin prick test was positive to grass (5/20 mm) plantago (6/20 mm), cat (7/40 mm as histamine 6/20 mm), Food panel was negative. Upper gastrointestinal endoscopy showed Schatzki ring in the distal esophagus with normal esophageal and gastric mucosa. Biopsies obtained from duodenum and stomach were normal, distal and proximal esophageal biopsies revealed >30 eosinophils per high power field and these findings were considered as eosinophilic esophagitis. Esophageal manometry, impedance and pH analysis results were normal. The patient was started on 400 μg once daily budesonide capsule treatment and sublingual immunotherapy (the five-grass pollen sublingual tablet-Oralair, Stallergenes®) for allergic rhinitis. His all symptoms resolved with this treatment in 3 months.

Conclusion: The incidence of eosinophilic esophagitis appears to be increasing, the higher rate of new diagnosis depends on the improved disease recognition and diagnostic methods. EoE should be considered in adults with a history of food impaction, persistan dysphagia, chest pain, regurgitation, vomiting and abdominal pain. An association with food allergy is most common in children, however there is strong association with allergic rhinitis-asthma in adults. The diagnosis of EoE should be based upon symptoms, endoscopic appearance and histological findings. In addition, other disorders that can cause esophageal eosinophilia, such as GERD, should be ruled out. Topical corticosteroids (budesonide, fluticasone etc.) and dietary regulation in case of food allergy are usually recommended for treatment.

1089
Cephalopods and bivalve allergy: a new protein different to tropomyosin?

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Background: Seafood allergy is one of the most frequent in the Mediterranean area, but is unusual to have it to cephalopods or bivalves tolerating crustaceans.
Method: A 16 year-old boy with nuts and fish allergy, experienced immediately oral pruritus, labial angioedema and some wheals around his mouth when he ate squid and cuttlefish. Occasionally he has had similar symptoms eating bivalve as clams but he tolerate crustaceans as prawns or lobster.

Skin prick test (SPT) with commercial extracts of squid, cod, tuna, prawn and clam was performed. Specific IgE to squid, cod, tuna, prawn and clam as well as tropomyosin detected by ImmunoCAP was done and immunoblotting with homemade extracts of squid and clam, as well as with commercial extract of cod, prawn and mussel were performed in the patient's serum and with a pool of sera of negative controls.

Results: SPT were positive for squid, cod and tuna and negative for prawn, and clam. Specific IgE to squid (2.26 kU/l), cod (4.72 kU/l) and tuna (3.53 kU/l) were positive and negative for clam (0.3 kU/l), prawn (0.1 kU/l) and tropomyosin. Immunoblotting with squid under reducted conditions showed a band of 10 kDa that bound IgE in the sera of the patient and the immunoblotting with mussel showed a band of 10 kDa and another of 20 kDa.
Conclusion: We report an IgE mediated case of specific allergy to squid *and bivalves* confirmed by SPT and immunobotting that tolerates crustaceans.

Poster Session TPS 31

Allergy epidemiology

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Relationship between dogs′ parasites and atopic diseases symptoms in children

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Background: Contamination of the soil with dog′s faeces is a consequence of having pets. This situation increases the possibilities of having a zoonosis, and children are the most exposed population at risk.

Toxocara and Ancylostoma are the most prevalent parasites in dogs; however, they can induce ocular or pulmonary toxocariosis as well as larva cutaneous migrans in humans, provoking symptoms of dermatitis as well as cough and wheezing

Aims:

1 To identify the presence of parasites in dog′s faeces.
2 To determine the presence of eosinophilia, IgE and specific IgG anti-Toxocara antibodies in children living at these selected places.
3 To confirm symptoms of asthma, rhinitis and eczema in those children, and their correlation with previous variables.

Method: Dog′s faeces were obtained both indoors and at public places surrounding.

Blood samples have been taken from exposed children.

Clinical evaluation for atopic manifestations in children living at selected places was done.

Professor of Immunology and of Parasites Cathedra performed collection and evaluation of samples. Specialist in Allergy / Immunology searched for atopic diseases symptoms.

Contingency 2 × 2 tables and Fisher′s exact test were used to determine the risks of association; P value < 0.05 was considered significant.

Signed consent was previously obtained by families, having the approval from Ethics Committee at UCaSal.

Results: From 37 samples of faeces obtained, 78.4% were positive for any parasite.

Blood samples were obtained from 88 children, having 32.95% positive for Toxocara antibodies.

Eighty-two children were clinically evaluated, with 35.36% of them presenting any of the mentioned atopic condition.

No statistical significant association was found between the presence of asthma, rhinitis or eczema symptoms neither with eosinophils or IgE levels, nor with specific anti Toxocara antibodies.

Conclusion: Even not finding a significant risk for atopic manifestations, parasites exposure is notably high in our population. Preventive measures in our communities should be considered, as well as in families having pets, in order to avoid not just having asthma and eczema symptoms but the whole zoonosis manifestations.

1091

Prevalence of allergic cat and dog sensitization in adult patients with allergic rhinitis from two German Federal States

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Background: Frequency of allergic cat and dog sensitization is well investigated in pediatric patients with allergic symptoms, but data about prevalence of sensitization and allergic symptoms to cat or dog in adult patients are sparse. We analyzed sensitization and prevalence of allergic symptoms to cat and dog in adult patients with allergic rhinitis from two German Federal States: North Rhine-Westphalia (NRW) and Bavaria.

Method: From 2011 to 2013, we recruited 952 adult patients suffering from allergic symptoms of the upper respiratory tract, 476 living for at least 20 years in NRW and 476 living for at least 20 years in Bavaria, as part of a study initiated by the German Federal Environment Agency.

All patients underwent GA^{2}LEN skin prick testing (SPT). We analyzed and compared the frequency of patients with positive SPT to cat and dog, respectively, and associated positive SPT results with patients′ answers on the question, if positive prick test results are of relevance to the patient. Bivariate testing for significant group differences was performed with the Chi Square test, P values < 0.05 (two tailed) were considered significant.

Results: From 952 investigated patients, 904 patients were considered to suffer from intermittent or persistent allergic rhinitis. All of these patients underwent valid SPT. 38.8% (n = 351) of these patients had positive SPT (wheal ≥3 mm) to cat allergen extract and 31.7% (n = 287) had positive SPT to dog allergen extract (P = 0.0019). From the patients with positive SPT to cat allergen extract, 75.5% (n = 265) reported clinical relevance of this finding, in contrast to 36.9% (n = 106) of patients with positive SPT to dog allergen extract (P < 0.001). There were no significant differences in these parameters between the two German Federal States (data not shown).

Conclusion: Our data showed higher sensitization rates as well as clinically relevant sensitization rates to cat then was reported before in adult patients in Germany (GA^{2}LEN skin test study II, Heinzerling et al., Allergy 2009), but sensitization rates as well as clinically relevant sensitization rates to dog were similar.

The limitations of the present study were, however, that:

1 participating patients were generally very interested in allergological diagnostics meaning that the data are not representative for adult patients with allergic rhinitis, and
2 data on clinical relevance were self-reported.

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IgE development from birth to preschool age and its influence on skin and respiratory symptoms in Chinese cohort

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Background: IgE is the key antibody related to Type I allergy. In this study we

investigated the development of IgE from birth to preschool age and its association with development of allergy-related symptoms in early childhood.
Method: The cohort consisted of 205 children (120 boys and 85 girls), which were recruited from a consecutive birth cohort of 1000 children in 2008–2009 in Second People's hospital of Wuhu city, China. Cord blood was collected at the day of birth and tested for total IgE. At the age of 3–4 years, subjects completed a questionnaire on the history and current status of skin-, wheeze- and rhinitis symptoms as well as serum total and specific IgE against house dust mite (HDM) extracts and HDM group 1 and 2 major allergens.
Results: At birth, 92 (45%) children had cord blood total IgE > 0.35 kU/l. At age 3- 4 years, 50% of children had total IgE > 60 kU/l. Specific IgE positive rates at age 3–4 years were for *Dermatophagoides pteronyssinus* (Dp): 24%, *Dermatophagoides farina* (Df): 19%, Der p 1: 18%, Der f 1: 17%, Der p 2: 16% and Der f 2: 16%. The reported history incident rate of infant eczema was 43% and 22% for wheezing. At age 3–4 years the reported incidence rates were 19% for frequent skin rash, 16% for frequent wheeze, 46% for rhinitis symptoms and 42% for no symptom. Cord blood IgE was not associated with any of the symptoms investigated, but it associated with total IgE levels at age 3–4 years. Total IgE was associated with history of infant eczema (OR [95% CI]:2.45 [1.38–4.34], $P = 0.0020$), but not with skin rash symptom or other respiratory symptoms at age 3–4 years. Rhinitis symptoms at age 3–4 years was associated with Dp specific IgE (OR [95% CI]: 2.10 [1.09–4.07], $P = 0.0254$), Der p 2 specific IgE (OR [95% CI]: 2.68 [1.23–5.88], $P = 0.0115$) and Der f 2 IgE (OR [95% CI]: 2.98 [1.33–6.68], $P = 0.0062$). Wheezing symptoms was not associated with total or specific IgE.
Conclusion: Cord blood IgE is a poor predictor for development of allergy related symptoms. The IgE levels increase significantly after birth. Eczema during lactation relates to high total IgE level at age 3–4 years, but not to HDM specific IgE. Prevalence of HDM IgE sensitization is close to 25% at age 3–4 years among the investigated children and dominated by IgE sensitization towards HDM major allergens. HDM specific IgE is a risk factor for the development of rhinitis symptom at age 3–4 years.

1093
Aeroallergen sensitization profiles in Northern Greece

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Background: It is well known that the prevalence of respiratory allergies varies not only between different countries but also between different regions within the same country. This may be attributed not only to different socio-economic or climatic characteristics but also to different aeroallergens that influence sensitization. The purpose of this study was to determine the sensitization profiles to common aeroallergens among individuals with respiratory allergies living in Northern Greece, since such data are lacking in the literature.
Method: The records of all patients with respiratory allergy under active allergen immunotherapy between 2013 and 2015 were reviewed. Their sensitization profile, which was based on skin prick test results with the standard Pan-European skin prick test panel for respiratory allergens, was recorded. All patients had at least one clinically relevant sensitization.
Results: 166 allergic individuals (70.5% males) with mean age 31.3 ± 13.1 yo (range 5–66 yo) were evaluated. 144 of them (87%) had allergic rhinitis, 20 (12%) allergic rhinitis and asthma and 2 (1%) allergic asthma alone. 39 patients (23.5%) were monosensitized: 11 to grass pollen, 8 to tree pollen, 8 to weed pollen, 7 to house dust mites (HDM), 3 to molds, 1 to animal epithelia and 1 to cockroach. Overall, 64.5% were sensitized to tree pollen (olive 44%; cypress 33.1%; platanus 9.6%; birch related pollen 7.2%), 60.8% to grass pollen, 48.2% to weed pollen (parietaria 32%; chenopodium 22.3%; mugwort 15%; ragweed 9%), 39.25% to HDM, 22.3% to molds (Alternaria alternata 18%; Cladosporium herbarum 9% and Aspergillus fumigatus 9%), 18.7% to animal epithelia (cat 16.3%; dog 9.6%), 11.4% to cockroach and 2.4% to feathers.
Conclusion: Among Northern Greek allergic individuals with respiratory allergies, sensitization to grass pollen is the most common followed by olive pollen, HDM, cypress and parietaria pollen. Interestingly, tree pollen sensitization as a whole is the most prevalent group of sensitization. There are distinct, significant differences with the sensitization profiles found in South Greece and the Greek islands.

1095
Prevalence of ragweed sensitization at a clinical trial unit in northern Germany

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Background: While ragweed (*Ambrosia artemisiifolia)* is a common plant and a major cause for allergic reactions in North America it has originally not been native to Europe. However, there have been reports of ragweed plants in Germany since approx. 150 years and today it can be considered native to Germany, especially in the southern regions. Due to climatic changes ragweed plants constantly spread to northern Germany. The aim of this study was to assess the prevalence of sensitization against ragweed pollen in a population of allergic patients at a clinical trial unit in Hannover, Northern Germany.
Method: All patients with a history of allergic rhinitis, allergic asthma, or both, that received a skin prick test at the Fraunhofer Institute for Toxicology and Experimental Medicine in Hannover between 2009 and 2015 have been evaluated for a positive reaction to ragweed. The skin prick test was conducted according to the guidelines of the German Society of Allergology and Clinical Immunology (DGAKI) and consisted of a panel of 16 allergens, mainly pollen, including ragweed.
Results: Between 2009 and 2015 a total of 666 patients with either allergic rhinitis ($n = 452$), allergic asthma ($n = 14$), or both ($n = 200$) have received a skin prick test. 178 patients (26.7%) showed a positive reaction to ragweed. The prevalence per year ranged from 17% to 39% with no increase over the years.
Conclusion: Although ragweed is still not common in northern Germany there is a high rate of sensitization in the investigated population. An increase in the ratio of sensitization between 2009 and 2015 was not observed.

1096
Allergic phenotyping and prevalence of skin prick test positive subjects in a New Jersey, USA consistent with a more northern clinical site located in the Greater Toronto Area (GTA), Canada

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Background: Allergic disease is influenced by both genetic predisposition and environmental exposure. As such, geographic location may play a role in the phenotypes and demographics of a population in different

geographies. In this study, a diverse population of individuals residing in New Jersey (NJ) were screened for self-reported allergies. NJ is identified as a warm temperate environment with dry winters and wet summers (Köppen: Cfa). The area has high rainfall levels and warm temperatures in the summer, coinciding with a peak in pollen levels. We examined whether the phenotype and prevalence were similar in NJ to the GTA in Canada (Köppen: Dfa).

Methods: A population of 369 subjects were screened at NJ for a history of allergy. The skin prick test (SPT) panel of 15 allergens included 4 perennial allergens and 11 seasonal allergens. A positive SPT was a wheal diameter ≥3 mm larger than the neg. control. These data were analyzed with regression and statistical methods with respect to the prevalence of allergy. As well, this population was compared to a known population from Southern Canada.

Results: This population had a high prevalence of grass (55.4%) SPT positive allergic responses. A high proportion of subjects (16.2%) had *Alternaria alternata* positive SPT with a mean wheal diameter of 9.1 mm. However, only 2.2 and 5.2% of subjects were allergic to the other mold screened, *Aspergillus fumigatus* and *Cladosporium cladosporioides*, respectively. Comparatively, the both populations showed a high similarity for both the most prevalent perennial (cat, 45.5%-NJ and 54.3%-GTA) and seasonal allergens (birch, 48.4%-NJ and 47.7%-GTA). A notable difference between the populations can be seen in the greater prevalence of positive SPT results for ragweed in the GTA (67.4%) compared to NJ (40.4%), despite similar ragweed seasons.

Conclusion: The distribution of positive SPT to seasonal and perennial allergens from the GTA is consistent with that observed in a more southern NJ site. Despite the GTA population being a demographically diverse group, the high similarity of allergen response with the NJ can potentially lead to successful future studies being run at both sites with a degree of consistency, despite geographical differences. Such allergy prevalence mapping is important to the successful recruitment and conduct of large pivotal multicenter trials where patients are recruited from diverse geographical and climate regions across North America.

1097
Are infants with food allergies candidate for allergic diseases of the respiratory tract?

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Background: Allergic sensitization usually develops against food allergens in infancy and to inhalant allergens in the older. Although having food allergies is considered a risk factor for development of asthma according to the modified API index, such a relationship has not been established for allergic rhinitis. Our goal is to investigate inhalant allergen sensitivity and frequency of allergic diseases of respiratory tract after the age of five in infants with milk and/or egg allergies.

Method: Children with milk and/or egg allergy proven by oral provocation test, that were followed up by Izmir Dr. Behcet UZ children′s Hospital′s Allergy Clinic between the dates 01.01.2010 31.12.2015, were involved in this retrospective cross-sectional study. All patients were performed skin prick test (SPT) involving major inhalant allergens. Patient demographics, concomitant allergic diseases and aeroallergens they were sensitive have been recorded.

Results: The study included a total of 51 patients and 36 (70.5%) were male. 16 of the cases (31.4%) had only milk, 16 (31.4%) only eggs and 19 (37.2%) had both milk and egg allergies. The average age of inhalant SPT was 68.78 ± 11.96 months. 19 of the cases (37.3%) were found to be sensitive to inhalant allergens. 10 of the cases (19.6%) were sensitive to only domestic allergens, 6 (% 11.8) to only pollen and 3 (5.9%) to both. 11 of the cases (%21.5) were being followed up with the diagnosis of allergic rhinitis and 2 with asthma. The remaining 6 patients lacking clinical signs were considered as only sensitization. There were no correlation between inhalant allergen sensitization and food-specific IgE levels identified during the diagnosis of food allergy and the diameter of SPT enduration. Also, when subjects were grouped according to the type of nutrients they were sensitive (milk, eggs, or milk+eggs) no statistically significant difference was detected between the groups in terms of development of inhalant allergen sensitivity ($P > 0.05$).

Conclusion: Inhalant allergen sensitivity and development of respiratory allergy including allergic rhinitis are high in infants with milk and/or egg allergies. Although tolerance to food allergens usually develops, patient monitoring is required for probable allergic respiratory diseases that may occur.

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The role of cutaneous *Staphylococcus aureus* in the development of atopic dermatitis during infancy

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Background: *Staphylococcus aureus* (SA) often colonizes the skin of patients with atopic dermatitis (AD) and exacerbates the disease. However, its role in the development of AD during infancy remains unclear.

Methods: We prospectively evaluated children who visited community-based health centres for checkups at 4, 18, and 42 months of age. Paediatric allergists examined the patients for the presence and severity of eczema at each visit. Skin culture of the cheeks for detecting SA was performed at 4 and 18 months.

Results: Colonization of SA was significantly associated with the presence and severity of AD at 4 months ($n = 585$) and 18 months ($n = 353$). The presence of AD at 18 months in infants without AD at 4 months was significantly higher in SA-positive infants (14.9%, $n = 47$) than in SA-negative infants (5.4%, $n = 294$) at 4 months ($P = 0.026$). Similarly, presence of AD at 42 months in infants without AD at 4 and 18 months was higher in SA positive infants ($n = 35$, 17.1%) than in SA negative infants (7.2%, $n = 208$) at 18 months ($P = 0.094$). A multiple regression analysis including sex, body weight at birth > 3000 g, breast feeding, 1 or more siblings, cat ownership, parental history of AD, and parental smoking showed that being SA positive at 4 months was significantly associated with development of AD at 18 months in infants without AD at 4 months (adjusted odds ratio: 3.5, 95% confidence intervals: 1.48.2) and that being SA positive at 18 months was also significantly associated with development of AD at 42 months in infants without AD at 4 and 18 months (adjusted odds ratio: 3.8, 95% confidential intervals: 1.2–11.7).

Conclusion: Our results suggest that cutaneous colonization of SA may precede development of AD in early childhood, which highlights the need to control SA colonization for the prevention of AD.

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Allergic disease is associated with nasal *Staphylococcus aureus* colonization in late adolescence

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Background: Asthma, allergic rhinitis (AR) and eczema are common chronic diseases in children and adolescents worldwide, but limited epidemiological data are available in the transition into adulthood. Nasal carriage of *Staphylococcus aureus* is in some studies linked to increased prevalence of allergic diseases, and *S. aureus* colonization of the atopic skin may exacerbate eczema.
Objective: The aims of our study were to find prevalence rates of allergic diseases and allergic multimorbidity among individuals in late adolescence above the Arctic Circle in Northern Norway and to analyze the associations between *S. aureus* colonization and allergic diseases.
Methods: We invited a school-based cohort of 1177 women and men aged 17–19 years to participate in a cross-sectional follow up on lifestyle and health, and 868 of the adolescents (77.7%) attended. We used MeDALL and POEM questionnaires to collect data on allergic diseases and severity of eczema, spirometry with reversibility test, exhaled nitric oxide and swabs for bacterial culture from nose and eczematous skin areas.
Results: We found asthma, eczema and AR in 11.5%, 10.0% and 25.1% of the participants, respectively, and at least one allergic disease in 35.0% of the participants, whereas 9.9% had two or more allergic diseases. Lifetime prevalence for any allergic disease was 43.3%. Women had more eczema ($P = 0.001$) and multimorbidity ($P = 0.024$) than men. Eczema (OR = 1.71, 95% CI = 1.06–2.77), but not asthma and AR, was associated with nasal *S. aureus* colonization. Severe eczema (OR = 2.27, 95% CI = 1.18–4.35), severe asthma (OR = 3.26, 95% CI = 1.28–8.30) and severe AR (OR = 1.71, 95% CI = 1.09–2.66) were associated with nasal *S. aureus* colonization. FeNO >25 ppb was associated with asthma (OR = 2.48, 95% CI = 1.41–4.35) and nasal *S. aureus* colonization (OR = 2.03, 95% CI = 1.26–3.24). The association between FeNO and nasal *S. aureus* colonization remained significant after adjusting for asthma (OR = 2.10, 95% CI = 1.30–3.40), and the association between FeNO and asthma remained significant after adjusting for nasal *S. aureus* colonization (OR = 2.49, 95% CI = 1.41–4.40). FEV_1 below lower limit of normal was not associated with nasal. *S. aureus* colonization.
Conclusion: Asthma, eczema and allergic rhinitis are common among adolescents above the Arctic Circle in Northern Norway. Allergic disease is associated with *S. aureus* colonization, but the role in the pathogenesis and severity of such colonisation is not established.

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Distribution characteristics of the concentration of house dust mites in patients with allergic airway diseases

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Background: The burden of allergic airway diseases represents a major health problem. Despite many different options are currently available for the management, is not yet satisfactory. Clinical studies have demonstrated that house dust mites (HDM) are the major allergen. Use HDM control practices were known by patients, however, we are not sure which environmental factors affects the concentration of HDM. In order to understand the distribution characteristics of HDM in patients with allergic airway diseases in Guangzhou and the effects of environmental factors on the it, aiming at better clinical guidelines for the HDM control.
Method: A total of 38 patients (15 males and 23 females) with allergic airway diseases were selected, including 5 patients with bronchial asthma, 12 with allergic rhinitis and 21 with allergic rhinitis combined with asthma. ISSAC questionnaire and the Swedish Dampness in Buildings and Health questionnaire were filled by patients. Dust samples from air and bedding as well as form a static collected device in 1 month in the bedroom were collected. ELISA was applied for the measurement of the concentration of Derp1 and Derf1 in above dust samples, SPSS21.0 statistical software for data entry and analysis, descriptive statistics for measurement data, and spearman correlation analysis for the correlations between environmental factors and HDM concentrations. $P < 0.05$ was considered as a statistically significant difference.
Results:
1 The concentration of Derp1 and Derf1 in air was 1.06 ± 0.06 μg/g and 1.00 (0.70, 1.30) μg/g, in bedding was 7.24 (1.34, 39.41) μg/g and 21.72 ± 11.29 μg/g, and samples from static collecting device was 1.06 (0.70, 1.12) μg/g and 1.00 (0.28, 1.00) μg/g, respectively.
2 The concentration of Derp1 in air was positively correlated with residence near to traffic arteries or expressways within 200 m; while was negatively correlated with mildew phenomenon in bedroom and damp phenomenon in bedroom.
3 The concentration of Derp1 in the dust samples from bedding was positively correlated with living in the city; on the other hand, the concentration of Derf1 was positively correlated with cleaning once a week for bedroom.
4 The concentration of Derp1 in the static collected device was correlated with cleaning once a week for bedroom ($r = -0.559$, $P = 0.004$) and airing quilt once half a year.
Conclusion: The concentration of dust mites is closely correlated with home environment, we might be careful with these factors.

1101
Evaluation of patients attending to an emergency department with suspicious of an allergic reaction

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Background: Allergic reactions represent a significant clinical problem in emergency departments (ED), being food (fruits/vegetables, tree nuts and crustaceans) and drugs (NSAIDs and antibiotics) the main triggers. These patients could be labelled as allergic without an allergological study. The aim of this study was to assess benefits of a thorough allergy evaluation after an ED visit and to compare concordance of clinical characteristics, triggers and diagnosis.
Method: A trained allergist screened electronic medical records of patients attending to an ED of Málaga, with suspicious of allergic reaction (primary evaluation) between April 2013 and June 2014. A group of them were reevaluated at the Allergy Unit (final evaluation). The clinical history was then reassessed and, if necessary, skin tests, specific IgE, basophil activation test and/or double-blind placebo-controlled food challenge or single-blind

placebo-controlled drug provocation test were done.

Results: One thousand patients were included in primary evaluation and 341 were considered for the final evaluation, 264 of them completed the study. One hundred and seventeen participants (44.3%) were confirmed as allergic and 147 (55.7%) were diagnosed otherwise. The identified allergic causes were, drugs (49.57%) and food (36.75%). The main non-allergic cause was acute or chronic urticaria with no specific triggers (39.7%).

For food allergy, most common clinical presentation was anaphylaxis (54.8%), and fruits and vegetables were the main prevalent triggers (44.2%). In drug allergy, also anaphylaxis was the most common clinical presentation (40.4%), main triggers were NSAIDs (62.1%) followed by β-Lactams (22.4%).

A concordant results between ED physician and the Allergy Unit team was found in 123/264 cases (46.6%) and between the trained allergist and Allergy Unit team in 141/264 cases (53.41%). Finally, concordant results between ED physician and the trained allergist was were found in 179/264 cases (67.8%), which represents a moderate level of agreement between the two observers.

Conclusion: These data show that drug and food hypersensitivity are the main inductors of hypersensitivity reactions evaluated in ED, being anaphylaxis the main clinical entity. Less than 50% of patients initially labelled as allergic in ED were finally confirmed. These results highlight the importance of evaluating patients in Allergy Units to get an accurate diagnostic and further management.

1102
Severity of anaphylaxis is associated to higher comorbidity. Analysis of hospitalized patients in Spain during the period 1998–2011

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Background: We have evaluated in the Spanish database of patients admitted, if presence of high level of comorbidities different than cardiovascular and respiratory diseases is associated to higher severity of anaphylaxis.

Method: The study was carried out using the Spanish Minimun Basic Data Set for the period 1998–2011. The system uses the codes of the Spanish version of the ICD-9-CM and covers 98% of public hospitals in Spain.

Possible cases of anaphylaxis were obtained only in the principal diagnostic field. We use two strategies: First, we chose the codes ICD-9-CM specifically associated with anaphylaxis. Secondly, we used combined codes of causes of anaphylaxis and symptoms or signs of organ and systems in order to select episodes that met the criteria for the definition of anaphylaxis following an adapted Harduar-Murano′s strategy. Proxies of severity in anaphylaxis admissions were deaths, use of invasive mechanical ventilation or vasopressor drug administration (IMV) and length of stay. The *Elixhauser′s score modified by van Walraven* was used as index of comorbidity. This score is validated to estimate the risk of deaths, longer stay admissions and hospital charges in admitted patients. We adjusted the estimated risks in the logistic regressions by age, sex and causes of anaphylaxis.

Results: 5261 admissions whose main diagnosis was anaphylaxis were found. Out of them, there were 116 cases of deaths and 318 cases required IMV and 66 vasopressor drug administration (375 IMV or vasopressor drug).

We observed in all studied outcomes, the Elixhauser′s score was associated to higher severity of anaphylaxis. For deaths and length of stay the C-statistics or discrimination was high (deahts 0.76; 95% CI 0.75 to 0.77; length of stay 0.73; 95% from 0.71 to 0.74). Good calibration was noted for both ($P = 0.39$, Hosmer-Lemeshow test). For Mechanical invasive ventilation or vasopressor drug administration discrimination was lower (0.66, 95% CI 0.64 to 0.67) with good calibration ($P = 0.12$).

Conclusion: Severity of anaphylaxis is increased not only due to presence of cardio-vascular and respiratory diseases, but also by presence of other comorbidities. For the most sick people are more likely to have more severe anaphylaxis.

	Odds Ratio by unit of Elixhauser′s score (modified by van Walraven)	$P > z$	Lower interval 95%	Upper interval 95%
Deaths	1.10	<0.001	1.06	1.14
Length of stay	1.02	0.0140	1.00	1.03
Mechanical invasive ventilation or vasopressor drug administration	1.03	0.0410	1.00	1.05

1104
Assessment of Fel d1 allergen characteristics in domestic house cats

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Background: Cat dander is ubiquitous and is one of the most potent indoor allergens causing an IgE mediated Type 1 allergic response. The purpose of this preliminary work was to measure the levels of Fel d1 found in fur, saliva and urine of male and female domestic house cats and to determine whether there are differences in allergen levels dependent on breed, gender, sterilization status and age.

Method: Cats volunteered by owners from a local animal hospital were used for this study. Owners signed an informed consent prior to any sample collection. In this initial exploratory investigation, fur, saliva and urine samples from 10 cats of various breeds, ages and sex were studied. Commercially available ELISA kits were used to measure the allergen levels.

Result: The sample size included 8 domestic short and 2 long hair breeds, with 4 males (mean age, 8.43 years) and 6 females (mean age, 4.34 years). All male cats were castrated. Overall mean Fel d1 levels in the fur was 23.33 μg/g with males having a mean value of 21.05 μg/g and females 24.85 μg/g. Mean fur Fel d1 levels in non-spayed cats was 28.03 μg/g compared to 18.48 μg/g in spayed cats. Mean values for short hair vs long hair were 26.09 and 16.88 μg/g respectively. Mean values by sex were 21.05 μg/g in males and 24.85 μg/g in females. Overall values for saliva and urine were 2.65 and 0.0197 μg/ml respectfully.

Conclusion: We have been able to demonstrate that even in this small sample size, that short and long hair cats irrespective of their gender, sterilization status and age produce levels of Fel d1 allergen to pose a significant health risk for sensitization. Further we have demonstrated these general characteristics will help us to identify cats to be housed in a cat allergen

challenge room in order to obtain consistent levels of airborne Fel d1 allergen.

1105
Allergic reaction induced by pollen in the upper respiratory tract affects eosinophils and basophils in peripheral blood as well as in the lower respiratory tract

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Background: In Japan, Japanese cedar pollen (JCP) is the most important causal pollen allergen and induces widespread pollinosis. However, asthma directly caused by JCP is rare because the large size of the pollen prevents its entry into the lower respiratory tract. JCP pollinosis frequently aggravates the symptoms of patients with concomitant asthma, but the detailed mechanism of this interaction remains unclear. We examined the effect of JCP on the allergic reaction in the nasal mucosa, in peripheral blood cells, and in the lower respiratory tract, using an experimental challenge chamber.
Method: A total of 50 patients with JCP pollinosis who did not have any symptoms or a history of lower respiratory tract diseases was enrolled in this study. These included 39 females (78%) and 11 males (22%), with a mean (± standard deviation) age of 47.9 ± 9.1 years. The mean JCP ImmunoCAP test score was 3.5 ± 0.9. The study was performed in November 2015, a period outside the pollen dispersal season (February to May). JCP exposure (8000 grains/m^3) was performed for 3 h on 2 consecutive days using an experimental challenge chamber. Before and after JCP exposure, we examined blood parameters as well as physiological changes in the nasal mucosa and lower respiratory tract.
Results: All patients complained of nasal symptoms after JCP exposure, but no lower respiratory symptoms were observed. The blood eosinophil count significantly increased in most patients after two consecutive JCP exposures (average count before exposure, 223/μL; after exposure, 302/μL; $P < 0.0001$), and the eosinophil cationic protein (ECP) titer also significantly increased (average titer before exposure, 7.4 μg/l; after exposure, 11.8 μg/l; $P = 0001$). The average fractional exhaled nitric oxide (FeNO) titer significantly increased after pollen exposure (average titer before exposure, 27.1 PPV; after exposure, 31.7 PPV; $P < 0.01$). In 25 cases with a high level of FeNO, forced expiratory volume in 1 s (FEV1) tended to decrease (average volume before exposure, 2.68 l; after exposure, 2.59 l; $P = 0.08$).
Conclusion: The allergic reaction induced by JCP in the upper respiratory mucosa can evoke a generalized allergic inflammatory response, including that in the lower respiratory tract.

1107
Innovative nasal filters allow for allergen exposure monitoring and are acceptable to wear

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Background: For over 25 years the examination of environmental allergens has shaped our understanding of the role of allergen exposure in the development of allergic disease. These studies have highlighted the important role allergens play in allergic sensitisation and exacerbation. The most common sample type analysed for monitoring allergen exposure is settled dust. It is an easily available source which yields lots of allergen. However, this sample type is only a snap shot of the allergen reservoir and may not take into account the full spectrum of allergen which a subject breathes in during their whole day. In this study, we sought to assess the feasibility of using a new nasal filter for the assessment of allergen exposure.
Method: The nasal filter consists of a membrane that removes particles by means of interception and impaction. Volunteers wore the nasal filter for up to 24 h during their normal daily routine. For comparison settled dust was collected from each volunteer′s home. Allergen was extracted from nasal filters and settled dust by gentle rocking in phosphate buffered saline with tween for 2 h. The levels of ten major allergens captured by these sampling methods were quantified using a multiplex array for quantification of indoor allergens which is very sensitive and allows for quantification of airborne allergens down to 0.01 ng/ml (for mouse allergen Mus m 1). Finally, in a randomized control trial the device was evaluated on usability and tolerance.
Results: Significant levels of allergens were readily detectable in the nasal filter extracts and ranged from 39 ng/filter to 0.01 ng/filter. These included allergens from house dust mite (Der p 1, Mite Group 2), cat (Fel d 1), dog (Can f 1), mouse (Mus m 1) and pollen (Bet v 1). There was some correlation with corresponding samples collected from settled dust. We found that most people (90%) seemed to quickly (within 60 min) forget that they were wearing the nasal filter. Most (85%) did not experience a difference in breathing resistance.
Conclusion: These data indicate that nasal filters may be considered a simple and easily wearable method for monitoring allergen exposure. This sampling method which takes into account a wider spectrum of potential allergen exposure sources may improve our understanding of the role of allergens in the development of allergic disease.

Poster Session TPS 32

Epidemiology of food allergy

1108

Patterns of food allergen sensitization in urban and rural populations - the EuroPrevall-INCO surveys

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Background: Food allergy is a common condition affecting children and adults in developed countries. Food induced anaphylaxis has been documented to be increasing in the recent decade. Food allergy has been perceived to be less common in developing countries. There is limited published data outside Europe and North America.
Methods: We used the standardized EuroPrevall methodology to investigate random samples of school children from Russia, India, and China to evaluate the patterns of food allergen sensitization in primary school children. Children aged 7–10 years were screened for the presences of possible food allergies. Subsamples of subjects with or without possible food allergies were studied by detailed face-to-face questionnaires, SPT, and serum specific IgE testings.
Results: A total of 35 549 children were recruited, of who 2891 participated in the second clinical stage. Using a cut off 0.35 kU/l as positive, the weight-adjusted prevalence rates of food-specific IgE sensitisation to at least one food were 29.7%, in Hong Kong, 14.5% in Guangzhou, 25.8% in rural Shaoguan, 13.2% in Tomsk, and 26.7% in India. The differences in the prevalence were statistically significant ($P < 0.01$). The patterns were very different among the different populations. In Hong Kong, sensitization to milk, hen's egg, and shrimp were the top three allergens while sensitization to nuts and vegetables were more common in Russia and India. For children recruited from Hong Kong, both sensitisation and food allergy were significantly higher ($P < 0.01$) in children who were born and raised in Hong Kong when compared to those who were born in mainland China and migrated to Hong Kong highlighting the potential importance of early life exposure in affecting the subsequent development of food sensitisation and allergy.
Conclusions: There are wide variations in the prevalence of food specific IgE sensitisation in the three participating countries. Despite high degree of sensitization in rural areas, food allergies were uncommon highlighting that other factors are important in the clinical manifestation of food allergies other than just sensitization.
Acknowledgement: Supported by the HKRGC CUHK477110, NNSFC 81261130023 and EU

1109

Study of patients with positive skin tests to LTP and/or profilin in a Mediterranean area

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Background: The use of LTP and other panallergens in skin tests joined to *in vitro* IgE to molecular components to study fruit allergy patients has been recently introduced. Our aim was to study molecular component of positive patients to panallergens by skin tests referred to allergy outpatient clinics in a highly prevalent Mediterranean area in Spain.
Method: A cross sectional study of patients positive to panallergens (LTP, profilin and/or polcalcin) by skin tests, from the outpatient clinic of Alicante University hospital, between 2012 and 2014 was carried out. Clinical history, skin tests to the major allergens of our area as pollens (olive, chenopods, and grasses), mites, fungi, epithelia and fruits extracts were done. ImmunoCAP ISAC array (Thermo Fisher Scientic, U.K.) were carried out in all of them. The ISAC tests were considered positive when they were greater than 0.35 ISU. Descriptive statistical analysis was performed with SPSS 20 MAC.
Results: 219 allergy patients were studied. The sample has a mean age of young adults (30.35 ± 11.8), and predominantly women (59%). Most of them suffered from any allergy disease, such as rhinitis (73%), food allergy (72%), asthma (28%) or atopic Dermatitis (7%). Pollen was responsible for 64% sensitization, presenting symptoms of rhinitis (100%) and asthma (53%). Among the different positive panallergens, LTPs were the most important. Pru p 3 was found positive in 84.7% of the sample, followed by Jur g 3(74.6%), Pla a 3(61.9%), Ara h 9 (55.8%), Art v 3 (51.6%), Cor a 8 (47%) y Ole e 7 (22.8%). Mostly they featured multiple sensitization (49% gave positive to 5 LTPs, 31% between 2 and 4, and only 18% to one). This multiple sensitization was related with food allergy symptoms (4.6 LTPs) vs asymptomatic (2.6 LTPs, $P < 0.001$). Although there was not a clear relationship between Ole e 1 and Ole e 7, there was a good correlation (OR 19.3, $P < 0.01$) between them. Profilin represented less than 10% of sensitizations.
Conclusion: LTP was found the most important panallergen in our Mediterranean area. The profile of different LTPs may vary from place to place depending on food habits or pollen count.

1110

Sensitization to profilin in Greek adults and correlation to oral allergy syndrome: results of a prospective study

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Background: Profilin is a panallergen often responsible for cross-reactivity between pollen and plant food. Oral allergy syndrome is a clinical expression of this cross-reactivity. The aim of our study was to determine the prevalence of sensitization to profilin and the correlation between its sensitization and manifestation of OAS.
Method: 264 adult atopic patients were included in our study. They had a history of respiratory (allergic rhinitis and/or asthma) or food allergy and presented at least one positive SPT out of the relative panel used in our Clinic. SPTs with an extra panel were conducted for the study including one profilin extract, four plant food extracts (peach skin and pulp, walnut

and apple), and three pollen (Olea europea, Parietaria judaica, Phleum pratense).
Results: 29/264 of our atopic patients (11%) resulted positive to profilin. 79/264 patients (30%) referred symptoms of OAS. The foods of plant origin most implicated in OAS were peach, walnut, kiwi, banana, hazelnut, peanut, apricot, eggplant and melon. No statistically significant correlation was found between sensitization to profilin and OAS, or between pollen extracts and OAS. A significant trend of profilin-sensitization was found in patients with allergic rhinitis ($P = 0.054$), but not in asthmatics. OAS was connected to peach pulp's sensitivity ($P < 0.0001$), but also to other plant foods. Cases with positive SPT to peach pulp extract had the highest correlation to OAS [OR = 5.77, 95%CI: (2.754–12.102)], in comparison to other food extracts.
Conclusion: Our results show a low prevalence of sensitization to profilin, in Greece. The *in vivo* sensitization to profilin's extract was not correlated to OAS, maybe due to the limited number of patients, or due to the fact that OAS in our country might be caused by other allergens.

1111
A retrospective study on clinical manifestations of fruits and vegetable allergy between adults and pediatric patients

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Background: The prevalence of allergy to fruits and vegetables has increased and has become important in children and adults. The aim of study aim is to clinical manifestations of fruits and vegetable allergy between adults and pediatric patients.
Methods: We retrospectively analyzed clinical manifestations in 148 patients (70 children and 78 adults) with allergy to fruits and vegetables.
Results: The patients showed allergy to 52 kinds of fruits and vegetables. Children were allergy to a total of 196 kinds, and adults were allergy to a total of 352 kinds, of fruits and vegetables. Eight of the 10 leading allergens were the same in children and adults; apple, peach, cherry, melon, kiwi, pear, banana, strawberry. Apple and peach were the most frequently implicated foods. The allergic symptoms appeared form at 8.1 years old on average in children and at 24.1 years old on average in adults. Allergic symptoms (children/adults) were oral itchiness (75.7%/91%), skin symptoms (17.1%/32.1%), gastrointestinal symptoms (12.9%/16.7%), and respiratory symptoms (12.9%/21.8%). Only adults patients reported headache in 2, and fatigue in 1. Twelve children and 16 adults experienced anaphylaxis to fruits and vegetable allergy. Five children were allergic to melon and 4 adults were allergic to apple, which are the most causal anaphylaxis fruits. A hundred twenty patients (54 children and adults 66 adults) had pollinosis as the most frequently complicated allergy and of whose patients were allergic to birch (35 children and adults 40 adults).
Conclusion: Symptoms of fruits and vegetable allergy were similar both children and adults. More investigations toward the prognosis and management, which including the risk of anaphylaxis, are necessary.

1113
Egg allergy: onset in adult age

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Background: The onset of egg allergy in adulthood is unusual. It frequently occurs as bird-egg (BES) or occupational egg-egg syndrome. However it may also manifest as a rare selective immediate food egg allergy (FEA).
Methods: A retrospective-descriptive study from Jan 2008 to Dec 2014 of patients with late-onset egg allergy (after 18 years old) in a third-level hospital was conducted. It was aimed to study and compare the specific characteristics of FEA and BES.
Results: Only 17 patients were found to have late onset-immediate egg reactions. Ten had been diagnosed with FEA and 7 patients with BES. At the onset of the disease the mean age was 30 years (SD = 10), 60% women, in FEA and 44 years (SD±16), 100% women in BES (n.s.). Seventy percent, and 100% had previous atopic diseases respectively (n.s). The delay on diagnosis was 9 years (median) in FEA and 5 years in BES. The main symptoms upon egg ingestion were: 80% cutaneous, 20% respiratory, 20% gastrointestinal in FEA and 57%, 42.85%, 57% in BES, respectively. Two patients presented with anaphylaxis in each group.

In FEA skin prick tests were positive in 100% of the patients to white egg, 50% to yolk, 70% ovomucoid (OVM) and 50% ovalbumin (OVA). In BES it was positive in 100% of the patients to white egg, 100% to yolk, and 71.4% to OVA. Prick test to OVM was negative in all of them.

Specific IgE (sIgE) were present in 100% of patients to white egg (median: 2.14 KU/l, range: 0.37–100), in 50% to yolk (0.6, 0.39–22.9), 60% to OVM (3.04, 1.69–65) and 70% to OVA (0.98, 0.65–100) in FEA. It was present in 100% of patients to white egg (median: 11.1 kU/l, range: 0.65–39.3), in 100% to yolk (11.29, 0.51–100), 43% to OVM (27.2, 0.69–100) and 71.4% to OVA (2.9, 0.35–46) in BEA patients.

In the FEA all tolerated chicken meet and 40% had tried and tolerate eggs from different species (ostrich, quail).

In BES only 42% did not tolerate chicken meat. The median sIgE to chicken meat was 18.9 kU/l (range: 7.09–33.6. All of them avoided all eggs.
Conclusions: FEA and BES have a similar incidence in the adult age, being both of them rare pathologies, with a considerable delay in the diagnosis. The clinical pattern of both entities look dissimilar, being cutaneous symptoms the main clinical presentation in FEA, whereas in BES patients, cutaneous and gastrointestinal and respiratory symptoms are developed at the same rate. Anaphylaxis may occur in both groups.

1114
Food allergy in a pediatric food allergy unit at Centro Hospitalar Porto, Portugal: 2 years of experience

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Background: The prevalence of food allergy (FA) in childhood increased in the last decades, affecting almost 10% of the pediatric population and being, across Europe, the leading cause of anaphylaxis in children aged 0–14 years. The aim of our study was to investigate the prevalence and characteristics of the principal foods implicated in a Pediatric population with suspected FA.
Method: A retrospective review was performed on children with suspected FA referred to our Pediatric Food Allergy Unit from Jan/2014 to Dec/2015. The evaluation involved skin prick test (SPT); Prick-to-prick test (PPT); specific IgE (sIgE); component-resolved diagnostics (CRD); Basophil Activation Test (BAT) and Oral Food Challenges (OFC).
Results: 109 children aged 10 months to 18 years (median 6) were analysed, most of them males (57%) and referred by general Allergist (35%), followed by primary care Physicians (32.7%) and Pediatrician (21%). Most frequent causes and clinical signs were: FA screening in high risk infants (18%); symptons involved the skin (urticaria and/or angioedema (42%),

followed by gastrointestinal (17%), anaphylaxis (10%), food sensitization (8.3%), oral allergy syndrome (4.6%) and respiratory symptoms (1.8%).

A total of 190 food allergens were found in result of positive SPT (88%), PPT (63%), sIgE (56%) and CRD (12%). We performed 4 BAT, in patients with persistent Cow's milk allergy (CMA), which were all positive. One of these patients underwent oral immunotherapy to CM, being fully desensitized.

A total of 67 OFCs were performed. 57 to confirm suspicion of FA. Of these, 27 (47%) were positive: 10 to Cow's milk (CM), 6 to hen's egg (HE), 6 to fish and crustaceans, 2 to peanut, 2 to wheat and 1 to vegetable.

Twelve (18%) OFC were performed to evaluate the acquisition of tolerance to CM and HE, and they were all negative.

Diagnosis of IgE-mediated FA was established in 77 patients. Of these, 65 are on elimination diet and 12 acquired tolerance. In 21 patients FA was excluded. 5 patients droup out the follow-up evaluation and 6 are in investigation. Most patients with FA reacted to one or two foods (89%). Only 11% of patients reacted to 3 or more foods, mostly to fish and crustaceans.

Conclusion: CMA was the most frequent FA. The most frequent symptoms involved the skin. Anaphylaxis was reported in 10% of patients. The SPT were the most used diagnostic tests and OFC was used as *gold standard* to confirm the diagnosis or the acquisition of tolerance.

1115
Early associations with asthma in young children with cow's milk allergy

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Background: Cow's milk allergy (CMA) is a common disease in infancy. It is hypothesized that these children have an increased risk for developing other allergic diseases, such as asthma, later in childhood. However, it is not clear how many will develop asthma. We hypothesized that children with CMA more likely had an aero-allergen sensitization, asthma-like symptoms and inhalation medication use compared to controls in the first 2.5 years of life.

Method: All children, aged 0–2.5 years, with challenge proven CMA participating in the Dutch EuroPrevall birth cohort study were investigated. They were age-matched and matched for age at aero-allergen sensitization sampling with healthy controls. Aero-allergen sensitization was defined according to Phadiatop reference values. Asthma-like symptoms were defined as having doctors diagnosed wheeze, and/or coughing at night without common colds, and/or doctors diagnosed asthma. Inhalation medication included use of prescribed inhalation medication. A logistic regression model was created for aero-allergen sensitization, asthma-like symptoms and inhalation medication use, separately.

Results: In total 45 children with CMA were included. The crude model regarding asthma-like symptoms was significantly different between children with CMA and matched controls ($P = 0.01$). This effect just disappeared after correction for confounders ($P = 0.05$). None of the other models showed significant results.

Conclusion: Children with CMA seem to have a higher probability of asthma-like symptoms in the first 2.5 years of life, compared to controls. Since this is the first study including young children with challenge proven CMA, investigating early signs of asthma, we consider our results, although with limited power, relevant.

1118
Tolerance to cow's milk protein development in children with IgE mediated cow's milk allergy

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Background: Cow's milk is a major allergen and one of the main nutrient in first years children. Development of tolerance to cow's milk is important task up to date allergology.

Method: Under our supervision were 143 1-st year children with cow milk allergy (skin and/or gastrointestinal symptoms approved with increased levels of specific IgE to cow milk fractions) 12 children had severe oral allergy syndrome to cows milk. ($n = 7$ rash, angioedema; $n = 3$ angioedema, vomiting; $n = 2$ vomiting). All children had high IgE level to cows milk ($n = 6$-α,β lactoglobulin and casein; 4 = α, β lactoglobulin, 1 = casein) and negative IgG levels to cows milk. To all children straight avoiding diet were recommended. At the age of three in the case of necessity oral immunotherapy were suspected. During supervision time control should be provided by oral provocation with cows milk and measuring IgE and IgG to cow milk proteins.

Results: At the age of three we found significant decrease of specific IgE and significant increase of specific IgG in 9 children. The tolerance development in these children approved with negative oral provocation. After diet analyses were found that in ratio of this children small doses of such products as beef, bred and other bakery were present.

3 other children had no violations in the diet and significant decrease of specific IgE and still negative IgG. 2 children had positive oral provocation result and 1 negative.

Conclusion:

1. Avoidance of cow's milk significantly reduces the risk of development oral allergy syndrome in children allergic with cow's milk allergy.
2. Including in diet products with small quantities of cows milk can lead to food tolerance development
3. Provocative tests to products with small quantities of cows milk can be reasonable and used for diet widening and food tolerance formation

1119
Rare case of late onset of allergy to chicken egg white

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Background: Food allergy is most commonly acquired during the first year of life. The onset of disease, in most cases, is closely related to the time of introduction, predominantly before the second year. Allergy to egg is among the eight most common food allergies across different age groups and regions in Europe. Most children outgrow allergy to egg. The onset in adolescent and adults is very rare.

Aim: The aim of this presentation is to demonstrate a rare case of late onset allergy to chicken egg white.

Method: Seventeen year old boy was referred to evaluate the reason for urticaria and angioedema, appeared for the first time 1 month ago and repeated twice. In order to diagnose the reason, a thorough history was acquired. Skin prick test with milk, whole egg, egg yolk, egg white, wheat was performed evaluated according to European Academy of Allergy and Clinical Immunology.

Results: From the detailed history of the disease it was clarified the urticaria and angioedema appeared within 20 min after raw egg shake was taken and repeated

once again after pancake was eaten. No adverse reactions had appeared when eating either pancakes or boiled eggs up to that time. There was no history of accompanying allergic disease and no family history of allergy. Sensitization to egg white was demonstrated by skin prick test.

Conclusion: The presented case is interesting because it demonstrates the onset of allergy to egg white in 17 year old boy who consumed eggs before that. Although rare, food allergy can begin at any time throughout life. It should be evaluated in cases of adverse reactions to food not only in children but in adolescence and adults too.

1120
An interesting case of persistent cow's milk allergy in adulthood

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Background: Milk allergy in the adulthood is scarce. The vast majority of children with cow's milk allergy (CMA) outgrow it in puberty. The evidence of sustained CMA in adulthood is limited.

We present an interesting case of persistent CMA in adulthood.

Case presentation: A 49 years old ♀ referred to us stating a revulsion to milk since childhood, although occasionally eated cheese uneventfully. For the first time at the age of 27 years, she presented an immediate reaction after eating pizza with cheese. Since then, she reported moderate-severe systemic reactions (SR) with skin, respiratory and cardiovascular symptoms in any case of cheese ingestion. Additionally, one reaction occurred after cucumber consumption that was cut by knife used before on cheese and another one manifested as contact urticaria after the use of milk foam bath. From her medical history a well controlled asthma was reported and skin testing documented positive atopic background with sensitization in pollen (Olea, grasses, artemisia) and mould (alternaria) allergens. Sensitization to CM was detected by skin prick tests (SPTs), Prick to Prick tests (PTP) and specific IgE to CM allergens (Immunocap, Phadia). Besides, PTPs were performed to amino acid-based and partially-extensively hydrolysed formulas (TABLE). An oral provocation with baked milk was proposed in order to investigate possible tolerance but the patient was reluctant to any further diagnostic and therapeutic intervention.

Table 1 Sensitization profile in CM & formulas

	SPTs (mm)	PTP (mm)	sIgE	VALUE (Ku/l)
Cow's milk	5	+NP	f2	>100
a-LAL *	5	+NP	f76	+NP
β-LGL #	–	+NP	f77	+NP
Casein	12	+NP	f78	>100
NAN HA 2	+NP	12	+NP	+NP
Alfare/Frisolac AC	+NP	9	+NP	+NP
Nutriben AT	+NP	8	+NP	+NP
Neocate	+NP	–	+NP	+NP
Histamine/Control	5/–	+NP	+NP	+NP

*α-lactalbumin #β-lactoglobulin +NP: not performed / NAN HA: partially hydrolysed; Alfare, Frisolac AC: extensively hydrolysed; Nutriben AT: milk free-lactose;Neocate: amino-acid based formula.

Conclusion: CMA may cause severe reactions in adults even with the consumption of traces of milk proteins. Sufferers must be aware of the multiple different markings of milk in food products and be well educated in treating anaphylaxis with emergency kit and auto-injectable adrenaline.

1121
Cow's milk allergy thought to be related to dog keeping: two case reports

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Background: Exposure to the allergens of furry animals is considered a risk factor for the development of a certain type of food allergy. However, few reports have described allergies to milk associated with pet keeping.

Method: Of 180 patients with cow's milk allergy who were orally challenged, we report the clinical features of two patients whose serum casein-specific IgE levels were appreciably lower than whole cow's milk-specific IgE levels.

Results: Two girls aged 10 and 15 years reported abdominal pain, nausea, and mild hives beginning 20–30 min after ingesting cow's milk. These symptoms were considered to be psychological-based reactions to a dislike for milk because they used to drink it before enrolling in primary school. However, the skin prick test and oral milk challenge showed positive results; serum specific IgEs to cow's milk and bovine serum albumin were noted, whereas those to casein were negative. Both patients had been previously diagnosed with dog allergy, because they developed rash on their faces when licked by their dogs, and they had positive Can f 3-specific IgE. Taken together, the results suggested that the allergic reaction was triggered by bovine serum albumin because of cross-reacting IgEs to dog dander or saliva, similar to pork-cat syndrome.

Conclusion: To our knowledge, this is the first report of milk allergy associated with dog keeping. It may be important that different countries have different processes and temperatures for milk pasteurization. Clear distinguishing between IgEs to whole milk and those to casein would be helpful for suspecting a furry animals-food allergy association, and allergen component testing can help establish it.

1122
Direct effects of fermented rice with lactobacillus paracasei CBA L74 on Th1/Th2 response in children with cow's milk allergy

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Background: Probiotic fermented foods may modulate allergic response. We aimed to evaluate the effects of fermented rice with *L. paracasei* CBA L74 (RM-CBAL74) on Th1 / Th2 cytokines response in peripheral blood mononuclear cells (PBMCs) from children affected by IgE-mediated cow′s milk allergy (CMA).

Method: PBMCs from 3 children with sure diagnosis of IgE-mediated CMA (2 males, all Caucasian, mean age 3.5, range 1–5 years) were stimulated with beta-lactoglobulin (BLG, 100 μg/ml) in the absence or presence of RM- CBL74 at different doses (0.115- 115 mg/ml) for 48 h. IL-4, IL-5, IL-10 and IFN-γ production was analyzed on cell supernatant, by ELISA.

Results: PBMCs stimulation with BLG resulted in a significant increase in IL-4 and IL-5 production, but not in IL-10 and IFN-γ production, that remained stable after stimulation. RM- CBL74 stimulated, in a dose-dependent manner (maximal effective dose 11.5 mg/ml), IL-10 and IFN-γ production and inhibited IL-4 and IL-5 production.

Conclusion: Through a direct interaction with the PBMCs from IgE-mediated CMA children, RM-CBAL74 regulates allergic response modulating Th1/Th2 cytokines

production. These data suggest a potential use of probiotic fermented food for prevention and treatment of food allergies.

1123
Nutritional implications of elimination diet in patients with suspected food allergy

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Background: It has been estimated that up to 15% of the population is subjected to an elimination diet only for the suspicious of food allergy. The indiscriminate measure as in current medical practice of subjecting patients to strict elimination diets only for the suspicious of food allergy without a proper approach, leads to the patients undergoing restrictions of basic foods and often multiple foods, decreasing the calorie intake, the amount of macro and micronutrients in the end, all causes changes in the growth side malnutrition. The aim of this study was to compare the nutritional status and identify the impact of elimination diets in the daily nutrient intake of patients who have elimination diets for a suspected food allergy on a group of healthy children.
Method: A cross-sectional study was carried out from January to October 2014 at the Hospital Infantil de Mexico Federico Gomez. Patients 1–11 years old with a history of elimination of at least one of five foods (eggs, milk, wheat, corn, soybeans) for a minimum of 6 months were included. Full nutritional assessment was performed by comparing the anthropometric indexes to z score for age, total caloric intake was identified, and the amount of nutrients ingested between the two groups was compared, addition levels of calcium, vitamin D and total proteins were evaluated. Data analysis used descriptive statistics. Kruskal-Wallis and Spearman correlation were performed.
Results: The most frequent eliminated foods were milk, soy, egg, corn, and wheat. Comparing the number of foods eliminated with different anthropometric indexes, with a greater amount of eliminated food, the z-score of weight/age (W/A), height/age (H/A) and weight/height (W/H) were lower and the most affected index was fat reserve. Furthermore a significant difference in the amount of ingested nutrients (calcium and protein) and caloric intake between the elimination diet group and control with a $P < 0.001$ was observed, low calcium, vitamin D and total proteins were observed ($P < 0.001$) in patients undergoing elimination diets. Only in 5% of children was food allergy confirmed.
Conclusion: The study confirms the need for nutrition counseling for patients who have elimination diets and an overdiagnosis of food allergy.

1124
Risk-benefit assessment of nutritional immune interventions during early life

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Background: The immune health status is strongly determined during early life stages. Many immune-related diseases are thought to find their origin in adverse shifts in immune balances during pregnancy or the first 2–3 years of life, including atopic diseases. Therefore, immune health interventions during these stages of life may be most effective in reducing the loss of health, loss of quality of life and costs to society due to immune-related diseases and disorders. Several starting points for immune health interventions have been identified and are being developed into prophylactic or therapeutic approaches, particularly targeted at the early life stages. Unfortunately, there is no consensus on which parameters should be addressed to assess the safety and/or efficacy of the interventions and how all the available data should be interpreted at the end. Hence, it would be extremely helpful to address this issue by developing a pragmatic, flexible and science-based risk-benefit assessment.
Method: We adapted the risk-benefit approach published by Renwick et al. (2004), to develop a framework for risk-benefit assessment of immune health interventions during early life stages. As case studies, we collected all available *in vitro*/*vivo*/*silico* and human data on galacto-oligosaccharides and fructo-oligosaccharides.
Results: The severity of hazard and beneficial effects observed and the incidence at which such an effect may be considered acceptable, were used to weigh the risk and beneficial effects. This risk-benefit framework enables us to evaluate all intervention data available and forms the basis to derive the optimal dose levels of intake.
Conclusion: This novel approach enables risk assessors to take the multitude of different types of data available covering toxicity and efficacy studies into account, by ranking and weighing all available data. Ultimately, this assessment will help to determine optimal beneficial and safe dose levels of intake.

1125
The effect of anthropometric measurements made elimination diet due to food allergy

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Background: There is an increase in the incidences of food allergies, which is a particularly impotant disease that affects especially early infants. The removal of allergens from the diet pose a risk for nutritional deficiencies. The aim of this sectional study is to compare antropometric measurements and calorie intakes of a food allergic child who has a restricted allergen diet, with that of a healthy child.
Method: A cross-sectional study was perfomed with children, whose ages were between 0–36 months, whom were diagnosed as food allergic by pediatric allergens according to history, physical examination, laboratuary findings, and response to elimination diet. Food allergic children's food allergy status, demographic datas, duration of breast-feeding, age at the onset of complementary foods, clinical presentations, age at the onset of symptoms, age of diagnosis, age at the onset of elimination diet and the type and the amount of the food consumed during the elimination diet were measured via a survey sheet.
Results: 112 children (62 food allergic, 50 healthy) took part in the study. The mean of the food allergic group's age was 15.75 ± 7.84 months and %61.3 (*n*:38) of them were male. The mean of the control groups's age was 14.79 ± 6.77 months and %50 (*n*:25) of them were female. %25.8 (*n*:18) of the patients had an allergy only to milk, %25.8 (*n*:16) of them had an allergy only to egg, and %45.2 (*n*:28) of them had an allergy to both milk and egg. There were no significant difference concerning the weight, height, weight-for-height, weight-for-age and height-for-age found in both groups ($P > 0.05$). When the patients were compared according to their pre-elimination diet and post-elimination diet, there were 27 (%43) patients who had lost weight percentile rank after the elimination diet. There were no meaningful

correlation between the elimination diet span and the percentile loss ($P > 0.05$). A significant decrease in weight-to-age in patients after the elimination diet was found (P:0.01). While the patient group's intake of callories and proteins per kilogram was lesser compared to the control group's intake, the patient group's intake of carbonhydrates and fats was more when compared to the control group.

Conclusion: It is important for patients who had undergone the elimination diet because of the food allergies to have their growth monitored and cooperation with a dietitian is strongly advised.

Poster Session TPS 33

Diagnosis and management of food allergy

1127
Searching predictors for boiled egg oral challenge

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Background: A high percentage off egg-allergic children will outgrow its allergy throughout chilhood and adolescence. Boiled egg tolerance usually develops years before raw egg. Predictors of natural tolerance development are needed in egg-allergic patients to improve their management. Ovomucoid specific IgE antibody levels have been suggested to predict boiled egg tolerance. We have studied the relationship between boiled and raw egg tolerance with the ratio between ovomucoid (OVM) specific IgE / egg white specific IgE in order to evaluate its usefulness and value as a predictor of tolerance.
Method: Children aged 9 months - 23 years with IgE mediated egg allergy diagnosis, all of them with a boiled or raw egg challenge test were restrospectively recruited between October 2014 and December 2015. We have registered ovoalbumin, ovomucoid and egg white specific IgE levels and results of boiled and raw egg challenges. We have calculated the ratio between ovomucoid specific IgE and specific egg white IgE in all of them. Then we established the predictive value of this ratio.
Results: We have recruited 163 patients. By boiled and raw egg challenges patients were classified as boiled egg allergic (14) or tolerant (81), and uncooked egg allergic (22) or tolerant (45).

In the 36 positive challenge, 23 patients experienced cutaneous symptoms (urticaria and erythema), 7 patients had gastrointestinal symptoms, 6 presented with nasal symptoms and only 4 developed ocular reactions.

Ovomucoid specific IgE and Ovomucoid specific IgE/ egg white specific IgE ratio are the variables with a highest performance to predict a boiled egg positive oral challenge, both with an area under the curve (AUC) of 0.8. Despite of this fact the statistical association is higher with ovomucoid specific IgE/egg white IgE ratio (OR 1.5 OR 2.5) than using ovomucoid specific IgE isolated.

Both ovoalbumin specific IgE and egg white specific IgE in isolation have a low performance to predict a boiled egg challenge outcome.

Egg white specific IgE is the best variable to predict a raw egg challenge outcome (AUC 0.69).
Conclusion: Both ovomucoid specific IgE and ovomucoid specific IgE/specific egg white IgE ratio are good predictors for boiled egg positive challenge.

1128
Analysis on the characteristics of egg and milk allergy with low level of sIgE

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Background: Egg and milk were the common allergy food in children. Some children with low level of sIgE had obvious allergic reaction after ingesting the sensitized food. In this study, we want to find out the biological marker for the diagnosis of milk or egg allergy with low sIgE level.
Method: One hundred and twenty-three children (average 3 (2.4) years) and One hundred and forty-eight children (average 3 (1.4) years) were detected egg and milk sIgE separately, the level of sIgE below 17.5 kUA/l. They were divided into self-reported allergy group and not allergy group, sIgE positive group and sIgE negative group. Serum levels of egg and three components sIgE, egg sIgG and sIgG4, milk and three components sIgE, milk sIgG and sIgG4 were analysed with ImmunoCAP.
Results: The level of egg allergy group (1.12 (0.40, 3.47) kUA/l) is higher than not egg allergy group (0.59(0.24, 1.04) kUA/l) ($P = 0.01$); The level of milk allergy group (0.95 (0.52, 2.71) kUA/l) is lower than not milk allergy group (0.59 (0.24, 1.04) kUA/l.) ($P = 0.01$); There were no statistical difference of sex, family history of allergy, sIgE level between self-reported allergy group and not allergy group, sIgE positive group and sIgE negative group of egg and milk. There were no statistical difference of component sIgE level between self-reported allergy group and not allergy group. The correlation of egg sIgG and sIgG4 was higher than milk sIgG and sIgG4 ($r_s = 0.909$ vs $r_s = 0.675$). The level of sIgE/sIgG4 of egg allergy group was higher than not allergy group ($Z = -2.463$, $P = 0.014$). The level of sIgE/sIgG4 of milk allergy group was lower than not allergy group ($Z = -1.453$, $P = 0.146$), there was no statistical difference. The level of sIgG4/sIgG of milk allergy group was higher than not allergy group ($Z = -2.163$, $P = 0.031$). The level of sIgG of milk allergy group was lower than not allergy group ($Z = -2.531$, $P = 0.011$).
Conclusion: The sensitized mode of egg allergy was difference than milk allergy with low sIgE level. sIgE/sIgG4 had diagnostic value for egg allergy but not for milk allergy.

1129
Ana o 3-specific IgE antibodies improve diagnosis of cashew nut allergy in Japanese children

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Background: There are few studies on the diagnostic utility of component test for Ana o 3-specific IgE in cashew nut allergy. The aim of this study was to determine the usefulness of Ana o 3-specific IgE measurement in the diagnosis of cashew nut allergy based on the results of oral food challenge (OFC).
Methods: Thirty-three children with suspected cashew nut allergy were retrospectively enrolled to this study. We divided the subjects into two groups; positive and negative results of OFCs against cashew nut. Possible relationships between cashew nut allergy diagnosis and Ana o 3-specific IgE antibody measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) were analyzed. Diagnostic value was evaluated by receiver operating characteristic (ROC) analysis.
Results: Median age was 6.7 years (range; 2.5–11.9 years). The median specific IgE to cashew nut and Ana o 3 was 2.4 kUA/l

(<0.1–28.6) and 0.2 kUA/l (<0.1–36.9), respectively. Positive OFC was observed in 9 subjects (27%), anaphylaxis was seen in 3 (11%) of them. In the subjects with positive OFC, specific IgE to cashew nut and Ana o 3 was significant higher than those in subjects with negative OFC (6.1 kUA/l vs 1.4 kUA/l, $P = 0.0009$, 4.1 kUA/l vs <0.1 kUA/l, $P < 0.0001$). No subjects in positive OFC had negative specific IgE to Ana o 3. ROC analysis showed that Ana o 3-specific IgE had a superior area under the curve (0.9537; 95% confidence interval (CI), 0.8864–1.021) compared to cashew nut specific IgE (0.8611; 95% CI, 0.7098–1.021). Sensitivity and specificity of specific IgE were 83% and 89% to Ana o 3, 83% and 89% to cashew nut, which can be used to distinguish the optimal cut off point based on the ROC analysis.

Conclusion: Measurement of Ana o 3-specific IgE was a useful diagnostic marker, and combination of cashew nut and Ana o 3-specific IgE particularly improved diagnostic value in cashew nut allergy.

1130
Fluorescent immunosorbent assay for detection bovine β-lactoglobulin by a monoclonal antibody against human IgE binding epitope

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Background: The traditional method for detecting bovine β-lactoglobulin (BLG) is by immunoassay. However, antibodies used in the conventional methods cannot specifically recognize human IgE-binding epitope of BLG, resulting in the content of β-lactoglobulin allergic residues in dairy products (such as hydrolyzed formulas) can not be determined. Since quantum dots (QDs) are a kind of fluorescent nanometer-sized particles with unique photophysical properties, it has been widely used in immunoassays, molecular imaging, and *in vivo* biological labels. This work aimed to develop a new approach to detect β-lactoglobulin by fluorescent immunosorbent assay based on quantum dots with new antibody.

Method: A monoclonal antibody against human IgE binding epitope was developed. The H_2O_2-sensitive QDs were introduced to develop a fluorescent immunosorbent assay (FLISA) for detection BLG and BLG allergic residues in dairy products. The content of BLG in dairy samples and the content of BLG allergic residues in hydrolyzed formulas were analyzed, and the results were in compared with the tested by the conventional ELISA.

Results: The linear range for BLG detection was 125–4 × 10^3 ng/ml, and the limit of detection of FLISA was 0.49 ng/ml, it is 16-fold higher than that by ELISA with LOD of 7.81 ng/ml. The assay exhibited intra- (CV ≤ 12.95%) and inter-assay variability (CV ≤ 17.34%). The content of BLG in dairy samples has been detected, and average recoveries for spiked milk, whey and whey power were 99.26–106.55%, 103.93–108.92% and 100.87–112.31%, respectively.

Conclusion: The developed method could be a practicable approach to determine BLG and BLG allergic residues in dairy products with the advantages of sensitivity, accuracy, and high recovery.

1131
Structural analysis and allergenicity assessment of cross-linked bovine α-lactalbumin by polyphenol oxidase

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Background: Bovine α-lactalbumin is one of the most common and severe food allergen in milk, and enzymatic cross-linking processing is known to influence the allergenicity of food proteins. We aimed to investigate the relationship between structure and allergenicity of bovine α-lactalbumin cross-linked by polyphenol oxidase.

Method: Various polymers of α-lactalbumin were obtained by cross-linking with Polyphenol oxidase from agaricus bisporus. After separation of dimer, trimer and polymers, the structure were characterized by circular dichroism spectroscopy, ultraviolet absorption spectroscopy and fluorescence spectroscopy. The allergenicity of the various α-lactalbumin polymers was evaluated through IgE inhibition ELISA, *in vitro* digestibility and *in vivo* animal model.

Results: The secondary and tertiary structure of various α-lactalbumin polymers appeared a significant variation compared with nomomer of α-lactalbumin. Meanwhile, polymers had a higher hydrophobicity and a more loosely structure. In addition, the IgE-binding capacity of dimer, trimer and polymer significantly reduced compared with monomer of α-lactalbumin. More importantly, high polymer had lower IgE-binding capacity than dimer and trimer. Besides this, the dimer and trimer from cross-linked α-lactalbumin were easy to be degraded by gastric and intestinal digestion, but the polymer was relatively resistant to gastrointestinal digestion. At last, compared with cross-linked and native α-lactalbumin in animal model, levels of specific antibodies (IgG_1/IgE), histamine content in plasma were decreased significantly. Moreover, the levels of IL-4, IL-5, and IL-13 derived from spleen cells of mice sensitized by cross-linked α-lactalbumin were remarkably reduced, while INF-γ had no evident change.

Conclusion: The allergenicity of α-lactalbumin significantly reduce or eliminate by cross-linking the protein.

1132
Dietary non-digestible oligosaccharides reduce the sensitizing capacity of deoxynivalenol in a dose-dependent manner

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Background: Detrimental compound-exposure in early life can negatively impact normal immune development. Recently, we showed that the mycotoxin deoxynivalenol (DON), a fungal metabolite found in grain-based human diets, can disrupt intestinal tight junctions and can subsequently promote allergic sensitization. Since specific dietary non-digestible oligosaccharides have been shown to protect the gastro-intestinal barrier against DON-induced damage, we hypothesized that these oligosaccharides might also protect against sensitization to cow's milk proteins due to the inhibition of DON-induced gut damage.

Method: Upon arrival, female C3H/HeOuJ mice were fed either control cow's milk free AIN93G diet or AIN93G diet supplemented with a 0.5, 1, 2 or 4 w/v% mixture of a 9:1 ratio of short chain galacto-oligosaccharides and long chain fructo-oligosaccharides throughout the study. After 2 weeks, mice were sensitized five times weekly with 5 mg/kg DON with or without 20 mg whey protein. At D35, whey was i.d. injected (10 μg whey/20 μl PBS/ear) in the ear pinnae and the corresponding delta ear swelling at 1 h was measured as readout for the local activation of mast cells. Serum (D37) was collected 30 min after the subsequent oral challenge (50 mg whey/0.5 ml PBS/mouse) to assess the mucosal mast cell response (mMCP-1). At

D37, blood and immunological relevant organs were isolated.

Results: DON + whey exposure induced an increased acute allergic ear (skin) swelling as compared to DON + PBS exposed animals, both on control diet. The specific oligosaccharide mixture decreased the allergic ear swelling response in a dose-dependent manner as compared to the positive control animals. No alterations in the overall low allergen-specific antibody or mMCP-1 levels were found, whereas there was a trend towards a dose-dependent reduction of serum ST2 (IL-33 receptor) levels in mice on the oligosaccharide-containing diet.

Conclusion: Our study suggests that supplementation with dietary non-digestible oligosaccharides can help to protect the epithelial barrier disruption by DON, and to reduce the allergy-inducing capacity of DON.

1133
The role of activated leukocyte cell adhesion molecule (ALCAM) in food allergy murine model

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Background: Food allergy is abnormal immune response resulting from fail to establish oral tolerance and considered one of the worldwide major health problems. Activated leukocyte cell adhesion molecule (ALCAM), member of immunoglobulin superfamily transmembrane glycoproteins, is known for affecting immune response. However, there are currently no studies directly investigating the impact and functions of ALCAM in food allergy. So, we aimed to investigate functions of ALCAM in experimental food allergy.

Methods: Female C57BL/6 wild type mice and ALCAM-/- mice were intraperitoneally sensitized and orally fed with ovalbumin (OVA). We assessed parameters of experimental food allergy including symptom and diarrhea score, incidence of hypothermia, H&E stained intestine histology, serum IgE, and intestinal Th2 immune responses. We also checked changes of intestinal tight junction using electron microscope.

Results:

1 As severe symptoms were observed, experimental food allergy is successfully induced in wild type mice (Clinical score, 3.7 points; Diarrhea score 2.7 points; incidence of hypothermia 67%). In contrast, mild symptoms were observed in ALCAM-/- mice (Clinical score 2.75 points; Diarrhea score 1.5 points; incidence of hypothermia 25%).
2 We obtained correlate result from histology of H&E stained small intestine. That is, intestinal damages of ALCAM-/- mice are milder than wild type mice.
3 Besides, level of serum IgE and intestinal Th2 cytokines (IL4, IL5, IL13) were significantly suppressed in ALCAM-/- mice compared to wild type mice.
4 The change of intestinal permeability of tight junction also indicates that attenuated symptom is showed in ALCAM-/- mice.

Conclusions: According to our data, ALCAM may play a key role in OVA-induced experimental food allergy by affecting systemic immune responses.

1134
New perspective in predicting of food tolerance in early age children with cow's milk protein allergy

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Background: Cow's milk protein allergy (CMPA) is one of the most often allergy problem in early childhood, that leads to great socio-economic damage. Whereas minimum lengths of elimination diet is determined, there are still not determined individual criteria of adequate and needed lengths of it. In this study we present results of determination and evaluating of predictive markers of tolerance to CMP, that is quite important in management of food allergy, especially in children.

Objective: To determine and evaluate laboratory markers of developing tolerance to CMP in early age children with CMPA.

Methods: The prospective observational study included children ($n = 153$) with CMPA aged from 1 to 18 months, both males and females; and control group - 118 healthy children without allergy and clinical history of any allergy both in parents and sibs. Children with CMPA underwent clinical and laboratory examination twice (before 6–12 months of elimination diet and after reintroducing CMP), that included measurements of sIgE concentration (UniCAP) to cow's and goat's milk and it's fractions; measurements of sIgG4 to the same allergens (0–3 classes of concentrations). Blood samples of control group were studied once for measurement of serum sIgG4 for the same allergens.

Results: Serum sIgG4 before elimination diet were detected in 65% of patients with CMPA and in 86% of patients of control group, that significally higher vs group of children with food allergy ($P < 0.05$). 77 children (50.3%) with CMPA became tolerated to CMP after 6–12 months of elimination diet, that was significally associated with high (3+) class of concentration of sIgG4 to CMP before elimination diet, increasing of sIgG4 to high class of concentration in dynamics in patients with sIgE $\leq$0.7 kUA/l to CMP; decreasing of sIgE to CMP during elimination diet vs group of children, who had not become tolerated ($P < 0.05$).

Conclusion: sIgG4 can't be used in diagnosis of food allergy. High class of concentration of sIgG4 to CMP before elimination diet can be used as a favorable predictive marker of tolerance to CMP in early age children.

1135
Usefulness of component-specific IgE identifying risk factors for severe kiwifruit allergy in children

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Background: There are few reports about pediatric kiwifruit allergy. The aim of the study is to investigate the clinical feature of pediatric kiwifruit allergy, and validate the performance of specific IgE to alder, Bet v 1 and Act d 8 as risk factors for severe kiwifruit allergy in children.

Methods: We retrospectively analyzed patients' characteristics, specific IgE and clinical symptoms of kiwifruit allergic children who had visited our hospital between 2008 and 2013. We measured specific IgE to alder, Bet v 1 and Act d 8. We classified kiwifruit allergy into the local reaction group (Local) and the systemic reaction group (Systemic). Logistic regression analysis was performed to compare the two groups.

Results: Fifty four patients were included. Onset age was ranged from 1 to 13 years (median 6 years). Mucosal symptom was the most common symptom, appearing in 43 patients (78%). Thirty one patients (57%) had only mucosal symptom. Onset age was significantly lower in Systemic than Local. Specific IgE to alder, Bet v 1 and Act d 8 in Systemic were also lower than those in Local. Sensitivity and specificity of specific IgE were 67.7% and 78.3% to alder, 71.0% and 82.6% to Bet v 1, 83.9% and 78.3% to Act d 8 with optimal cut off point to distinguish Local from Systemic. Specific IgE to Bet v 1 and Act d 8 negative were also more likely to be seen in Systemic even after adjusted for onset age. Adjusted odds ratio (95% confidence

interval) of specific IgE to Bet v 1 and Act d 8 for Systemic were 4.4 (1.2–17) and 12 (3.0–52) with optimal cut off point.
Conclusion: Negative specific IgE to Bet v 1 or Act d 8 were identified as risk factors for severe symptoms in kiwifruit allergic children sensitized to kiwifruit.

1136
Peanut sIgE sensitized without symptoms is caused by the tree pollen allergen

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Background: As all kown, peanut is a common food allergen and can cause anaphylactic shock in Europe, while it rarely cause a severe allergic reaction in China. Although peanut sIgE can be found in patients serum, but are usually no peanut related symptoms, this study focuses on Chinese patients with peanut sensitization, and analyzes its components and the relationship with palne tree and birch sensitization.
Method: 33 cases of peanut-sIgE-positive patients were selected, their serum sIgE of peanut components Ara h 1, Ara h 8 and plane tree and birch and CCD were dectected by UnitCAP. And questionnaire survey were carried out on all patient. 25 cases of peanut-sIgE-negative patients also included.
Results: 18%(6/33) peanut sIgE positive patients were sensitized to Ara h 1, only 9% (3/33) sensitized to Ara h 8. And 91% of them were sIgE-positve to palne tree, 55% (18/33) were sIgE-positve to birch, 70% (23/33) were sIgE-positive to CCD. Only 8% (2/25) peanut negative patients were sensitized to plane tree and 4% (1/25) to birch.

The 6 Ara h 1-postive patients were all sensitized to plane tree and CCD, 5 of them were birch-postive, 2 were Ara h 8-postive.

Peanut positive patients had higher plane tree positve rates and higher birch positve rates than the peanut negative patients ($P < 0.01$).

Only 2 patients has mild oral allergy syndrome after consuming peanut, which with Ara h 1-sIgE of 3.33 and 1.64 kU/l. The patients with Ara h 1-sIgE lower than 1.64 kU/l were had no peanut allergy, but 94% of them has pollen related allergic rhinitis and/or asthma.
Conclusion: Peanut positive patients had higher plane tree positve rates and higher birch positve rates than the peanut negative patients. Peanut-sIgE positive patients in China without symptoms might be caused by plane tree and birch pollen allergen.

1137
Age of patient at time of skin prick testing affects accuracy at predicting challenge outcome

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Background: Skin prick test (SPT) is an important diagnostic tool for IgE mediated food allergy. It is utilised to assess the probability of tolerance acquisition and determine when it is appropriate to proceed to confirmatory oral food challenge (OFC) testing. There is limited published data whether accuracy and performance characteristics of SPT vary across different age groups. The aim of this study was to compare food specific SPT predictive accuracy between age groups.
Method: This is a retrospective review of an OFC database of children presenting to a paediatric allergy clinic in a tertiary referral private hospital in Melbourne, Australia. OFC were performed according to standard protocols. An OFC was considered positive in the presence of an objective clinical reaction (urticaria, angioedema, rhinitis, conjunctivitis, persistent cough, wheeze, vomiting, or hypotension) or with reproducible/persistent subjective symptoms (throat tightness, oropharyngeal pruritis, abdominal pain). Using SPT results and OFC outcomes, we generated age-stratified SPT predictive accuracy [area under the curve (AUC) of receiver operating characteristic (ROC) curve] and SPT performance characteristics of predetermined SPT thresholds for baked egg, cooked egg, raw egg and peanut.
Results: Between April 2011 and March 2014, 1515 OFC were conducted in 1083 children [median age 5.3, interquartile range (IQR) 2.8–8.5 years]. Overall rate of allergic reaction during OFC was 20.2% (306/1515). For raw egg, SPT predictive accuracy was higher in children ≤2yo than in children aged 2–5yo (AUC = 0.82, 95%CI 0.68–0.95 vs AUC = 0.55, 95%CI 0.39–0.71; $P < 0.05$). For peanut OFC, SPT predictive accuracy was higher in children aged 2–5yo than in children aged ≤2yo (AUC = 0.92, 95%CI 0.86–0.98 vs AUC = 0.63, 95%CI 0.45–0.80; $P < 0.005$). On age stratification, food-specific performance characteristics of predetermined thresholds varied between age groups. For example, for raw egg OFC, the sensitivity and specificity associated with a 3 mm SPT threshold were both higher in children ≤2yo (100%, 95%CI 75.3–100%; 50.0%, 95%CI 28.2–71.8%) than in children aged 2–5yo (56.3%, 95%CI 29.9–80.2%; 43.1%, 95%CI 29.3–57.8%).
Conclusion: Age at time of SPT affects its accuracy at predicting OFC outcome. To improve the accuracy and performance of this important diagnostic tool, age-specific cut-offs should be used in clinical practice.

1138
Milk components sensitivity with goat's and sheep's milk sensitivity in cow's milk allergy: effects on prognosis

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Background: Cow's milk allergy is the most common food allergy in infancy. Cross reaction with goat's milk and sheep's milk can be seen and milk komponent sensitivity can also be present.
Method: Sixty-six patients diagnosed with cow's milk allergy (CMA) were evaluated for milk allergen components sensitivity as well as goat's milk and sheep's milk cross reactions. Elimination and tolerance groups were compared to identify risk factors of not developing tolerance .
Results: Onset of symptoms of 20.3% patients were before 3 months of age. Mean age of onset and diagnosis were 4.7 ± 2.8 (1–18) and 7.8 ± 4.7(1–24) months. At first admission 24.3% of patients had tolerance. Only 2 patients developed tolerance after a mean of 31.9 ± 45.5 months elimination. Mean cow's milk (CM)-spIgE was 33.4 ± 108(0–862) kUA/l, goat's milk (GM) spIgE was 18.7 ± 28.2 kUA/l, sheep's milk (SM)-spIgE was 21 ± 30.0 kUA/l and GM-spIgE and SM-spIgE were both 84.8% positive. Mean α-lactalbumine-spIgE was 9.8 ± 17.6 kUA/l, β-lactoglobuline-spIgE was 9.8 ± 17.6 kUA/l, casein-sIgE was 21.9 ± 32.2 kUA/l and percentage of positivity of all were respectively 69.7%, 62.7%, 77.3%.

CM-spIgE levels of elimination and tolerance groups were significantly different as 42.3 ± 123.8 kUA/l and 7.8 ± 11.6 kUA/l respectively. There was no difference between the groups for total IgE levels, eozinophilia, gender, consanguinity, age of onset and diagnosis ($P > 0.05$).

α-lactalbumine-spIgE (74%), β-lactoglobuline-spIgE (82%), casein-sIgE (86%),

GM-spIgE (92%) and SM-spIgE (92%) positivity of elimination group significantly higher than tolerance group. CM-spIgE levels were associated with milk komponent-spIgE and also with GM-spIgE and SM-spIgE. Casein-spIgE, SM-spIgE, GM-spIgE levels and high induration diameter of CM at skin prick tests were inverse related with tolerance. Respiratory symptoms and anaphilaxis were seen mostly with higher CM-spIgE levels. There was no relation between milk component levels and different symptoms.

Induration diameters of CM and SM at skin prick tests were respectively 8.5 ± 7 (0–35) mm and 7.5 ± 7(0–30) mm and induration diameter of CM was significantly high in elimination group (no difference of GM). CM provocation tests were positive in elimination group with a mean provocation dosage of 16 ± 27.5 ml.

Conclusion: Patients with sheep's milk and goat's milk cross reactions, high casein-spIgE levels and large induration diameters of CM in skin prick tests were in risk of peristant cow's milk allergy.

1140
Open oral food challenge testing - a 90-month retrospective study

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Background: Despite advances in food allergy diagnosis, the combination of both *in vivo* and *in vitro* testing is often insufficient in predicting tolerance. Oral food challenges (OFCs) remain the gold standard for effectively confirming or ruling out clinical allergy to a specific food. Challenges should be done in specialized centers and monitored by skilled allergy specialists. We aimed to summarize our experience in OFCs, performed in our Immunoallergology Department over the course of seven and a half years (January 2008 to June 2015), extending the data on a previous 3-year study presented at EAACI 2011.

Method: Data were compiled from clinical files. All OFCs were open and followed an age-adapted protocol of progressive food intake, after which followed a 150-min observation period. A negative OFC required the uneventful ingestion of a meal-sized portion of the tested food.

Results: We performed 373 open OFCs in 242 different patients (51.5% female, mean age 20.8 years-old, between 3 months and 91 years-old). Egg was the most frequently tested food (94 challenges), followed by cow milk (61), shrimp (37), peach (22), salmon (10), peanut (10), apple (8) and wheat flour (7). The result was negative in 347 challenges (93%). 172 had a positive skin prick test (SPT) and 135 patients tested positive for food-specific IgE-antibodies (mean: 4.76 kU/l). Both tests were positive in 95 patients (27.4%). OFCs were positive in 26 challenges (7%) (fish-6, cow milk-6, mollusks-3, shrimp-2, egg-2, tree nuts-2, spinach, peanut, wheat, orange, apple). In these patients, SPTs were positive in 14 cases (53.58%), the mean specific IgE level was 2.81 kU/l, with both tests being positive in 11 patients (42.3%). Symptoms were mild to moderate in severity and included mostly cutaneous (urticaria), upper respiratory and gastrointestinal (abdominal pain, vomiting) manifestations. One challenge had a delayed positive result (milk-delayed rash). There was no difference between food groups concerning the severity of manifestations or their treatment.

Conclusion: OFCs in a controlled setting are a useful diagnostic tool in order to avoid unnecessary dietary restrictions. The safety of the procedure relies on the supervision of skilled allergy specialists in a center where these tests are frequently performed.

1141
Food challenges in a secondary care setting - a service evaluation

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Background: Food challenges are the gold standard method for confirming diagnosis or excluding ongoing IgE mediated food allergy, but are resource-intense and run the risk of anaphylaxis. Appropriate patient selection and timing is important; studies have attempted to determine levels of sensitisation (specific IgE bloods or skin prick test) that indicate whether a challenge should be arranged or avoided. Tertiary centres with high throughput will have algorithms for patient selection; a secondary setting such as our department may be able to offer a more personalised service, but is this safe / effective?

Method: Timing of challenges in our service is agreed between the consultant and families, taking into account information from investigations, but also other factors such as importance to the family as getting a definite answer at a particular point as well as their approach to risk. All challenges are supervised by the consultant. We undertook a retrospective review of challenges December 2011- October 2015, using information from clinical letters before and after the challenge.

Results: Of 43 patients during this time, 35 (81%) were under 8 years old. Fifteen (35%) had a positive challenge, compared with 19% at our nearest tertiary centre. Positive challenge was more likely for peanut (55%) than egg (14%) or milk (0%). 0/5 patients with negative SPT reacted;1/5 patients with negative specific IgE had a skin reaction and the challenge was abandoned by family choice. 1 of 43 patients required intramuscular adrenaline, 3 patients had nebulised salbutamol - these had all had peanut challenge. Some patients with positive challenges did not require any treatment.

Conclusion: Our approach has a relatively high proportion of positive challenges, especially peanut, probably patients with mid-range sensitisation but no history to guide decision making. However the overall safety profile was satisfactory. Fewer negative challenges with egg and milk was expected: there would usually have been evidence from serial investigations that an allergy may have been outgrown. Our approach does enable families to have clarity, and many are then able to avoid unnecessary ongoing food allergen restriction even when some sensitisation persists. Informal feedback from families is that, whatever the outcome of the challenge, they are pleased with the choice they made, and they feel it has been a collaborative service. More formal structured feedback is planned.

1142
Determining the usefulness of allergometric tests in predicting the outcome of oral food challenges in Portuguese patients

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Background: Oral food challenges (OFCs) remain the gold standard for effectively confirming tolerance to a specific food. However, challenges are inherently risky procedures and methods to determine their outcome would greatly improve food allergy management. We aimed to assess if the results of allergometric tests such as skin prick tests (SPT) and serum specific-IgE (sIgE) could be used to predict the safety of OFCs in a group of Portuguese patients.

Method: Data were compiled from clinical files of patients in our department that had undergone OFCs from January 2011 to June 2015. All OFCs were open and

followed an age-adapted protocol. A negative OFC required the uneventful ingestion of a meal-sized portion of the tested food. The diameter of SPTs wheals and sIgE values prior to the OFC were recorded, with food fractions specified for egg (yolk, white, ovomucoid) and cow milk (casein). A 95% confidence interval (95CI) was calculated for the means of the parameters obtained from the largest series of OFCs. The results were analyzed using IBM SPSS Statistics Version 23.

Results: We recorded 284 OFCs in our outpatient clinic, mainly in children (64.1%). Only 31% had a positive history of respiratory (25%) or cutaneous (5.6%) allergic disease. The most tested foods were egg (91 challenges), cow milk (53 challenges), and shrimp (27 challenges). Seventeen challenges (6%) were considered positive. Most patients showed cutaneous symptoms (urticaria-12) or gastrointestinal symptoms (abdominal pain/vomiting-4). One patient showed respiratory symptoms (milk-wheezing). A 95CI was calculated for the means of the parameters obtained from the largest series of OFCs (egg, cow milk, and shrimp). We established that negative OFCs had an upper limit of the 95CI for mean SPT wheal of 4.5 mm for egg white, 2.7 mm for egg yolk, 6.6 mm for ovomucoid, 4.1 mm for cow milk, 5 mm for casein, and 3.9 mm for shrimp. Correspondent values of sIgE were determined as 7.8, 7.7, and 8.8 kU/l for egg white, yolk, and ovomucoid, respectively; 2 and 1.1 kU/l for cow milk and casein, respectively; and 1.2 kU/l for shrimp.

Conclusion: We postulate that wheal diameter of SPTs and sIgE results above the 95CI upper limit for the mean of negative OFCs cannot be considered likely to result in a negative OFC and, therefore, correspond to higher risk procedures. Such values vary depending on the allergen and, most likely, on the studied population (in this case, Portuguese patients).

1143
Which is the next nut to crack?

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Background: Nut allergy is the most common cause of anaphylaxis in children. With peanut immunotherapy treatment close to clinical practice, tree nuts are now being considered. However, there are many nut types, and there needs to be prioritisation according to prevalence, severity, and patient opinion. It is important to consider how allergy to each nut type impacts nut allergic families. We therefore designed a questionnaire to study this.

Method: Patient interviews were used to identify and prioritise domains and questions. The questionnaire was trialed on consultants and medical students. Questionnaires were offered to parents of allergic patients (nut and non-nut allergic), and staff members (medical and non-medical) in paediatric allergy clinics. Microsoft excel was used for analysis.

Results: 30 parents and 12 staff members completed and returned the questionnaire. Parents deemed takeaways and restaurant food as the most troublesome factor; whilst staff thought poor labelling and unsuspected nut content in food caused the most difficulties. The top tree nuts that were selected by parents to be the next target of immunotherapy were almond (32%) and hazelnut (28%). Staff chose hazelnut (33%), followed by cashew nut (27%). Additionally, the questionnaire revealed that amongst all groups, more than half mistakenly believed that nut allergic patients should also avoid pine nuts (58%) and chestnuts (62%). In all groups, more than 90% felt that tree nut immunotherapy would vastly improve quality of life.

Conclusion: Parents chose almond and hazelnut due to perceived lifestyle disruption and prevalence in food. Staff selected hazelnut and cashew nut based on allergy prevalence and severity of the allergy. As almond allergy is rare, this study suggests that hazelnut and cashew nut would be the best targets for tree nut immunotherapy.

1144
Knowledge and practices of general practioners in UK about food allergy: a survey

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Background: Food allergy (FA) has significantly increased in last two decades. It is the leading cause of anaphylaxis in children and adolescents. Initially children with FAs are expected to present to general practitioners (GPs) or Primary Care Physicians. This study aims to provide insight into knowledge and perceptions about FA among GPs in the region of Harrogate (United Kingdom).

Method: A validated web-based Chicago Food Allergy Research Survey for Primary Care Physician was sent to hundred and twelve GPs in our area. Findings were analysed to provide itemised knowledge score and to look into the practices of our local GPs.

Results: Response rate for our survey was over 40%. Majority of our participants had more than 5 years of working experience. Overall, GPs answered 55.3% of knowledge-based questions. Our survey demonstrated that 73.9% of GPs were aware of the fact that food specific IgE or skin prick test is not enough to diagnose FA. However, only half of the GPs were able to identify cow's milk as potential cause for anaphylaxis. Survey further highlighted that among GPs who were aware of cow's milk as potential fatal allergen, 21.7% would still advice parents to continue giving cheese and yogurt to children with known Cow's milk allergy (CMA). In addition, eczema was recognized by 77% of our respondents as an isolated symptom of CMA but only 53% will change infant formula to hydrolysed formula. Vast majority of our GPs demonstrated good knowledge about how to manage anaphylaxis however, only 47.2% were aware of correct adrenaline dose. Regarding vaccines, only half of the participants knew that MMR could be safely administered in community in children with egg allergy. Minority of GPs (22.2%) mentioned increase in life threatening episodes associated with FA but 64.4% knew that there is no cure for FA.

Conclusion: Our survey clearly demonstrated sub optimal knowledge at certain domains of FAs and anaphylaxis among GPs. GPs also recognised the need of education in allergy. We recommend that periodic educational programmes to be incorporated in monthly GPs updates and online modules should be started by regional paediatric specialists in order to enhance knowledge of primary care doctors. These programmes will also help GPs to become aware of recent advances in field of paediatric allergy.

1145
Safety profile of oral immunotherapy with cow's milk and hen's egg: a 10-year experience in controlled trials

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Background: Oral immunotherapy (OIT) for food allergy is gaining interest, due to the favorable clinical results reported with cow's milk, hen egg an peanut. The safety of the procedure remains a major aspects, that can limit the introduction of OIT in clinical practice.

Method: The selection and exclusion criteria were the same across the trials, where children who did not overcome their sensitization were enrolled. The clinical records of 68 children receiving an active treatment

(40 cow milk and 28 egg) were carefully reviewed. Out of 68 children, 6 (9%) had to discontinue the OIT procedure due to the onset of severe adverse events. 50% of children received the build-up and maintenance phase without adverse reactions. Mild to moderate reactions were documented in 28 patients, who could anyway complete the desensitization. Most reactions were mild or moderate, requiring only symptomatic treatment, and often occurring in concomitance of acute events.
Results: We describe herein in detail the occurrence and characteristics of adverse events (AEs) in children carefully selected for OIT and participating in controlled trials at our Unit.
Conclusion: In conclusion, a careful review of the patients receiving food-OIT in controlled trials confirmed that the occurrence of adverse events is not negligible, but that around 90% of children can achieve an effective desensitization. The procedure remains investigational, and should be performed only by trained physicians, especially in the pediatric setting.

1146
The long-term prognosis of oral immunotherapy for eggs and cow's milk allergy

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Background: Current standard of care for childhood food allergy is dietary avoidance while awaiting natural outgrow. Recently, efficacy and safety of oral immunotherapy (OIT) as a disease-modifying treatment has been reported. However, there have not been many reports on long-term outcome of OIT.
Objective: The aims of the study were to evaluate the long-term prognosis of OIT for egg and cow's milk allergy and safety of the OIT.
Methods: We previously reported randomized controlled trials (RCT) of rush OIT for 45 children with IgE-mediated hen's egg allergy and 32 with cow's milk allergy confirmed by double-blind placebo-controlled food challenge (DBPCFC). Most of the patient had history of anaphylaxis by small amount of ingestion of the food. We employed the delayed control group who continued food avoidance for 3 months while the treatment group started rush OIT. The primary outcome was threshold dose (TD) of DBPCFC at 3 months and we found that significant increase in TD in the treatment group compared with the control in both egg and milk OIT. Then, the control group performed rush OIT and we continued to follow the both groups in the maintenance phase of OIT. In this study, we evaluated clinical status such as the daily intake of treatment food and adverse events in the third years of OIT.
Results: In egg OIT group, 65% of the patients could take one or more boiled eggs, 23% could take a little amount of boiled eggs, 11.6% had not yet reached to the third year at this study point and none returned to the complete elimination of egg. In cow's milk OIT group, 25% of the patients had 200 ml or more of milk, 6.2% had 50–200 ml, 6.2% had 10- 50 ml of milk, 62% had not yet reached to the third year and only one patient returned to the complete elimination diet of milk. No significant adverse events was noted in the third year except for one patient with milk allergy who had to use epinephrine injection.
Conclusions: With OIT, many patients could take moderate amount of eggs or milk without fear of anaphylaxis that they experienced before OIT although the amount of the food that they could take was different.

1148
Allergen-specific oral immunotherapy with wheat

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Background: Wheat is one of the most important food allergens in childhood but data about oral immunotherapy (OIT) in wheat allergic children are lacking.
Objective: To evaluate the effectiveness and safety of an OIT protocol developed by the authors, applied to children with IgE-mediated wheat allergy and with at least 12 months follow-up period after the up-dosing phase.
Method: Included 2 cases of children with IgE-mediated wheat allergy diagnosis since the first year of life, with moderate mucocutaneous symptoms, that successfully completed the up-dosing phase of an OIT protocol and a minimum follow-up of 12 months after reaching maintenance phase. The applied protocol, using bread/pasta/flakes as allergen extract, began with sub-lingual doses followed by oral ingestion of increasing doses of wheat, always in hospital settings, until reaching the target dose of 100 g/day of wheat.
Results: The 2 children aged 4 and 10 years-old, with IgE-mediated wheat allergy, were symptomatic at the beginning of the protocol. Both children successfully completed the up-dosing phase achieving the target dose of 100 g of wheat/day in 4 months, in 4 and 6 hospital sessions. During the up-dosing phase, mild to moderate adverse reactions (mucocutaneous/gastrointestinal symptoms) were recorded, which resolved spontaneously or with oral

	Patient 1	Patient 2
Age (years, months) Gender	9 months Male	3 years and 7 months Male
Wheat-allergy history	8 months old: Cough, generalized urticaria and facial angioedema	7 months old: Generalized urticaria and angioedema, bronchospasm
Wheal diameter in skin prick testing before treatment (mm)	Wheat: 3 Gluten: 3.5 Gliadin: 8.5 Prick by prick with gluten-containing cereals: 12 Other cereals: negative	Wheat: 10 Gluten: 11 Gliadin: 8 Oat: 4 Barley: 10 Rye: 9.5 Prick by prick with gluten-containing cereals: 15
s-IgE levels before treatment (KU/l)	Wheat: 1.3, rye: 1.69, barley: 0.49, oat: <0.1, 5-ω-gliadin: 0.11, r tri a 14 < 0.1	Wheat: >100, rye: 100, barley: 100, oat: 88.5, 5-ω-gliadin: 21.7, r tri a 14 2.7
Wheal diameter in skin prick testing after treatment (mm)	Wheat: negative Gluten: negative Gliadin: negative Prick by prick with gluten-containing cereals: 4 Other cereals: negative	Wheat: 7 Gluten: 9 Gliadin: 4 Oat: 4 Barley: 10 Rye: 5 Prick by prick with gluten-containing cereals: 14
s-IgE levels after treatment (KU/l)	All cereals <0.1	Wheat: 77.5, rye: 78.7, barley: 64.6, oat: 27.7, 5-ω-gliadin: 1.78, r tri a 14 0.68

Patients characteristics.

anti-histamines. After 1 year follow-up children maintain wheat daily ingestion. A substantial decrease in wheat sensitization was observed by serum specific IgE measurements.
Conclusion: Our wheat OIT protocol guaranteed a clinical tolerance state after 1 year with great improvement in the quality of life of those children and caregivers. Large controlled trials are needed to investigate the short- and long-term effectiveness of OIT in moderate to severe wheat allergic patients.

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Oral immunotherapy in clidren with IgE-mediated wheat allergy: is the treatment possible from the diagnosis moment?

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Background: Current management of wheat allergy is based on avoidance. We propose an active intervention to promote tolerance in IgE wheat-allergic children.
Objetives: To evaluate the safety and efficacy of our oral immunotherapy (OIT) protocol with wheat.
Methods: 2 patients (table 1) underwent OIT treatment with an up-dosing phase, until appropriated doses for their age were reached, followed by a 6-months maintenance phase. Treatment started with an open oral food challenge (OOFC) and the last dose tolerated without symptoms was considered as the starting point for the build-up phase. Weekly increases were performed in hospital and they continued the daily home-dosing.
Results: For the OFC and the first doses of treatment gluten-containing 5 cereals baby food was used (9.3% protein) Threshold doses during the OFC were 1 g of cereal porridge for patient 1 and 0.1 g for patient 2. No pre-medication was administered during the treatment. The food used in the build up phase was adapted to the patient age. Patient 1 completed the escalation phase in 9 weeks, when 35 g of cereal baby food were achieved (3 g of wheat protein). In patient 2, porridge was substituted with an equivalent amount of wheat pasta until 60 g (3.5 g of wheat protein) were reached (14 weeks). Both patients successfully finished this phase with no elicited reactions during the increases or home doses. After the up-dosing, patient 2 continued the ingestion of wheat, and avoided other gluten-containing cereals during a month. Then, OFC with oat, rye and barley were successfully performed. Patient 1 has cotinued to ingest multi-cereal baby food daily. For the maintenance phase parents were given a detailed chart of foods containg 3 g of wheat protein as examples for the daily home-dosing. Table 1 shows the decrease of s-IgE levels and wheal diameter in prick tests after the treatment.
Conclusion: Our wheat OIT protocol was safe and efficient. Also, it shows the possibility of a normalization of the diet and daily routines even, from de diagnosis moment before the first year of life.

1150
Doses of major allergens in peanut associated with oral tolerance

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Background: The LEAP study showed that peanut consumption in early life dramatically reduced the prevalence of peanut allergy among high risk children. The preferred peanut snack used for the study was Bamba, a corn puff containing ~50% peanut. Our objectives were to compare Arah1, Arah2 and Arah6 levels in Bamba and to estimate the weekly doses of specific peanut allergens associated with oral tolerance.
Method: Extracts of Bamba (100 mg/sample) from either the UK ($n = 7$) or the US ($n = 8$), or 25 individual Bamba sticks, were analyzed by ELISA for Arah1, Arah2 and Arah6 using purified natural allergen standards. The limits of detection of the ELISA were: Ara h 1, 32 ng/ml; Ara h 2, 2 ng/ml and Ara h 6, 0.8 ng/ml). Allergen consumption in the LEAP study was estimated by calculating the amount of allergen/Bamba stick and extrapolating from the median peanut consumption reported in the study (7.7 g peanut protein/week).
Results: The absolute amounts of peanut allergens in Bamba were remarkably consistent: $n = 15$, Ara h 1, 2427 μg/g (11% CV); Ara h 2, 1970 μg/g (15% CV); and Ara h 6, 2379 μg/g (15% CV), with no significant differences between lots purchased in the UK or the US. Moreover, the levels of each allergen were present in ~1:1:1 ratio. Median weekly doses of allergens were calculated based on consumption of 80 Bamba sticks (equivalent to 7.7 g peanut protein) and amounted to: 83 mg Ara h 1, 120 mg Ara h 2 and 127 mg Ara h 6 (total 330 mg/week).
Conclusion: Unlike other peanut food products, Bamba is a reproducible and consistent formulation of peanut allergens with each of these three major allergens present in uniform amounts. The results provide, for the first time, target doses of specific peanut allergens that are associated with prevention of peanut allergy and which, by extension, could apply to the induction of tolerance to other food allergens.

1152
Systematic education for staffs of schools, nursery schools and kindergartens in pre-hospital care including adrenaline auto-injector use in an anaphylactic emergency

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Background: Anaphylaxis is a serious hypersensitivity reaction that is rapid in onset and potentially life-threatening. The self-administered adrenaline auto-injector (e.g., EpiPen®) is an essential treatment agent in pre-hospital care for anaphylaxis. However, education for school staff is crucial, as the adrenaline auto-injector is not necessarily used appropriately, even in instances when its use is warranted.
Objective: We investigated effective education methods for the staffs of schools, nursery schools and kindergartens in pre-hospital care including adrenaline auto-injector use in an anaphylactic emergency.
Method: Lectures were held for 286 staff members of schools, nursery schools and kindergartens (14 lectures with 20–22 participants). A survey was conducted before and after the lecture, and problems in the use of the adrenaline auto-injector indicated by the school staff members were examined using the Visual Analogue Scale. The lecture included discussions of food allergy, anaphylaxis, how to use the adrenaline auto-injector, and post-administration measures; practical instruction on adrenaline auto-injector use; and the viewing of an original DVD on basic initial treatment of anaphylaxis.
Results: Participants demonstrated a better understanding of food allergy and anaphylaxis and knowledge of methods and the timing for adrenaline auto-injector use following the lecture ($P < 0.001$). Multivariate analysis of 'confidence in the ability to use the adrenaline auto-injector' showed a significant correlation with 'understanding of the timing of adrenaline auto-injector use' ($\beta = 0.271$, $P < 0.005$), 'understanding of anaphylaxis' ($\beta = 0.265$, $P < 0.001$),

'acquisition of skill in adrenaline auto-injector use' ($\beta = 0.238$, $P < 0.001$), 'understanding of the basic initial treatment of anaphylaxis' ($\beta = 0.224$, $P < 0.01$) and 'recognition of the need for adrenaline injection' ($\beta = 0.165$, $P < 0.005$).

Conclusions: Education that provides a heightened understanding of anaphylaxis, acquisition of skill in and the timing of adrenaline auto-injector use, understanding of the basic initial treatment of anaphylaxis and recognition of the need for adrenaline injection is important for the staffs of schools, nursery schools and kindergartens in promoting appropriate pre-hospital care including adrenaline auto-injector use in an anaphylactic emergency.

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Food allergy education program at elementary school as science communication: a pilot study

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Background: Food allergy (FA) is one of the most important health issues in schoolchildren. Schools are not rare places where anaphylaxis caused by FA happens. Although it is common that FA education is provided for patients with FA at hospitals or clinics, we do not have the standard curriculum for FA at schools. The aim of the study was to evaluate the acceptability and effectiveness of FA education program as science communication at elementary school.

Method: We developed the FA education program as science communication with allergists, pediatricians, a science communicator, and a medical illustrator, schoolteachers and parents. The program topics included as follows:

1 FA signs/symptoms,
2 immunological reaction in the body,
3 food allergens,
4 food label-reading,
5 how to be a good pal with classmates with FA,
6 how to take an action for an emergent case of FA; and
7 epinephrine auto-injector.

We conducted 60-min FA education program for children at public elementary schools in August, 2015. The participants completed the pre and post questionnaire for evaluating the program acceptability and the knowledge and attitudes towards FA.

Results: We had 42 participants in the FA program. The questionnaire was completed by 36 participants. There were 32 participants who considered the FA program was good and understandable. Furthermore, 32 participants recommended the FA program should be offered in regular school class for all children. The number of participants who had confidence in taking an action for an emergent case of FA following the FA program increased after joining FA program (32/36 vs 12/36, $P < 0.05$). The knowledge and attitudes toward FA were also improved after this program.

Conclusion: To make a proactive management for FA at schools, not only children with FA but also children without are encouraged to have an opportunity to learn FA at school on a regular basis.

1154
Impact of food allergy on quality of life - FAQLQ QUESTIONNAIRE

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Introduction: Food allergy (FA) affects 8.5% percent of children in Portugal. This study evaluates the impact of food allergy on quality of life (QoL).

Methods: We performed a study using the Food Allergy Quality of Life Questionnaire *FAQLQ*. The appropriate questionnaire will depend on the patient's age. *FAQLQ-PF* (0–12 years) as noticed by the parents. *FAQLQ-CF* and *FAQLQ-TF* are self-administered tools that measure the impact of FA on children (8–12 years) and teenagers (13–17 years). We applied the questionnaire to patients under 18 years diagnosed with FA in the last 3 months.

Information on food allergens and demographic data was collected for all children.

Results: The questionnaire FAQLP-PF was applied to 13 parents of children under 12 years. The questionnaires FAQLP-CF and FAQLQ-TF were applied to 9 children and 9 teenagers, respectively.

The mean age of the population with food allergy was 10 ± 5.4 (1–17 years). 18 patients (58.1%) were male; 38.7% had rhinitis, 27.6% had atopic dermatitis and 16.1% had asthma. 19 (61.3%) were allergic to 1 or 2 foods; 12 (41.4%) were allergic to 3 or more foods. The egg are the most common food allergen implicated in children (38.7%), followed by milk proteins (35.5%), shrimp (31.09%), and fresh fruits (27.6%).

The median score of the questionnaires were: FAQLQ-PF = 5.2; FAQLQ-CF = 4.9; FAQLQ-TF = 4.

The correlation between the severity of the reaction (Mueller classification) and the FAQLQ is 0.3 ($P = 0.05$). Positive correlation between the number of food allergies and impairment in the QoL was not found.

Conclusions: The parents were the most affected group at level of the impact on quality of life (FAQLQ-PF 5.2), as indicated by them FA had significant impact in meal preparation and on their stress level, it affected the family social activities and the school absenteeism. We found a positive but weak correlation between the severity of the reaction and the impairment in the quality of life (FAQLQ).

The results demonstrate that FA impairs the children's quality of life in all age groups and also the quality of life of their families. We suggest the regular evaluation of the quality of life in the clinical management of children with FA.

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Instruction and key points regarding the use of adrenaline auto injector

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Background: The adrenaline auto injector, e.g. EpiPen®, is a treatment agent with a central role in pre-hospital care for anaphylaxis. However, education for patients and families is crucial, as the adrenaline auto injector is not necessarily used appropriately, even in instances when its use is warranted.

Method: A lecture was held for 38 pediatric patients that had been prescribed the adrenaline auto injector and 61 parents of the patients. A questionnaire was conducted before and after the lecture, and problems in use of the adrenaline auto injector indicated by the parents were examined using the Visual Analogue Scale. The lecture included a discussion on food allergy, anaphylaxis, how to use of the adrenaline auto injector, and post-administration measures; practical instruction on

adrenaline auto injector use; and viewing of an original DVD.

Results: Participants demonstrated understanding of food allergies and anaphylaxis and knowledge on methods of adrenaline auto injector use following the lecture. Multivariate analysis on 'awareness about whether the adrenaline auto injector can be used' showed a significant correlation with 'understanding of anaphylaxis' ($P < 0.05$) and 'understanding about the timing for adrenaline auto injector use' ($P < 0.01$). The primary administrator of the adrenaline auto injector within the home was most often the mother. Fathers tended to have limited understanding prior to the lecture. After the lecture, fathers demonstrated a similar degree of understanding as mothers, suggesting the possibility of increased appropriate administration of the adrenaline auto injector.

Conclusions: Patient education that allows for heightened understanding of anaphylaxis ($P < 0.05$) and understanding about the timing for adrenaline auto injector use may be important in promoting appropriate adrenaline auto injector use.