257. Clinical aspects and treatment of asthma and allergic respiratory diseases

P2338

The APEX study: A retrospective review of outcomes in patients with severe allergic asthma who were or were not hospitalised in the year prior to omalizumab initiation in UK clinical practice

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The link between increasingly severe asthma and increased hospitalisation risk is well established. We retrospectively reviewed medical records 12 months pre- and post-omalizumab initiation in patients (≥12 years) with severe persistent allergic asthma who were (n=81) or were not (n=55) hospitalised for asthma in the year before omalizumab initiation. Baseline characteristics in hospitalised and non-hospitalised patients were similar: mean age 39.7 and 43.6 years; 27.2% and 38.2% male; mean IgE 278 and 309 IU/mL, respectively. Post-omalizumab initiation there were significant improvements in oral corticosteroid (OCS) burden (primary endpoint), % patients stopping OCS, exacerbation rates and Asthma Quality of Life Questionnaire (AQLQ) scores.

	Hospitalised (n=81)	Non hospitalised (n=55)
Responders†, n (%)	67 (82.7)	45 (81.8)
Patients stopping OCS, n (%)	40 (49.4)	26 (47.3)
Total OCS burden (g)		
Mean change	–1.81*	–1.96*
12 months pre-→12 months post-omalizumab	5.77→3.96 (–31.4%)	5.08→3.12 (–38.6%)
Exacerbations		
Mean change	–1.56*	–2.51*
12 months pre-→12 months post-omalizumab	3.4→1.84 (–45.9%)	4.07→1.56 (–61.7%)
AQLQ scores at 16 weeks		
Mean change	+2.03*	+1.87*
Baseline→Week 16	3.11→5.13 (+65.3%)[a]	2.91→4.78 (+64.3%)[b]

*p<0.001 vs pre-omalizumab; † significant improvement on physician's assessment at 16 weeks; [a]n=49; [b]n=34.

Overall, similar benefits were seen regardless of hospitalisation in the previous year. This suggests that prior hospitalisation is not a good predictive discriminator of response to omalizumab in patients with severe allergic asthma.

P2339

Effectiveness of omalizumab in improving quality of life in patients with 'steroid-resistant' asthma and severe allergic rhinitis

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Asthma is a heterogeneous disease, not only in its clinical expression and course but also in its response to treatment with deleterious effects on Quality of life (QoL). Anti- IgE can spare these patients with unnecessary exacerbations and have a better QoL. The objective of this study was to evaluate the effectiveness of omalizumab treatment in improving QoL in patients with severe allergic rhinitis and asthma.

Methods: 41 patients aged > 18 years with steroid-resistant asthma were enrolled in this open label study. Patients were examined at baseline and were treated with omalizumab administered subcutaneously every 2 or 4 weeks (at least 0.016 mg/kg/IgE IU/ml), in addition to existing treatment. At both visits, investigators assessed QoL on a 4 point scale in the following domains: nasal, ocular and asthmatic symptoms. Scores were calculated for individual symptoms, total scores for each domain. Patients were also assessed on impairment of sleep and daily activities.

Results: Omalizumab significantly reduced scores from baseline in both nasal and ocular symptoms. Reductions were also seen in the asthmatic symptom scores: significance was noted in wheezing (P=0.0002) and breathless scores (P=0.0002). At baseline, 62% of patients had some degree of daily activity impairment, whereas at the final visit only 31% had daily activity impairment. Similarly, while 55% of patients had some sleep impairment at baseline, this was reduced to 28% at the final visit.

Conclusions: This open label study demonstrated that omalizumab was an effective treatment for the symptoms and sleep/daily life impairments associated with severe allergic rhinitis and asthma.

P2340

Population pharmacokinetics of tralokinumab, an investigational anti-IL-13 monoclonal antibody, in asthmatic and healthy adults

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Interleukin-13 (IL-13) is considered a critical mediator in the development and maintenance of asthma. Tralokinumab (CAT-354), a human IgG4 monoclonal antibody that specifically neutralizes IL-13, is currently trialled in subjects with uncontrolled, severe asthma.

The aim of this study was to develop and evaluate a population pharmacokinetic (PK) model of tralokinumab.

Four phase 1 studies and one phase 2a study constitute the data to be analysed comprising a population of 247 healthy and asthmatic adults. Nonlinear mixed-effects modeling of pooled data was conducted using the software NONMEM7. The influence of demographic features on tralokinumab PK was evaluated by covariate analysis. Predictive performance of the model was assessed through simulations.

The PK parameters for a 2-compartment model after IV and SC dosing were all precisely estimated (RSE<26%) with mean values (CV% of between-subject variability) of clearance (CL), central volume (Vc), inter-compartment clearance (Q), and peripheral volume (Vp) respectively equal to 0.22 L·day-1 (33%), 2 L (64%), 3.4 L (28%), and 1.4 L·day-1 (64%). Body weight explained a minor portion of the variability in CL and Vp, 11% and 34% respectively. No PK difference was detected between healthy and asthmatic subjects. SC bioavailability was estimated at 82%. Model appropriateness was demonstrated by good predictive behaviours of the model.

The population PK model successfully described the concentration time-course of tralokinumab and adequately predicted the variability in the studied population. It therefore constitutes a useful tool for guiding the design and dosing of tralokinumab in future clinical trials.

P2341

Cough variant asthma may be a incipience of bronchial asthma

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Cough variant asthma (CVA) is characterized by chronic cough that persists for more than two months and suggested to be a precursor of bronchial asthma (BA). To analogize if the position of cough variant asthma is early or mild stage of the classical bronchial asthma analyzed according to the airway inflammation,

bronchial hyperresponsiveness, airway obstructive damage, newly diagnosed 46 cough variant asthma patients and 57 bronchial asthma patients naive to oral or inhaled corticosteroids and free of asthma execerbation were subjected to spirometry, impulse oscillometry (IOS), bronchial hyperesponsiveness test, induction of sputum, and measurement of fractional exhaled nitric oxide (FeNO).
Spirometry revealed lower values of FEV1.0/FVC, FEV1.0%pred, V50%pred, and V25%pred in patients with BA than in those with CVA ($p<0.01$). Both IOS parameters and FeNO values were significantly higher in patients with BA than in those with CVA ($p<0.01$). The log PC20 was significantly lower in patients with BA than in those with CVA ($p<0.05$). Induced sputum eosinophil counts were significantly higher in patients with BA than in those with CVA for both central and peripheral airways ($p<0.001$). However, the values of IOS, PC20, FeNO, and induced sputum eosinophil counts did not differ significantly between patients with mild intermittent asthma and those with CVA.
All measures of central and peripheral airway obstruction, eosinophilic inflammation, and airway hyperresponsiveness were milder in patients with CVA than in those with BA but paralleled with intermittent asthma. Our data suggest that CVA is an allergic and inflammatory precursor of BA.

P2342
Effects of budesonide/formoterol combination therapy versus budesonide on airway dimensions in asthma
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Background: The combination of inhaled corticosteroids and long-acting β_2-agonists results in improved asthma symptom control compared with inhaled corticosteroids alone, but the effects of combination therapy on airway structural changes and inflammation are still unknown.
Aims and objectives: The aim of the study was to compare the effects of budesonide/formoterol versus budesonide on airway dimensions and inflammation in asthma.
Methods: Fifty asthmatic patients were randomized to treatment with budesonide/formoterol (200/6 μg, two inhalations bd) or budesonide (200 μg, two inhalations bd) for 24 weeks. Airway dimensions were assessed by CT, and wall area corrected for body surface area (WA/BSA), percentage wall area (WA%), wall thickness (T)/$\sqrt{\text{BSA}}$, and luminal area (Ai)/BSA at the right apical segmental bronchus were measured. The percentage of eosinophils in induced sputum, pulmonary function, and Asthma Quality of Life Questionnaire (AQLQ) were also evaluated.
Results: Significantly decreases in WA/BSA ($p < 0.05$), WA% ($p < 0.001$) and T/$\sqrt{\text{BSA}}$ ($p < 0.05$), and increases in Ai/BSA ($p < 0.05$), and improvements in the AQLQ scores were observed in patients treated with budesonide/formoterol compared with budesonide. The reduction in sputum eosinophils and increase in FEV_1% were greater for budesonide/formoterol compared with budesonide. The changes in WA% were significantly correlated with changes in sputum eosinophils and FEV_1% ($r = 0.84$ and $r = 064$).
Conclusions: Budesonide/formoterol combination is more effective than budesonide for reducing airway wall thickness and inflammation in asthma.

P2343
Effects of breast feeding on the prevalence rates of asthma, rhinitis and eczema in Chinese school children
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Background: Exclusive breastfeeding for at least 4 months is recommended by many governments and allergy organizations to prevent allergic disease. There is conflicting evidence concerning the relationship between breast feeding and asthma, wheezing illness and allergic disorders. The objective of this study was to investigate whether there is any association between breast feeding and asthma and allergic disorders in Chinese schoolchildren.
Methods: Study subjects comprised 10824 randomly selected 6 to 18 year-old schoolchildren from Shijiazhuang in Hebei Province in China. Information on breast feeding, asthma, rhinitis and eczema was gathered by parental questionnaire using the Chinese version of ISAAC questionnaire.
Results: Children who have been breastfed had significantly lower prevalence rates of exercise-induced wheezing, asthma ever, and rhinitis ever than those who have not been breastfed (3.1% vs 4.2%, $p<0.05$; 1.0% vs 1.6%, $p<0.05$; and 13.3% vs 15.8%, $p<0.01$; respectively).There was a similar trend with chronic rash ever. Children who have been breastfed more than or equal to 12 months had lower prevalence rates of ever wheezed, wheeze in the past year, exercise-induced wheezing, persistent cough past year, ever had rhinitis, and ever had eczema than those who have been breastfed less than 12 months (5.3% vs 6.8%, $P<0.05$; 1.6% vs 2.7%, $P<0.05$; 2.9% vs 3.9%, $P<0.05$; 10.7% vs 12.4%, $P<0.05$; 12.5% vs 16.2%, $P<0.001$ and 11.4% vs 13.2%, $P<0.05$, respectively). The present study confirms the protective effect of breastfeeding on symptoms of asthma, rhinitis and eczema.

P2344
Effects of water aerosol on pediatric allergic asthma
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Objective: Ionized water aerosols have been suggested to exert beneficial health effects on pediatric allergic asthma. Their effectwas evaluated in a controlled randomized clinical trial as part of a summer asthma camp.
Methods: Asthmatic allergic children (n=54) spent three weeks in an alpine asthma camp; half of the group was exposed to water aerosol for one hour per day, whereas the other half spent the same time at a "control site". Immunological analysis, lung function and FeNO testing was performed during the stay, and sustaining effects were evaluated after 2 months. Symptom score testing was done over a period of 140 days.
Results: The water aerosol group showed a significant improvement in all lung function parameters whereas the control group only in peek expiratory flow. All patients showed significant improvement in symptom score and significant decrease of FeNO after the camp. Only the water aerosol group exhibited a long lasting effect on asthma symptoms, lung function and inflammation in the follow-up examination. Induction of IL-10 and regulatory (Treg) cells was measured in both groups, with a pronounced increase in the water aerosol group. IL-13 was significantly decreased in both groups, whereas IL-5 and eosinophil cationic protein were decreased only in the water aerosol group.
Conclusion: Our findings confirm the induction of Treg cells and reduction of inflammation by climate therapy. They indicate a synergistic effect of water aerosols resulting in a long lasting beneficial effect on asthma symptoms, lung function and airway inflammation.

P2345
Simultaneous analysis of clinical markers for predicting increased lung function fluctability in stable asthma
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Background: Airway hyperresponsiveness (AHR) has been shown to be associated with the loss of asthma control. Predicting the increased fluctuation of lung function might be useful to regulate the future risk of poor asthma control because peak expiratory flow (PEF) variability well correlates with AHR.
Objective: We simultaneously analyzed the clinical markers for predicting increased PEF variability in stable asthma.
Methods: We studied non-smoking asthmatic patients who were receiving conventional therapy and clinically stable for 8 weeks. Patient medical records were obtained and asthma control questionnaire (ACQ), spirometry, and exhaled nitric oxide fraction (FENO) were measured. Associations between these variables and PEF variability over a week (Min%Max) were prospectively assessed.
Results: 52 of 297 asthmatics (17.5%) showed the increased PEF variability (Min%Max < 80%). These subjects were receiving more intensive therapy, but had more severe asthma symptoms, more airflow obstruction, and more evidence of airway inflammation. Especially, ACQ, forced expiratory volume in one second % of predicted (%FEV1), and FENO were identified to be independent predictors of Min%Max < 80%. When we combine baseline %FEV1 $\leq$ 85% and/or FENO $\geq$ 40 ppb, this index was associated with the highest combination of sensitivity (94.2%) and specificity (80.4%) for increased PEF variability.
Conclusions: These results suggested that ACQ, %FEV1 and FENO can stratify risk for increased fluctuation of lung function among the clinically stable asthmatics.

P2346
Impact of allergy diagnosis on patients' perceptions and experience of HDM allergy: A European survey
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Background: We assessed allergy awareness and diagnosis in a survey in four European countries. A post-hoc analysis determined the impact of diagnostic status on the perception of house dust mite (HDM) allergy and its management.
Methods: 4016 adults (France: n=1001; Germany: n=1002; Italy: n=1004; Spain: n=1009) answered an anonymous, online, questionnaire on their perception and personal experience of HDM allergy. The results were analyzed according to whether the subjects had been diagnosed with HDM allergy by a physician (n=611) or not. Survey procedures complied with the ESOMAR International Code of Marketing and Social Research Practice.
Results: 56% of the overall survey population stated that they experienced symp-

toms (repetitive sneezing, nasal discharge, stuffy nose, eye irritation and breathing difficulties). 15% had been diagnosed with HDM allergy and another 23% thought that they were allergic to HDMs but had not been diagnosed. Of the diagnosed patients, 47% presented year-round symptoms, 35% had seasonal symptoms and 14% rarely had symptoms. A high proportion of diagnosed patients considered that their symptoms were due to dust (66%) or indoor air pollution (27%), versus 66% for HDMs. 87% of diagnosed patients felt well informed, whereas 37% of the latter had not identified HDMs as the cause of their symptoms. Diagnosed patients appeared to be more aware that untreated HDM allergy can progress to asthma and that HDM allergy is difficult to treat.
Conclusion: Physician-diagnosed HDM allergy patients had greater levels of awareness of HDM allergy and its management than non-diagnosed patients. However, some topics need to be reinforced through health education measures.

P2347
Helminths for asthma: Findings of a Cochrane systematic review
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Background: Helminths modulate the natural immune responses of their human hosts, and may prevent or cure immune-mediated or allergic diseases, such as asthma. Non-randomised studies support this hypothesis.
Objectives: To assess the safety and effectiveness of helminth therapy in people with asthma.
Methods: We searched the Cochrane Airways Group Specialised Trials Register and additional sources for published and unpublished trials. We included all randomised controlled trials where the intervention was any helminth species administered to people with asthma. We combined dichotomous data using risk ratio (RR) and continuous data using mean difference (MD).
Results: We found 5 published reports, describing 2 studies (64 adult participants). Both studies used a single percutaneous application of 10 third stage *Necator americanus* (i.e. hookworm) larvae. Pooling of data showed no difference in airway hyperresponsiveness between the helminth and placebo groups (MD 0.51, 95% CI –0.54 to 1.56) and no difference in study dropouts (OR 2.15, 95% CI 0.36 to 12.76). Other outcomes (asthma symptoms, use of reliever inhalers, quality of life) did not differ between the groups. Adverse events were few.
Conclusions: There was no clinical benefit from helminth therapy. The trials however were small and not powered to show effectiveness. Administered to humans in carefully measured doses, helminths appear to be safe. More preclinical studies should be performed, before larger and extended duration trials of helminths for asthma are carried out. 'Trickle colonisation' with helminths may be more effective than the administration to patients of a single large helminth bolus, but this therapeutic approach has not yet been tested for asthma.

P2348
Changes in total and specific IgE following treatment with mebendazole in patients with persistent asthma and IgE to Ascaris lumbricoides
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Background: Recent studies have reported that patients with ascaridiasis and high IgE levels may suffer from asthma. This study aims at evaluating the changes in total and Ascaris-specific IgE, as well as in symptoms, following anti-helminthic therapy in patients with asthma not controlled with standard drug treatment.
Methods: 30 adult patients with persistent asthma and high levels of total and Ascaris-specific IgE were included in the study. Though they had been treated by associations of inhaled corticosteroids (ICS) and long-acting beta-agonists (LABA), they shared irregular and unjustified asthma attacks and therefore referred to us in order to have a further check-up. They underwent spirometry, skin prick tests, total and specific IgE (aeroallergens + *A. lumbricoides*). To all patients a treatment by mebendazole 100 mg b.i.d for 3 days, based on two courses with a 20-day interval, was proposed. After 6 and 12 months, in case of persistent positivity, 2 other courses of mebendazole were prescribed.
Results: 24 patients underwent the treatment. The mean value of total IgE increased after 6 months of treatment from 1556 to 2206 but decreased after 12 months to 1352 kU/L. Similarly, specific IgE increased from 3.1 to 4.5 after 6 months and decreased to 2.4 kU/L after 12 months. Spirometry showed a basal FEV1 mean value of 59% and a rise to 71% after 6 months and to 78% after 12 months.
Conclusion: These findings confirm the association between Ascaris infestation and allergy-like symptoms and demonstrate that antiparasitic therapy remarkably reduces asthma attacks in patients who show high levels of total and specific IgE for A. *lumbricoides.*

P2349
High incidence of sinusitis in asthmatic patients detected by computed tomography
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Background: Allergic rhinitis and sinusitis are frequent comorbidities in patients with bronchial asthma, and these nasal and sinus complications are reported to correlate with worsening of symptoms of asthma. Diagnosis of rhinitis and sinusitis are commonly diagnosed by clinical symptoms, X-ray, laryngoscope and sinus CT, but there are only a few reports of CT findings of sinus in patients with bronchial asthma.
Patients and methods: From April 2010 to December 2011, 115 patients with bronchial asthma were enrolled in this study. Duration of disease, treatment steps (JGL2009), medications and symptoms of bronchial asthma (Asthma Control Questionnaire; ACQ, etc.), nasal symptoms (nasal discharge, nasal obstruction and nasal voice) and spirometry in addition to sinus CT findings were evaluated.
Results: Eighty-four patients (73%) showed sinusitis by sinus CT in these 115 patients. Nasal polyps were detected in 15 (13%) patients, and higher treatment steps were observed in patients with bronchial asthma complication sinusitis ($p<0.05$). Nasal symptoms were detected in 76 (66%), and nasal voice (61, 53%) is significantly highly detected in patients with bronchial asthma complicating sinusitis. ACQ and parameters of pulmonary function were not significantly different in asthmatic patients with or without sinusitis.
Conclusion: Incidence of sinusitis in our study was relatively higher than the incidence of 66.3% previously reported by Matsuno et al. (2008). Patients with sinusitis detected by sinus CT tend to receive higher treatment steps, and it is speculated that sinus CT is useful for detecting and evaluating sinusitis as a complication of bronchial asthma.

P2350
Chronic paranasal sinusitis exacerbates allergic inflammation in patients with asthma and contributes to refractoriness to treatment
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Background: Factors such as airway inflammation, airway hyperresponsiveness, and airway remodeling contribute to the pathogenesis of refractory asthma in a complex fashion. Many studies have reported the development of severe disease in patients with asthma associated with allergic rhinitis. However, the relation between chronic paranasal sinusitis and severe asthma remains largely uninvestigated. In the present study, we examined whether the concurrent presence of paranasal sinusitis contributes to the development of refractory asthma.
Subjects: Three groups of patients were studied: those with asthma, those with chronic paranasal sinusitis, and those with both asthma and paranasal sinusitis. Peripheral eosinophil counts, serum IgE levels, exhaled nitric oxide (FeNo) levels as a maker of airway inflammation, and airway hyperresponsiveness were compared among the groups.
Results: Peripheral eosinophil counts, FeNo levels, and serum IgE levels were higher in patients with asthma and chronic paranasal sinusitis than in patients with asthma alone and patients with chronic paranasal sinusitis alone. Airway hyperresponsiveness was slightly increased in patients with chronic paranasal sinusitis, but was further increased in patients with asthma, and was significantly increased in patients with asthma plus chronic paranasal sinusitis.
Conclusions: Our results suggest that chronic paranasal sinusitis may modify airway inflammation in patients with asthma and contribute to the exacerbation of disease. Paranasal sinusitis should thus be adequately treated in patients with asthma complicated by chronic paranasal sinusitis.

P2351
Hospital admission in adults with asthma exacerbations: Do demographic factors play a role?
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Aim: To determine whether demography affects hospitalisation in asthma exacerbations in adults.
Methods: We included 100 asthmatics admitted with an acute exacerbation over 14 months; matched for age and sex with a 100 well-controlled asthmatics from asthma clinic. Information on sociodemographic variables, clinical and laboratory data was collected. Acute and convalescent (at 6 weeks) titres of serum immunoglobulin E (Se Ig E) and serum eosinophil count were taken. SPSS was used for statistical analysis.
Results: The study population was 73% female and the median age was 49 years. Univariate analysis using t-test and Chi-square showed a significant difference in compliance ($p<0.0001$), smoking status ($p=0.007$) and hospitalisation in the previous year between controls and cases ($p=0.0001$). There was no significant difference in: influenza immunisation ($p=0.105$), exhaled CO ($p=0.85$),

BMI (p=0.27), Se Ig E levels (p=0.517), history of atopy (p=0.637), family history of atopy (p=0.121), level of education (p=0.210), age of asthma onset (p=0.320) and pets at home (p=1.0). The mean decrease in Se Ig E between acute and convalescent titres was 36.1%. There was no correlation between % predicted PEFR on admission (as a measure of severity) with length of stay (p=0.376), white cell count (p=0.165), CRP (p=0.199), or Se IgE (p=0.767), however this was negatively correlated with eosinophil count (p=0.045).
Conclusions: A history of previous hospitalisation, non-compliance and smoking are significant risk factors for asthma exacerbations requiring hospital admission. An increased eosinophil count correlates with severity of exacerbation.

P2352
Efficacy and safety of 300IR 5-grass pollen sublingual tablet in allergic patients with and without asthma
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Background: Efficacy and safety of 300IR tablet has been demonstrated. Here we report the impact of asthma status on efficacy and safety.
Methods: Grass pollen allergic adults were randomised to placebo or 300IR pre- and co-seasonally for 3 seasons, starting 4 months (4M) or 2 months (2M) prior to each season and continuing for its duration. Asthmatic patients requiring no more than GINA Step 1 therapy could be included. The primary efficacy endpoint, Average Adjusted Symptom Score (AAdSS, adjusting rhinoconjunctivitis symptoms for rescue medication use, scale 0-18) during the pollen period in Year 3, was analysed by ANCOVA. Asthma presence at baseline was a pre-specified covariate. Treatment by asthma status interaction was tested.
Results: Among 581 patients included in the Year 1 full analysis set, 14.1% were asthmatic, with balance between groups. In Year 3, differences in AAdSS Least-Squares means vs. placebo during the pollen period were significant in the two active groups ($p<0.0001$) corresponding to a relative difference of -34.9% in the 4M group and -37.6% in the 2M group. Asthma status was not a significant predictor of outcome. Interaction between treatment and asthma status was not significant (p=0.62) indicating that treatment effect was independent of asthma status. No significant difference was observed between the 4M and 2M groups.
During the 3 treatment years, 3 patients had an asthma exacerbation (moderate): 2 in Year 1 (placebo) and one in Year 3 (4M). None was drug-related.
Conclusion: Efficacy and tolerability of 300IR 5-grass pollen sublingual tablet in patients with grass pollen allergic rhinoconjunctivitis were similar in those with and without asthma.

P2353
IgE sensitisation to food allergens relates to increased airway and systemic inflammation in asthmatic children – Results from the MIDAS study
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Food allergy is common among children with allergic asthma and has been linked to asthma severity. However, the relation between IgE sensitisation to food allergens and local airways inflammation or systemic inflammation in subjects with allergic asthma has been little studied.
Within the frame of an industry-academy collaboration on minimally-invasive diagnostics (MIDAS), fraction of NO in exhaled air (FeNO), serum eosinophil cationic protein (sECP) and IgE against aero- or food allergen mix was measured in 151 asthmatic children aged 10-18 years. Three asthma groups were defined: non-atopic (n=31, median age 15 yrs), IgE-sensitised to only aeroallergens (n=59, median age 15 yrs) and IgE-sensitised to both aero- and food allergens (n=61, median age 14 yrs).
FeNO levels were 8.9 ppb (7.1, 11.1) in non-atopic asthmatics, 14.2 ppb (11.7, 17.2) in aeroallergen-sensitised asthmatics and 23.4 ppb (19.4, 28.3) in asthmatics sensitised to both aero- and food allergens ($p<0.01$ for all comparisons). Corresponding sECP levels for the three groups were: 9.6 ng/mL (7.9, 11.8), 11.9 ng/mL (9.7, 14.5) (p=0.55 vs. non-atopic asthma), 21.9 ng/mL (18.6, 25.7) ($p<0.001$ vs. each of the other two groups). Asthmatic subjects sensitized to both aero- and food allergens had higher levels of FeNO and sECP than non-sensitised or aeroallergens-sensitised subjects, after adjustments for gender, age, height, lung function, total IgE.
In conclusion, sensitisation to food allergens is common among children with allergic asthma and is related to increased local as well as systemic inflammation. The clinical implications of these findings warrant further studies.

P2354
The results of inferon administration in the treatment of chronic obstructive pulmonary disease
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Immunity disorders play an important role in the latent inflammatory formation in patients with chronic obstructive pulmonary disease (COPD). A low γ-IFN level may be one of them. The aim was to study γ-IFN level in patients with COPD and the efficacy of immunomodulator inferon (IFN) in its treatment.
Methods: The study included 45 patients with moderate to severe COPD. The level of γ-interferon, CD3+, CD4+, CD8+, lymphocytes, phagocytic activity of neutrophils by nitro-blue tetrazolium (NBT) test was determined in the patients blood. 23 patients with COPD received standard therapy. IFN was used in the complex therapy of 22 patients.
Results: In patients with COPD the level of γ–interferon has been found to be reduced by 2.0 times, the level of CD3+, CD4+, CD8+ lympocytes by 1.6-1.8 times, the values of NBT –test by 2.5 times. Administration of IFN increased the level of γ–interferon by 1.5 times, improved T-cells and neutrophils activity, produced positive effect on the course of the inflammation. In patients who received standard therapy γ–interferon content remained at a lowered level, impairment of the immune status and symptoms of inflammation have been found.
Conclusion: In patients with COPD γ–interferon content was found to be decreased. IFN administration increased γ–interferon production, eliminated immunity disorders, improved the results of the treatment.

P2355
Application of a new mass-spectrometric platform for determination of lipid mediators in urine reveals increased oxidative stress during allergen bronchoprovocation of subjects with atopic asthma
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Background: Traditionally, mechanisms in allergen-induced bronchoconstriction have been investigated by measurement of a few metabolites of lipid mediators (LMs) in urine. Mass spectrometry enables quantification of a wider panel of compounds per analysis. We applied a new platform that included isoprostanes (IPs), markers of oxidative stress.
Aim: To assess the levels of IPs in urine before and after allergen provocation in asthma patients.
Methods: Eighteen subjects with mild atopic asthma and airway hyperresponsiveness to methacholine were challenged with allergen to produce at least a 20% drop in FEV_1. Urine was collected before and after the provocation. Metabolites were extracted and analyzed by a new mass spectrometry platform. Data were normalized per mmol of creatinine.
Results (Fig. 1, p. 427s): As expected, metabolites of prostaglandin D_2, thromboxane A_2, and leukotriene E_4 increased after the provocation. However, two IPs (2,3-dinor-8-isoPGF$_{2\alpha}$ and 8,12-iPF$_{2\alpha}$-VI) also increased significantly. Multivariate analysis showed gender differences in basal levels, potentially due to higher excretion of creatinine by males.
Conclusions: We discovered that allergen provocation of atopic asthmatics increased the level of oxidative stress, suggesting that IPs might represent a new target for therapeutic intervention.

P2356
Putting patients at the heart of healthcare: Respiratory allergy care in 18 European countries
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Aim: To evaluate, from the patients' perspective, how Europe cares for patients with respiratory allergies (RAs; allergic rhinitis and asthma) in order to identify national gaps and patients' needs. The survey was part of the 4-year Allergy Awareness Project of the European Federation of Allergy and Airways Disease Patients Associations (EFA).
Methods: Data were collected via an online 3-part questionnaire: 1) Basic facts: epidemiology, disease definitions, prevalence and costs; 2) Access to care: diagnosis, management, role of healthcare professionals in patient management and follow-up; 3) Quality of care: national policies and best practices. EFA member associations (n. 38) received the questionnaire. Data were also obtained from governmental sources and the scientific literature.
Results: Associations from 18 countries returned the questionnaire. RAs affect 20%-30% of the European population. But RAs, and particularly allergic rhinitis, are not considered serious diseases, and thus often remain underdiagnosed and undertreated despite the heavy burden they place on patients and society (in all 18 countries, direct RA costs reach millions of euros). In most countries, patients have difficulty in seeing specialists, and coordination among physicians is lacking. However, countries that implement national programs (Finland, Czech Republic) have seen reduced costs and better quality of care.

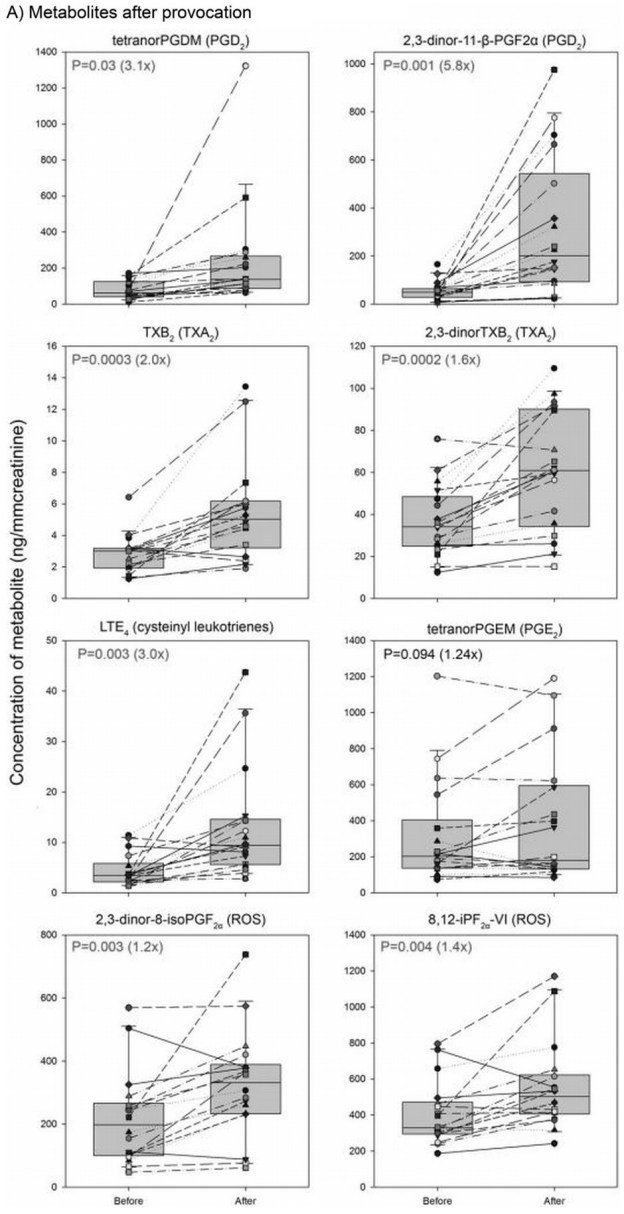

Fig 1. Levels of LMs after provocation with allergen. A) Comparison of levels of metabolites of prostaglandin D_2 (PGD_2), thromboxane A_2 (TXA_2), cysteinyl leukotrienes, prostablandin E_2 and isoprostanes (markers of oxidative stress as are produce by reactive oxygen species, ROS). In every panel the P-value for paired-t tests is shown, as well as the times of increase of the metabolite. Those with a significant increase are highlighted in red. B) Unsupervised multivariate analysis of basal levels. The first two principal components are shown. The first one shows gender separation.

Conclusions: Awareness of RAs and their social burden is low. There is a need for better prevention and coordination among healthcare professionals. Patients' associations can help increase public awareness, and must be actively involved in devising and implementing RA management and education programs.

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The effects of inspiratory muscle training on the interleukin-6 response to intense volitional hyperpnoea

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Vassilakopoulos et al. (*Am. J. Physiol* 1999; 277:R1013–R1019) demonstrated a breathing-induced interleukin-6 (IL-6) response. Whether inspiratory muscle training (IMT) can attenuate this response is unknown. Therefore, we tested the hypothesis that the IL-6 response to volitional hyperpnoea (VH) could be reduced with IMT and investigated whether this response was related to diaphragm fatigue (assessed by phrenic nerve stimulation) and/or changes in blood lactate concentration ($[Lac^-]_B$).

Twelve male participants performed either 6 weeks of pressure-threshold IMT (n=6) or placebo (PLA) training (n=6). Prior to training, a maximal incremental cycling test (max) was performed. Before and after training, participants undertook two 1 h experimental trials on separate days: passive rest or VH. In VH, they voluntarily mimicked at rest the breathing and respiratory muscle recruitment pattern equal to 70-80% of the maximum minute ventilation achieved during max. IL-6 increased ($P<0.01$) following the pre-training VH and was (mean ± SD) 5.02±0.63 and 4.87±0.86 pg·mL^{-1} at 2 h post for IMT and PLA groups, respectively. $[Lac^-]_B$ remained ($P<0.01$) elevated above baseline values for the duration of VH at 1.36±0.24 and 1.29±0.18 mmol L^{-1}. The IL-6 (-29%) and $[Lac^-]_B$ (-11%) responses were reduced ($P<0.05$) for the IMT, but not for the PLA group. There were no increases in IL-6 or $[Lac^-]_B$ over time for either group during passive rest and no evidence of diaphragm fatigue during any trial.

In conclusion, 6 weeks of IMT reduces the magnitude of the IL-6 response to VH with no evidence of diaphragm fatigue. The reduction in IL-6 may be related to the post-IMT reduction in $[Lac^-]_B$.