EAACI PO EAACI 2017

Golnik, 7. september 2017

Allergen Immunotherapy Guidelines

Part 1: Systematic reviews

www.eaaci.org/resources/guidelines/ait-guidelines-part-1.html

Translating knowledge into clinical practice

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Allergy European Journal of Allergy and Clinical Immunology

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Position Paper

EAACI Guidelines on Allergen Immunotherapy: Hymenoptera venom allergy

Gunter J Sturm, Eva-Maria Varga, Graham Roberts, Holger Mosbech, M. Beatrice Bilò, Cezmi A Akdis, Darío Antolín-Amérigo, Ewa Cichocka-Jarosz, Radoslaw Gawlik, Thilo Jakob, Mitja Kosnik, Joanna Lange, Ervin Mingomataj, Dimitris I Mitsias, Markus Ollert, Joanna N.G. Oude Elberink, Oliver Pfaar, Constantinos Pitsios, Valerio Pravettoni, Franziska Ruëff, Betül Ayşe Sin, Ioana Agache, Elizabeth Angier, Stefania Arasi, Moises A Calderón, Montserrat Fernandez-Rivas, Susanne Halken, Marek Jutel, Susanne Lau, Giovanni B Pajno, Ronald van Ree, Dermot Ryan, Otto Spranger, Roy Gerth van Wijk, Sangeeta Dhami, Hadar Zaman, Aziz Sheikh, Antonella Muraro ✉

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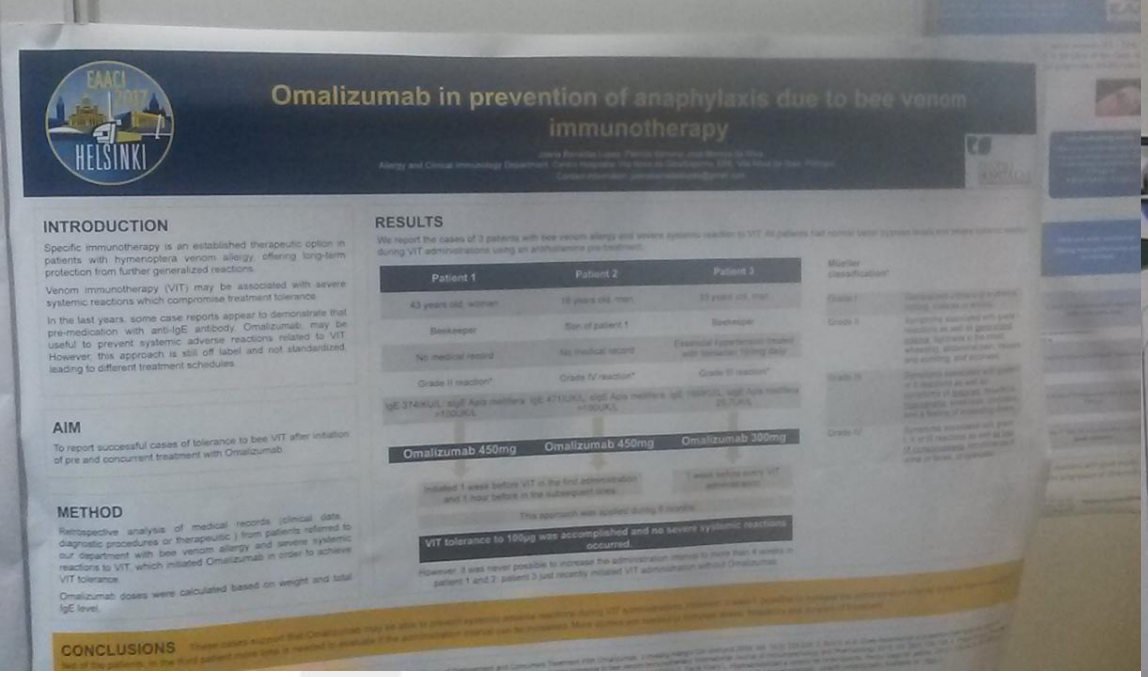
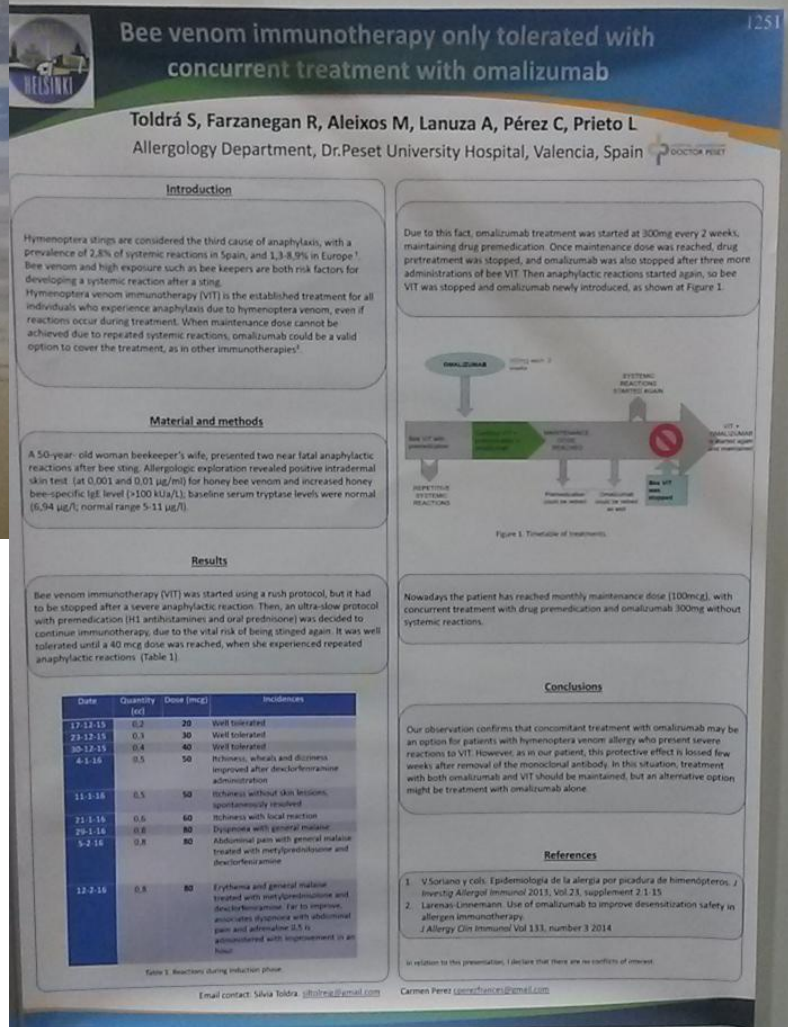
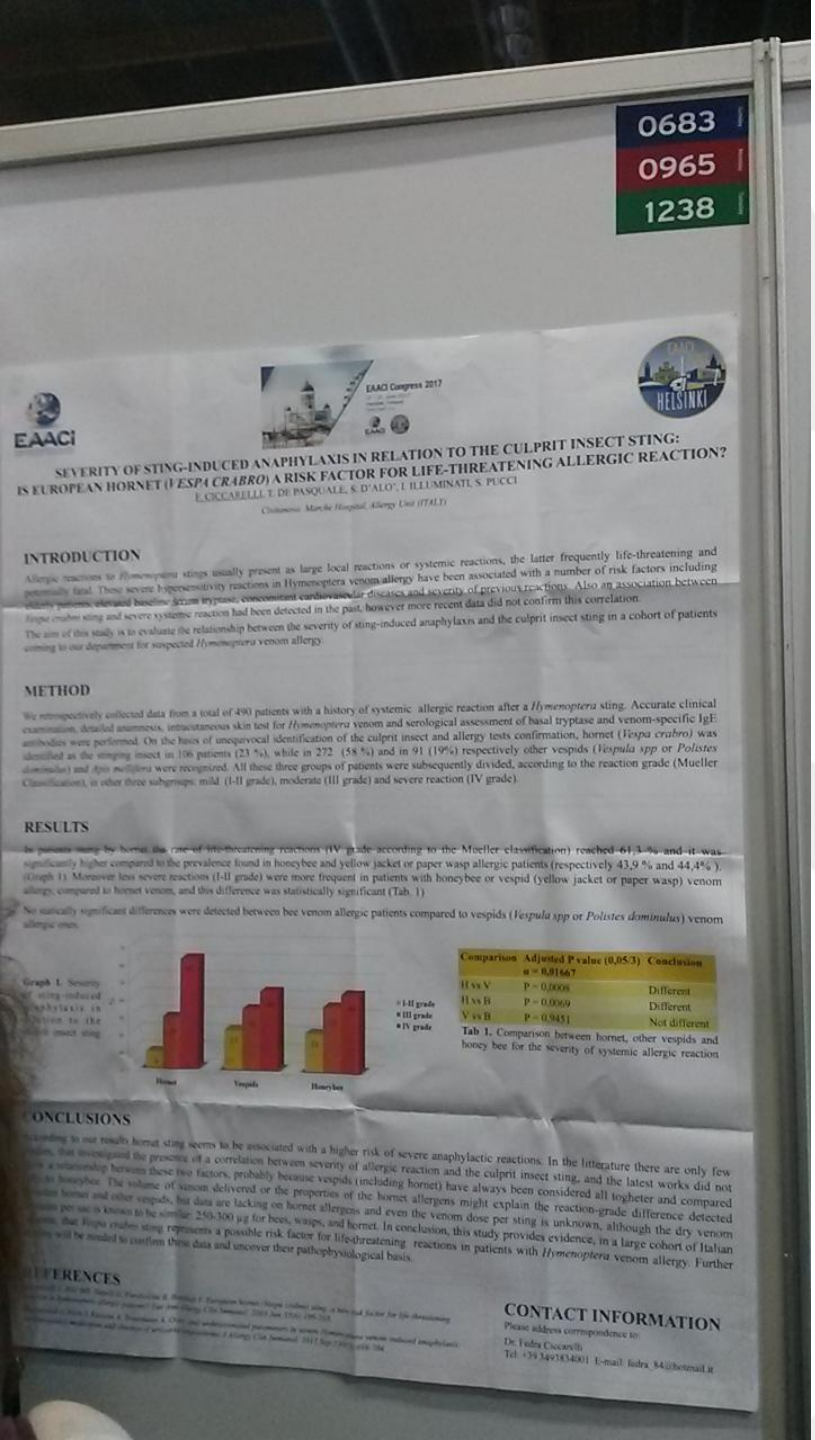
Abstract

Hymenoptera venom allergy is a potentially life-threatening allergic reaction following a honeybee, vespid or ant sting. Systemic allergic sting reactions have been reported in up to 7.5% of adults and up to 3.4% of children. They can be mild and restricted to the skin or moderate-to-severe with a risk of life-threatening anaphylaxis. Patients should carry an emergency kit containing an adrenaline autoinjector, H_1-antihistamines, and corticosteroids depending on the severity of their previous sting reaction(s). The only treatment to prevent further systemic sting reactions is venom immunotherapy. This guideline has been prepared by the European Academy of Allergy and Clinical Immunology's (EAACI) Taskforce on Venom Immunotherapy as part of the EAACI Guidelines on Allergen Immunotherapy initiative. The guideline aims to provide evidence-based recommendations for the use of venom immunotherapy, has been informed by a formal systematic review and meta-analysis and produced using the Appraisal of Guidelines for Research and Evaluation (AGREE II) approach. The process included representation from a range of stakeholders. Venom immunotherapy is indicated in venom allergic children and adults to prevent further moderate to severe systemic sting reactions. Venom immunotherapy is also recommended in adults with only generalized skin reactions as it results in significant improvements in quality of life compared to carrying an adrenaline auto-injector. This guideline aims to give practical advice on performing venom immunotherapy. Key sections cover general considerations before initiating venom immunotherapy, evidence-based clinical recommendations, risk factors for adverse events and for relapse of systemic sting reaction, and a summary of gaps in the evidence.





Omalizumab pri bolnikih, ki imajo hude zaplete imunoterapije z žuželkami



Anafilaksija po pikih sršenov

Ko gre znanstvenik v privatno prakso

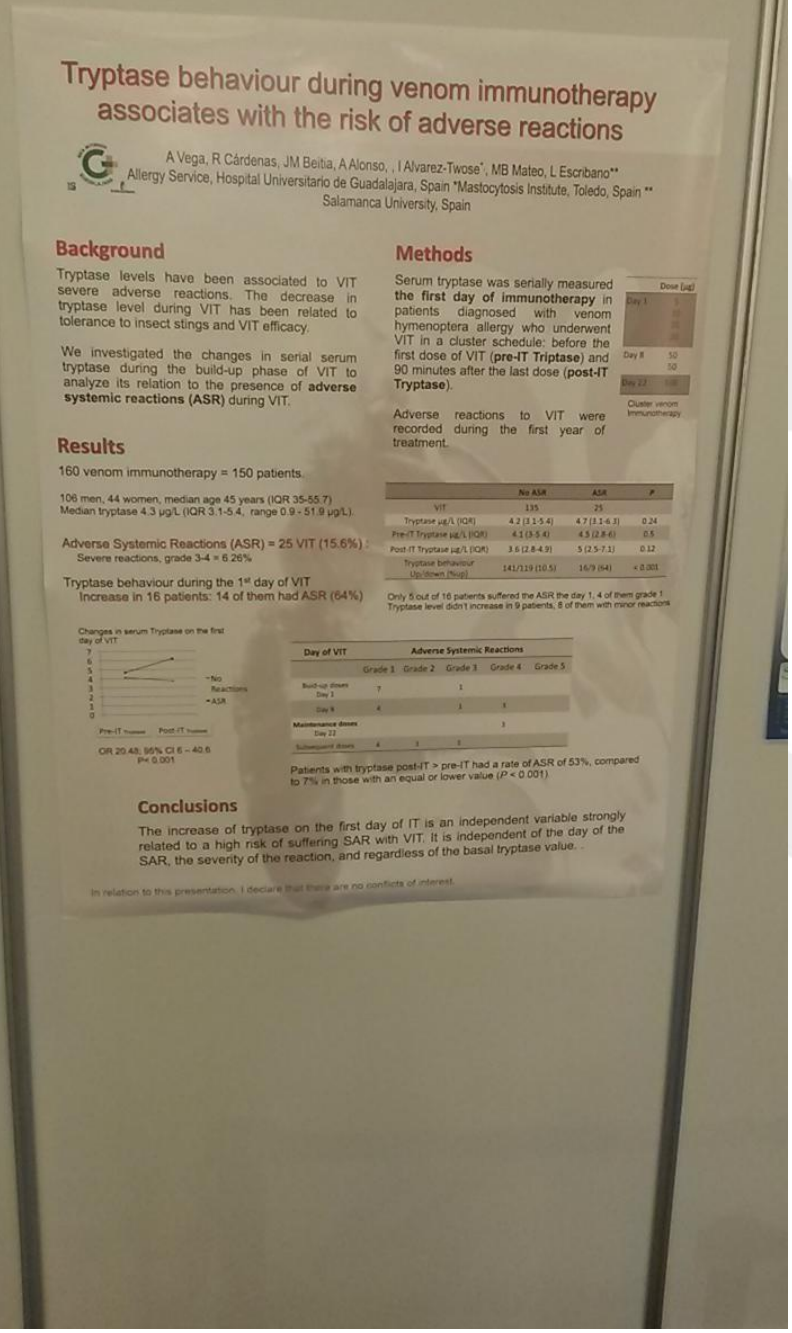
#1233 - Is the skin prick test sufficient to diagnose vespid venom allergy?

4 of 51 allergic subjects (8%) were positive at the concentration of 10 µg/ml vespid venom extract, (65%) at 100 µg/ml and 45/51 (88%) at 300 µg/ml.

Adding serological testing for sIgE, all SPT negative subjects were positive for sIgE to vespid venom extract.

In the IDT positive results were obtained in 51/51 (100%) at 1 µg/ml.

In subjects with clinically irrelevant sensitization the IDT was positive in 86% of cases. In contrast, only 38% were positive in SPT.



Napoved zapletov imunoterapije

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Serum tryptase was serially measured the first day of cluster. Tryptase level decrease after the 4 doses of IT.

15,6% developed ASR with VIT. In 16 (64%) out of 25 patients who developed ASR, tryptase post-IT the first day of VIT was higher after the 4 doses, than tryptase pre-IT. Mean tryptase increase was 26.5%.

The kinetics of peanut allergen absorption using autologous serum in a human model of passive cutaneous anaphylaxis

Anja Pahlow Mose, Esben Eller, Charlotte Gotthard Mørtz, Carsten Bindslev-Jensen
Department of Dermatology and Allergy Center, Odense Research Center for Anaphylaxis (ORCA), Odense University Hospital, Denmark
e-mail: anja.pahlow.mose@rsyd.dk

BACKGROUND
Anaphylaxis is the result of a complex series of events; however, the anaphylactic reaction is rapid in onset and usually occurs within one hour of food intake. The rate of allergen absorption is most likely a key factor in the

METHOD
Healthy, non-atopic volunteers (n= 5, all men) aged 25–66 years (median age 30 years) were used as recipients of a human serum obtained from a donor with severe peanut allergy through the passive transfer of cutaneous anaphylaxis and challenged

samples. One of the recipients showed a p
with the serum sampled at 48 hours afte
peanut.

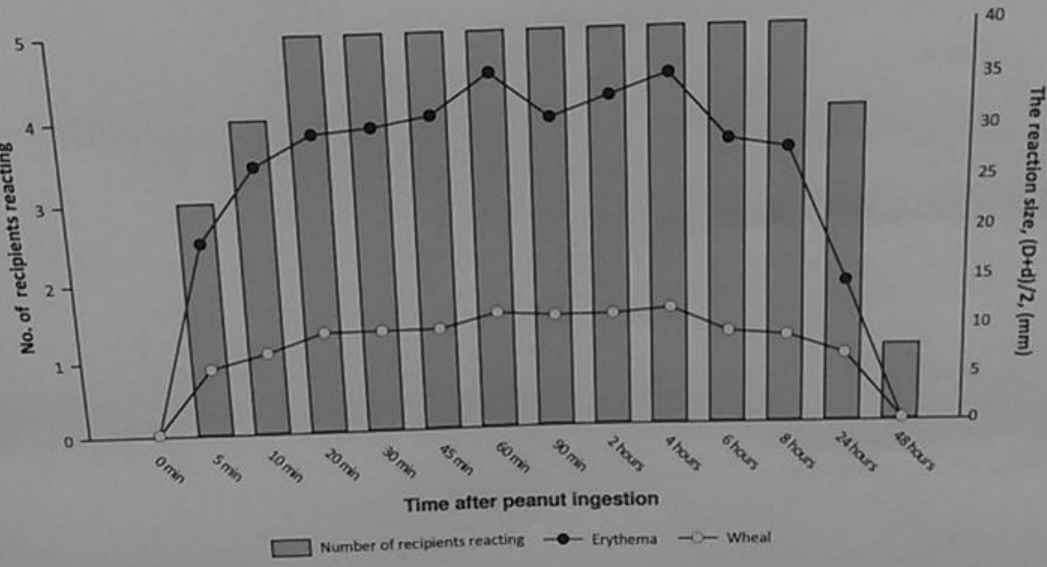
CONCLUSION
Ingested peanut protein is absorbed systemically and retains its immunoreactive capacity in non-atopic persons.

The gastrointestinal absorption of peanut proteins can run very fast (≤ 5minutes).

The concentration of peanut proteins in the blood peaks between 1 and 4 hours.

Peanut proteins can circulate in the blood up to 48 hours after oral intake.

Autologous Prausnitz-Küstner test



Graph I. The results of the autologous Prausnitz-Küstner test as a proxy for immunoreactive peanut protein absorption over a 48-hour period in 5 non-atopic volunteers passively sensitized in the skin with a serum from a donor with severe peanut allergy.

CONCLUSION
Ingested peanu
cally and retain
non-atopic pers

The gastrointes
proteins can run

The concentratio
blood peaks betw

Peanut proteins ca
48 hours after oral

Evaluation of a hypoallergenic wheat line 1BS-18 lacking omega-5 gliadin

Kunie Kohno[1*], Hitoshi Takahashi [2], Takashi R Endo [3], Hiroaki Matsuo [2], Kunimori Shiwaku [1], Eishin Morita [1]

1. Shimane University Faculty of Medicine, Shimane Japan, 2. Hiroshima University, Hiroshima Japan, 3. Ryukoku University , Kyoto Japan

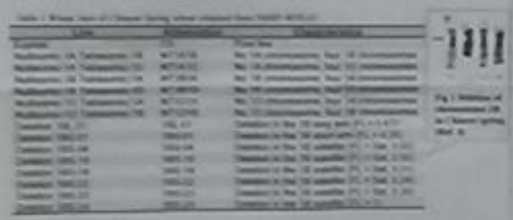
ABSTRACT

Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a distinct form of wheat allergy typically induced by exercise after the ingestion of wheat products. Prevalence of wheat allergy is estimated to be 0.1–3.9% among Europeans in a meta-analysis, and, is 0.21% among Japanese adults in a cross-sectional study of rural mountainous area in Japan (Shimane CoHRE Study). There is no established treatment for WDEIA, patients are forced to limit their intake of wheat products. As wheat is one of the dietary staple, patient's quality of life is significantly lowered by this limitation. Among wheat allergens, ω-5 gliadin is one of the dominant allergens affecting WDEIA patients. Possible explanation for the higher allergenicity of ω-5 gliadin, the intestinal translocation capabilities via transcellular route is suggested in Caco-2 cell model (Bodinier et al., 2007). The use of ω-5 gliadin-free wheat flour in the regular diet is considered to be one of the prophylactic approaches against the sensitization to ω-5 gliadin.

METHODS

Selection of wheat strains

The ω-5 gliadin gene is located on the short arm of chromosome 1B in wheat. We searched for candidate wheat lines among the deletion stocks of common wheat on the website of the National Bioresource Project (NBRP) (shigen.nig.ac.jp/wheat/komugi); and obtained candidate deletion lines and other lines from NBRP-Wheat (Fig 1 and Table 1).



Evaluation of allergenicity

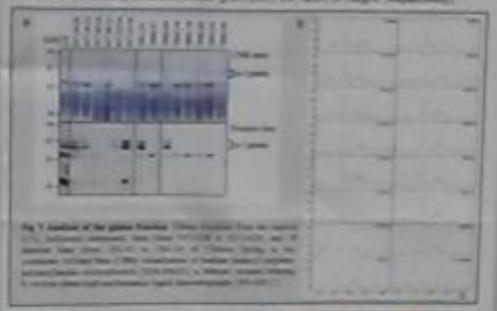
We screened the deletion lines of bread wheat by western blotting and reverse phase-high performance liquid chromatography (RP-HPLC) to ascertain common wheat lines lacking the ω-5 gliadin locus. To assess sensitization ability of gluten from the selected deletion line, guinea pigs were fed with either the gluten from the selected deletion line or commercially available gluten and allergic score was evaluated after challenging the same gluten preparations (Fig 2).

OBJECTIVES

We sought to evaluate hypoallergenic bread wheat that lacked the genes encoding ω-5 gliadin.

RESULTS

The deletion lines of bread wheat 1BS-18 were selected among deletion line of Chinese Spring, a well-established cultivar in wheat research field. Sensitization ability of gluten from deletion line 1BS-18 was much less than that of gluten from commercially available wheat. However the practical feasibility of deletion line 1BS-18 was low from the point of cost-effectiveness. In addition, bread making property of 1BS-18 whole-grain was low because of less expansion when compared with the one of commercially available whole-grain (5cm vs. 12cm of height, respectively).



CONCLUSIONS

The use of the wheat products of the deletion line 1BS-18 in daily life have possibility to provide a feasible solution for the onset of wheat allergy. Further study is needed to confirm this hypoallergenic ability of 1BS-18. The bread making property of 1BS-18 Chinese spring is low; repeated backcrossing of the 1BS-18 line to elite commercial cultivars is desirable for better quality and practical feasibility.

COI: *None*

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CHARITÉ

Benefit from mepolizumab treatment in a patient with chronic spontaneous urticaria

Magerl M, Terhorst D, Metz M, Altrichter S, Zuberbier T, Maurer M, Bergmann KC

Allergie-Centrum-Charité, Urticaria Center of Reference and Excellence (UCARE), Dpt. of Dermatology and Allergy, Charité - Universitätsmedizin Berlin

Chronic spontaneous urticaria (CSU) is a common and debilitating disease that come with recurrent wheals, angioedema or both. Key features of the pathogenesis of CSU include skin mast cell activation, release of histamine and other mediators, subsequent vasodilation, extravasation and nerve stimulation, and the recruitment of inflammatory cells including basophils and eosinophils. Antihistamine and omalizumab, the only two licensed CSU treatment options are effective, but many patients do not respond to either or both of these treatments, and additional and better therapies are needed.

Mepolizumab is a humanized monoclonal antibody directed against IL-5, and is licensed for the treatment of severe asthma in patients aged ≥12 years (EU only adults) with an eosinophilic phenotype as an add-on treatment. Eosinophils are held to contribute to the pathogenesis of asthma. Eosinophils have also been suggested to contribute to the development of the signs and symptoms of CSU. Here, we report the case of a 27 year old women with both, severe refractory eosinophilic asthma and CSU, who was treated successfully with 100mg mepolizumab every 4 weeks. The asthma control test (ACT, ranging from 0 to 25 with a score of <20 indicating uncontrolled disease) increased from 13 points, i.e. uncontrolled asthma, before treatment to 23 points 4 weeks after the first injection of mepolizumab. FEV1 increased in the same period of time from 2.5 L (60% predictive) to 3.6 L (90% predictive). ACT scores improved further, to the maximum possible 25 points another 8 weeks later, indicating complete control of her asthma. The patient was maintained on mepolizumab for a total of 16 weeks, after which treatment had to be discontinued due to the occurrence of the signs and symptoms of an immune complex reaction. After discontinuation, the patient's asthma remained stable and well controlled with inhalative steroids (800 ug/day) and long-acting beta-agonist (twice/day) treatment.

In addition to her asthma, our patient had long standing and difficult to treat CSU. Her CSU had started 5 years prior to mepolizumab treatment and was characterized by wheals and episodic angioedema, which were mostly appearing during phases of infections, most notably respiratory tract infections. Sleep and daily activities were then severely impaired, primarily due to the severe itch. The patient reported that her CSU symptoms are exacerbated by infections, the only known trigger or underlying cause. Previous treatments with several different antihistamines, at [illegible] than standard doses, alone or in combination, only had limited effects and did not result in CSU control. Over the course of the year previous to mepolizumab treatment, her CSU episodes led to several sick leaves for at least two weeks, indicating a very poorly controlled disease.

From the day after the onset of treatment with mepolizumab, the patient reported a dramatic and sustained improvement of her urticarial symptoms, both, the spontaneous wheals as well as the infection-triggered episodes. Four weeks after the first injection, the urticaria control test (UCT) was 12 (Firgure 1). The UCT ranges from 0 (no control at all) to 16 (complete control), a score of 12 or higher indicates controlled disease. Another 8 weeks later, the UCT was 16, and the patient reported about an ongoing and complete absence of the urticarial lesions, despite several infectious episodes during the wintertime. When we discontinued mepolizumab treatment, her CSU signs and symptoms returned during infectious episodes.

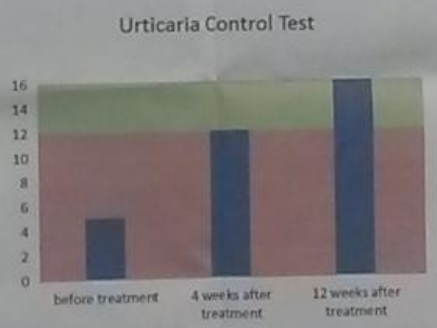

Figure 1: UCT values before and under treatment with Mepolizumab

To our knowledge, this is the first report of a therapeutic response to mepolizumab in a patient with CSU. The most likely explanation is that mepolizumab and its effects on IL-5 and eosinophils interfere with the pathogenic chain of events that leads to whealing and itch in CSU. It is unlikey that the CSU improved because of the effects of mepolizumab on asthma. Interestingly, the number of eosinophils in the skin of CSU patients has recently been reported to be higher than in healthy controls (Kay et al., 2014), and eosinophils have been proposed to contribute to the pathogenesis of CSU. Little is known about the role of eosinophils in CSU, and even less is known about IL-5. Our findings call for [illegible] studies on the role of IL-5 and eosinophils in chronic urticaria.

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#0110 - Causal association between IgE anti-TPO and chronic urticaria.

IgE anti-TPO expression in the three groups (CSU: 34%, ATD: 16,6%, healthy subjects 8,1%). Between those patients with positive IgE anti-TPO, flow cytometry showed CD203c induction with serial additions of TPO in 76,4% of CSU group and 40% ATD but not in healthy subjects.

#1321 - Increased risk of chronic spontaneous urticaria in patients with autoimmune thyroid diseases: a nationwide population-based study

AITD group (N= 3,659), control group (N=18,295). Each subject was tracked for whether CSU occurs or not. Subjects with AITD had a significantly higher rate of CSU compared to the control group (HR, 1,46).

Presence and family distribution of SERPING1 mutations in Macedonian HAE type I patients

Vesna Grivcheva – Panovska, MD PhD1; Matija Rijavec PhD2;
1[University Clinic of Dermatology, School of Medicine, University St. Cyril and Methodius, Skopje, Macedonia], 2[University Clinic Golnik, Ljubljana, Slovenia]

AIM

Authors investigated presence and family distribution of SERPING1 mutations in Macedonian HAE type I patients.

METHODS

- C1-INH-HAE diagnosis was established based on clinical and anamnestic criteria in 23 patients from 15 families; 4 patients are silent carriers.
- Genetic studies were carried out using PCR and sequencing to detect *SERPING1* mutations in promoter, noncoding exon 1, the 7 coding exons, and exon-intron boundaries
- Multiplex ligation-dependent probe amplification was performed in order to search for large deletions/duplications in *SERPING1* gene

RESULTS

Disease-causing mutations in SERPING1 were identified in all patients. In C1-INH-HAE type I, we identified 13 different mutations, and 2 large deletions. Two of the mutations (c.813_818delCAACAAC>T and c.1188_T>G) are reported here for the first time. Depending on the type of SERPING1 gene mutation, patients were divided into two groups: group 1 (nonsense, frameshift, large deletions/insertions, splicing defect, and mutations at Arg444) or group 2 (missense, excluding mutations at Arg444).

CONCLUSIONS

Authors have identified 13 different disease-causing mutations, including two novel mutations, contributing the heterogeneity of mutations in the SERPING1 gene

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#0333 - Are patients prone to using penicillin after testing negative for penicillin allergy at a specialist centre?

Of the 103 patients, 30 patients (29%) had taken penicillin since the investigation. Twenty nine patients (28%) were still hesitant to take penicillin. Eight patients (8%) answered that a doctor had hesitated to prescribe penicillin after the investigation.

#0336 - Outpatient collaboration between allergist and pharmacists results in long-term increase in ß-Lactam antibiotic prescriptions among patients with a history of penicillin allergy

A cohort of PCN allergy patients were identified by a pharmacist at the local pharmacy. 27% of 496 pts underwent PCN skin test, 93% were negative. During 10 Y follow up among patients evaluated by an allergist compared to those who were not 56 (68%) were prescribed a β-Lactam antibiotic compared to 65 (25%; $p < 0.0001$);

Omalizumab for idiopathic anaphylaxis – a case series

Kobir P.[1], Kokelj S.[1], Zidarn M.[2], Erzen R.[2], Bajrovic N.[2], Kopac P.[2], Silar M.[2], Korosec P.[2], Kosnik M.[1,2]
[1]Medical faculty, Ljubljana, Slovenia
[2]University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia

Introduction

Idiopathic anaphylaxis is a rare disease with no discernible cause. It is due to mast cell activation. Idiopathic anaphylaxis accounted for aproximatelly 10% of all cases of anaphylaxis. A large specter of allergy tests and other diagnostic tests (basal tryptase, histamine intolerance, chromogranin, 5-HIAA) have to be done to exclude relevant allergen sensitization and diseases that could mimic it. According to guidelines patients with more than 6 episodes per year should be put on long term systemic glucocorticoid prophylaxis.

Objectives

Omalizumab is a monoclonal antibody, that binds to IgE and decrease mast cell reactivity. Therefore omalizumab might be helpful in prevention of the anaphylactic reactions.

Materials and Methods

We reviewed the medical files of 3 patients who started omalizumab treratment due to recurent episodes of anaphylactic reactions with no discernible reason. Skin prick test were performed with a set of common respiratory allergens, common food allergens and fresh foods like nuts, peanuts, spices. Specific IgE against omega-5-gliadin, and alphy-3-gal were determined with ImmunoCAP system. Extended specter of sIgE sensitization was tested with ISAC microchip (Termo Fisher, Waltham, Massachusetts, USA).
Basal tryptase was determined. Serum chromogranin and diaminooxidase (D-HIT, Sciotec, Austria) determinations were ordered in routine diagnostic laboratories.

Results

Three women (56, 43 and 28 years) with recurrent spontaneous episodes of anaphylaxis (4-10 in year 2015), confirmed by tryptase elevation during episode. They were repeatedly treated by epinephrine at the emergency unit. Diagnostic workup didn't reveal any relevant allergy, neither cofactor. Two patients have concomitant chronic urticaria. Because of frequent and severe episodes, patients were started off-label omalizumab 300 mg monthly and are without anaphylactic episodes since then (9-13 months). Table 1.

Table 1. Demographic and clinical data on 3 patients with idiopathic anaphylaxis).

	Comorbidities	First episode	No. of episodes in 12 months	Tryptase during attack / basal	Symptoms	Positive diagnostic tests	Negative tests	Previous therapy	Outcome after omalizumab therapy
B.G. 1988	Chronic urticaria	2015	>4	18 10.4	Broncho spasm	IgE alpha-GAL; Dermographism	sIgE against common allergens negative, DAO, ISAC	epinephrine	No systemic reactions
S.J. 1973	Chronic urticaria	2015	8	5,51/ 1.62	Broncho spasm, hypotension	IgE for inhalatory and food allergens (celery); low diamonioxidase , ISAC Ves v 5	ANA	epinephrine	2 mild systemic reaction (urticaria) 2 and 13 months after start of omalizumab
R.D. 1960	Hyperthyrosis, Mb Crohn	2014	4	135/ 10.9	Broncho spasm, hypotension		IgE; Bone marrow biopsy, Octreoscan, OPT diclophenac	epinephrine	No systemic reactions

Conclusion

All three patients are in remission since the administration of omalizumab. Omalizumab seems an effective drug for prevention of recurrent episodes of idiopathic anaphylaxis.

Finski alergološki program

mag. Peter Kecelj, dr. med.
REMEDA d.o.o.

- program obvladovanja alergijskih bolezni na Finskem
- začetek programa 2008
- dogovor ekspertov (domači in gostujoči)
- finančna podpora finskega ministrstva za zdravje in njihovega nacinalnega inštituta za javno zdravje
- dolgoročni cilji

Načini delovanja v programu

- **<u>ciljne skupine:</u>**
  - splošna populacija
  - alergološki bolniki in njihove družine
  - nevladne organizacije in združenja bolnikov
  - zdravniki, zdravstveni delavci(posebni cilji)
  - zdravstvena politika (oblast)

Glavni poudarki programa

Endorse health, not allergy

Strengthen tolerance

Adopt a new attitude to allergy, and avoid allergens only if mandatory

Recognise and treat severe allergies early; prevent exacerbations

Improve air quality; stop smoking

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Organiziranost zdravstva na Finskem (5,5 miljonov prebivalcev)

- 21 bolnišničnih okrožij
- 5 univerzitetnih bolnišnic
- 250 centrov primarne oskrbe (22 000/center)
- 1000 izvajalcev medicine dela in športa (MDŠP)(5500/izvajalca)

Izvedba

- 20 000 zdravnikov in ostalih zdravstenih delavcev se je udeležilo usmerjenih izobraževalnih programov
- ustvarili so mrežo posebej usposobljenih zdravnikov in med. sester (1500)
- 14 regionalnih strokovnih alergoloških skupin- koordinacija implementacije novih priporočil

- **Primary prevention**

- Support breastfeeding, with solid foods from 4–6 months onwards

- Do not avoid exposure to environmental allergens (foods, pets), if not proven necessary

- Strengthen immunity by increasing contact with natural environments (*e.g.* by taking **regular physical exercise** and following a **healthy diet** such as a traditional Mediterranean or Baltic diet)

- **Antibiotics** should only be used in cases of **true need** (the majority of microbes are useful and build a healthy immune function)

- Probiotic bacteria in fermented food or other preparations may balance the immune function

- Do not smoke (parental smoking increases the risk of asthma in children)

European Respiratory Journal 2017

- **Secondary and tertiary prevention:**

- Regular physical exercise is anti-inflammatory

- Healthy diets are anti-inflammatory (a traditional Mediterranean or Baltic diet may improve asthma control)

- Probiotic bacteria in fermented food or other preparations may be anti-inflammatory

- Respiratory/skin inflammation should be treated early and effectively; maintenance treatment titrated for long-term control

- To stop symptom exacerbations proactively, instructions for guided self-management are provided for 10 allergic conditions (available in both paper and electronic formats)

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- **<u>Allergen-specific immunotherapy is recommended for more severe symptoms, *e.g*:</u>**

- allergens as such (for foods)

- sublingual tablets or drops (sublingual immunotherapy, or SLIT) (for pollens)

- subcutaneous injections (for pollens, pets, mites, insect stings)

- Smoking should be strictly avoided (the effectiveness of asthma and allergy drugs is reduced in smokers)

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Doseženi cilji po 5 letih programa

- **1) Prevent allergy**
- *Indicator*: asthma, rhinitis and atopic eczema prevalence reduced by 20%
- ***Outcome*: no information yet**
- **2) Improve tolerance**
- *Indicator*: food allergy diets reduced by 50%
- ***Outcome*: allergy diets in day-care settings −40%**
- **3) Improve allergy diagnostics**
- *Indicator*: skin prick testing practised in certified testing centres
- ***Outcome*: 30 hospitals and other centres educated, audited and certified**

- **4) Reduce work-related allergies**
- *Indicator*: occupational allergies reduced by 50%
- ***Outcome*: occupational allergies reduced by 40%**
- **5) Focus on severe allergies and treat in time**
- *Indicator*: effective allergy practice; asthma emergency visits reduced by 40%
- ***Outcome*: emergency visits −46%; asthma hospital days −67%**
- **6) Reduce allergy and asthma costs**
- *Indicator*: allergy costs reduced by 20%
- ***Outcome*: total costs in the 2000s −15%; in 2007–2013 −5%**

Zdravstvena vzgoja na EAACI 2017

Perko Karmen

DMS

- Pacientovo vedenje o njegovi bolezni je pomemben del njegovega zdravljenja
- Največ gradiva oz študij, ki so bile na kongresu predstavljene, so naredili na področju pacientov z diagnozo astme
- Zanimiva je študija o uporabi epipena pri pacientih z alergijo za hrano
- Sestrski protokol – sprejem otroka z alergijo za hrano na testiranje v bolnišnico – kratka primerjava z našim delom

Prilagajanje zdravstvene vzgoje pri starejših pacientih

- Saratov State Medical University , Russia
- Starejši se pogosto soočajo z težjimi oblikami poslabšanj, njihova zmožnost samokontrole je manjša kot pri mlajših.
- Namen je bil preveriti znanje o astmi, poiskati pomanjkljivosti in ugotoviti, na kakšen način pridobivajo znanje oz kako jim pomagati
- Vključenih 50 pacientov z dg. astma, starejših od 64 let, zdravljenih v letih 2014 in 2015

- Ugotovili so: 36% - pomanjkljivo znanje o bolezni

  : napačna pričakovanja - kar 56% jih je pričakovalo popolno ozdravitev

  : 56% - napačna tehnika jemanja th

  : neredno prejemanje th, strah pred stranskimi učinki, brez načrta samozdravljenja
- Ugotovili so, da so starejši manj prizadevni za izobraževanje, poiščejo si manj gradiva
- Večina bolnikov je dobila navodila od zdr. osebja, nekaj jih je obiskalo astma šolo, dobili so pisno gradivo – brošure. Samo 12 % se jih je poslužilo interneta.

* Več jih je obiskalo poljudne strani kot strokovno literaturo.

- Zaključek in povzetek študije je, da starejši še vedno potrebujejo zdravstveno vzgojo
- V primeru spletnega izobraževanja potrebujejo podporo in sodelovanje strokovnih delavcev, ki jim s svojim znanjem pomagajo .

Avtoinjektor in hrana – kdaj mladi nosijo s seboj zdravilo, kako dojemajo tveganje v različnih situacijah?

- Brighton&Sussex Medical schoolm Brightom, UK skupaj z LKC Medicinem Nanyang Tehnological University Singapore
- Najbolj uspešno je izogibanje alergenu. Včasih se zgodi, da pride do reakcije zaradi nenamerne izpostavljenosti alergenu.
- 188 mladostnikov starih med 13 in 23 let, ki so imeli potrjeno alergijo za hrano in predpisan epipen, 50% žensk
- Izvedeno na podlagi vprašalnika (ali nosijo avtoinjektor (AI) s seboj, ali se zavedajo tveganj za al. reakcijo)
- Poročajo o različnih navadah – večina , 90% nosi AI s seboj na potovanje. Ob športni aktivnosti ga ima pri sebi le 21% sodelujočih.

Avtoinjektor in hrana – kdaj mladi nosijo s seboj zdravilo, kako dojemajo tveganje v različnih situacijah?

- Kot najbolj tvegano dejanje so izpostavili poljub s partnerjem, ki je zaužil alergen, manj jih je skrbel pojav reakcije ob obisku šole;).
- Ženske so zaznale večje tveganje kot moški.
- Rezultate so primerjali z predhodno izvedeno študijo v Ameriki, bistvenih odstopanj niso opazili.

* Zaznali so, da so ženske predstavnice bolj dovzetne za izobraževanju o tveganih situacijah.

Sestrski protokol sprejema otroka v dnevno bolnišnico (povzeto po Infanta Leonor University Hospital, Madrid Spain

- Postavljen z željo po najboljši oskrbi ob sprejemu v bolnišnico
- Vpis pacienta in preverjanje podatkov - identifikacija
- Zagotoviti sodelovanje pacienta
- Zdravnik opravi intervju s pacientom in starši
- Natančno opredelijo, kaj in kako bo potekalo testiranje
- Podobno se ravnamo v alergološki enoti UKPA Golnik
- Administrativni sprejem
- Osebni kontakt z osebjem
- Zagotovimo intimo pri razgovoru
- Plan testiranja dogovorjen s pacientom

Sestrski protokol sprejema otroka v dnevno bolnišnico (povzeto po Infanta Leonor University Hospital, Madrid Spain

- Identifikacija alergena
- Po testiranju opazovanje
- Ob zaključku podrobna navodila za doma

- Označimo katerikoli alergen z bolnikovimi podatki (nalepka)
- Po testiranju opazovanje
- Ob zaključku odpustnica z navodili

A NURSING PROTOCOL OF ASSISTANCE IN A PEDIATRIC DAILY HOSPITAL OF ALLERGY.

López M. , Rojas A. , Rodríguez F., Rodríguez MA. , Canto G.
Infanta Leonor University Hospital.

INTRODUCTION

The nursing assistance to the children who attend to an Allergy daily hospital has as a main priority to provide the best care to the patients with specialized and well trained nurses.

OBJECTIVES

The aim of this work was to perform a nursing protocol which summarized all the steps to follow up and all the actions to perform in order to assess the best assistance to the children attended in our paediatric allergy daily hospital.

Patient (> 1 y.o.) undergoing DPT.

Patient (> 1 y.o.) undergoing DPT.

Paediatric DPT/OFC average per year = 1.920.

MATERIAL AND METHODS

- **RECEPTION OF PATIENTS:**
  - Name/family name of patients are verified.
  - Confirmation of personal data of the children with the parents.
  - Introduction of the nursing staff.
- **IDENTIFICATION OF PATIENTS:**
  - Placement of a personal sticker with the name and the picture of the allergen in study (food or drug) on the back (if younger than 1 year old) or on the chest (if older than 1 year old).
- **CLINICAL ASPECTS:**
  - Interview concerning health problems within the previous 24 hours (fever, cough, rhinitis, diarrhoea, vomiting...) and any medication undertaken (vaccines, antibiotics, antihistamines, corticosteroids...).
  - Confirmation that the child has eaten before the procedure (children must not fast).
- **CONTROLLED ADMINISTRATION:**
  - Verification of the correct drug/food dose before each step and after every controlled administration.
  - Confirmation that the dose corresponds to the one prescribed by the allergist.
  - Avoidance of any contamination from other allergens (food/drug).
- **RECOMMENDATIONS:**
  - Parents/caregivers must keep the patient under surveillance over the next 6-8 hours after the discharge from the hospital.
  - A written information form is provided to the parents or caregivers with the guidelines to be followed at home.

RESULTS

With this nursing protocol we avoid any mistake that could occur during the oral controlled administration concerning allergen-dose, as well as we achieve a better compliance with the guidelines given to the children and their families.

CONCLUSIONS

This protocol ensure an appropriate nursing assistance as well as avoid any mistake during the oral challenge procedure.

Patient (< 1 y.o.) undergoing oral cow's milk challenge.

Patient (> 1 y.o.) undergoing oral hen's egg challenge.

Hand delivery of guidelines to parents upon patient's discharge.

Pediatrična alergologija

Tina Vesel Tajnšek

Služba za alergologijo, revmatologijo in klinično imunologijo, Univerzitetna pediatrična klinika, Ljubljana

Golnik, EAACI po EAACI, 7.9.2017

Pristop k otroku z anafilaksijo in alergijo na hrano

3. preventiva?

Dogovor o obravnavi anafilaksije

Smernice za ukrepanje pri anafilaksiji otroka in mladostnika, Zdrav Vestn 2014

PREPOZNAVA ANAFILAKSIJE

ZDRAVLJENJE ANAFILAKSIJE

VZROKI

DEL[illegible] PEDIATROV ALERGOLOGOV

[illegible]A [illegible]EV DELA

SAMOINJEKTOR ADRENALINA

ZORNI KOT:

ZDRAVNIKI

OTROK, NJEGOVI BLIŽNJI

ZAKONODAJA

PSIHOLOGIJA

2. bulling-ustrahovanje

IZOBRAŽEVANJE

OZAVEŠČANJE

1. Uporabnost opredelitve kvalitete življenja ?

1. Ocena kvalitete življenja-QoL/HRQL otrok in mladostnikov z alergijo na hrano in anafilaksijo

Vprašalniki QoL- kazalec izida številnih bolezni

- AD, astma, rinitis, urtikarija, piki kožekrilcev,..
- alergija na hrano- ocena dobrega počutja bolnika?

Box 4: Recommendations for clinicians

1 To date, the use of food allergy-specific HRQL tools in clinical practice has been little documented. Clinicians should be aware of this and be cautious when using HRQL measurements to guide management decisions.

2 There is currently also no information on the use of HRQL measurements as a form of bench-marking in food allergy.

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines. Food allergy health-related quality of life measures

A. Muraro[1,†], A. E. J. Dubois[2,3,†], A. DunnGalvin[4], J. O'B. Hourihane[5], N. W. de Jong[6], R. Mey
S. S. Panesar[8], G. Roberts[9,10,11], S. Salvilla[8], A. Sheikh[8,12], A. Worth[8] & B. M. J. Flokstra-de Bl

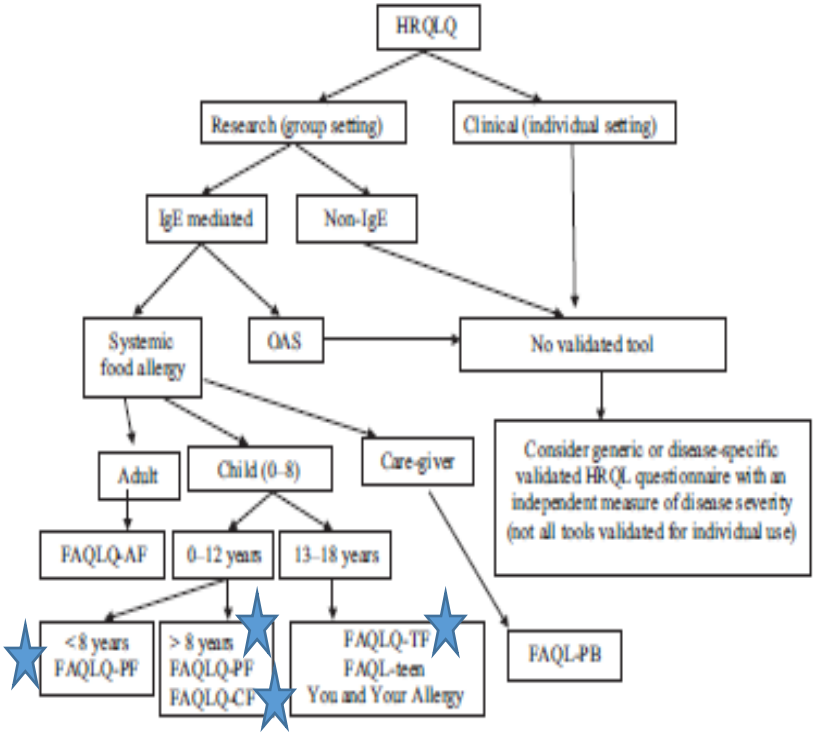

Figure 1 Choosing an appropriate Food Allergy HRQLQ

Starši otrok z alergijo na hrano: višja QoL bolj poučeni, manj alergij, starejši

Knibb RC PAI 2016

Odrasli- Evropa: nižja QoL- prizadetost dihal/KVS, alergija na mleko, ribe, ženski spol

Otroci- Evropa: nižja QoL- alergija na arašide, sojo

Saleh-Langenberg J, Allergy 2015

Provokacijski test s hrano: višja QoL

Na vsako vprašanje naj otrok odgovori s pomočjo naslednjih odgovorov z izbiro ENE možnosti:

ne **komaj** **malo** **kar** **precej** **zelo** **ekstremno**

Food Allergy Quality Of Life Questionnaire – Child Form (8–12 years)

Koliko težav imaš ker…

1. moraš vedno biti pozoren na to kaj poješ?
2. lahko ješ manj stvari?
3. si omejen pri tem, da bi si kupil tisto, kar si želiš?
4. moraš brati o sestavi živil (deklaracije)?
5. moraš zavrniti hrano ko počneš stvari z drugimi?
6. manj pogosto lahko poješ obrok/ kosilo pri nekom?
7. lahko preskušaš manj stvari, ko ješ zunaj?
8. moraš vnaprej povedati, česa ne smeš jesti, ko ješ zunaj?
9. moraš sam preveriti ali lahko nekaj poješ zunaj?
10. oklevaš, da bi jedel, ko ne veš, če je zate določena hrana varna?
11. moraš biti previden, ko se dotikaš določene hrane?
12. ne dobiš ničesar, ko nekdo v šoli razdeli sladkarije?

Koliko težav imaš zaradi alergije na hrano ker…

13. se sestavine proizvodov spreminjajo?
14. na živilu piše »lahko vsebuje sledi«?
15. moraš drugim razlagati, da imaš alergijo na hrano?
16. drugi okrog tebe pozabijo da imaš alergijo na hrano?
17. ko si v družbi lahko drugi okrog tebe uživajo hrano, na katero si alergičen?
18. ne veš kakšnega okusa je hrana, ki je ne smeš jesti?

Koliko te skrbi zaradi tvoje alergije na hrano…

19. alergijska reakcija
20. da pomotoma zaužiješ napačno hrano?
21. poješ nekaj kar sploh še nisi?

Odgovori prosim še na naslednja vprašanja:

22. Koliko te skrbi, da se ne boš nikdar znebil svoje alergjje
23. Koliko si razočaran, ko drugi ne upoštevajo resno tvoje alergije?
24. Kako razočaran si, ker imaš svojo alergijo?

FAIM- Ocena resnosti bolezni s strani bolnika

Food Allergy Independent Measure – Child Form (8–12 years)

0	1	2	3	4	5	6
never (0% chance)	very small chance	small chance	fair chance	big chance	very big chance	always (100% chance)

	How big do you think the chance is that you . . .	0	1	2	3	4	5	6
a.	will accidentally eat something to which you are allergic?	☐	☐	☐	☐	☐	☐	☐
b.	will have a severe reaction if you accidentally eat something to which you are allergic?	☐	☐	☐	☐	☐	☐	☐
c.	will die if you accidentally eat something to which you are allergic?	☐	☐	☐	☐	☐	☐	☐
d.	can not do the right things for your allergic reaction should you accidentally eat something to which you are allergic?	☐	☐	☐	☐	☐	☐	☐

e. How many foods are you unable to eat because of your food allergy?

- ☐ almost none
- ☐ very few
- ☐ a few
- ☐ some
- ☐ many
- ☐ very many
- ☐ almost all

f. Everyone does things with other people, such as; playing with friends, going to a birthday party, visiting, staying over with someone for a meal or eating out. How much does your food allergy affect things you do with others?

- ☐ so little I don't actually notice it
- ☐ very little
- ☐ a little
- ☐ moderately
- ☐ a good deal
- ☐ a great deal
- ☐ a very great deal

Velde JL et al, Allergy 2010

IMPAIRED HEALTH-RELATED QUALITY OF LIFE IN FOOD ALLERGIC CHILDREN AND TEENAGERS IN SLOVENIA

Tina Vesel[1], Mateja Sever[1], Poredoš T[2], Avčin T[1]

[1]Department of Allergology, Rheumatology and Clinical Immunology, University Children's Hospital, University Medical Center, Ljubljana, Slovenia

[2]Department of Dietotherapy and Hospital Nutrition, University Children's Hospital, University Medical Center, Ljubljana, Slovenia

INTRODUCTION

- Food allergy may impair health-related quality of life (HRQL).
- Predictors of HRQL have been found in greater extent in adults than in children and teenagers. For children HRQL varied with perceived disease severity, peanut or soy allergy and country of origin (1).
- There are no data on HRQL of children and teenagers with food allergies in Slovenia.

AIMS:

- to identify HRQL of food allergic children and teenagers in Slovenia
- to examine clinical usefulness of HRQL and food allergy independent measure (FAIM)

METHOD

- 69 children were examined (Table 1). Eight adolescent completed Food Allergy Quality of Life Questionnaire (FAQLQ)-Teenager Form, 20 children FAQLQ- Child Form and 42 parents Parent Form of FAQLQ.
- A new questionnaire assessing HRQL in kindergarten and school was also developed and applied.
- The FAQLQ and FAIM scores were the sum of item scores divided by the number of completed items (ranging from 1- minimal impairment to 7- maximal impairment).

RESULTS

Table 1. Characteristics of 69 children

Gender	Number (%) of children
Female	21 (30)
Male	48 (70)
Age (years)	
0-3	4 (6)
4-6	22 (32)
7-12	35 (51)
13-17	8 (11)
Clinics	
Anaphylaxis/ urticaria	17/18 (25/26)
Atopic dermatitis	45 (65)
Asthma	21 (30)
OAS	9 (13)
Peanut allergy	52 (75)
Multiple food allergy	27 (40)

Legend: OAS- oral allergy syndrome

Table 2. Health-related quality of life and food allergy independent measure in 69 children

	Children 8-12 years	Teenagers 13-17 yeras	Parents of 1-12 years old children
1. FAQLQ (mean, SD)			
General emotional impact	3.9± 1.6	4.1± 1.9	2.6± 1.1
Food anxiety	3.4± 1.2	3.9± 1.7	2.7± 1.5
Social and dietery restrictions	4.8 ± 1.6	4.8± 2.1	2.7± 1.5
Total score	**3.9± 1.2**	**4.13± 1.8**	**2.7± 1.3**
School/kindergarden domain	2.4± 0.7	2.8± 1.4	2.4± 1.2
2. FAIM (mean, SD)	3.4± 1.0	3.6± 1.7	3.9± 1.2

1. Total FAQLQ score was worse when assessed by teenagers and children themselves (4.1 and 3.9, respectively), being most disturbed at the item of Social and dietary restrictions. Total FAQLQ score was moderate low when assessed by the parents (2.7) (Table 2).

2. Experience of anaphylaxis and having multiple food allergies impaired HRQL according to FAQLQ Parent Form ($p < 0.05$). Sex, having prescribed an adrenaline autoinjector, experience of food provocation test, peanut allergy and FAIM did not contribute to different HRQL.

3. HRQL in kindergarten and schools were moderately diminished (2.6 in schools vs 2.2 in kindergartens) ($p > 0.05$).

4. During FAIM 68% of participants' reported at least some possibility of dying if child/teenager would accidently eat a food allergen.

5. Clinical usefulness: After fulfilling FAQLQ and FAIM questionnaires, all participants expressed satisfaction, ten children/teenagers decided to approach food provocation tests de novo, employees of children's schools/kindergartens were encouraged in written invitations to assess anaphylaxes training programs and four families accepted additional psychological support.

CONCLUSIONS

- **Food allergies impair HRQL in children and teenagers- especially if asking children or teenagers. Social and dietary restrictions were most bothersome for children/ teenagers.**
- **Allergy to multiple foods and experience of anaphylaxis were associated with more severe impairment of HRQL.**
- **Regarding FAIM: the perception of disease severity in food allergic children, teenagers and their parents is independently present, including in two thirds the tough of possibility of death.**
- **HRQLQ and FAIM are useful, additional tools to assess and discuss child's/teenager's/parent's fears and obstacles because of food allergy and identify further needs of support.**

REFERENCES

1. Saleh-Lamgenberg J, Goossens NJ, Flokstra-de Blok BMJ, et al. Predictors of healh-realted quality of life of European food-allergic patients. Allergy 70 (2015) 616-24.

In relation to this presentation, we declare that there are no conflicts of interest.

CONTACT INFORMATION

tina.vesel@kclj.si.

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5. Clinical usefulness: all participants expressed satisfaction, ten children/teenagers decided to approach food provocation tests de novo, four families accepted additional psychological support.

Pre-service teachers' perception of allergic students' quality of life

Sonja Posega Devetak[1], Iztok Devetak[2], Tina Vesel[3]

[1] General and teaching hospital Izola, Department of pediatrics, Izola, Slovenia

[2] University of Ljubljana, Faculty of Education, Ljubljana, Slovenia

[3] University Medical Center, University Children's Hospital, Department of Allergology, Rheumatology and Clinical Immunology, Ljubljana, Slovenia

INTRODUCTION

- In management of allergic child in school, teacher's knowledge but also perspective of child's needs is important.
- The experience and perception of food allergy (FA) were lacking among caregivers of non-FA children (1).
- Health-related quality of life (HRQL) questionnaires have been applied with benefits in children with allergic diseases and in their families (2), but not in pre-service teachers or teachers.

AIM

The aim of our study was to assess:

- the knowledge of pre-service teachers about allergies
- pre-service teacher's awareness of the impact of allergic child diseases on
  1. children's and
  2. pre-service teacher's quality of life.

PARTICIPANTS AND METHODS

- 137 pre-service primary and lower secondary school teachers (8% male; 91% female; average age 23.9 (SD=1.5) years participated in this study. 23% of students were allergic themselves.
- Participants fulfilled:

  1. Allergy Quality of Life Questionnaire (AQLQ) - Teacher's Form which comprised 31 items about pre-service teachers' perception of HRQL of an allergic student (HRQLS) (in Box 1 items about FA are presented) and
  2. 31 items about pre-service teachers' own HRQL if they had to take care for an allergic student in school (HRQLT).
- The HRQL scores were the sum of item scores divided by the number of completed items (ranging from 0-minimal impairment to 6-maximal impairment).
- Cronbach Alpha: HRQLS 0.950; HRQLT 0.931
- Participants also answered edited Teachers' Health Competences Development–Allergy Questionnaire (THCDAQ2), which comprised 9

1. children's and
2. pre-service teacher's quality of life.

RESULTS

- Female pre-service teachers (*M*=18.01 (51.5%); *SD*=4.53) showed higher knowledge about allergies than males (*M*=14.73 (42.1%); *SD*=2.80); *t*(133)=-2.36; *p*=.020. [Max. 35 points.]
- The total HRQLS score was quite low, but assessed significantly higher by female (*M*=4.85; *SD*=.71) than male pre-service teachers (*M*=4.22; *SD*=.88); *t*(116)=-2.61; *p*=.010. Among items on food allergy assessed HRQLS was lowest at the items of Social and dietary restrictions.
- The total HRQLT score was comparably low when assessed by males (*M*=3.79; *SD*=1.39) or females (*M*=4.48; *SD*=1.10); *t*(116)=-1.85; *p*=.067. Among items on food allergy assessed HRQLS was again the lowest at the items of Social and dietary restrictions.
- The level of pre-service teachers' knowledge about allergies did not contribute significantly to different average HRQLS or HRQLT scores (*p*> 0.05).

CONCLUSIONS

- **Pre-service teachers recognised reduced HRQL of allergic children and expressed also theirs lower HRQL when taking care for allergic child.**
- **There was no significant correlation between knowledge and HRQL assessment.**
- **HRQL issues should be included in recommendation for the management of allergic child in school besides training how to prevent, recognise and manage allergic reactions.**

- Participants also answered edited Teachers' Health Competences Development–Allergy Questionnaire (THCDAQ2), which comprised 9 attitude items on managing children's health issues, 3 items about their formal education about allergies and 33 alternative knowledge items on allergic disease.

Box 1 Allergy Quality of Life Questionnaire (AQLQ) - Teacher's Form with 24 items about pre-service teachers' perception of HRQL of an food allergic student (HRQLS)

GENERAL EMOTION IMPACT OF FOOD ALLERGY: How troublesome do you find it, because of your students food allergy, that she/he . . .
1 ...must always watch what to eat?
2 ...can eat fewer things?
3 ...is limited in buying food?
4 ...have to read labels?
5 ...have to refuse food when eating outside?
6 ...can less easily except invitation to events organised by school when food is present?
7 ...can taste or try fewer things when eating outside?
8 ...have to check herself/himself whether can eat something when eating out?
9 ...hesitate eating certain foods when don't know if it is safe?
10 ...must refuse treats when delivering them at school?
11 ...must watch out when touching certain foods?
12 ...must carry Epipen (adrenaline auto-injector)?
FOOD ANXIETY: How troublesome is it for your student with food allergy ...
13 ...that the ingredients of a food change?
14 ...that the label states: 'May contain traces of . . .?
15...that declaration on a common box differentiates from declaration of inside items?
16...that student have to explain to people around having a food allergy?
17... that others can eat around the student the food student is allergic to?
18...that during social events others do not take food allergy seriously?
SOCIAL AND DIETERY RESTRICTIONS: How frightened is a student with food allergy because of his/hers food allergy . . .
19 ...of having an allergic reaction?
20 ...of eating the wrong food by accident?
21 ...to eat something never eaten before?
22. How disabled is a student with food allergy during allergic reaction?
23. How disappointed is a student with food allergy when people don't take food allergy into account ?
24. How disappointed is a student with food allergy when school can not take care of meals and she/he must carry food from home?

REFERENCES

1. Yamamoto-Hagada K, Futamura M, Tahakashi O, et al. Caregivers of children with no food allergy- their experience and perception of food allergy. PAI 2015; 26: 614-7.
2. Saleh-Lamgenberg J, Goossens NJ, Flokstra-de Blok BMJ, et al. Predictors of health-related quality of life of European food-allergic patients. Allergy 2015; 70: 616-24.

2. Ustrahovanje (bulling) otrok in mladostnikov z alergijo na hrano

Bullying in Australian children and adolescents with food allergies, EAACI 2017

Introduction

Recent international evidence suggests that food allergic children and adolescents experience an increased incidence of bullying compared to similar school-aged children, at rates of up to 30%. There have as yet been no studies to characterise this in Australian populations despite the high numbers of food allergic school children.

Objectives

Two survey tools were used; a questionnaire based on similar surveys done overseas, and the validated Food Allergy Quality of Life Questionnaire (FAQLQ).

Results

102 surveys have been collected at the time of writing of which 64 were answered by parents for young children. Overall, 44/97 **(45%) reported bullying, with a higher portion in older children and adolescents (22/37; 59%).** Of this group, 10/20 **(50%) reported being bullied or teased because of their food allergies. From parental reports, 11/19 (57%) stated that their child had experienced bullying or teasing because of food allergies.**

For those not bullied, parents mentioned that this may be due to their child having friends at school, being too young for bullying or because other children at school had a good understanding of the severity of allergies and were educated by teachers.

The most common location for bullying was "in the playground or sportsground" (36/39). The most common form of bullying involved being "teased, called names or someone has said mean things to me" (31/39). Whilst food allergens were involved in bullying in many cases (24/39), there were no reports of children being forced to eat food to which they are allergic. Of concern however, two adolescents reported experiencing an allergic reaction as a result of the bullying. The majority reported experiences of sadness from bullying (30/39) while seven stated that it had no effect.

Conclusions

Our current research shows that 45% of children and adolescents with food allergies experience bullying, and that 22% (21/97) experience bullying specifically because of their food allergies. This indicates a significant social problem that requires addressing to positively assist those children living with food allergies.

Table IIFrequency of general bullying for type of bullying among food-allergic students compared with nonallergic students*

Type of bullying	Status	Frequency (N = 120)				
		Never	Hardly ever	Sometimes	Often	Mostly
Verbal (being called mean names, or teased in a hurtful way)	Allergic	59.17	28.33	8.33	3.33	0.83
	Nonallergic	79.17	17.50	3.33	0	0
Relational (being target of rumors)	Allergic	70.83	19.17	8.33	0.83	0.83
	Nonallergic	82.50	13.33	4.17	0	0
Social (being intentionally excluded or isolated)	Allergic	75.83	16.67	5.83	0.83	0.83
	Nonallergic	81.67	15.83	2.50	0	0
Physical (being hit, kicked, or pushed)	Allergic	81.67	12.50	3.33	0.83	1.67
	Nonallergic	88.33	11.67	0	0	0

45.4% of food allergic children and 36.3% of parents of food allergic children reported bullying- Shemesh E, Pediatrics 2013

Comparison of bullying of food-allergic versus healthy schoolchildren in Italy- Muraro A, JACI 2014: **Food-allergic students have a probability of being bullied approximately 2 times higher than nonallergic peers**

IMPACT OF BULLYING IN FOOD ALLERGY

- 4.0% of incidents resulted in an allergic reaction
- 26.3% reported feeling sad/depressed,
- 20.2 % reported loneliness/social withdrawal, low self-esteem,
- 20% reported nervousness/anxiety,
- 5% insomnia & fatigue
- 23 % embarrassment/humiliation.

- Qualitative reports include :
  - Feeling angry, isolated, confused as to why they were targeted, vulnerable, and hesitant to eat at school after an incident
  - Trying to hide their food allergies because of past bullying, teasing, or harassment

Lieberman et al., Bullying among Pediatric Patients with food allergy. Ann allergy asthma Immunol 2010;105:282-6.
Shemesh et al. Child and parental reports of bullying in a consecutive sample of children with food allergy. Pediatrics 2013;131:e10-7.
Muraro et. al Comparison of bullying of food-allergic versus healthy schoolchildren in Italy JACI (2014) 134, 3
Koman, E; Raver E Adams Dunn Galvin, A. Living with food allergy : Bullying across 48 states in the US(submitted).

3. Preprečevanje alergijskih bolezni

PEDIATRIC JOURNAL CLUB

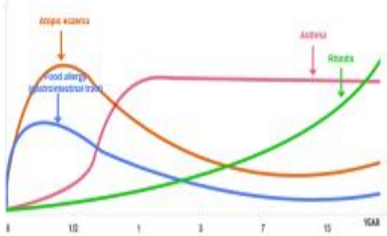
TO EAT OR NOT TO EAT ?

PEDIATRIC JOURNAL CLUB

EPIDEMIJA ALERGIJE NA HRANO

DRUGI VAL EPIDEMIJE ALERGIJ zadnjih 10-15 let

- alergije na hrano
- zgodnješe, težje potekajoče in dolgotrajnejše
- kumulativna incidenca 6 – 8 % prva 3 leta življenja, kasneje ≈2 %
- motnje zgodnje oralne imunske tolerance



ALERGIJSKI POHOD

PEDIATRIC JOURNAL CLUB

PRIPOROČILA - ZGODOVINA

60. leta

Večina dojenčkov uživa gosto hrano pred 4. mesecem

70. leta

Priporočila za uvajanje goste hrane po 4. mesecu

80. / 90. leta **IZOGIBANJE ALERGENOM**

Teorija povečane prepustnosti in "nezrelosti" GIT imunosti

Priporočila za kasnejše uvajanje alergene hrane za rizične (ZDA,UK,Australija...)

- izključno dojenje 6 mesecev
- KML po 12. mesecu
- jajce po 2. letu
- arašidi/oreščki/ribe po 3. letu

PEDIATRIC JOURNAL CLUB

PRIPOROČILA - ZGODOVINA

2008 (AAP*,ESPGHAN**,EAACI***)

- uvajanje goste hrane vključno s potencialnimi alergeni med 4. – 6. mesecem
- ni dokazov, da kasnejše uvajanje zmanjša verjetnost alergije
- nobene diete za rizične nosečnice
- uvajanje goste hrane še med dojenjem

AKTIVNO PROMOVIRANJE ORALNE TOLERANCE

ALERGIJA NA ARAŠIDE

- 1.4 – 3 % otrok v zahodnem svetu
- Najpogostejši vzrok anafilaksije in smrti zaradi alergije na hrano
- Velik vpliv na kvaliteto življenja
- Zgodaj se pojavi, redko izzveni

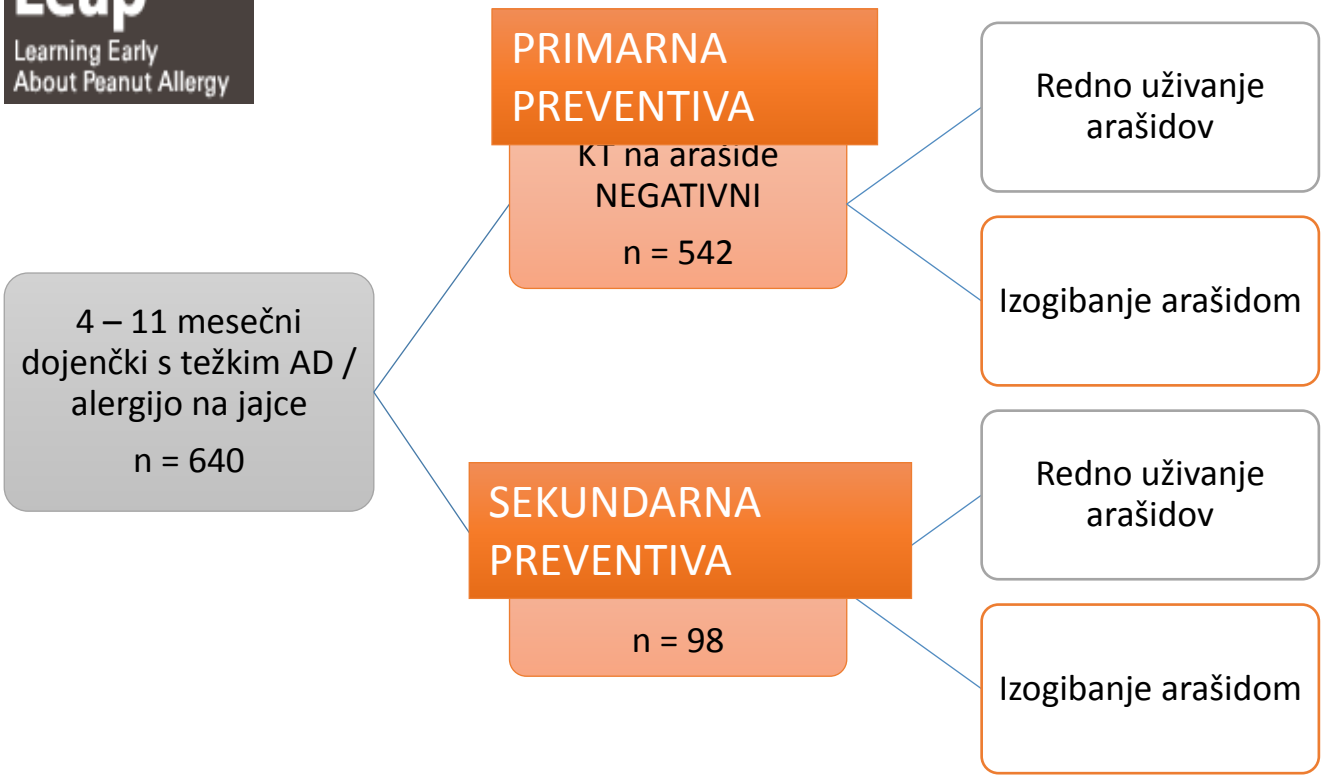
UŽIVANJE ARAŠIDOV V IZRAELU IN VELIKI BRITANIJI

	IZRAEL	VB
PREVALENCA ALERGIJE NA ARAŠIDE med šolarji	0,17 %	1,85 %
SREDNJA KOLIČINA MESEČNIH ZAUŽITIH BELJAKOVIN ARAŠIDOV med 8-14 mes	7,1 g	0 g
SREDNJE ŠTEVILO OBROKOV Z ARAŠIDI NA MESEC med 8-14 mes	8	0

Du Toit G et al. Early consumption of peanuts in infancy in associated with a low prevalence of peanut allergy. JACI 2008.

Študija "LEAP"

randomizirana, odprta, kontro
intervencijska študija



PRIMARNI IZID: DELEŽ OTROK Z ALERGIJO NA ARAŠIDE PRI 5 LETIH (PROVOKACIJSKI TEST)

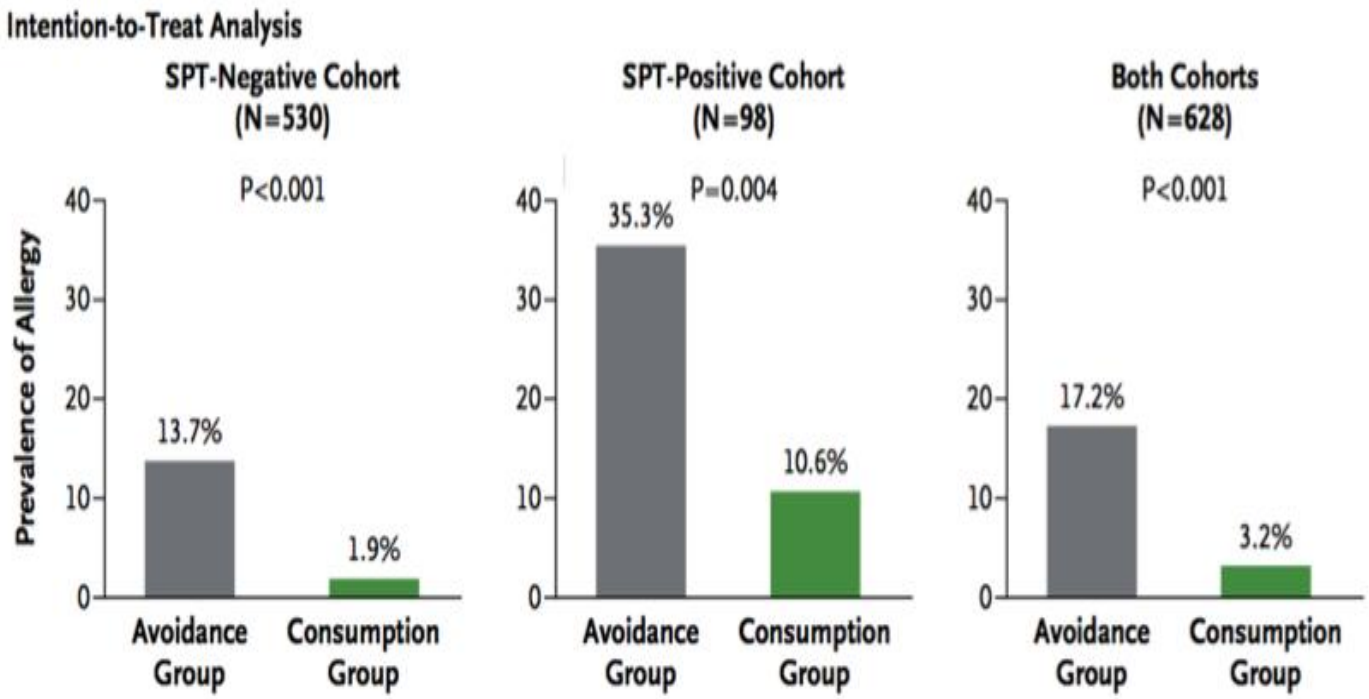
Du Toit, G. *et al.* Randomized trial of peanut consumption in infants at risk for peanut allergy.
N. Engl. J. Med. (2015).

LEAP študija

- arašidi
  - arašidovo maslo, Bamba, arašidova juha, z
  - vsaj 3 X na teden, 6 g beljakovin/teden
  - dojenčki so jih zelo dobro sprejeli
  - rast in pridobivanje na teži enaka

“LEAP” rezultati

intervencija je bila varna in zelo učinkovita tako v namen primarne kot tudi sekundarne preventive alergije na arašide



1° preventiva
86 % zmanjšano tvega

2° preventiva
70 % zmanjšano tveganje

Du Toit, G. *et al.* Randomized trial of peanut consumption in infants at risk for peanut allergy. *N. Engl. J. Med.* (2015)

CONSENSUS COMMUNICATION ON EARLY PEANUT INTRODUCTION AND THE PREVENTION OF PEANUT ALLERGY IN HIGH-RISK INFANTS

- AAAAI, AAP, ACAAI, ASCIA, CSACI, EAACI, ISACI, JSA, SPD, WAO
- JACI, Allergy, Pediatrics, WAO Journal, Pediatric Dermatology, Allergy, Asthma and Clinical Immunology, Annals of Allergy, Asthma and Immunology

obstaja znanstven dokaz (level 1) v prid uvajanja arašidov "visoko rizičnim" dojenčkom zgodaj v življenju (4-11 mes) v državah kjer je alergija na arašide pogosta, saj je kasnejše uvajanje arašidov lahko povezano s povečanim tveganjem razvoja alergije na arašide

- alergolog KT, PROVOKACIJSKI TEST (ne svetujejo sIgE)

- spodbujajo aktiven pristop pediatrov, alergologov in dermatologov za hitro implementacijo teh novih spoznanj

ADDENDUM GUIDELINES FOR THE PREVENTION OF PEANUT ALLERGY IN THE UNITED STATES: REPORT OF THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES–SPONSORED EXPERT PANEL

(J Allergy Clin Immunol 2017;139:29-44.)

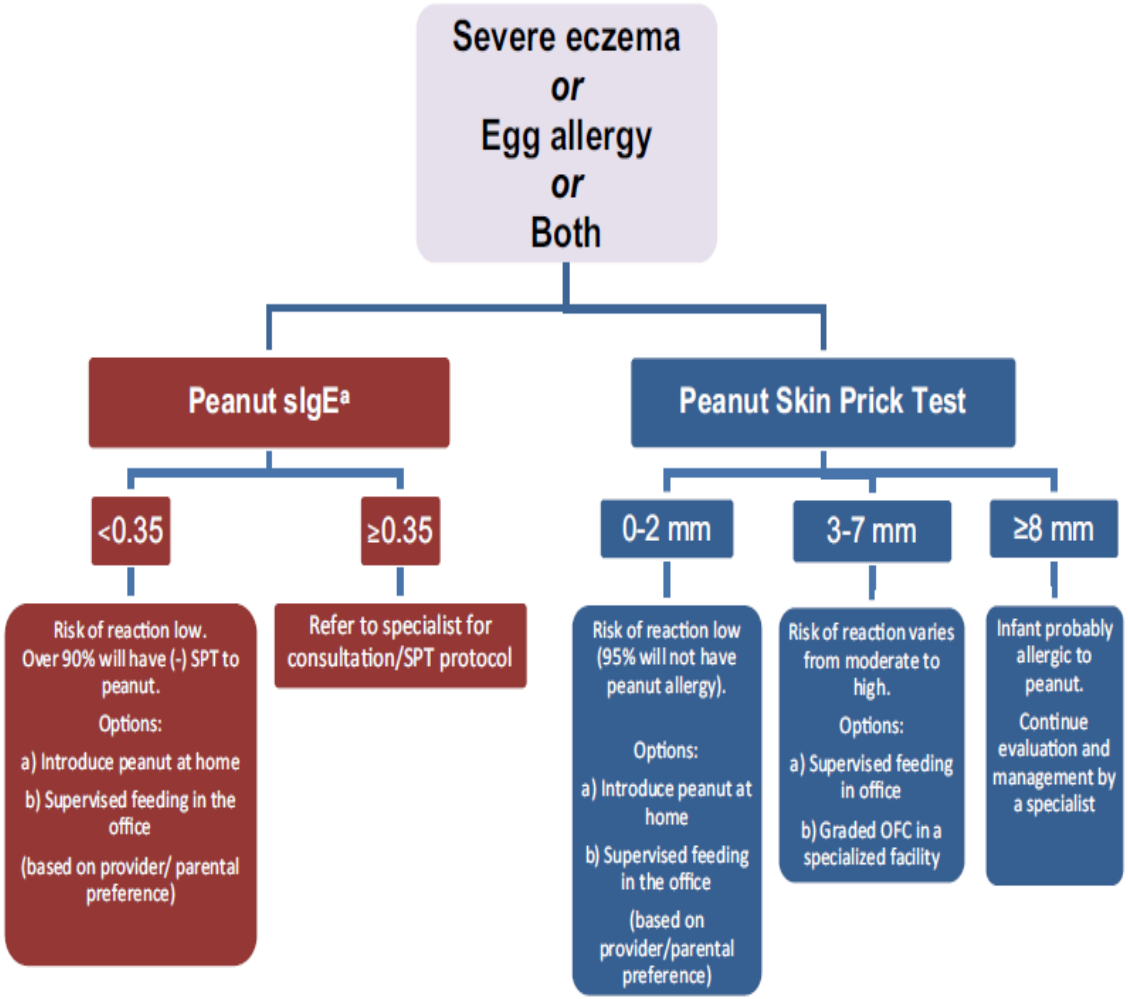
TABLE I. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices

Addendum Guidelines for the Prevention of Peanut Allergy in the United States: Summary of the National Institute of Allergy and Infectious Diseases–Sponsored Expert Panel

Table. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by peanut-sIgE[a] and/or SPT[b] and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods	4 to 6 months
2	Mild-to- moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices



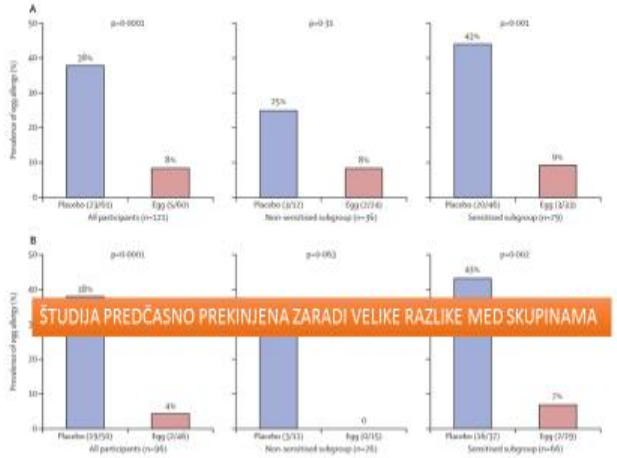
Vprašanja ?

- Ali lahko rezultate ekstrapoliramo na druge države oz populacije ? Druga hrana?
- Kako pogosto je treba jesti arašide ? Ali jih je treba jesti redno ? Ali je to praktično izvedljivo ? So arašidi zdrava hrana ?
- Ali je tak pristop smiseln za splošno populacijo ?
- Ali je tak pristop varen ?

RANDOMIZIRANE KONTROLIRANE ŠTUDIJE V TEKU

študija	načrt	primaren izzid
STEP (Australija)	uživanje jajc/placeba od 4-6 mes	alergija na jajce pri 12 mes
BEAT (Australija)	uživaje jajc/placeba od 4-6 mes	IgE senzibilizacija na jajce pri 8 in 12 mes
EAT (VB)	uvajanje jogurta, jajc, pšenice, sezama, rib, arašidov od 3 mes vs. nobene alergene hrane do 6 mes	alergija na 6 alergenov med 1 in 3 letom
HEAP (Nemčija)	uživanje jajc/placeba od 4-6 mes	alergija na jajce pri 12 mes
PEAAD (Nemčija)	uživanje arašidov od 5-30 mes vs. dieta brez arašidov	alergija na arašide po 12 mesecih

"PETIT" Rezultati



PREDLOG ZA IZVAJANJE PRIPOROČIL

RAZPOREDITEV OTROKA GLEDE NA RIZIČNOST	PRIPOROČILA
težek AD alergija na jajce	NAPOTITEV K SPECIALISTU ALERGOLOGU (SEKUNDARNI NIVO) za izvedbo alergoloških testov (KT, sIgE) • neg testi → uvajanje doma • nizko pozitivni testi → provokacija • visoko pozitivni testi → dieta
blag - zmeren AD	PRIMARNI PEDIATRI svetujejo uvajanje arašidov po 6. mesecu BREZ ALERGOLOŠKEGA TESTIRANJA
brez AD brez alergij	NOBENIH POSEBNIH NAVODIL

Mastocitoza in preobčutljivost za strup kožekrilcev

Mihaela Zidarn

Definicija mastocitoze

- Heterogena skupina klonalnih motenj
- Značilna je proliferacija in akumulacija mastocitov v različnih tkivih (predvsem koži in kosteh)
- Sistemska mastocitoza: prizadetost enega ali več organov (ne samo koža)
- Večinoma je prisotna mutacija v kodonu 816 gena za kit receptor
- Simptomi:
  - Pruritus, urtikarija, angioedem, zardevanje, bruhanje, bolečina trebuhu, diareja, anafilaksija, osteoporoza
- Redko agresivna bolezen: hipersplenizem, patološke frakture, ascites, malabsorcija, citopenia

Table 1. WHO Diagnostic Criteria for Systemic Mastocytosis

A firm diagnosis of systemic mastocytosis is established when at least 1 major and 1 minor or at least 3 minor criteria are present	
Major	Multifocal dense infiltrates of MCs in bone marrow sections or other extracutaneous organs (>15 MCs in aggregate).
Minor	a. MCs in bone marrow or other extracutaneous organs show an abnormal (spindle-shaped) morphology (>25%). b. Mutation at codon 816 of the *KIT* gene in extracutaneous organs. In most cases the mutation is D816V. c. MCs in bone marrow express CD2 and/or CD25. d. Serum tryptase >20 ng/mL (not in patients with AHNMD-type disease).
B findings	a. Bone marrow biopsy showing >30% infiltration by MCs (focal, dense aggregates) and/or serum tryptase level >200 ng/mL. b. Signs of dysplasia or myeloproliferation in non-MC lineages, but insufficient criteria for definitive diagnosis of a hematopoietic neoplasm (AHNMD), with normal or slightly abnormal blood counts. c. Hepatomegaly without impairment of liver function, and/or palpable splenomegaly without hypersplenism, and/or lymphadenopathy on palpation or imaging.
C findings	a. Bone marrow dysfunction manifesting as cytopenia (ANC <1.0 x 10^9/L, Hb <10 g/dL, or platelets <100 x 10^9/L), but no obvious non-MC hematopoietic malignancy. b. Palpable hepatomegaly with impairment of liver function, ascites, and/or portal hypertension. c. Skeletal involvement with large osteolytic lesions and/or pathological fractures. d. Palpable splenomegaly with hypersplenism. e. Malabsorption with weight loss due to gastrointestinal mast cell infiltrates.

Abbreviations: AHNMD, associated clonal hematologic non–mast cell lineage disease; ANC, absolute neutrophil count; Hb, hemoglobin; MC, mast cell.
Diagnosis of:
(a) Indolent SM (ISM): meets criteria for SM. No C findings. No evidence of AHNMD.
(b) Smoldering SM: as ISM, but with 2 or more B findings and no C findings.
(c) Isolated bone marrow mastocytosis: as ISM with bone marrow involvement, but without skin involvement.
(d) Aggressive SM: meets criteria for SM. One or more C findings. No evidence of mast cell leukemia.
(e) Mast cell leukemia: meets criteria for SM. Bone marrow biopsy shows a diffuse infiltration, usually compact, by atypical, immature mast cells. Bone marrow aspirate smears show ≥20% mast cells. In typical mast cell leukemia, mast cells account for ≥10% of peripheral white blood cells.

Monoclonal mast cell activation syndrome (MMAS)

- Nepojasnjene ali ponavljajoče se anafilaksije
- Brez kožnih lezij
- Ne izpolnjujejo kriterijev za sistemsko mastocitozo
- Prisotni so markerji klonalnosti mastocitov

Sistemska mastocitoza in alergijske bolezni

- Sprožilci anafilaksije
  - Kožekrilci
  - Hrana
  - Zdravila
  - Redkeje: alkohol, napor, temperaturne spremembe
  - Kombinacija več dejavnikov
  - Idiopatska

REMA kriteriji

- >2 napove prisotnost klonalne motnje mastocitov pri bolnikih z anafilaksijo, ki nimajo kožne mastocitoze

Table 2. REMA Scoring Model[a]

Variable		Score
Gender	Male Female	+1 –1
Clinical symptoms	Absence of urticaria and angioedema Urticaria and/or angioedema Presyncope and/or syncope	+1 –2 +3
Serum tryptase	<15 ng/mL >25 ng/mL	–1 +2

Abbreviation: REMA, Red Española de Mastocitosis (Spanish Network on Mastocytosis).

[a]Proposed as a screening method for the presence of clonal mast cells in patients presenting with anaphylaxis in the absence of cutaneous mastocytosis before a bone marrow study.

Epidemiologija

- Prevalenca alergije za strup kožekrilcev v splošni populaciji je okoli 3%
- Med bolniki s katerokoli obliko mastocitoze pa 20-30%
  - Večje je tveganje težke reakcije

Prevalenca mastocitoze v splošni populaciji je 1-1,3 na 10.000, med bolniki z alergijo za strup kožekrilcev pa je bistveno višja

Table 3. Prevalence of Clonal Mast Cell Disease in Patients With Systemic Reactions to Hymenoptera Venom Screened on the Basis of Elevated Tryptase

Author	Patients	Elevated Tryptase, No. %	Clonal Mast Cell Disease	%
Haeberli et al 2003[a] [69]	259	19 (7.3)	3 CM	1%
Dubois 2004[b] [47]	2375	32 (1.3)	22 SM	1%
Rueff et al 2006[c] [71]	1102	106 (9.6)	21 CM + 8 SM	2.6%
Bonadonna et al 2009 [24]	379	44 (11.6)	21 ISM + 9 MMAS	7.9%
Potier et al 2009[c] [72]	138	22 (15.9)	1 CM + 5 SM	4.4%
Guevara et al 2010[c,d] [73]	274	30 (10.9)	1 CM + 3 ISM	1.5%

Abbreviations: CM, cutaneous mastocytosis; ISM, indolent systemic mastocytosis; MMAS, monoclonal MC activation syndrome; SM, systemic mastocytosis.
[a]Bone marrow evaluation not performed.
[b]Screening with urinary histamine metabolite.
[c]Evaluation of CD25/CD2 mast cell coexpression and *KIT* mutation not performed or reported.
[d]Bone marrow evaluation performed if serum tryptase >15 ng/mL.

Priporočila

- VIT
- Reakcija med imunoterapijo po piku na terenu: povišati dozo na 200
- Opremljeni z vsaj 2 avtoinjektorjema adrenalina tudi če prenašajo imunoterapijo
- Podaljšana, doživljenska VIT? Verjetno pri bolnikih z težko izvorno reakcijo

Dvojna senzibilizacija pri alergiji za strupe kožekrilcev

- Razširjen panel komercialno dostopnih rekombinatnih sIgE ima še vedno nižjo senzitivnost kot nativni alergen, dvojna pozitivnost pa se po pogostnosti približuje nativnim alergenom
- Če je indeks pri sIgE več kot 5 naj bi to nakazovalo na monosenzibilizacijo

Carrier 12:32

Menu About us

The Allergy Diary was developed in collaboration between MACVIA-LR and ARIA.

MACVIA-LR

MACVIA-LR (Contre les Maladies Chroniques pour un Vieillissement Actif en Languedoc-Roussillon, France) is a reference site of the European Innovation Partnership on Active and Healthy Ageing aimed at fighting chronic disease.

The ARIA (Allergic Rhinitis and its Impact on Asthma) initiative aims to educate and implement evidenced-based management of allergic rhinitis in conjunction with asthma

Carrier 12:19

Menu My Profile

Me

Year of birth

Gender

First enter your profile

Entering your profile saves you time when using the app daily. To get started just enter your year of birth, gender and country. To continue using the app please complete your profile within 10 days.

OK

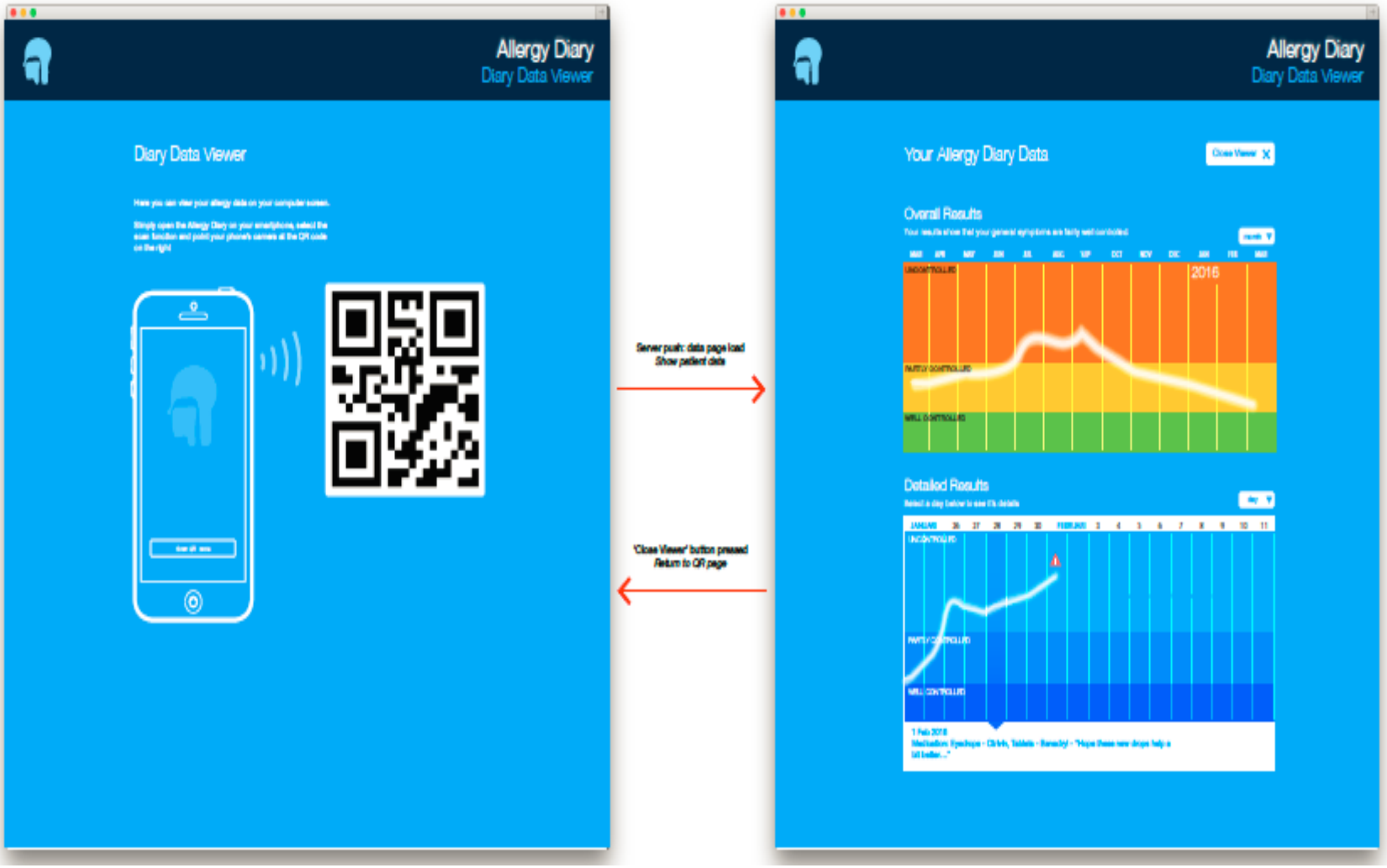
Symptoms

My symptoms

How they affect me

Medication

My usual allergy meds


Allergy Diary
Diary Data Viewer
Diary Data Viewer
Server push: data page load
Show patient data
'Close Viewer' button pressed
Return to QR page
Allergy Diary
Diary Data Viewer
Your Allergy Diary Data
Close Viewer
Overall Results
2016
Detailed Results

Diagnostic value of T cell analysis and *in vitro* release of interleukins in patients with nonimmediate hypersensitivity to amoxicillin

Background

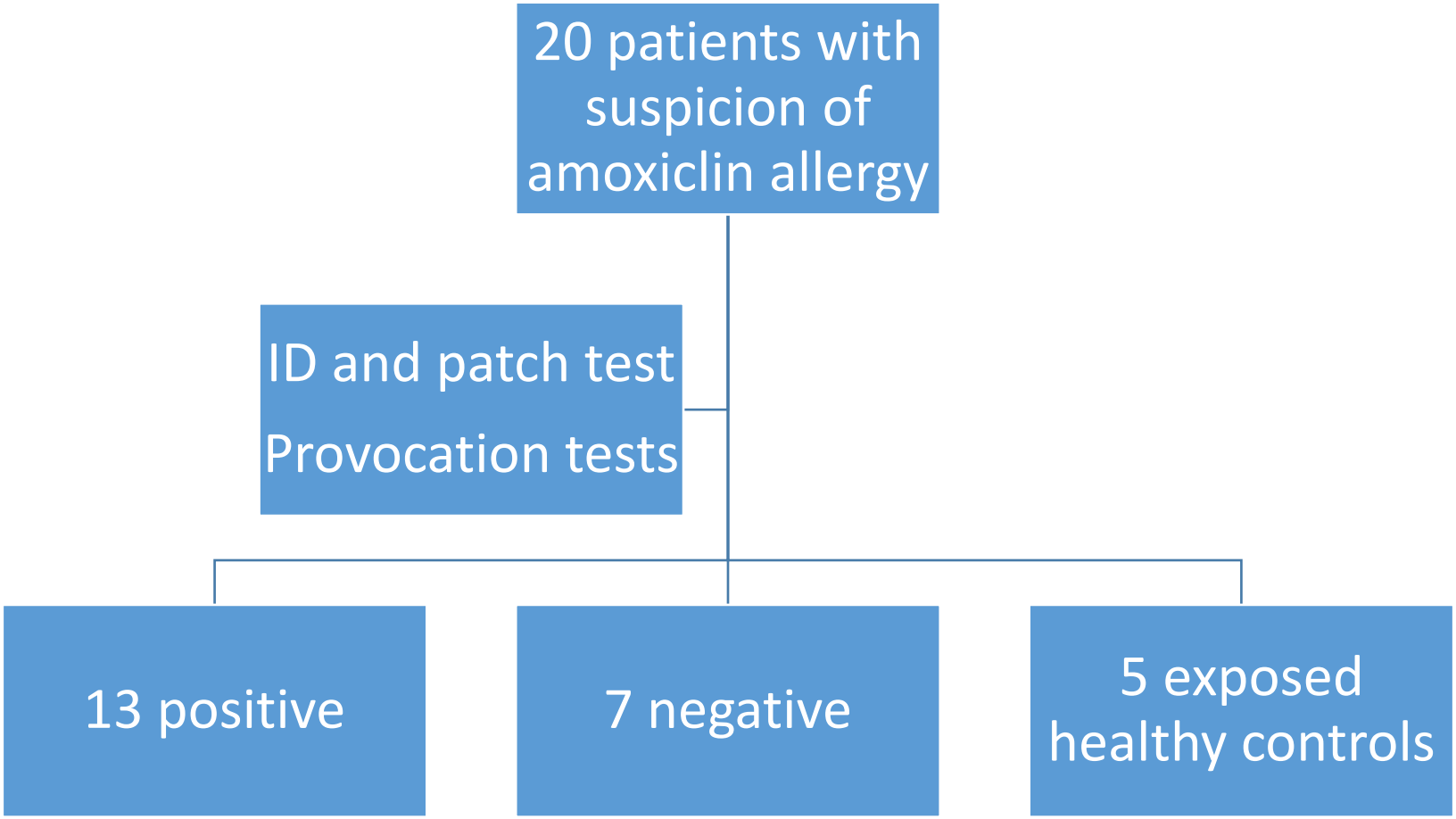
- Non immediate reactions caused by amoxicilin are most common drug hypersesnitivits reactions in our practice
- The clinical picture is heterogeneous
- Diagnostic procedure is hampered by lack of practical *in vitro* method

- CD69 is a marker of T cell activation
- Measurement of IL-2, IL-5, IL-13 and IFN-γ secretion in response to drugs were shown as potential in vitro tool for detection of T-cell sensitization to drugs

Study protocol

- Inclusion criteria
  - Convincing history of nonimmediate reaction to amoxicilin: urticaria, maculopapular exanthema: more than one hour after last dose of amoxicilin and up to 2 weeks after starting of the antibiotic
- Exclusion criteria
  - Immediate reactions: anaphylaxis, urticaria less than 1 hour after antibiotic exposure
  - Unconvincing history (expected side effects)
  - Reactions in early childhood
  - Severe skin reactions: DRESS, SJS/TEN
  - Organ specific reactions: hepatitis, nephritis, pneumonitis
  - Typ II. or III. Reactions: blood disorders or serum sickness
  - Other uncontrolled diseases

Flow chart


20 patients with suspicion of amoxiclin allergy
ID and patch test
Provocation tests
13 positive
7 negative
5 exposed healthy controls

Positive patients = confirmed drug allergy

- 13 patients with confirmed amoxicillin hypersensitivity:
  - 6 with skin tests:
    - 1 immediate reading ID
    - 4 late reading ID
    - 1 patch test
  - 7 with drug provocation tests:
    - In one patient with positive late reading of intradermal skin test a provocation test was performed that was positive
    - No provocation test positive on the first day

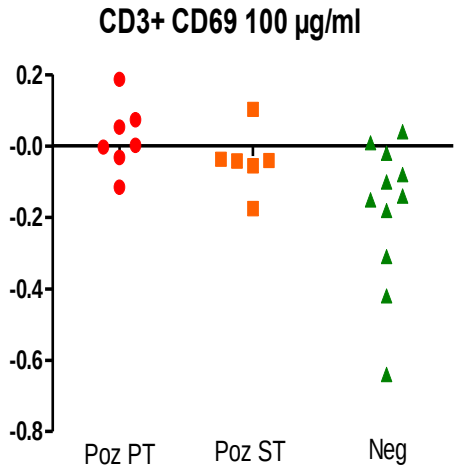
i*n vitro* tests

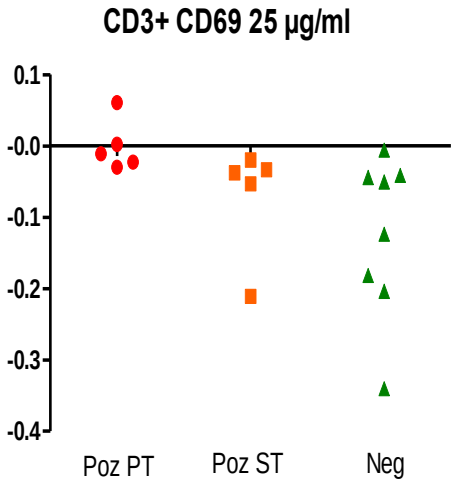
- **CD 69 upregulation** analyzed by flow cytometry
  - **absolute count** of CD69 upregulated CD3+, CD3+CD4+ and CD3+CD8+ after stimulation and incubation for 4 hours with 25µg/ml 100 µg/ml of **amoxicilin**

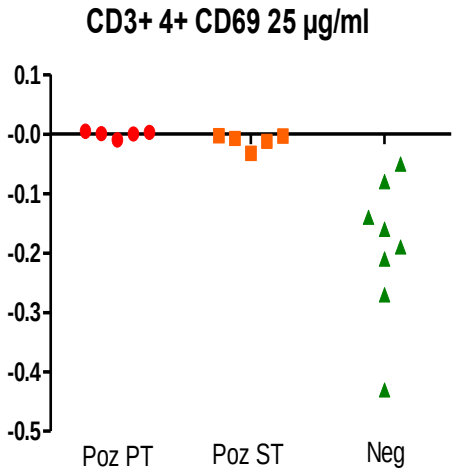
  minus
  - absolute count of CD69 upregulated CD3+, CD3+CD4+ and CD3+CD8+ after incubation with **culture media** alone

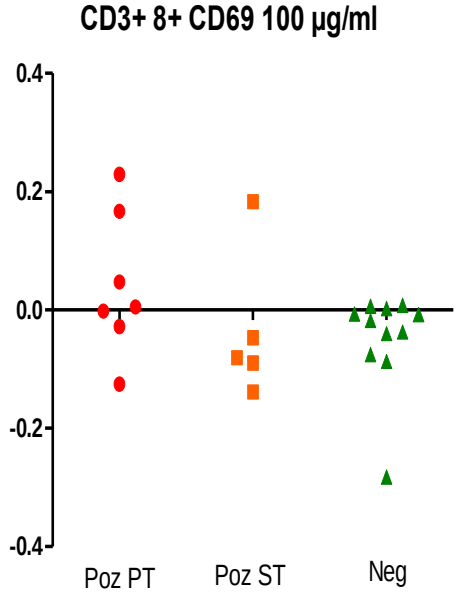
- Incubation of peripheral blood mononuclear cells (PBMC) for 48 hours, analysed by multiplex flow cytometry CBA Flex Array
  - **Concentration of IL-2, IL-5, IL-13 and IFN-γ in** supernatants after incubation with 25µg/ml 100 µg/ml of **amoxicilin**

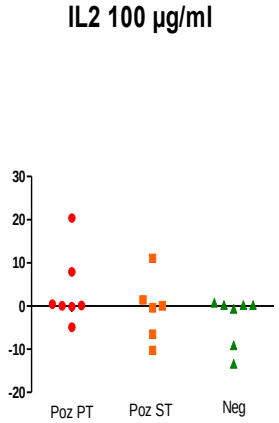
  minus
  - **Concentration of IL-2, IL-5, IL-13 and IFN-γ in** supernatants after incubation with culture media alone











Result were considered positive for values that were higher than values for all negative patients and controls.

For all provocation test positive patients at least one *in vitro* test was positive

Conclusion

- High number of positive patients 13/20 selected on the basis of clinical history
- Late reading of ID test is useful: 5/13 positive patients were confirmed with skin testing in one patient only patch test was positive
- All provocation tests were positive with prolonged provocation
- *In vitro* diagnostic tests are a potential possible surrogate for drug provocation test

THE ROLE OF BASOPHILS IN ACUTE ALLERGIC REACTIONS

Peter Korošec

Laboratorija za klinično imunologijo in molekularno genetiko

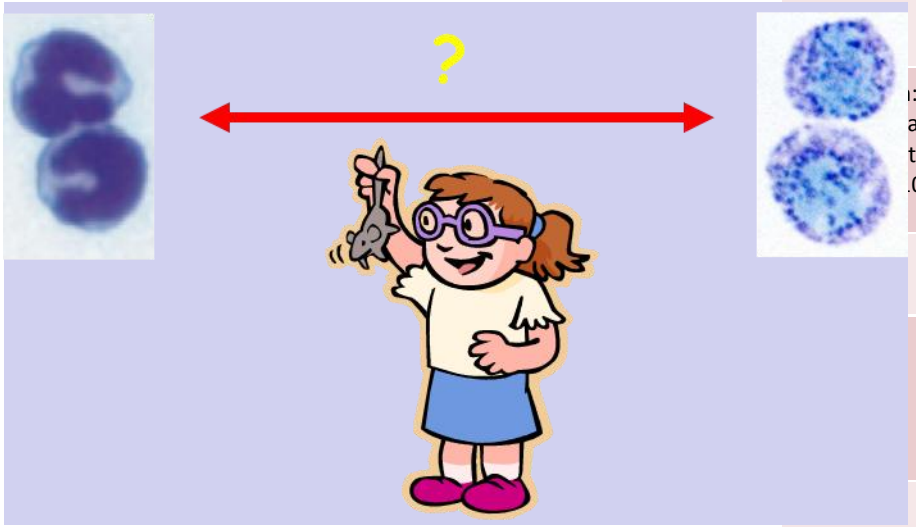
Univerzitetna Klinika za pljučne bolezni in alergijo Golnik

Summary

IgE-mediated allergic reactions involve the activation of effector cells, predominantly through the high-affinity IgE receptor (FcεRI) on mast cells and basophils. Although the mast cell is considered the major effector cell during acute allergic reactions, more recent studies indicate a specific and potentially important role for basophils and their migration which occurs rapidly upon *in vivo* allergen challenge.

OF MICE AND NOT MEN

Basophils in mice display **substantial differences in morphology, function** and immunomodulatory roles in comparison to human basophils. This highlights major pitfalls in extrapolating from animal basophil models to acute allergic reactions in humans.



Murine models		Humans
Polymeric IgA (low serum levels) IgD, IgE, IgM IgG1, IgG2a, IgG2b, IgG3	Immunoglobulins	Monomeric IgA, 2 serotypes (IgA_1, IgA_2), IgA_1 abundant in serum IgD, IgE, IgM IgG1, IgG2, IgG3, IgG4
Yes	High affinity IgE receptor (FcεRI) on mast cells and basophils	Yes
No	FcεRI receptor on antigen presenting cells	Yes
Yes	IgE-dependent anaphylaxis	Yes
Yes	IgG-dependent anaphylaxis	No evidence for IgG-mediated activation of human mast cells. If present, likely to require very high levels of antigen exposure
: in murine models of allergy, dose/weight t to a human eating of .000 peanuts!	Allergen dose required through oral exposure to cause anaphylaxis	Very low doses (mgs) e.g. for peanut allergy, 10% of individuals react to 1/70 of a peanut
+	Sensitivity to histamine	++++
Yes	Anaphylaxis inhibited by H1-antihistamines	Little clinical evidence for this. Significant interspecies differences exist in histamine receptor pharmacology.
Yes	Basophils secrete Platelet Activating Factor (PAF)	Data inconsistent

Histamine sensitivity

LD50 of histamine (thought to be an important mediator of anaphylaxis) in mice was greater than 20 mg/mouse – a sensitivity **several orders of magnitude lower than that in humans**. This may have contributed to the relative paucity of studies assessing the role of basophils in anaphylaxis, given that basophils are relatively uncommon in comparison to their tissue-fixed mast cell counterparts in both mice and humans. However, despite their relative rarity, human basophils are at least **one order of magnitude more sensitive to IgE-mediated provocation than mast cells.**

IgE versus IgG-mediated anaphylaxis

There are two major distinct pathways of anaphylaxis in mice: one is mediated by **basophils, allergen-IgG- FcγRII-III receptor** interactions and PAF release, whereas the other is mediated by **mast cells, allergen-IgE-FcεRI receptor** interactions and histamine release.

Antigen presentation

Human basophils are not able to present antigens.

Human experimental models of anaphylaxis

Controlled allergen challenge studies

Studies in the challenge setting do have the advantage of allowing comparison with pre-reaction samples, optimal sampling, and controlling potentially confounding factors (including acute treatment, where blood samples can often be taken prior to treatment. However, for safety reasons, in controlled allergen challenge studies, patients with **previous severe reactions are often excluded** from challenge studies due to the potential for life-threatening reactions. Furthermore, in the (oral food) challenge model, the reaction severity at challenge is also limited by the controlled nature of the challenge (allergen exposure is usually terminated at the onset of objective symptoms) and administration of pharmacologic interventions to treat the symptoms.

Emergency department-based studies

Patients with anaphylaxis are studied prospectively at the time of presentation to the ED, with sample collection typically occurring **1 to 2 hours after onset of symptoms**, and usually after initial treatment and stabilisation. In the case of field-treatment of anaphylaxis, patients are very often treated with systemic corticosteroids and antihistamines as well. Corticosteroids have broad immunological effects, albeit much delayed compared to other anti-allergic therapies. With respect to basophils, corticosteroids inhibit their pro-allergic functions and this might be an important confounder.

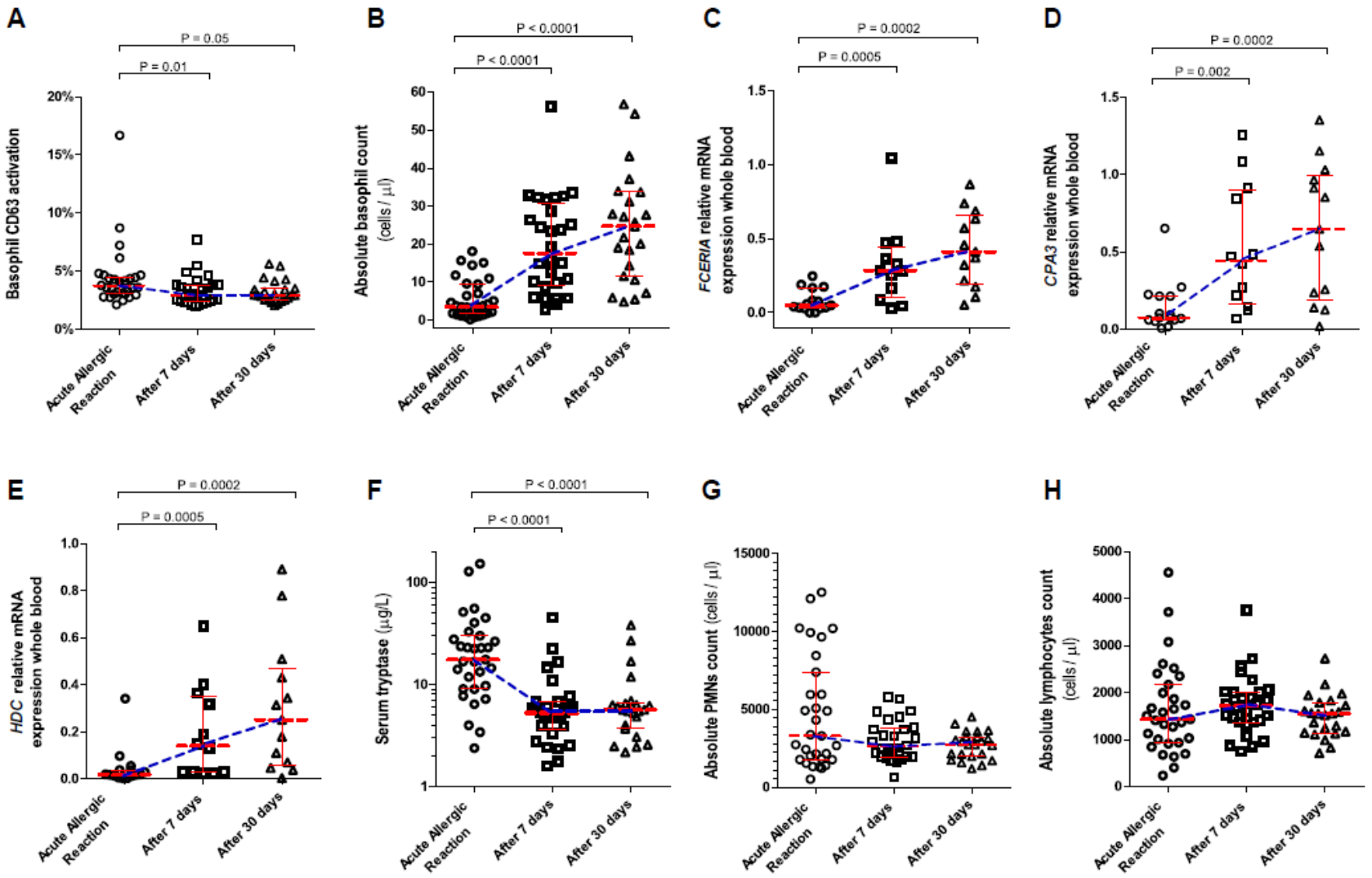


FIG 1. Basophil CD63 activation (**A**); absolute basophil counts (**B**); whole-blood *FCER1A* (**C**), *CPA3* (**D**) and *HDC* (**E**) expression; serum tryptase levels (**F**); and PMN (**G**) and lymphocyte (**H**) absolute counts in ED patients during acute anaphylactic reactions to Hymenoptera venom and 7 and 30 days after the anaphylactic episode. *Horizontal lines* represent median values with interquartile ranges.

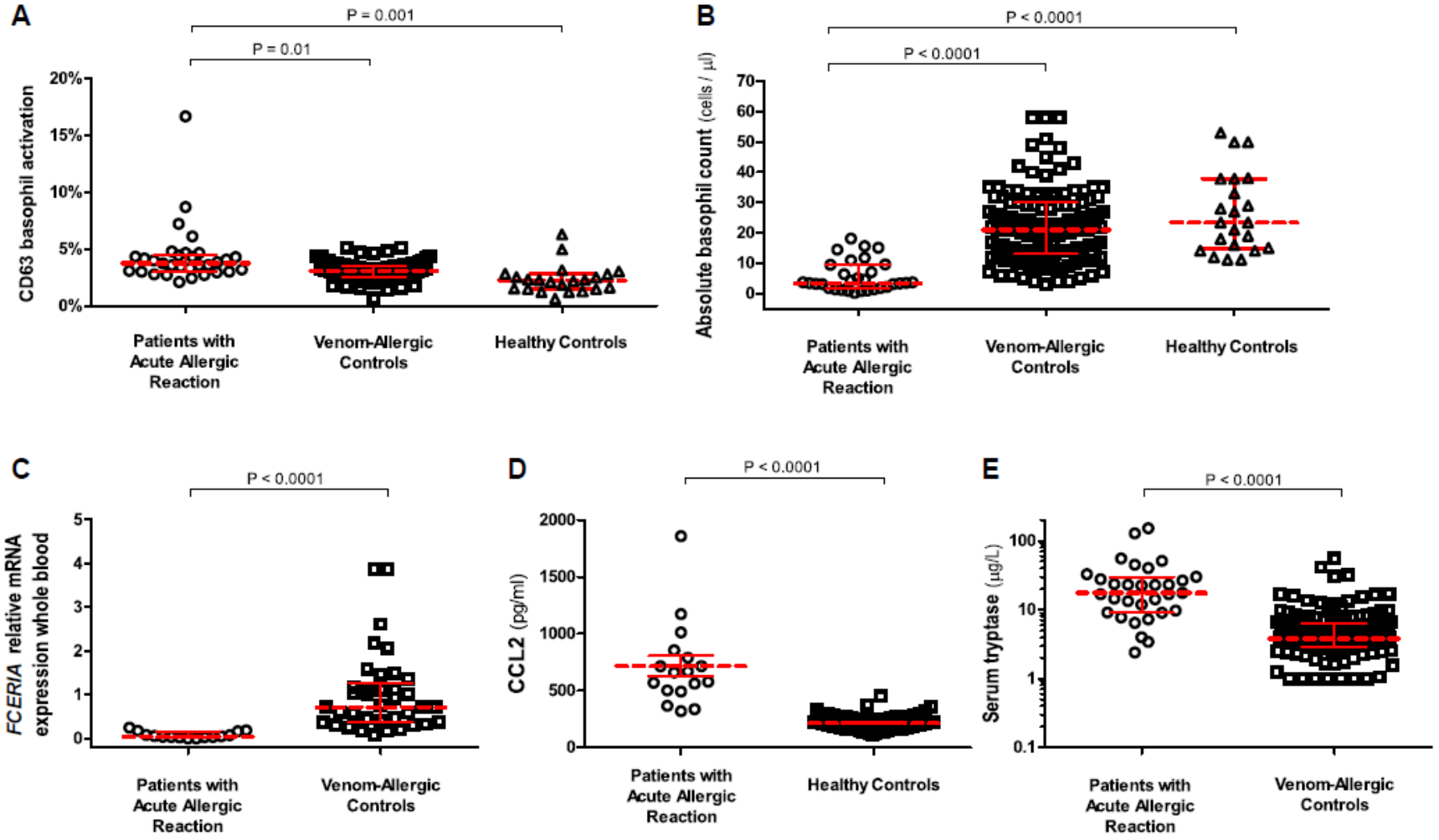


FIG 2. Comparison of basophil CD63 activation (A), absolute basophil counts (B), whole-blood *FCER1A* gene expression (C), CCL2 serum concentrations (D), and serum tryptase levels (E) between patients with acute anaphylactic reactions to Hymenoptera venom on ED presentation and patients with venom allergy or healthy control subjects. *Horizontal lines* represent median values with interquartile ranges.

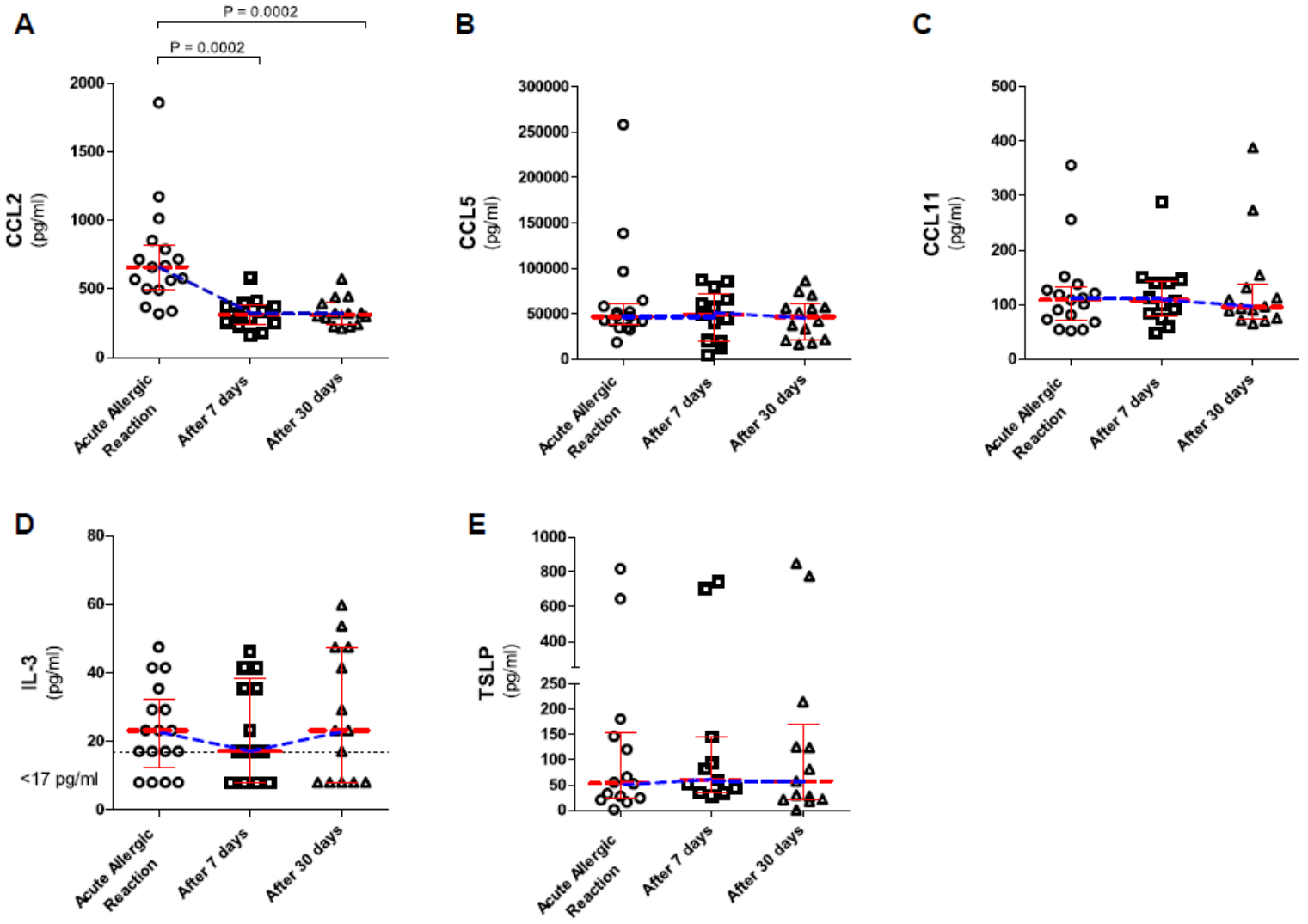


FIG 4. Serum CCL2 **(A)**, CCL5 **(B)**, CCL11 **(C)**, IL-3 **(D)**, and TSLP **(E)** levels in ED patients during acute anaphylactic reactions to Hymenoptera venom and 7 and 30 days after the anaphylactic episode. *Horizontal lines* represent median values with interquartile ranges.

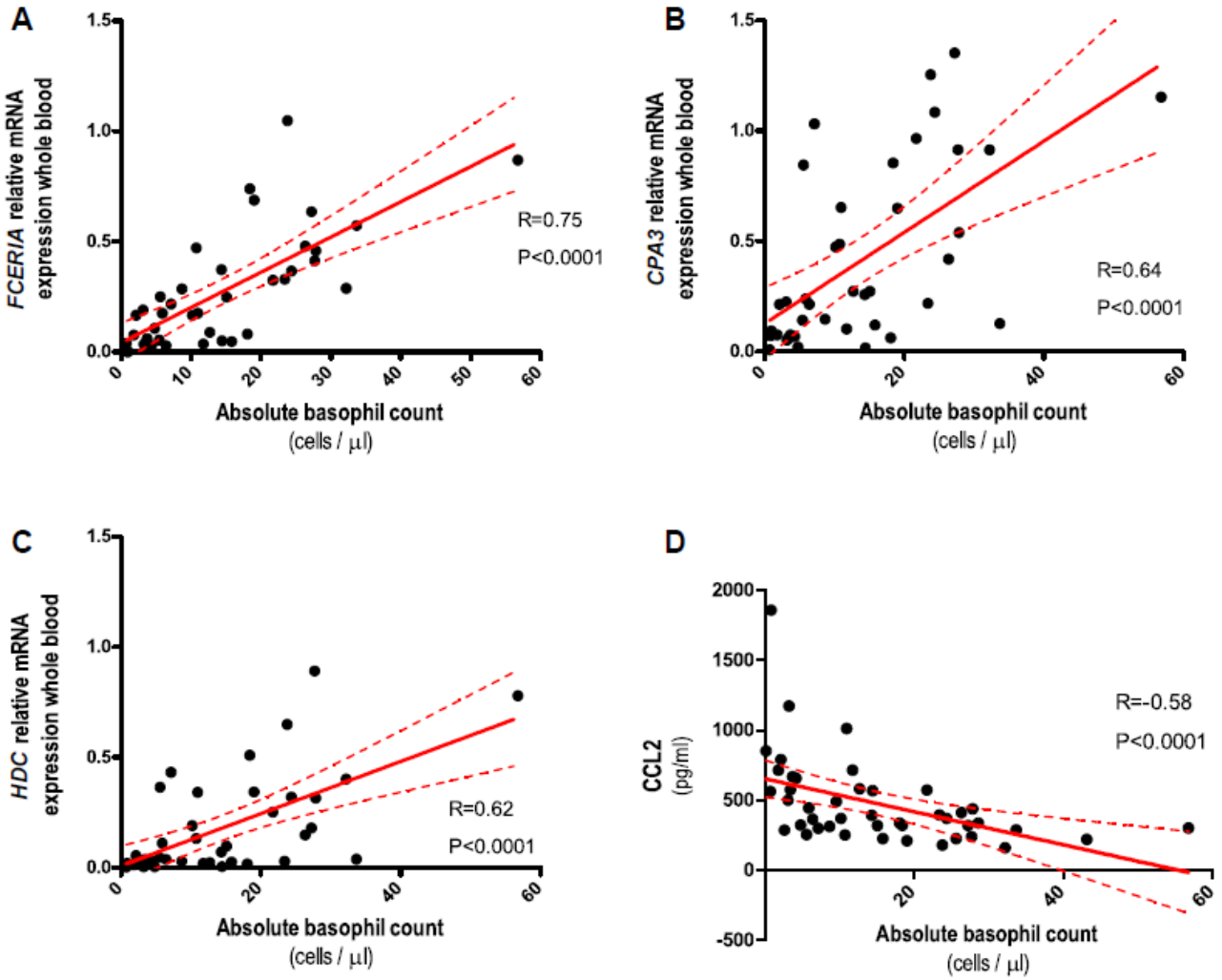


FIG 3. Correlation between absolute basophil counts and whole-blood *FCER1A* **(A)**, *CPA3* **(B)**, and *HDC* **(C)** gene expression and serum CCL2 concentrations **(D)** in patients with acute anaphylactic reactions presenting to the ED.

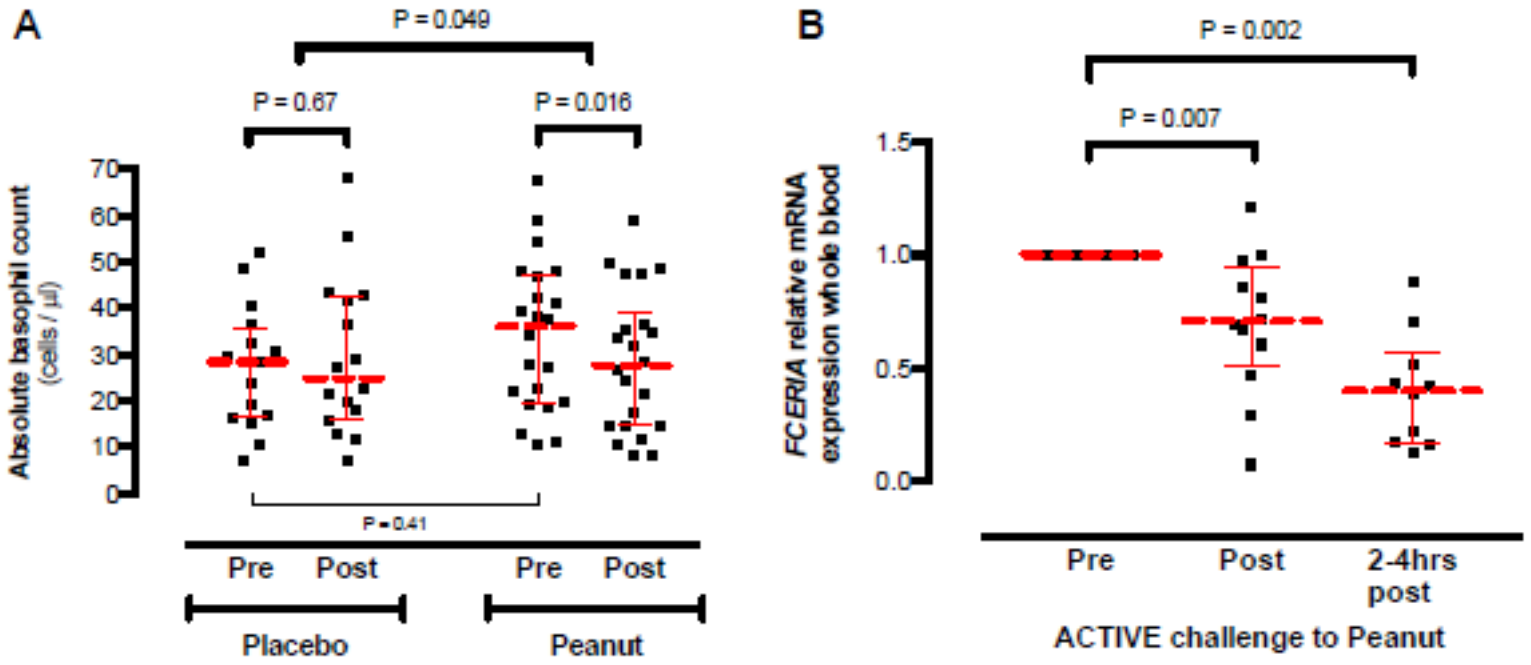
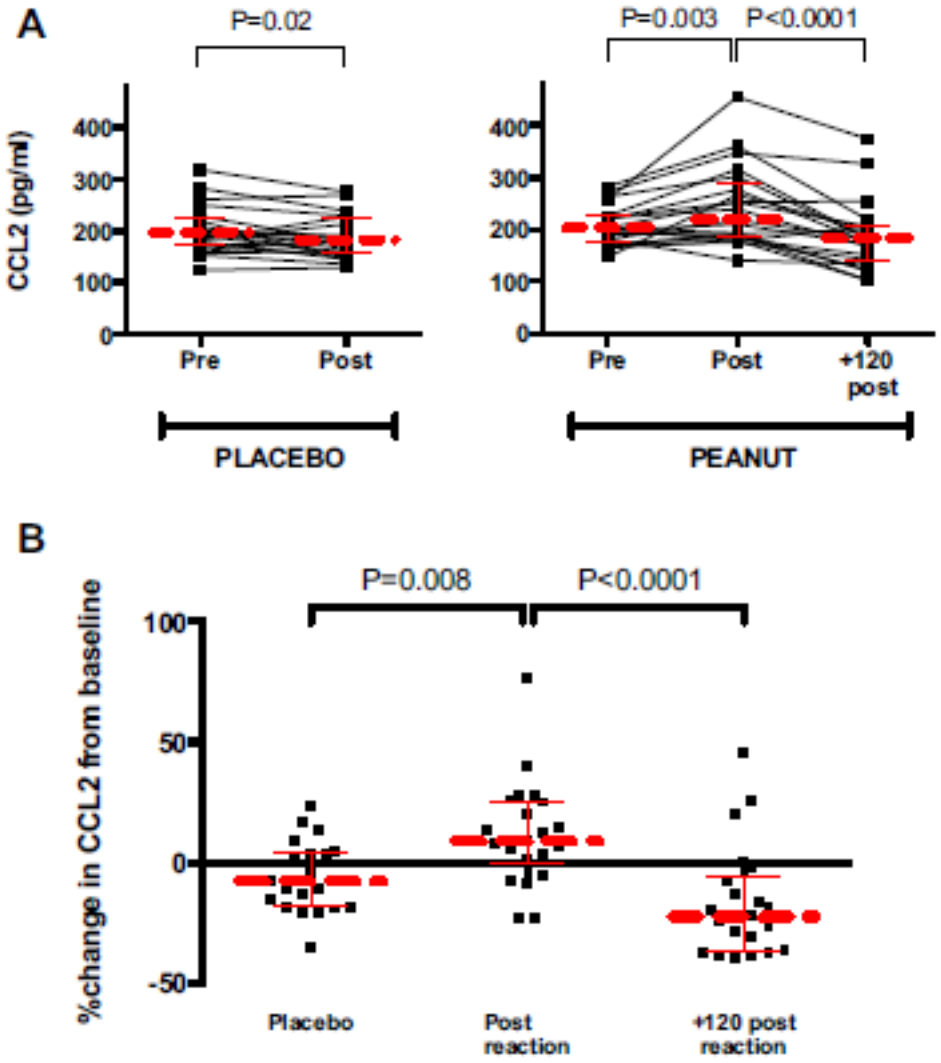


FIG 5. Absolute basophil counts **(A)** and whole-blood *FCER1A* gene expression **(B)** in patients with peanut allergy undergoing DBPCFCs to peanut. *Horizontal lines* represent median values with interquartile ranges.


A
P=0.02
P=0.003
P<0.0001
CCL2 (pg/ml)
400
300
200
100
0
Pre
Post
Pre
Post
+120 post
PLACEBO
PEANUT
B
P=0.008
P<0.0001
%change in CCL2 from baseline
100
50
0
-50
Placebo
Post reaction
+120 post reaction

Take-home messages

Basophil migration from the circulation might be one of the key events during anaphylaxis.

How can the understanding of the factors that regulate basophil trafficking and activation lead to new diagnostic and therapeutic strategies in anaphylaxis?

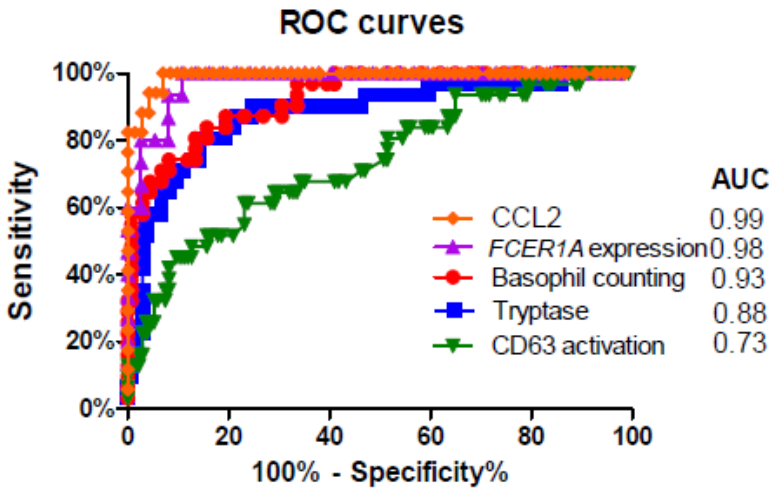


FIG E8. ROC curve analysis of basophil CD63 activation, absolute basophil counts, whole-blood *FCER1A* gene expression, CCL2 concentrations, and serum tryptase levels between patients with acute anaphylactic reactions to insect venoms on ED presentation and patients with venom allergy or healthy control subjects. *AUC*, Area under the curve.

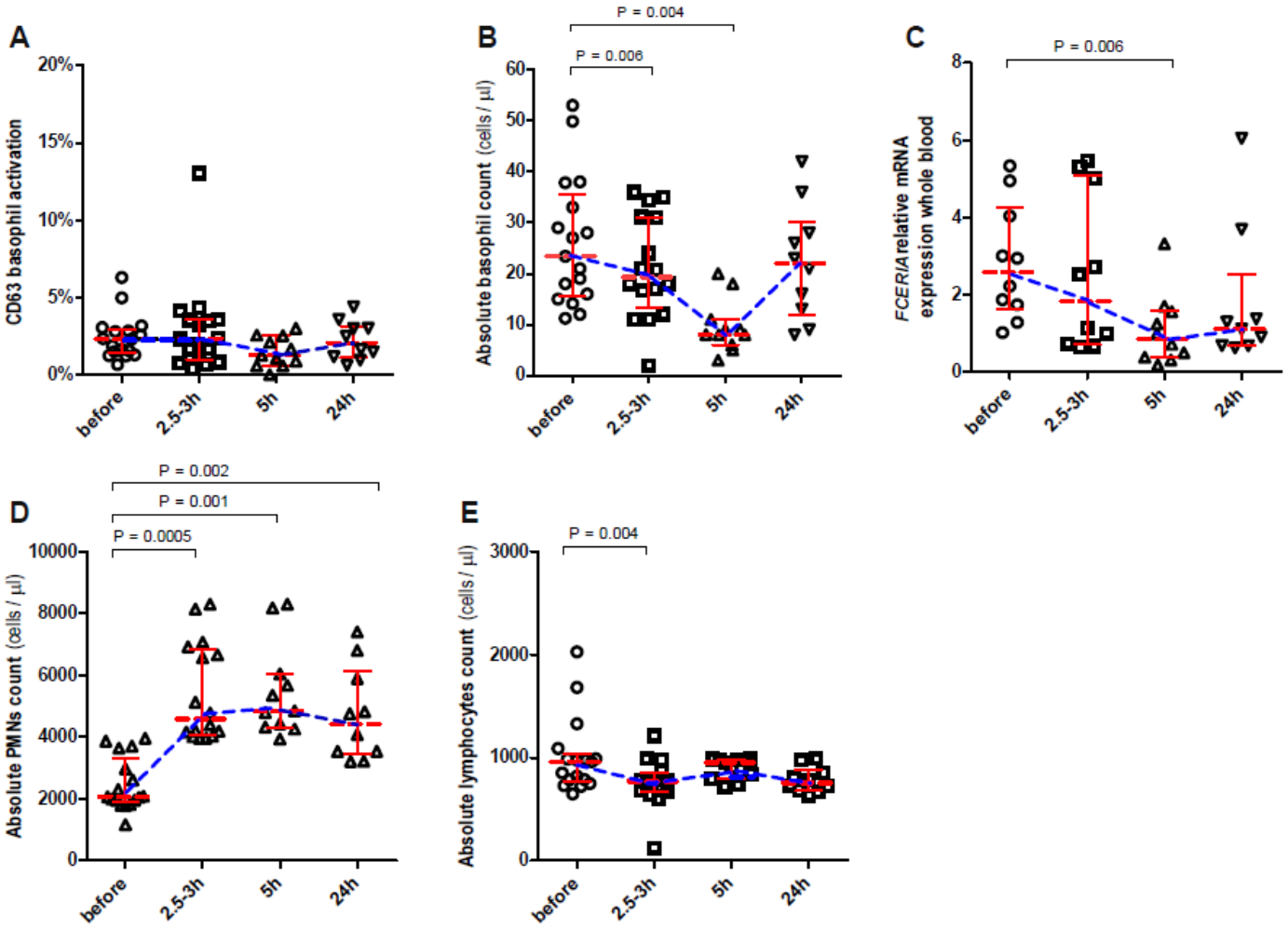


FIG E4. Basophil CD63 activation (**A**), basophil absolute count (**B**), whole-blood *FCER1A* gene expression (**C**), and lymphocyte (**D**), and PMN (**E**) absolute counts in healthy control subjects 2.5 to 3, 5, and 24 hours after the single dose of oral methylprednisolone (64 mg). *Horizontal lines* represent median values with interquartile ranges.

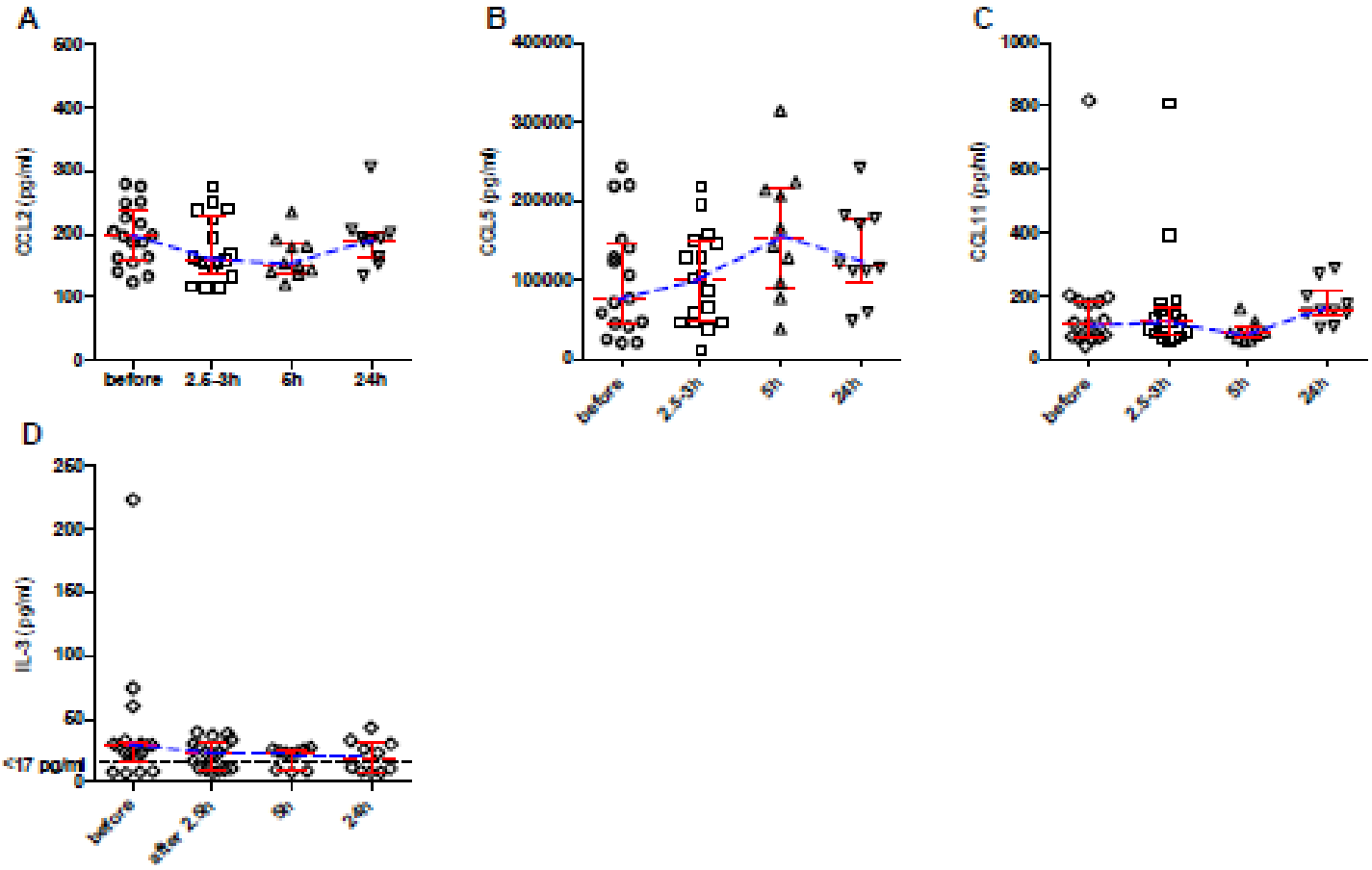
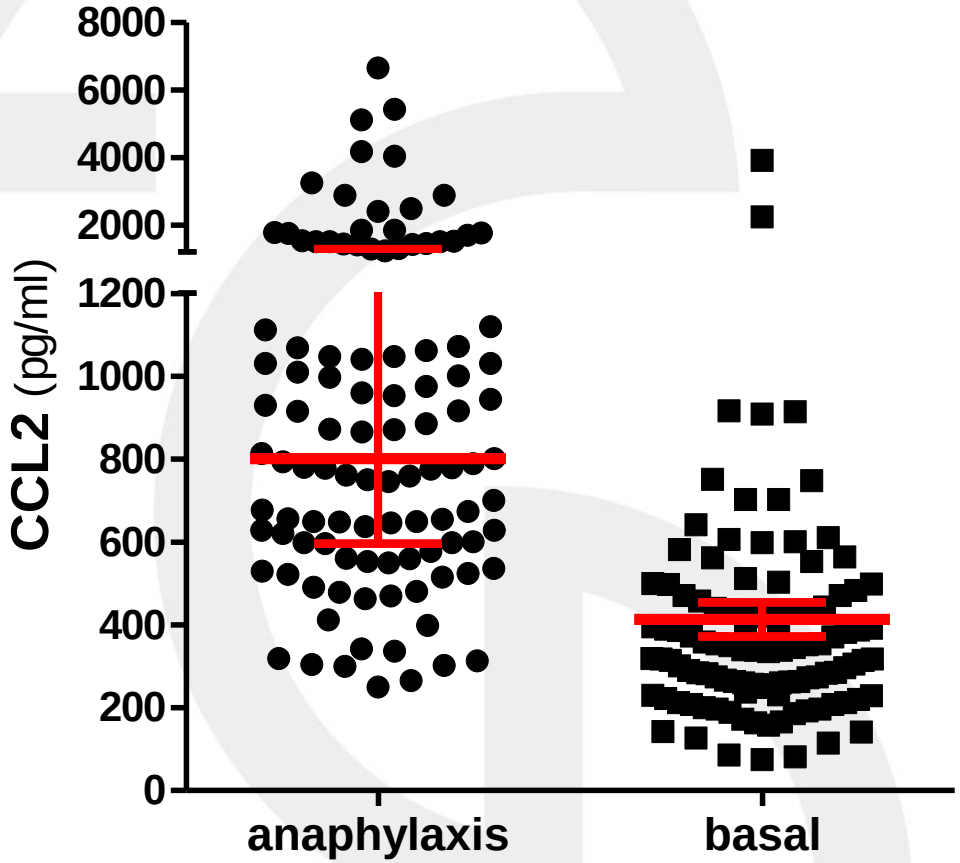


FIG E5. Serum concentrations of CCL2 **(A)**, CCL5 **(B)**, CCL11 **(C)**, and IL-3 **(D)** in healthy control subjects 2.5 to 3, 5, and 24 hours after the single dose of oral methylprednisolone (64 mg). *Horizontal lines* represent median values with interquartile ranges.

RESULTS – CCL2 measurements



CCL2	Anaphylaxis (pg/ml)	Basal (pg/ml)
Median	801,2	338,7
Range (min-max)	250,5 -6661	74,8 - 3925

Descriptive statistics of CCL2 measurements.

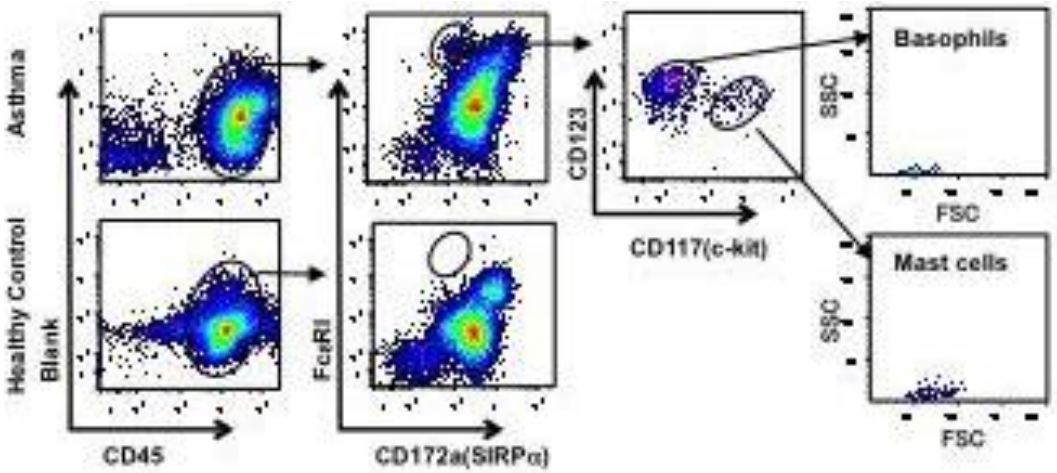
Serial CCL2 measurements in 107 patients (P > 0,0001)

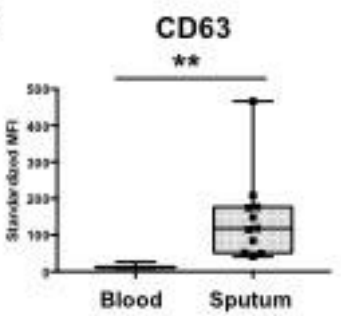
Early and late asthmatic response

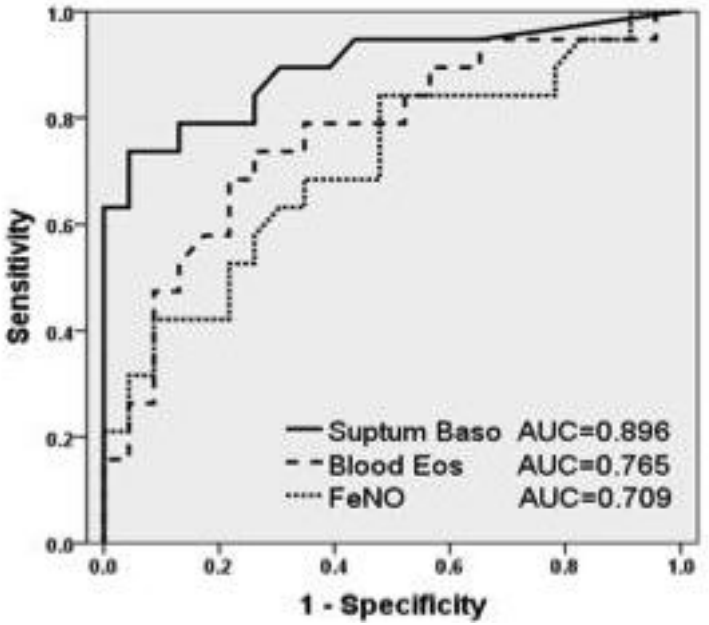
Inhalation of allergen leads to an **early asthmatic response**, which is associated with a decrease in lung function that occurs within 2 hours, caused by the release histamine and cysteinyl leukotrienes from mast cells. In some patients, the early response is followed by a late asthmatic response, a decline in lung function that occurs during the subsequent 24 hours. The **late response** is caused by the continued release of mast-cell and/or basophil mediators, as well as by the infiltration of inflammatory cells (eosinophils), which produce cytokines and other mediators, resulting in prolonged swelling of the airway mucosa and aggravating of the airway obstruction.

Basophils **ARE INCREASED** in induced sputum of asthmatic patients as well as in the sputum or bronchoalveolar lavage (BAL) fluid during exacerbation or after allergen challenge of asthma patients. Basophils were also observed in the lungs of patients with fatal asthma. This suggests that basophils infiltrate lung tissue in asthma patients. Basophils are increased in the sputum not only from allergic but also of non-allergic asthmatic patients.

The **highest numbers of basophils** were observed in the lungs of patients with **eosinophilic asthma**, and there is a strong positive correlation between sputum basophil and eosinophil counts.

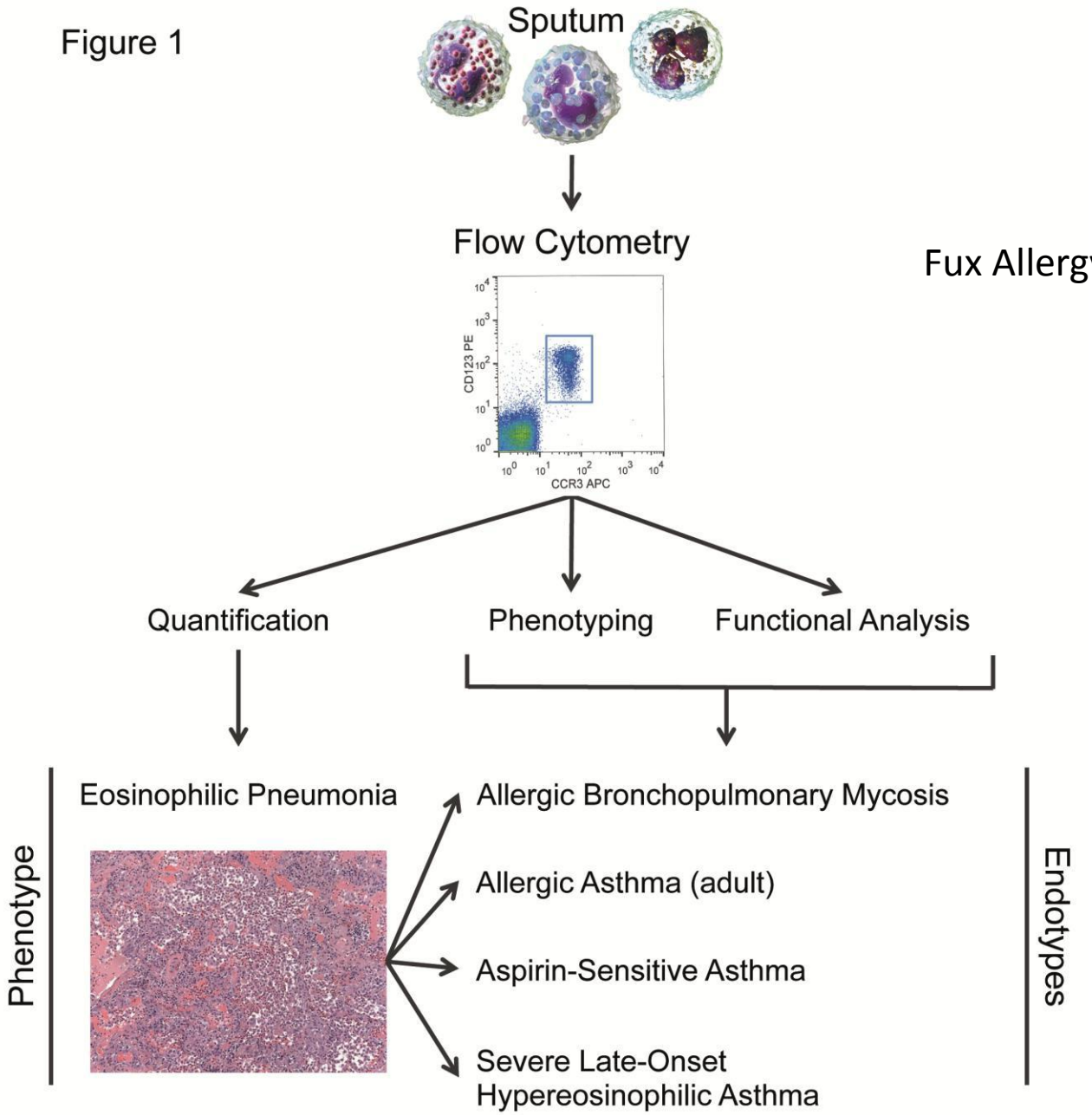






Suzuki Allergy 2017
Brooks Allergy 2017

Figure 1



Fux Allergy 2017

Take-home messages

A rapid basophil infiltration in the airways and subsequent activation or immunomodulatory roles might be an important part of asthma pathogenesis and/or exacerbation.

Mast cells and basophils seems to collaborate to cause acute allergic reactions. Basophil migration occurs rapidly upon in vivo allergen challenge to target affected organs together with mast cells.

klinika GOLNIK

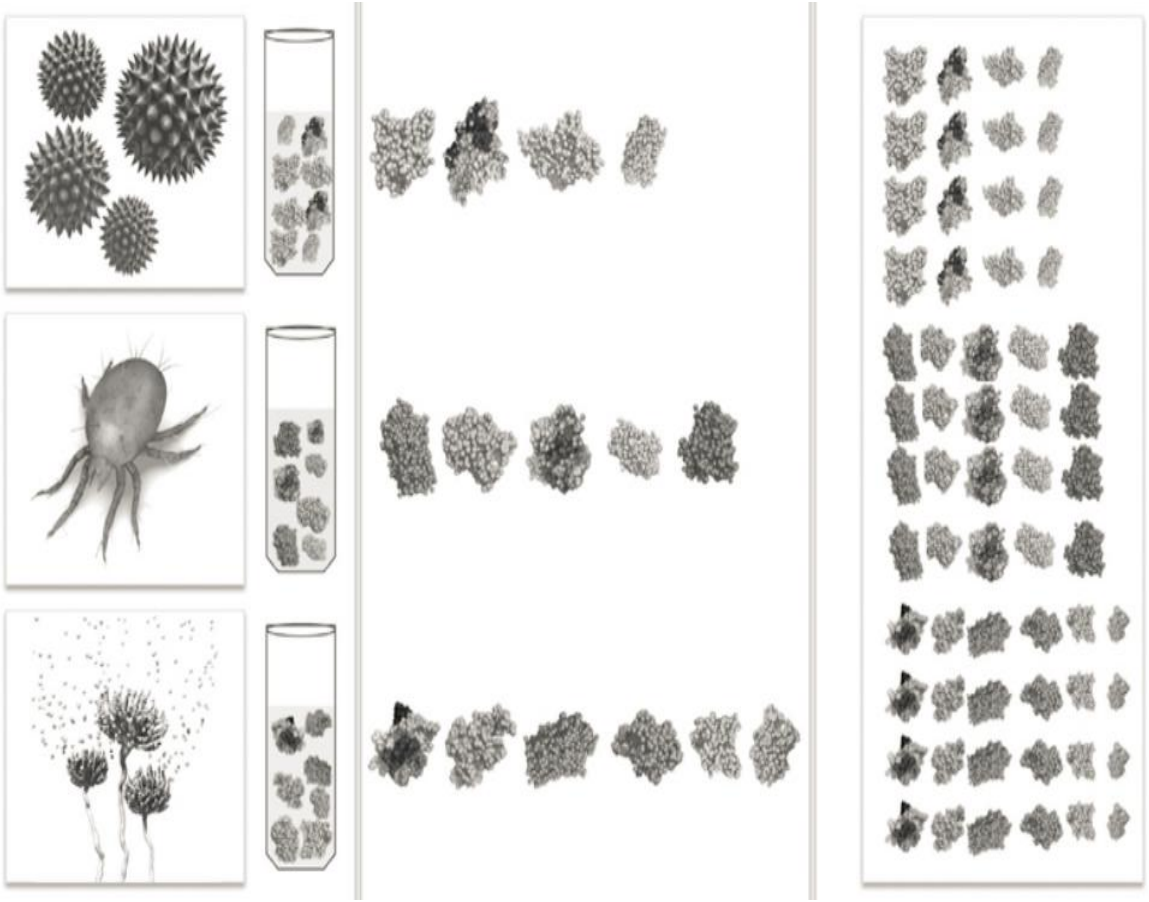
UNIVERZITETNA KLINIKA ZA PLJUČNE BOLEZNI IN ALERGIJO GOLNIK

REKOMBINANTNI ALERGENI

dr. Julij Šelb dr.med.

Molekularna diagnostika

klinika GOLNIK
UNIVERZITETNA KLINIKA ZA PLJUČNE BOLEZNI IN ALERGIJO GOLNIK



Vloga MD – splošni vidiki

- Razlikovanje med pristno (angl. ‚genuine‘) senzibilizacijo in navzkrižno reaktivnostjo – izboljšana identifikacija krivdnih alergenov, ki se uporabljajo pri IT
- Ocenjevanje tveganja (v izbranih primerih alergenov) za resnejšo obliko reakcije
  - Ara h 2, Cor a 9 – povezana z resnejšimi reakcijami
  - Ara h 8 – povezan z bolj blagimi reakcijami (saj je občutljiv na pH in temperaturo; za razliko od Ara h 2)

Pristna vs. navzkrižna rea

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- Proteini znotraj iste družine so si podobni → osnova navzkrižne reaktivnosti
- Večina navzkrižne reaktivnosti je klinično nepomembne
  - Vloga MD pri identifikaciji primarnega senzibilizatorja (kurativni ukrepi)
- V določenih primerih lahko pride do klinično pomembne navzkrižne reaktivnosti
  - OAS po določenem sadju pri določenih bolnikih, ki so alergični na brezo (navzkrižna reaktivnost med PR-10 proteini npr. Bet v 1 [breza] in Mal d 1 [jabolko])

Pristna vs. navzkrižna rea na cvetni prah

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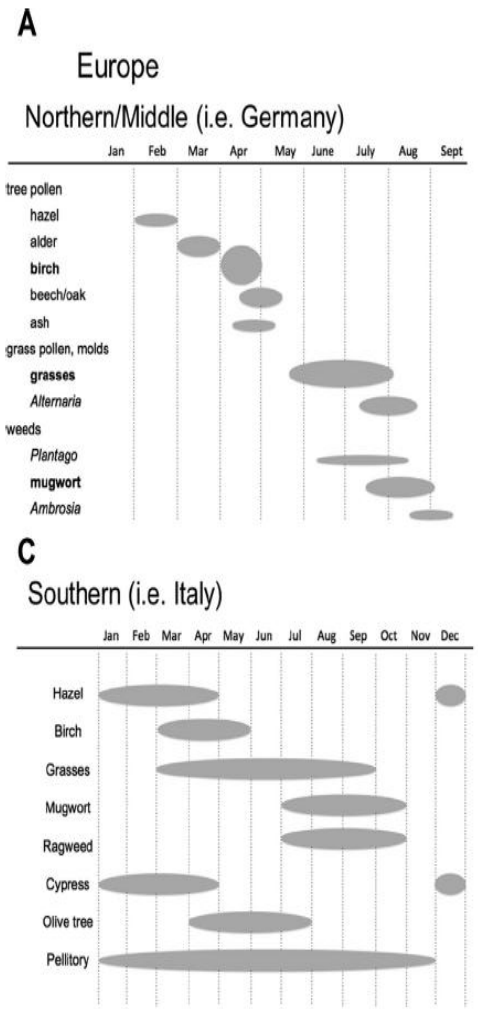
- Osnovni diagnostični korak: anamneza (časovno orientirana) in dokaz IgE senzibilizacije (ekstrakti) → diagnoza in zdravljenje
- Problem:
  - Prekrivanje obdobij cvetenja
  - Senzibilizacija na rastlinske pan-alergene

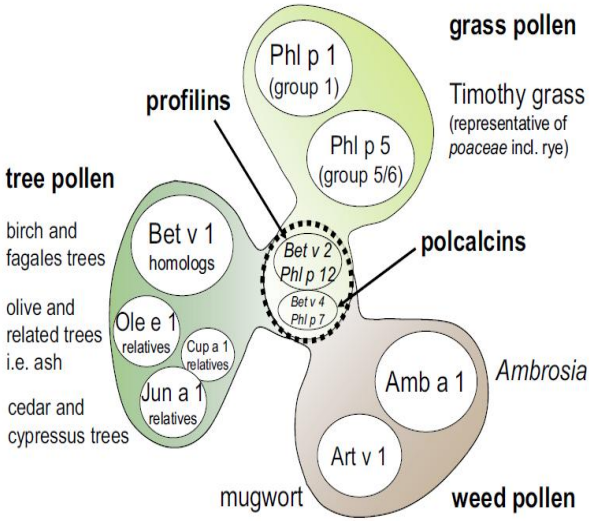
Pristna vs. navzkrižna rea na cvetni prah



do 30 % posameznikov, ki so senzibilizirani na aeroalergene, je senzibiliziranih na pan-alergene (predvsem profiline in polkalcine)

Pristna vs. navzkrižna rea na cvetni prah

- Dokaz IgE senzibilizacije na profiline (Phl p 12/Bet v 2)/polkalcine(Phl p 7/Bet v 4) → izguba diagnostične specifičnosti → nujna uporaba MD za dokaz specifičnih primarnih senzibilizatorjev → IT
  - Bet v 1 - pokrijemo bukovce (breza, leska, jelša, hrast, bukev, gaber in kostanj)
  - Ole e 1 – pokrijemo ustnatičevce kalina)
  - Cup a 1 – pokrijemo cipreso
  - Phl p 1 in Phl p 5 – pokrijemo trav
  - Art v 1 – pokrijemo artemezijo (p
  - Amb a 1 – pokrijemo ambrozijo
  - Par j 2 – pokrijemo krešino



Anafilaksa

- S kofaktorji povzročena anafilaksa (vadba, alkohol, zdravila …):
  - WDEIA – dokaz senzibilizacije na w-5-gliadin
  - CEFA - IgE proti nsLTP (v mediteranskih državah [velikokrat tudi pri WDEIA-i in neg. w-5-gliadinu])- pokrijemo s Pru p 3 in Tri a 14
- Anafilaksa na rdeče meso (zakasnjena; 3-6 h po zaužitju mesa sesalcev):
  - IgE proti a-Gal – senzibilizacija s piki klopov; pametne so večkratne meritve, saj IgE odgovor s časom pada (nekateri bolniki prenašajo meso sesalcev, če jih 1-2 leti ni pičil klop)
- Idiopatska anafilaksa
  - W-5-gliadin, alergeni rakcev, lateksa, ‚seed storage' proteini in nsLTP-ji

Ocena tveganja za težjo obliko reakcije pri alergiji na hrano

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Table 1 High- versus low-risk molecules from foods giving rise to anaphylaxis

Source	High risk	Low risk
Peanut	Ara h 1, 2, 3, 9	Ara h 8, profilin, CCD
Hazelnut	Cor a 8, 9, 14	Profilin, CCD
Walnut	Jug r 1, 2, 3	Profilin, CCD
Soy	Gly m 5, 6, (4)	Profilin, CCD
Rosacea fruits	Pru p 3, Mal d 3	Pru p 1, Mal d 1, profilin, CCD
Wheat	Tri a 14, Tri a 19	Profilin, CCD

KEY: *CCD* = Cross-reactive Carbohydrate Determinant.

Canonica *et al. World Allergy Organization Journal* 2013, **6**:17
http://www.waojournal.org/content/6/1/17

- Na temperaturo in pH odporni proteini načeloma povzročajo težje reakcije, dočim proteini, ki na temperaturo in pH niso odporni povzročajo blažje reakcije.

Navzkrižna alergija na hrano pri alergiji na aeroalergene

- Do 60 % alergij na hrano pri starejših otrocih, adolescentih in odraslih je povezanih z alergijo na aeroalergene
- Pri navzkrižni alergiji na hrano ob alergiji na aeroalergene, lahko do pride do alergične reakcije ob prvem zaužitju hrane.
- OAS je najpogostejša klinična manifestacija navzkrižne alergije na hrano, pri alergiji na aeroalergene, čeprav lahko pride tudi do resne prizadetosti (sistemska reakcija - najpogosteje generalizirane kožne manifestacije, lahko izolirane oz. v kombinaciji s prizadetostjo kakšnega drugega organskega sistema [izolirana prizadetost ostalih organskih sistemov, brez kožne prizadetosti, pri alergiji na hrano je redka]).

Navzkrižna alergija na hrano pri alergiji na aeroalergene

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- Breza
  - Večinoma OAS, (soja, zelena, korenje - lahko resna anafilaktična reakcija)
  - Alergenost hrane ponavadi izgine po toplotni obdelavi (pazi visoko senzibilizirani)
  - Večina posledica navzkrižne reaktivnosti z Bet v 1

Table 3 Birch pollen (Bet v 1*)-associated food allergies

Family	Food	Related food allergen	For *in vitro* testing available
Rosaceae	Apple	Mal d 1	✓
	Cherry	Pru av 1	
	Pear	Pyr c 1	
	Peach	Pru p 1	✓
Apiaceae	Celeriac	Api g 1	✓
	Carrot	Dau c 1	
Other	Hazelnut	Cor a 1.04†	✓
	Soybean	Gly m 4	✓
	Mungbean	Vig r 1	
	Kiwifruit	Act d 8	✓
	Peanut	Ara h 8	✓

*Bet v 1 is a member of pathogenesis-related (PR) protein family and the major source of pollen-related food allergy in central Europe.
†Hazelnut test is spiked with rCor a 1.04 in a commercial IgE test system.

POSITION PAPER

Position paper of the EAACI: food allergy due to immunological cross-reactions with common inhalant allergens

T. Werfel[1], R. Asero[2], B. K. Ballmer-Weber[3], K. Beyer[4], E. Enrique[5,*], A. C. Knulst[6], A. Mari[7], A. Muraro[8], M. Ollert[9], L. K. Poulsen[10], S. Vieths[11], M. Worm[12] & K. Hoffmann-Sommergruber[13]

MD pri alergiji na kožekrilce

- senzitivnost

  Vachova et al.; (84 % senzitivnost panela)
  Artz et al.(71.6% MS na ektstrakt; 92.7 % DS na ekstrakt)

- specifičnost

  Eberlin et al. JACI 2012; (95 % - DS)
  Frick et al. Allergy 2015;(75 % - 90 % DS)
  Michel et al. Allergy 2016; (75 % DS)

1560 | **Limited clinical utility of a panel of routine honeybee venom components**

Vachová M[1]; Šilar M[2]; Kosnik M[2]; Erzen R[2]; Panzner P[1]; Korošec P[2]

1237 | **The severity of hymenoptera sting reactions and the levels of recombinant sFsE and the bat response**

Šelb J; Košnik M; Šilar M; Eržen R; Korošec P

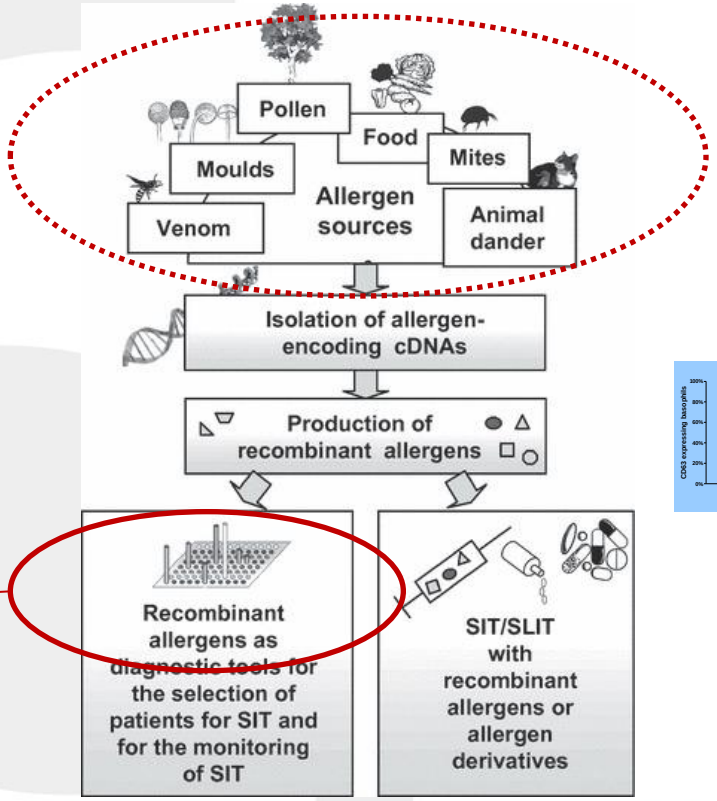
University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia

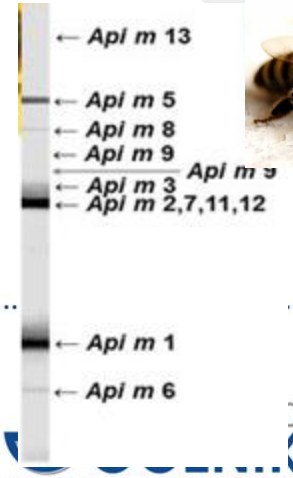
RECOMBINANT BASOPHIL ACTIVATION TEST (rBAT)

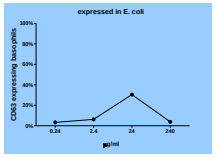
Mira Šilar

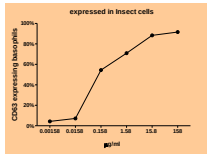
University Clinic for Respiratory and Allergic Diseases Golnik

BAT vs rBAT: **different allergen**



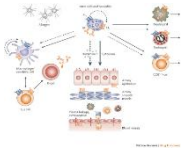


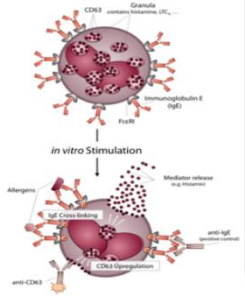




BAT vs rBAT: **same technology**

degranulation upon croos-linking of the sIgE bound on membrane-bound high affinity IgE-receptor by allergen exposure

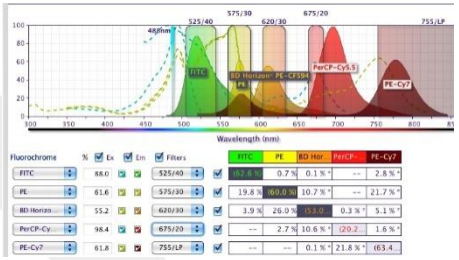




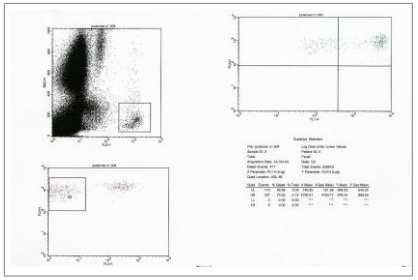
Upon cross-linking of membrane-bound IgE, basophils upregulate the expression of specific activation markers such as CD63. These phenotypic alterations can be acquired by flow cytometry using monoclonal staining antibodies.

(http://www.adr-ac.ch/en/diagnostics/bat)

Flow cytometer



Fluorochromes conjugated with different antigens exposed on the basophil surface can be used to identify basophils amongst leukocytes: CD123/HLA DR
activation markers: CD63



The % of degranulated basophils was determined by FL1 (CD63)

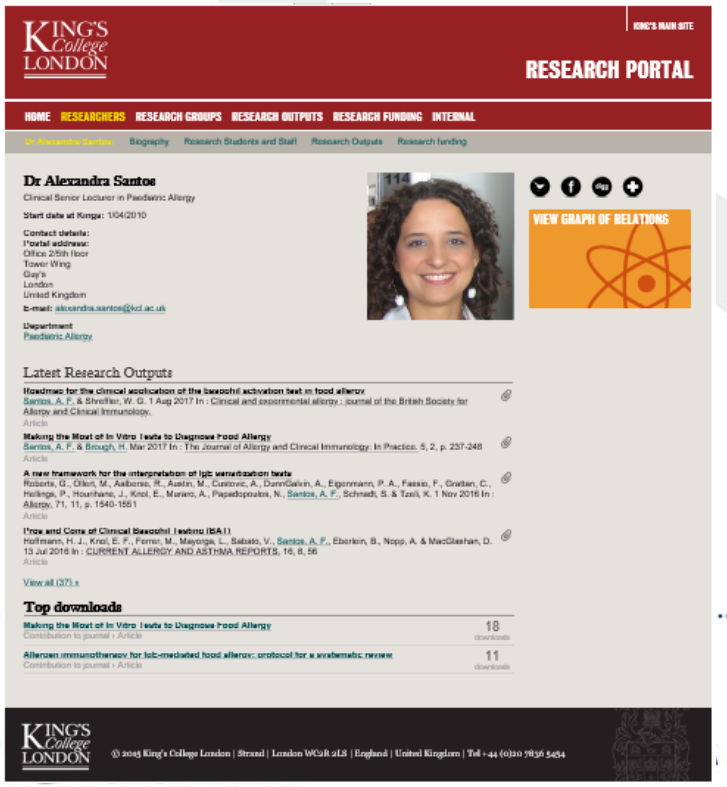
DOI: 10.1111/cea.12964

REVIEW

WILEY

Road map for the clinical application of the basophil activation test in food allergy

A. F. Santos[1] | W. G. Shreffler[2]



Summary

The diagnosis of IgE-mediated food allergy based solely on the clinical history and the documentation of specific IgE to whole allergen extract or single allergens is often ambiguous, requiring oral food challenges (OFCs), with the attendant risk and inconvenience to the patient, to confirm the diagnosis of food allergy. This is a considerable proportion of patients assessed in allergy clinics. The basophil activation test (BAT) has emerged as having superior specificity and comparable sensitivity to diagnose food allergy, when compared with skin prick test and specific IgE. BAT, therefore, may reduce the number of OFC required for accurate diagnosis, particularly positive OFC. BAT can also be used to monitor resolution of food allergy and the clinical response to immunomodulatory treatments. Given the practicalities involved in the performance of BAT, we propose that it can be applied for selected cases where the history, skin prick test and/or specific IgE are not definitive for the diagnosis of food allergy. In the cases that the BAT is positive, food allergy is sufficiently confirmed without OFC; in the cases that BAT is negative or the patient has non-responder basophils, OFC may still be indicated. However, broad clinical application of BAT demands further standardization of the laboratory procedure and of the flow cytometry data analyses, as well as clinical validation of BAT as a diagnostic test for multiple target allergens and confirmation of its feasibility and cost-effectiveness in multiple settings.

Santos AF, Shreffler WG. Road map for the clinical application of the basophil activation test in food allergy. Clin Exp Allergy. 2017;00:1–10. https://doi.org/10.1111/cea.12964

6 | WHAT WOULD BE THE VALUE OF USING BAT IN CLINICAL PRACTICE?

Basophil activation test can be performed using single allergen components, which for some foods can be more accurate than using allergen extracts in the BAT (Table 2). For example, BAT to ovomucoid and BAT to Pru p 3 showed improved diagnostic accuracy compared to BAT to egg white and BAT to peach to diagnose egg allergy (both baked and raw egg allergies) and peach allergy, respectively.[46,62] The use of single allergens has, however, the disadvantage of missing the contribution of minor allergens that are clinically relevant for some patients and of missing the combined effect of multiple allergens to which polysensitized patients produce IgE and which may increase the degree of basophil activation detected in the BAT.

TABLE 2 Examples of studies assessing the utility of the basophil activation test to diagnose food allergy using whole allergen extracts or single allergens

Food allergy	Food extract or allergen component	Study	Cut-offs	Sensitivity	Specificity
Cow's milk allergy	Cow's milk extract	Rubio (2011)[48]	>6% CD63+	91%	90%
		Sato (2010)[46]	SI CD203c ≥1.9	89%	83%
	Casein	Sato (2010)[46]	SI CD203c ≥1.3[46]	67%	71%
Egg allergy	Ovalbumin	Ocmant (2009)[48]	≥5% CD63+	77% for CD63	100% for CD63
			SI CD203c ≥1.6	63% for CD203c	96% for CD203c
Baked egg allergy	Egg white extract	Sato (2010)[46]	SI CD203c ≥2.4	74%	62%
	Ovomucoid		SI CD203c ≥1.7	80%	73%
Raw egg allergy	Egg white extract	Sato (2010)[46]	SI CD203c ≥1.7	77%	63%
	Ovomucoid		SI CD203c ≥1.6	83%	83%
Wheat allergy	Wheat extract	Tokuda (2009)[50]	>11.1% CD203c+	86%	58%
	Omega-5 gliadin (nTri a 19)		>14.4% CD203c+	86%	58%
	Omega-5 gliadin (rTri a 19)		>7.9% CD203c+	83%	63%
Peanut allergy	Peanut extract	Santos (2014)[4]	≥4.78% CD63+	98%	96%
	Ara h 2	Glaumann (2012)[22]	ND	92%	77%
Hazelnut allergy	Hazelnut extract	Brandstrom (2015)[58]	CD-sens >1.7	100%	97%
PFAS to hazelnut		Erdmann (2003)[65]	≥6.7% CD63+	85%	80%
Peach allergy	Peach extract	Gamboa (2007)[62]	>20% CD63+SI CD63 >2	87%	69%
	Pru p 3		>20% CD63+SI CD63 >2	77%	97%
PFAS to apple	Apple extract	Ebo (2005)[64]	≥17% CD63+	88%	75%
PFAS to carrot	Carrot	Erdmann (2003)[65]	≥8.9% CD63+[65]	85%	85%
PFAS to celery	Celery	Erdmann (2003)[65]	≥6.3% CD63+[65]	85%	80%

SI, stimulation index; PFAS, pollen-food syndrome; ND, not determined.

…it is necessary to achieve standardization of the laboratory procedure and data analyses and more rigorous validation.

Šilar, EAACI po EAACI, 7.9.17

EAACI: oral presentation

Recombinant basophil activation test and "fingerprint" modeling of allergenic activity

Mira Šilar[1], Renato Eržen[1], Yvonne Resch[2], Susanne Vrtala[2], Mihaela Zidarn[1], Peter Kopač[1], Minja Zorc[3], Tanja Kunej[3], Edzard Spillner[4], Rudolf Valenta[2], Mitja Košnik[1], Peter Korošec[1]

1. University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia
2. Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria
3. Department of Animal Science, Biotechnical Faculty, University of Ljubljana, Slovenia
4. Immunological Engineering, Department of Engineering, Aarhus University, Aarhus, Denmark

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The aim of this work:

To introduce a novel model of analysis of recombinant basophil activation test (rBAT), which allows displaying multi parameter features of allergenic activity of all major allergens of a specific allergen source on the level of individual patient.

Methods:

- 27 house dust mite (HDM) allergic patients
  3 healthy controls

- 30 patients with anaphylactic reactions to honey bee venom (HBV; n=24) or yellow jacket venom (YJV; n=6)
  4 healthy controls

Some HBV allergic patients were also followed during SIT

The protocol was performed in **two steps**:

1. **IgE reactivity** of recombinants was determined with dot blots or ELISA.

2. **Allergenic activity** was evaluated with basophil CD63 testing on heparinized whole blood with serial dilutions of:

   - **HDM**: nDer p 1, rDer p 2, rDer p 5, rDer p 7, rDer p 10, rDer p 21 and rDer p 23 allergens: 10^{-35} to 100 ng/ml
   - **HBV:** nApi m 1, rApi m 1, rApi m 2, rApi m 3, rApi m 5, rApi m 10, rApi m 11 allergens: 0.001–10 µg/ml

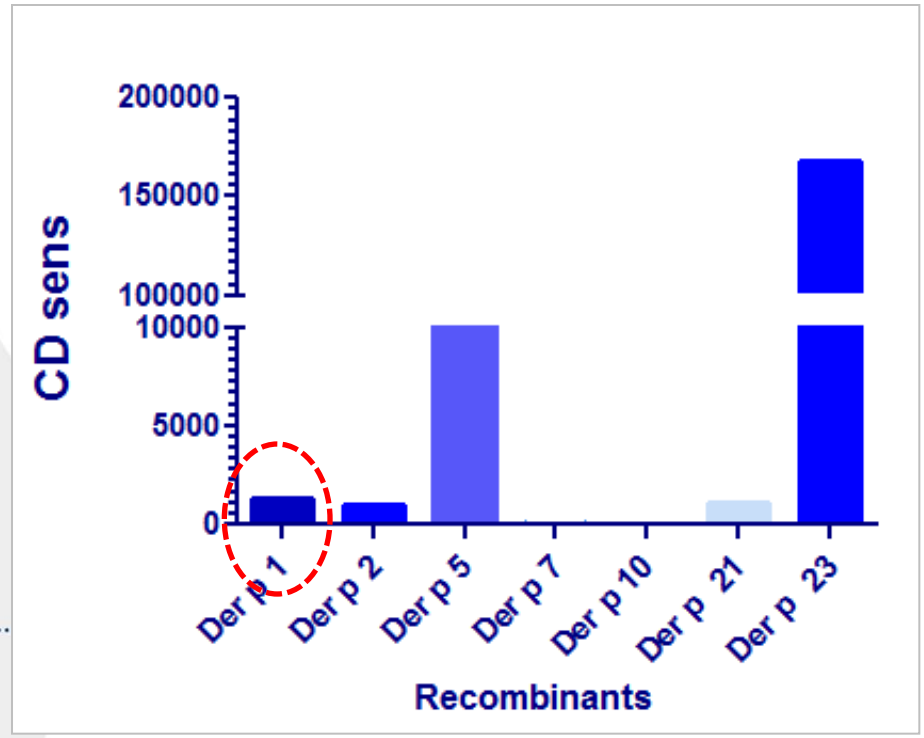
Results for HDM model:

1. **IgE reactivity** was determined in sera of **all** HDM allergic patients

2. **positive** recombinants were tested with BAT and quantified with CDsens

Basophil sensitivity was determined as the allergen concentration giving a 50% of maximum CD63% up-regulation. CD-sens was calculated as the inverse value of this threshold allergen concentration multiplied by 100. The higher value for CD-sens represents higher basophil sensitivity.

	Der p 1	Der p 2	Der p 5	Der p 7	Der p 10	Der p 21	Der p 23
1	x	x	x	x		x	x
2	x	x		x			x
3	x						
4		x					
5	x	x					
6		x					x
7	x	x	x			x	x
8	x	x					x
9							x
10	x	x					
11		x		x			x
12		x					x
13							
14		x	x			x	x
15	x	x	x	x	x		x
16	x	x		x			x
17	x	x	x			x	x
18							
19							
20							
21	x	x		x			x
22	x	x					x
23	x	x	x	x			x
24	x	x		x			x
25							
26	x	x	x	x		x	x
27	x	x	x	x	x		x
28	x	x	x	x		x	x
29							
30							

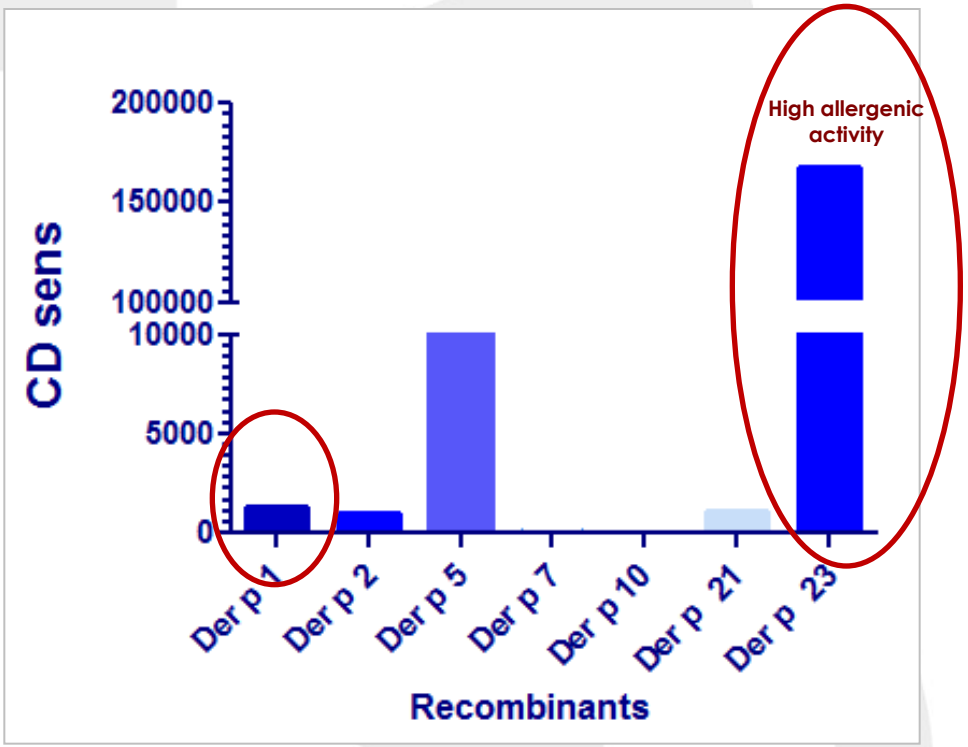


REACTIVITY ≠ **ALLERGENICITY**

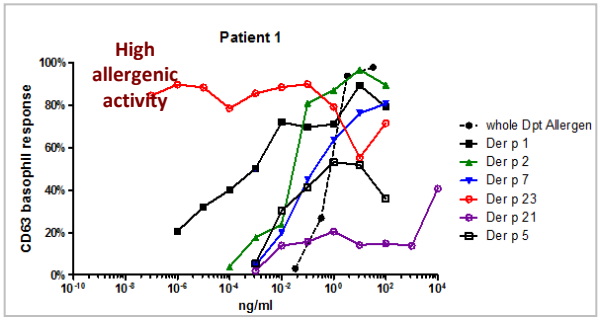
Silar, EAACI 2017

CDsens results showed extremely wide range

(as such different allergens could not be combined and compared in individual patients)



	Der p 1	Der p 23
mediana	1147	167293
range	0.6 – $3.4x10^{18}$	31.3 – $2.0x10^{32}$
SD	$7.6x10^{17}$	$4.7x10^{31}$



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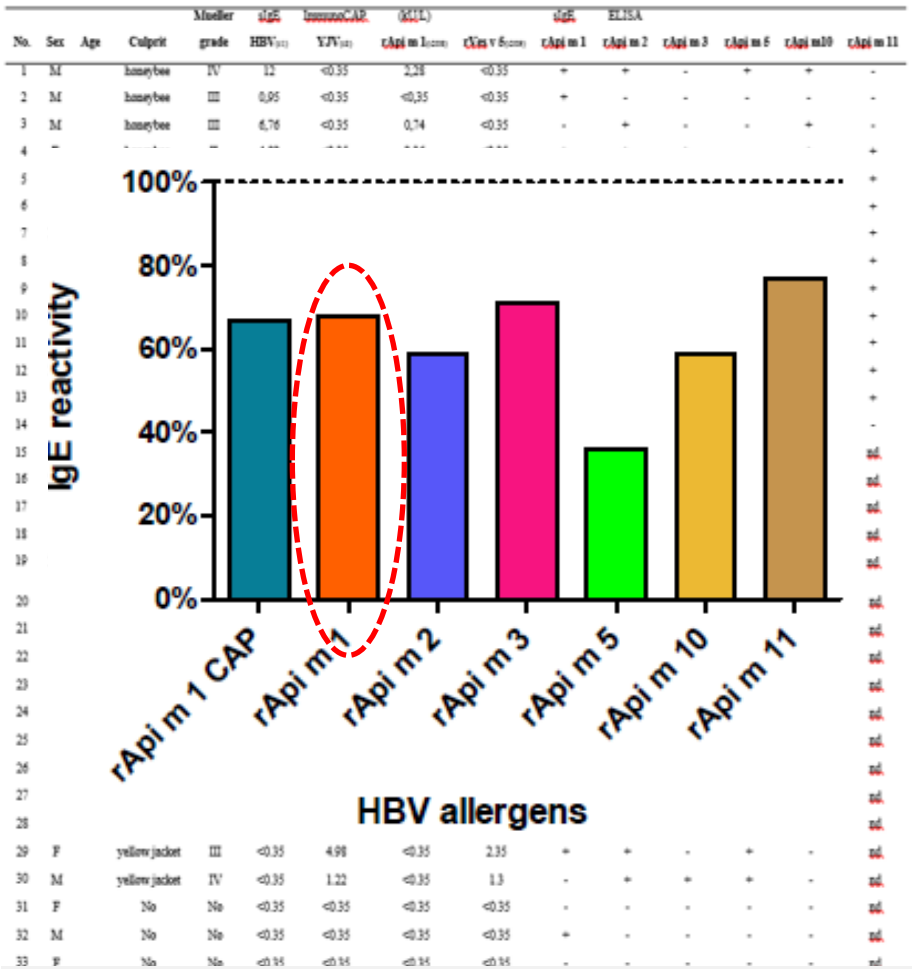
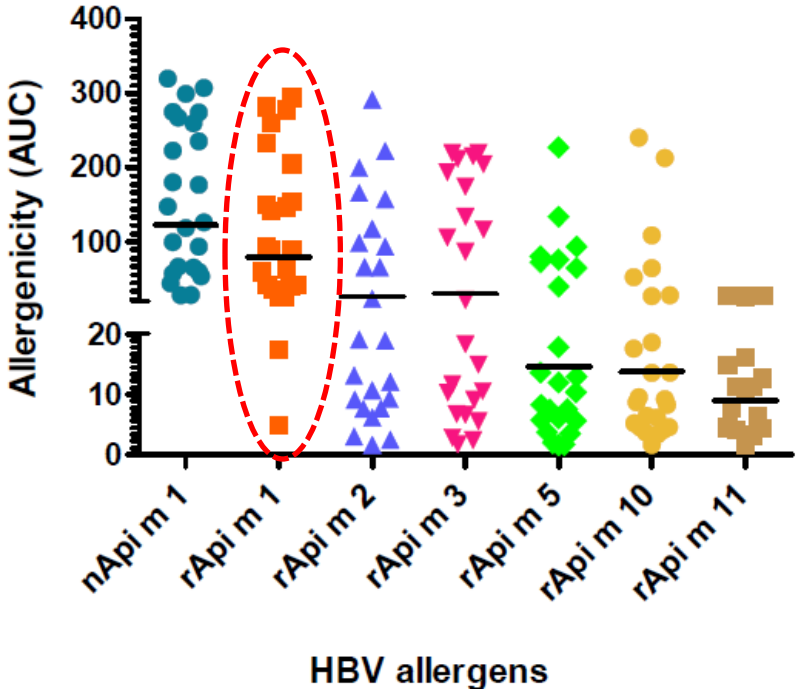
Results for HBV model:

1. **IgE reactivity** was determined in sera of **all** HBV allergic patients



2. **all** recombinants were tested with BAT and quantified with AUC

BAT AUC (area under the curve) was calculated using the trapezoid rule on the data representing CD63% up-regulation with 4 consecutive bee venom concentrations (0.001 - 10 ug/ml)



REACTIVITY ≠ **ALLERGENICITY**

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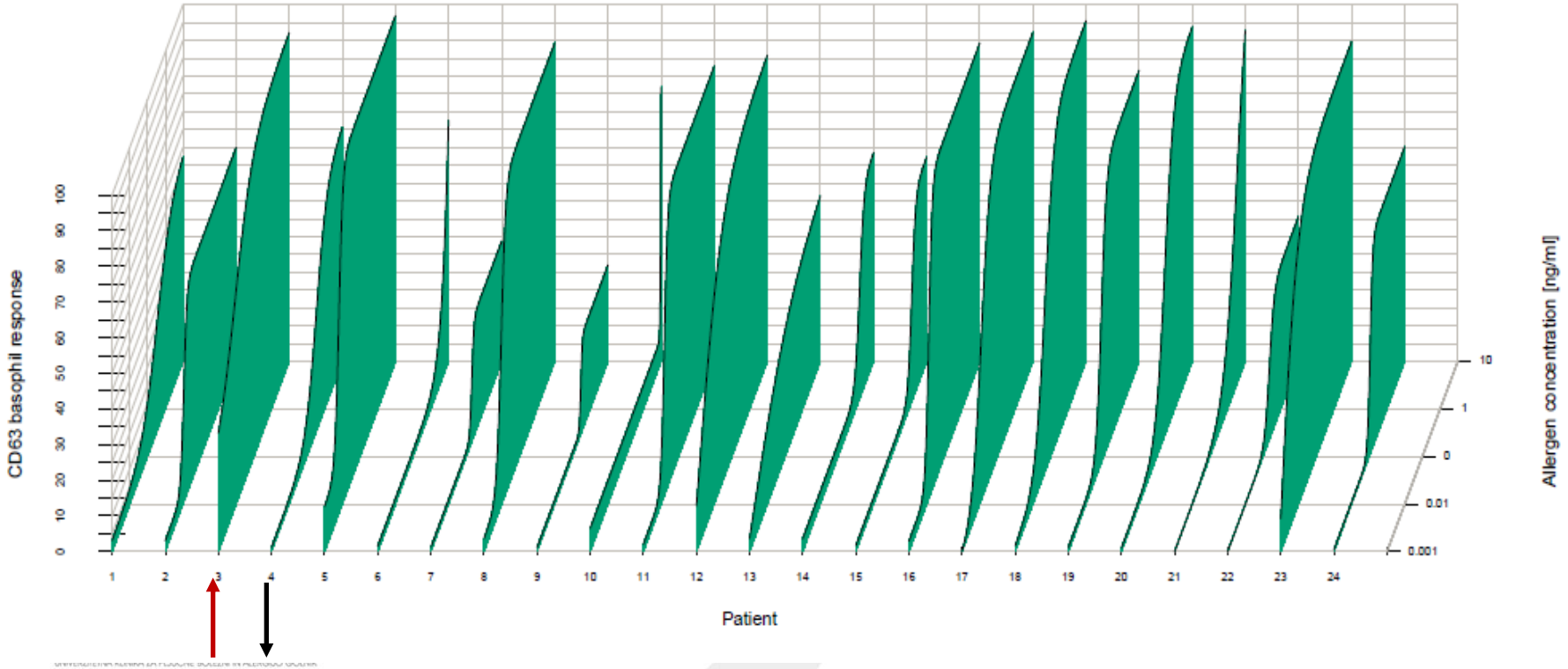
Quantification of allergenic activity for single allergen with new developed 3D-plot of AUCs

- all patients, 24/24 (100%) were positive for nApi m 1
- nApi m 1 showed the highest AUC (geometric mean 123)



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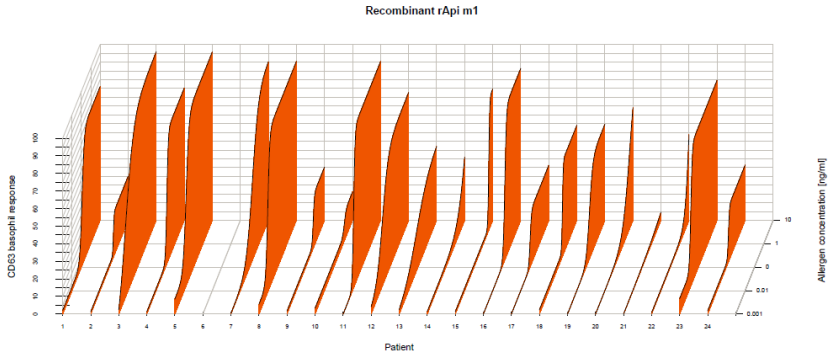
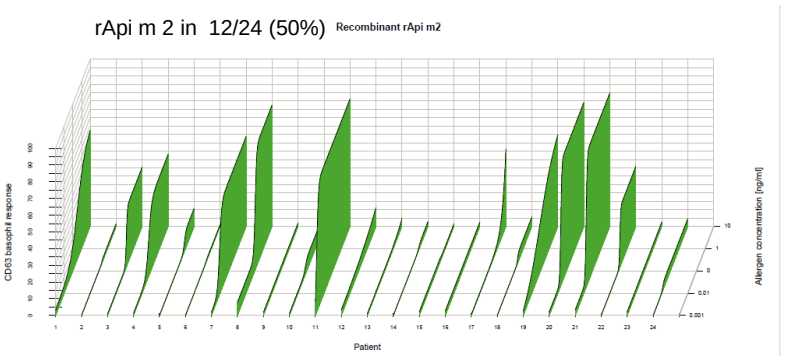
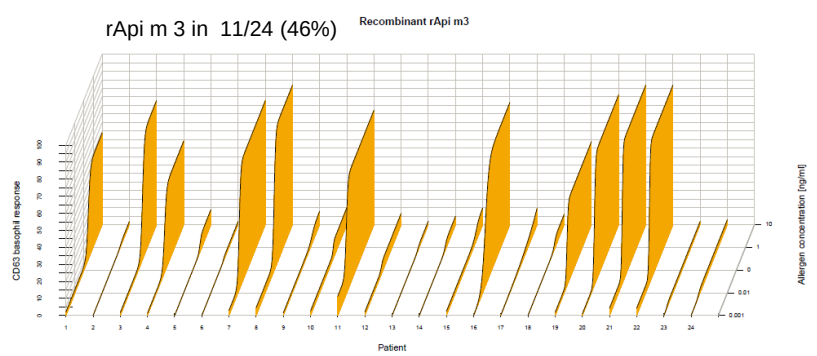
Allergenicity to rApi m 1 was detected in 22/23 (96%)



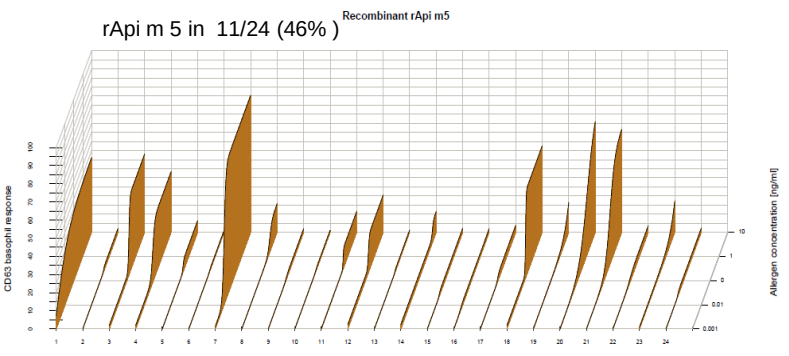
rApi m 2 in 12/24 (50%)



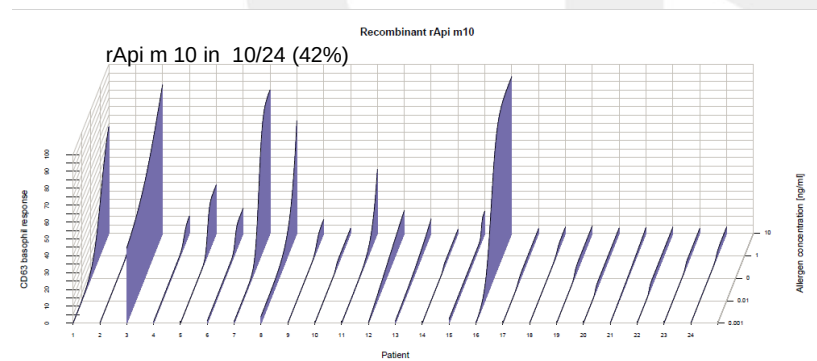
rApi m 3 in 11/24 (46%)



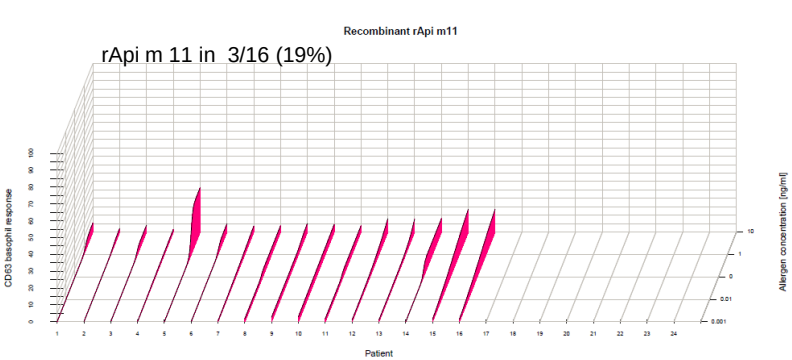
rApi m 5 in 11/24 (46%)



rApi m 10 in 10/24 (42%)



rApi m 11 in 3/16 (19%)



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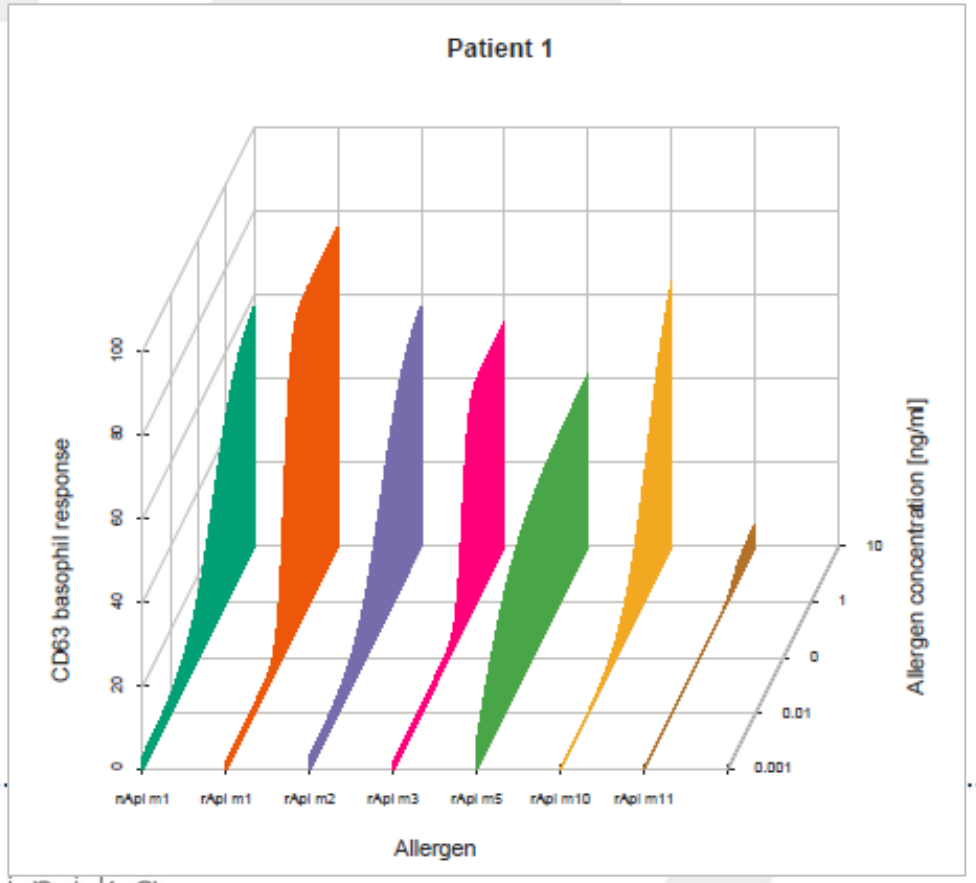
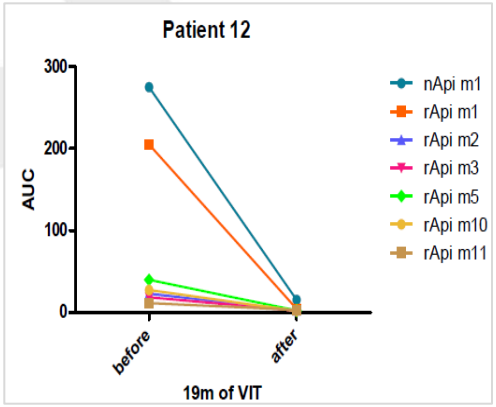
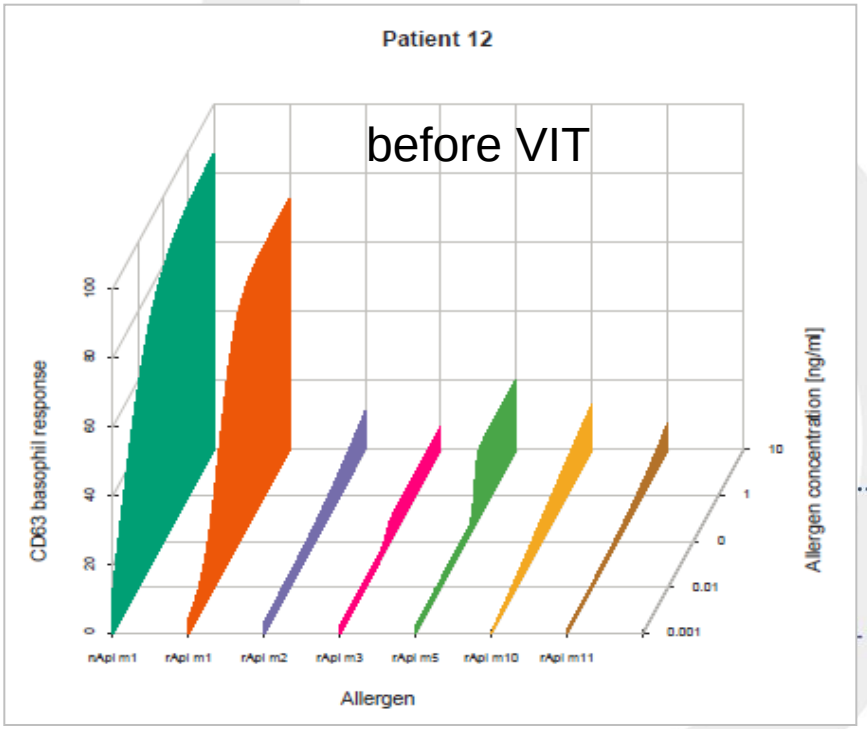
On the level of individual patient 3D-plot of AUCs represent multiparameter features of allergenic activity, including quantification for single allergen and summary for all tested allergens.

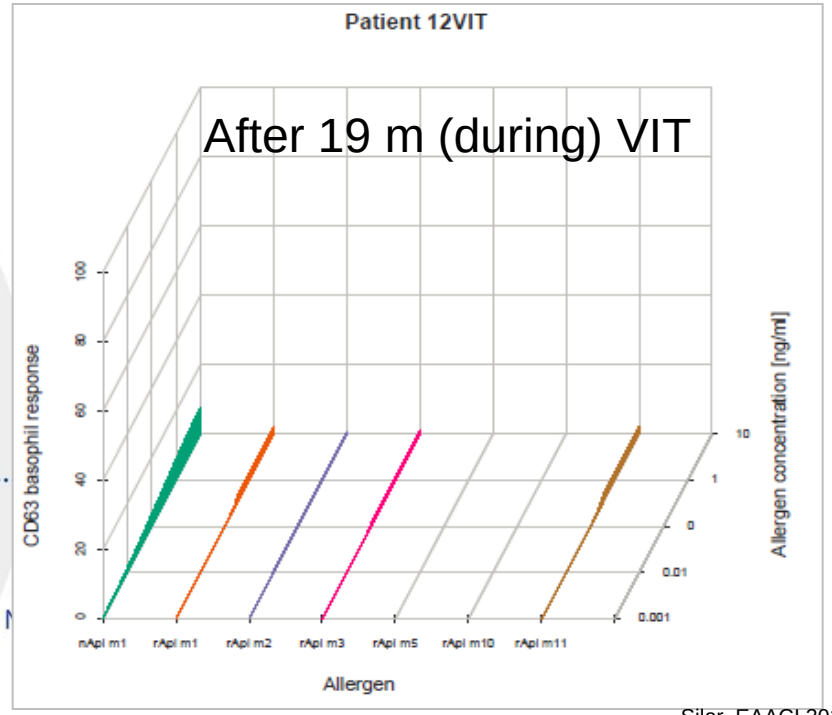


1 patient
7 rec BAT x 5 different conc. = **35 BAT**

3D-plot of AUC:
a new tool for monitoring allergen immunotherapy







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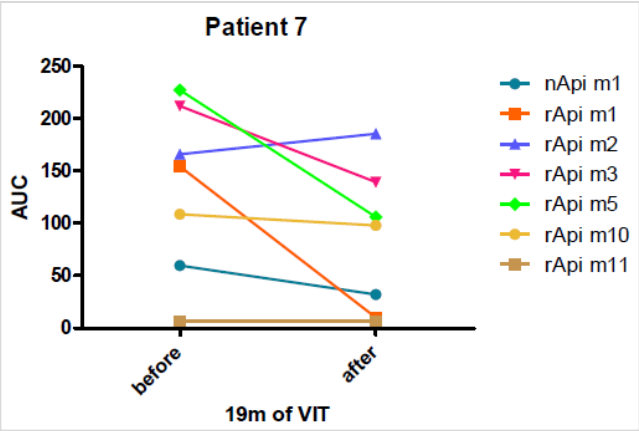
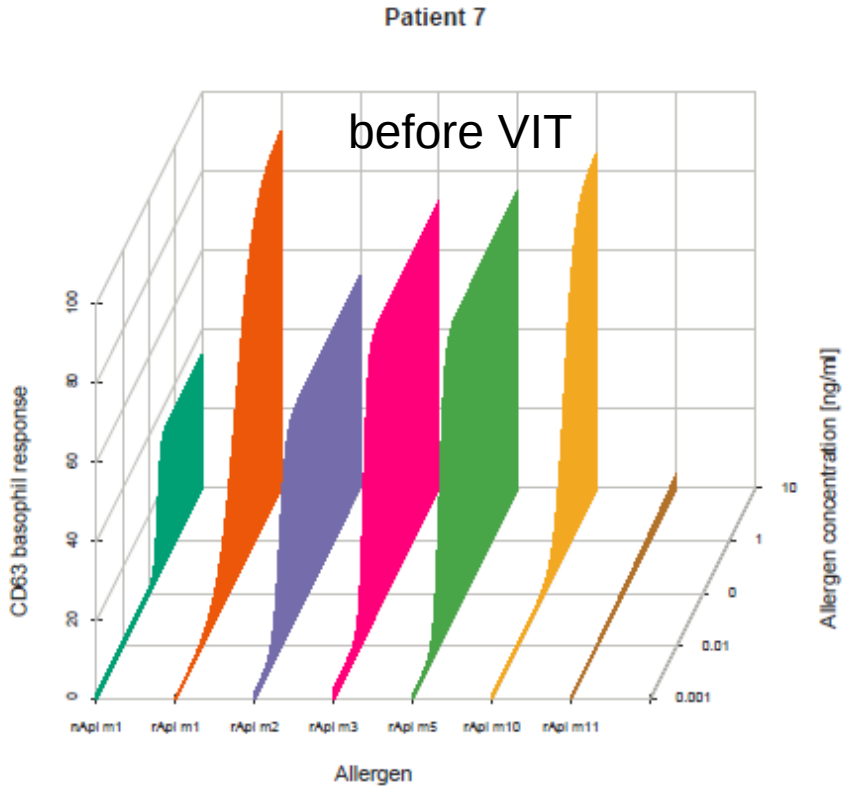
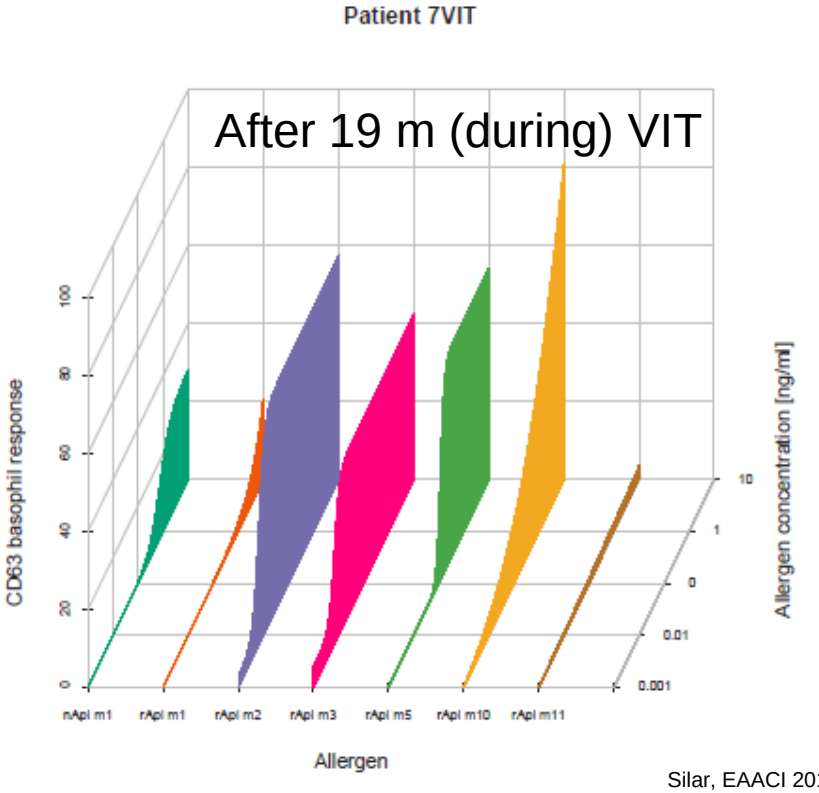
No.	Sex	Age	Culprit	Mueller grade	sIgE HBV(i1)	ImmunoCAP YJV(i3)	(kU/L) rApi m 1(i208)	rVes v 5(i209)	sIgE rApi m 1	ELISA rApi m 2	rApi m 3	rApi m 5	rApi m10	rApi m 11
7	M		honeybee	IV	1,13	<0.35	<0,35	<0.35	+	+	+	+	-	+



- Highly positive for multiple HBV allergens

- A significant decrease of allergenic activity was evident for rApi m1, but not for rApi m 2;
  less for rApi m 3 and 5 and minor for rApi m 10





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CONCLUSION

- ✓ Fingerprint modeling of allergenic activity pointing out the actual allergens from the offending allergen source that eliciting the allergic response in individual patients.

- ➢ This approach offers a new tool to address patient's individual clinical reactivity at the molecular level and to monitor allergen immunotherapy.

Major basophil chemotactic factor CCL2 is increased in chronic urticaria patients and correlates with basopenia

Ana Koren, Mira Silar, Matija Rijavec, Peter Kopac, Mitja Kosnik, Peter Korosec

University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia

INTRODUCTION

Chronic urticaria (CU) is associated with basopenia, but the underlying mechanism for reduced basophil numbers remains unknown. Our recent study indicates substantial reduction in circulating basophils during acute allergic reaction, which correlates with a significant increase in the major basophil chemotactic factor CCR2 ligand CCL2. The aim of our current study was to investigate relationship between CCL2 level and basophil number in CU patients.

METHODS

Concentration of CCL2 and absolute basophil count were measured in 64 patients with CU and 24 healthy controls. CCL2 was determined with ELISA (R&D Systems, USA) and the absolute basophil count (CD123+ HLA-DR− cells) was determined with flow cytometry (BD, USA). Study was approved by Slovenian National Committee for Medical Ethics. Written inform consent was obtained from each participant before entering the study.

RESULTS

Basophil numbers in CU were reduced compared to controls (P<0.0001) (Figure 1). Serum CCL2 concentration was significantly increased (*P*=0.0002) in patients with CU (median 279 pg/ml) compared to healthy controls (median 191 pg/ml) (Figure 2). A significant negative correlation (r=-0.24, *P*=0.025) between serum CCL2 concentration and the absolute number of circulating basophils was demonstrated (Figure 3).

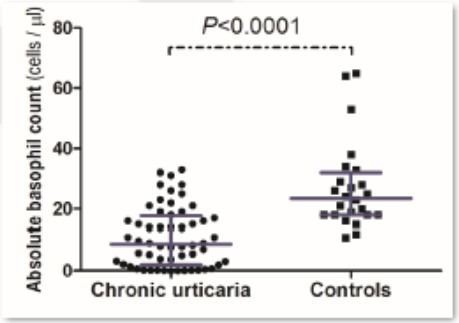


Figure 1: Absolute basophil count in chronic urticaria and healthy controls

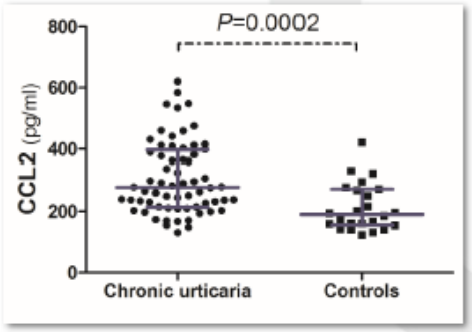


Figure 2: CCL2 expression in chronic urticaria and healthy controls

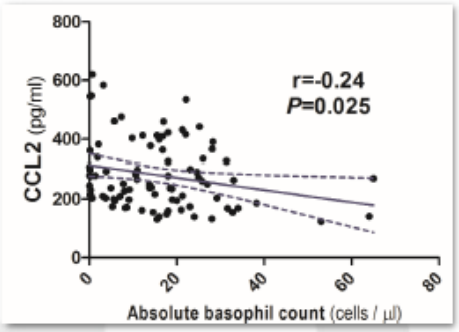


Figure 3: Correlation between CCL2 and basophils in chronic urticaria and healthy controls

CONCLUSIONS

Our study indicates increase in the level of CCL2 in CU patients, which is associated with a decrease in the number of circulating basophils. CCL2-mediated migration may represent a mechanism for the selective migration of human basophils in CU. Additional studies will help clarify the importance of these observations.

CONFLICT OF INTEREST In relation to this presentation, I declare that there are no conflicts of interest.

Patient tailored omalizumab treatment in chronic urticaria – our experiences

P.Kopač, M. Zidarn, N. Bajrović, R. Eržen, J. Šelb, M. Šilar, P. Korošec, M. Košnik
University Clinic of Respiratory and Allergic Diseases Golnik, Slovenia

Background

Omalizumab is effective treatment in chronic spontaneous urticaria (CSU). There are reports that treatment schedules should not be uniformed, but patient tailored.

Method

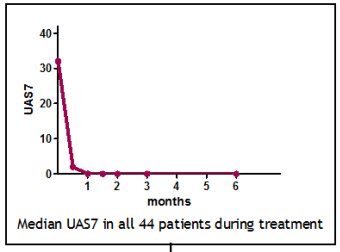
We have analysed clinical response to omalizumab 300 mg/4 weeks in 52 CSU patients (41 females, median age 48 years). Treatment was started by 300 mg/4 weeks. Patients daily reported urticaria activity score (UAS) via a web based application. We analysed UAS7 at the beginning, 2 weeks (W2), 3 months (M3), and 12 (M12) months after first omalizumab application. The following definition of response to treatment were based on UAS7: complete response (UAS7=0), well controlled (UAS7=1-6), not well controlled (UAS7>6) and among last group significant improvement if reduction of UAS7 was 90-30%. In patients with complete response omalizumab dose was stepwise decreased and interval extended to the minimal dose/interval on which patients stayed symptom free.

CLINICAL RESPONSE	UAS7
complete response	0
well controlled urticaria	1-6
not well controlled urticaria	>7

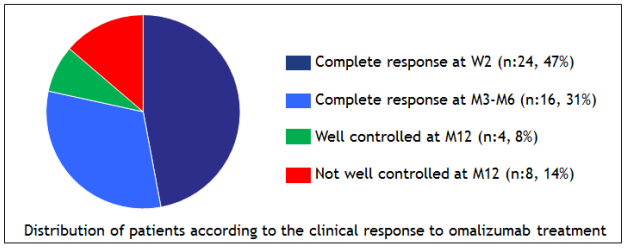
Classification of clinical response to omalizumab treatement

Results

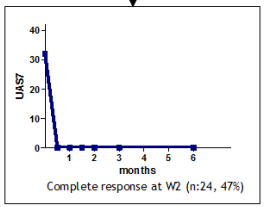
Complete response was achieved in 24/52 (46%) patients already at W2, in 11/52 (21%) patients at M3 and in 5/52 (10%) patients at M12. In 33/40 (82%) patients with complete response omalizumab treatment could be reduced to median 150mg/6 weeks. In 5 patients a remission was achieved after median 7 months of treatment (2-19 months) and were able to discontinue the treatment.
In 4/52(8%) patients CSU was well controlled at M12. 8/52 (15%) patients were not well controlled although in 4 patients significant improvement was achieved and patients continued with omalizumab 300 mg/4 weeks. In 4 patients with no significant improvement treatment was stopped after median 6 months (3-13months).



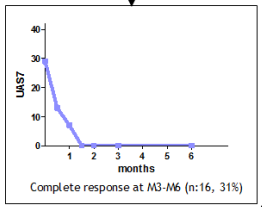
Median UAS7 in all 44 patients during treatment



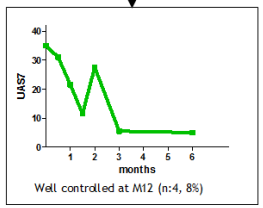
Distribution of patients according to the clinical response to omalizumab treatment



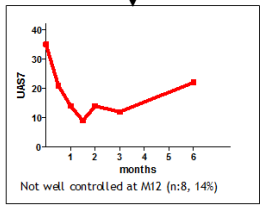
Complete response at W2 (n:24, 47%)



Complete response at M3-M6 (n:16, 31%)



Well controlled at M12 (n:4, 8%)



Not well controlled at M12 (n:8, 14%)

In 33/40 (82%) patients with complete response omalizumab treatment could be reduced to median 150mg/6 weeks. In 5 patients a remission was achieved after median 7 months of treatment (2-19 months) and were able to discontinue the treatment

In 4/8 not well controlled patients there was no no significant improvement and treatment was stopped after median 6 months (3-13months).

Conclusion

Half of the patients with CSU completely respond to omalizumab very rapid and in these patients lower dose (150mg/6 weeks) is sufficient. In third of the patients completely response is achieved in several months and also in these patients less intensive treatment is needed. In patients with partial response, even after year of treatment, higher omalizumab dose is needed, while minority of patients did not respond to treatment and omalizumab was stopped

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Abstract Prize Winner

CCL2 MEASUREMENT IN SERA AS A NOVEL BIOMARKER OF ANAPHYLAXIS

Romana Vantur BSc, Mira Silar BSc, Ana Koren PhD, Peter Kopac MD, Mitja Kosnik MD PhD, Paul J. Turner FRACP PhD, Adnan Custovic MD PhD, Peter Korosec PhD

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UNIVERZITETNA KLINIKA ZA PLJUČNE BOLEZNI IN ALERGIJO GOLNIK

UNIVERZITETNA KLINIKA ZA PLJUČNE BOLEZNI IN ALERGIJO GOLNIK
UNIVERSITY CLINIC OF RESPIRATORY AND ALLERGIC DISEASES GOLNIK

Golnik 36, 4204 Golnik, Slovenija
T: +386 (0)4 25 69 100 **F:** +386 (0)4 25 69 117 **E:** kopa.tajnistvo@klinika-golnik.si **W:** www.klinika-golnik.si

BACKGROUND

- Currently, the most widely used laboratory test to confirm anaphylaxis is the **measurement of total tryptase** levels in serum or plasma

- **LIMITATION**: even when blood samples are optimally timed, tryptase levels are often within normal limits

- **CCL2 –** major basophil chemotactic factor may be a useful biomarker of anaphylaxis

Korosec P, Turner PJ, Silar M, Kopac P, Kosnik M, Gibbs BF, Shamji MH, Custovic A, Rijavec M. **Basophils, high-affinity IgE receptors, and CCL2 in human anaphylaxis.** J Allergy Clin Immunol. 2017 Mar 22. pii: S0091-6749(17)30423-2. doi: 10.1016/j.jaci.2016.12.989. [Epub ahead of print]

WHY CCL2?

- Chemokine CCL2 is **increased** during acute anaphylactic reaction
- Induces strong basophil **transendothelial migration** to inflammatory tissue sites
- Reduction in circulating basophils correlates with increase in CCL2
- Therapy (corticosteroids) **has no affect** on CCL2

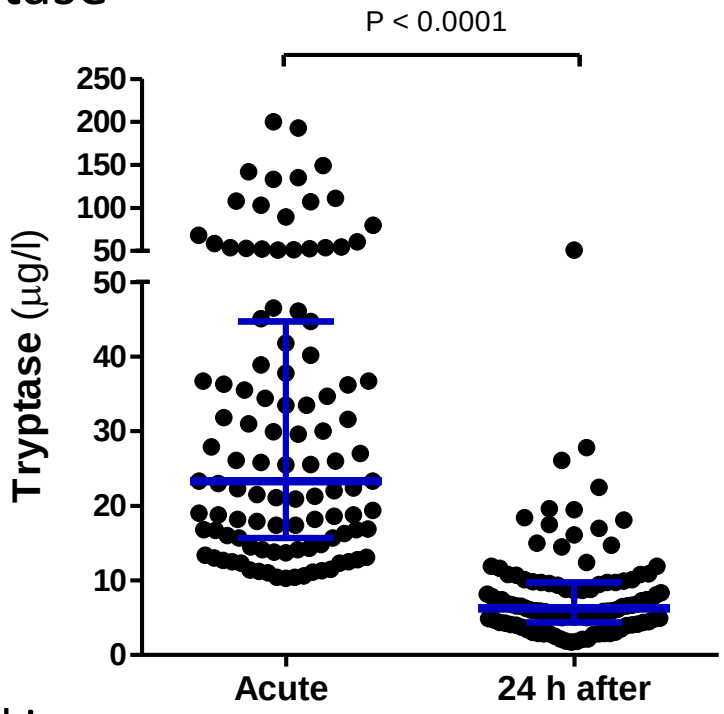
METHODS

- **107 patients** with clinical diagnosis of anaphylaxis and positive serial tryptase measurement (tryptase > 10 µg/l)

TIME POINTS:

Acute samples – reaction to 24h after

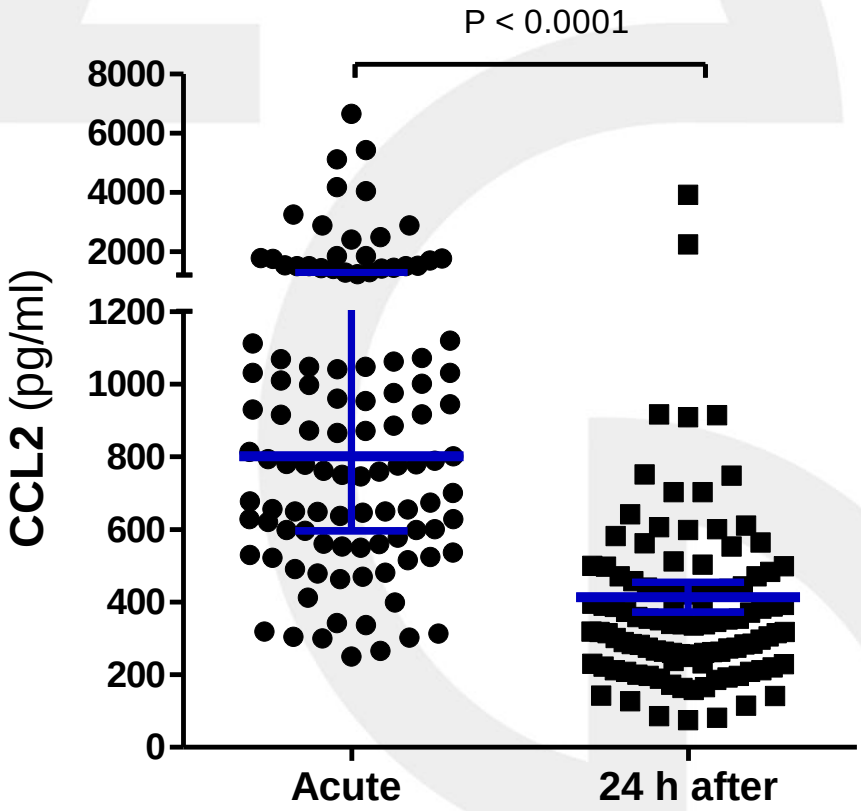
Basal samples – 24 h to 3 months after



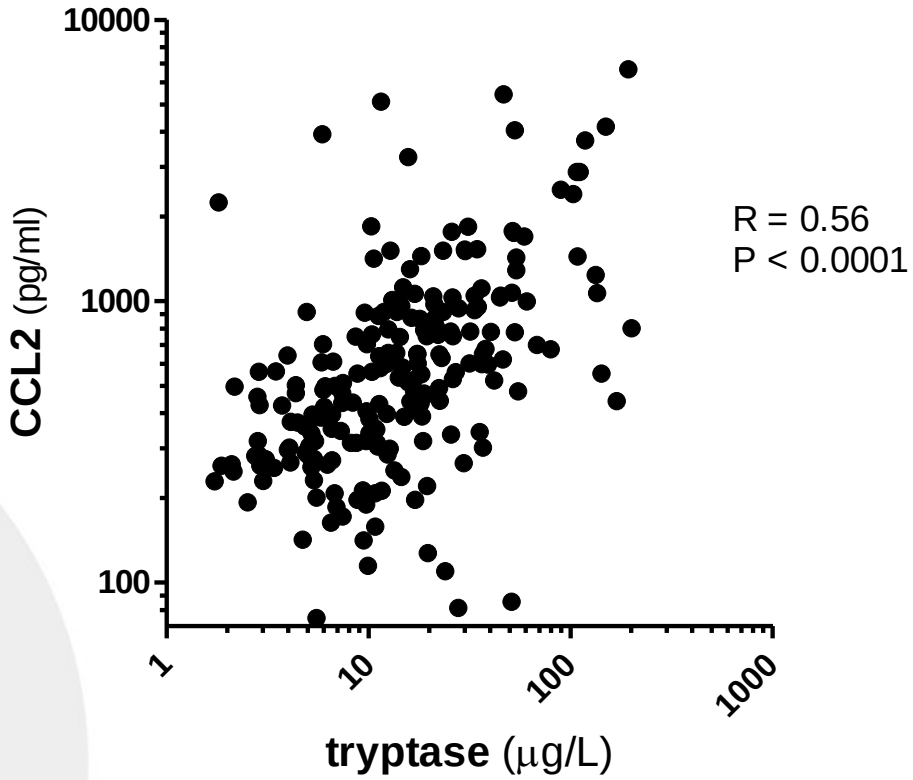
- **98 healthy controls**

- Measurement of CCL2 - ELISA test: Quantikine Human MCP-1 Immunoassay

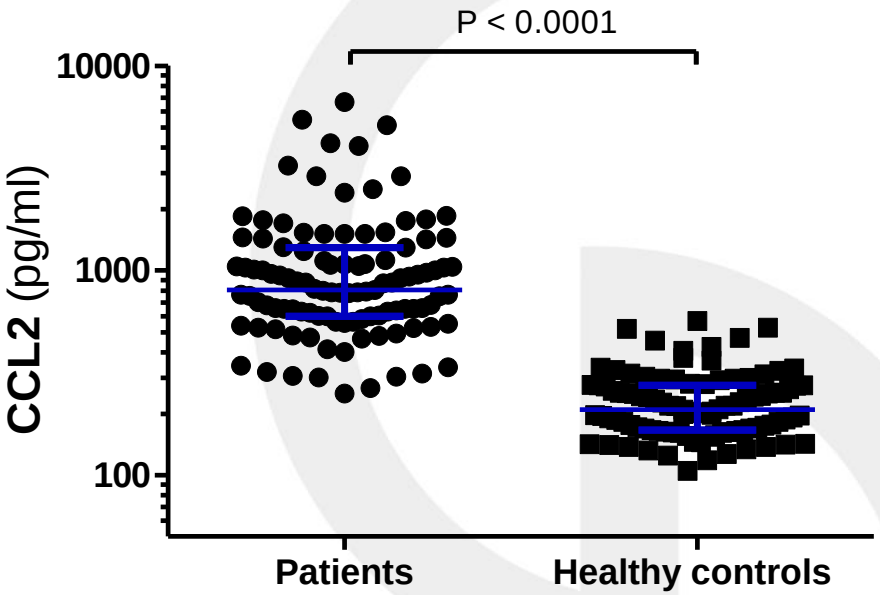
1. CCL2 levels are increased during anaphylaxis



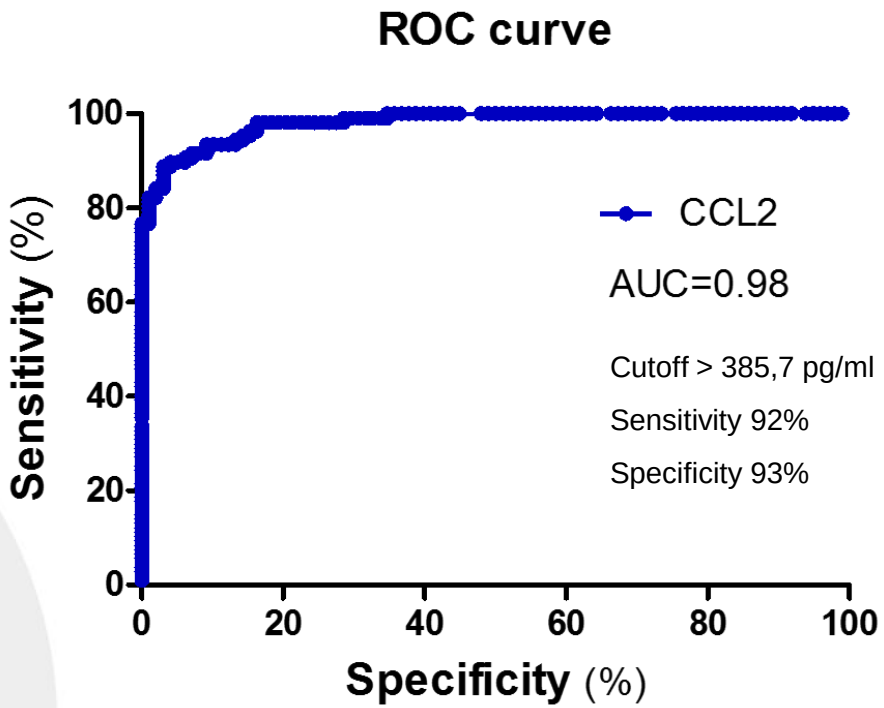
2. There is a strong positive correlation between serum tryptase and CCL2 levels



3. During anaphylaxis is CCL2 significantly higher compared to healthy controls (4-fold increase)



4. The ROC curve analysis showed AUC of 0.98



CONCLUSION

- We showed that in patients with clinical diagnosis of anaphylaxis there is a **significant increase in CCL2 serum levels**

- CCL2 measurement in sera could lead to an **improved ability** to confirm the clinical diagnosis of anaphylaxis

- … **work in progress** ☺
  - testing of „tryptase negative" group with clinical diagnosis of anaphylaxis
  - correlation with severity
  - testing of specificity (other ED patients, local allergic reactions etc)