ABSTRACTS

Friday, 12 April 2019
Oral Abstract Presentations

**O01 - Fluorescent Labelling Of Major Honeybee Allergens Api M 1 And Api M 2 With Quantum Dots And Development Of Multiplex Basophil Activation Test**

Ana Koren¹, Mojca Lunder², Peter Molek², Peter Kopac¹, Abida Zahirovic², Pia Gattinger³, Rudolf Valenta³, Irene Mittermann³, Peter Korosec¹

1. University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia
2. University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia
3. Medical University of Vienna, Department of Pathophysiology and Allergy Research, Vienna, Austria

**Background**

Api m 1 and Api m 2 are two major allergens of honeybee venom. Basophil activation test (BAT) is *in vitro* approach for evaluation of the biological relevance of IgE antibodies. Labelling of recombinant allergens with fluorescent probes could represent a new approach for multiplex assessment of allergenic activity with flow cytometry.

**Materials and methods**

nApi m 1 (Latoxan, France) and rApi m 2 (from Medical University of Vienna) were conjugated to Qdot® 705 or 800 ITK™ Amino (PEG) Quantum Dots and Qdot® 705 or 800 ITK™ Carboxyl Quantum Dots. IgE reactivity of Qdot-labelled allergens was assessed with immunodot assay using of rApi m1 or rApi m2 sIgE-positive sera of honeybee allergic patients. Allergic activity was assessed with BAT using CD123-PE/HLA-DR-APC/CD63-FITC labelled antibodies. Qdot 705 was measured with 670LP (exc. 488nm) and Qdot 800 was measured with 780/60 (exc. 488nm). Finally, usefulness of Qdot-labelled allergens for multiplex BAT analysis was tested in 12 bee venom-allergic patients and in 3 non-allergic controls. The stimulation of whole blood with amino Qdot 705-API m 1 and amino Qdot 800 API m 2 was done in separate tubes, then samples were merged, antibody labelled and analyzed as multiplex.

**Results**

Both Amino and Carboxyl Qdot-labelled nApi m 1 and rApi m2 showed positive and specific IgE reactivity evaluated with immunoblotting. We then tested weather Qdot labelled allergens are able to induce activation of the basophils in honeybee allergic patients. We demonstrated that only Amino but not Carboxyl Qdot-labelled nApi m 1 and rApi m 2 are able to activate basophils, suggesting that allergenic activity is preserved only in case of Amino Qdot-labelling. Furthermore, we showed that Qdot 705 Amino-labelled Api m 1 and Qdot 800 Amino-labelled Api m 2 could be used in multiplex analysis in which basophil subpopulations and their activations were
analysed according to the binding of fluorescent allergens. Multiplex BAT results were concordant with BAT result in 11/12 patients and 3/3 controls. Moreover, there were also comparable CD63 dose-response curves between labelled allergens used in multiplex approach and conventional BAT.

**Conclusion**
Quantum Dot labelling of allergens does not affect IgE reactivity; however IgE crosslinking and allergenic activity is preserved only in case of labelling with Amino (PEG) Qdot. Fluorescent labelling of venom components represents a new approach for multiplex BAT testing in *Hymenoptera* venom allergy.

**O02 - Pulling The Trigger In Clonal Mast Cell Disorders: Are Hymenoptera Stings The Only Actors?**

*Gustavo Jorge Molina Molina*, Paula Galván, Johana Gil Serrano, Jenny Tatiana Verdesoto, Moisés Labrador Horrillo, Anna Sala Cunill, Olga Luengo, Victoria Cardona, Mar Guilarte

Allergy Section. Department of Internal Medicine. Hospital Universitari Vall d’Hebron, Barcelona, Spain

**Background**
The implication of hymenoptera venom as a trigger of anaphylaxis in patients with clonal mast cells disorders (c-MCD) is well known. Currently, most anaphylaxis clinical guidelines recognize the need of assessing for an underlying c-MCD in case of hymenoptera sting and in idiopathic anaphylaxis but not so in case of other elicitors.

**OBJECTIVE:** To study the characteristics and triggers of anaphylaxis in patients with c-MCD, with special focus on hymenoptera sting anaphylaxis.

**Materials and methods**
Patients with a diagnosis of systemic c-MCD fulfilling the WHO 2016 criteria followed at our department from 2007 to 2018 were included. Anaphylactic reactions were carefully evaluated regarding their clinical characteristics, including triggers, severity of the reaction and skin involvement. Baseline serum tryptase (sBT) levels were recorded. The Spanish Network on Mastocytosis (REMA) score to assess the probability of systemic c-MCD (≥2) was performed. A subgroup of patients with hymenoptera sting anaphylaxis without c-MCD was selected as control group (H-A) and compared to those with hymenoptera sting anaphylaxis with c-MCD (H-SM).

**Results**
Data from 59 patients with a diagnosis of systemic c-MCD were collected. Anaphylaxis lead to c-MCD diagnosis in 26 patients (49%). The most frequent triggers were drugs (34.5%), hymenoptera stings (31%) and foods (15.5%). In 19% of patients no specific trigger could be identified (idiopathic). REMA score was ≥2 in 15/26 (58%) patients. The majority (67.5%) of H-SM developed a grade III anaphylaxis after hymenoptera sting compared to 50% of H-A. An inverse relationship between involvement of skin during anaphylaxis and having an underlying c-MCD was found (Fisher exact test 0.0012; p < 0.01). sBT was elevated (>11.4 mcg/dL) in 21/26 (81%) c-MCD patients. 3/5 patients with normal
sBT had as a trigger a hymenoptera sting, while 2/5 were idiopathic. In patients with drug or food induced anaphylaxis, c-MCD would have been missed in 50% of cases if sBT had not been assessed.

**Conclusion**
The absence of cutaneous manifestations during anaphylaxis due to hymenoptera sting is a sign suggestive of c-MCD. Moreover, sBT determination should be performed in all patients with an anaphylaxis, independently of the type of triggering agent in order not to miss mast-cell disorders.

**O03 - Mastocytosis And Anaphylaxis To Hymenoptera Venom: A Single Center Cohort Study**

Toon Ieven¹, Anne-Marie Kochuyt², Rik Schrijvers²⁻³, Dominique Bullens⁴⁻³, Christine Breynaert¹⁻³

1. University Hospitals Leuven, Department of Internal Medicine, Leuven, Belgium
2. University Hospitals Leuven, Department of General Internal Medicine (Allergy and Clinical Immunology), Leuven, Belgium
3. KU Leuven Department of Microbiology, Immunology and Transplantation, Allergy and Clinical Immunology Research Group, Leuven, Belgium
4. University Hospitals Leuven, Department of Pediatrics (Pediatric Allergology), Leuven, Belgium

**Background**
Patients with mastocytosis have an increased risk of severe anaphylaxis after hymenoptera stings.

**Materials and methods**
A retrospective analysis was performed on a cohort of patients with a diagnosis of mastocytosis from January 1990 to January 2018 in a single tertiary referral center. After informed consent, data were collected from the medical records on demographics, clinical history of anaphylaxis, sensitization to insect venom and venom immunotherapy (VIT).

**Results**
103 patients with a diagnosis of mastocytosis were included [female: n=52 (50.5%), age at time of inclusion: 28.9 years (7.4⁻53.0)]. 34/103 (33.0%) patients [3 cutaneous mastocytosis (CM)/31 systemic mastocytosis (SM)] indicated having been stung over the course of their lifetime. 6/34 patients (17.6%) experienced a large local reaction, 12/34 (38.2%) anaphylaxis and 15/34 (44.1%) no reaction. Of the 103 patients, n=29 [28.2%, serum basal tryptase (SBT) level 23.3 ng/ml (14.5⁻72.7)] had a history of anaphylaxis [indolent SM (ISM)/monoclonal mast cell activation syndrome (MMAS)/smouldering SM (SSM)/aggressive SM (ASM) respectively n=24/3/1/1]. 11/29 patients experienced anaphylaxis after a hymenoptera sting [hymenoptera venom allergy (HVA) group; MMAS/ISM without skin lesions (ISM⁻)/ISM with skin lesions (ISM⁺) respectively n=2/8/1, number of episodes 2 (1⁻3), age at first symptoms 42.1 years (38.4⁻55.1)]. 18/29 patients suffered anaphylaxis due to another cause [non-HVA group; number of episodes 2 (1⁻4), age at first symptoms 32.1 years (22.9⁻42.2; p=0.024 compared to the HVA...
group). In the HVA group, 3/11 had a positive major criterion for the diagnosis of SM vs. 14/18 in the non-HVA group (p=0.028). In contrast, c-kit D816V mutation was positive in 10/18 in the non-HVA group versus 10/10 in the HVA group (p=0.013). In the HVA group, anaphylaxis was the main symptom leading to the diagnosis of SM (11/11, 100%) vs. 8/18 (44.4%) in the non-HVA group (p<0.01). In the HVA group, 11/11 had documented hypotension after the sting, 9/11 loss of consciousness and 8/11 had no skin symptoms. All were started on VIT [yellow jacket venom (n=9), honeybee venom (n=1) or both (n=2)].

**Conclusion**
In our cohort, patients with mastocytosis suffering anaphylaxis after hymenoptera stings, had lower SBT levels, often lack typical skin lesions and rarely have the major bone marrow criterion for diagnosis of mastocytosis, compared to patients with mastocytosis and anaphylaxis due to another cause.

**Friday, 12 April 2019**
Poster Discussion Session
13:30 – 14:30

**P01 - Predictors Of Severe Anaphylactic Reactions In Patients With Hymenoptera Venom Allergy**

Maria Chapsa, Henriette Rönsch, Mathias Langner, Stefan Beissert, Andrea Bauer

Department of Dermatology, University Hospital Dresden, Dresden, Germany

**Background**
Severe anaphylaxis (SA) in hymenoptera venom allergy (HVA) has been associated with a number of risk factors. Baseline serum tryptase (BST), presence of mastocytosis and older age are well-established risk factors, whereas other factors including sex, personal health issues (comorbidities, concurrent medication) and anaphylaxis-associated findings (e.g. time interval between sting and onset of symptoms (TI), skin symptoms) have been also proposed to be taken into account for individual risk assessment. However, their impact on the severity of the anaphylactic reaction is poorly defined and discussed controversially. The aim of this study was to evaluate risk factors of SA due to hymenoptera field stings.

**Materials and methods**
A total of 500 patients, who referred to our department for the diagnosis of HVA over a period of 11 years (2007-2018), were included in this retrospective single-center observational cohort study.

**Results**
Six significant indicators and risk factors for SA were identified (P<0,05): short TI, absence of urticaria/angioedema (U/A) during anaphylaxis, older age, male sex, elevation of BST and diagnosis of indolent mastocytosis. Moreover, BST elevation was significantly related to the absence of U/A and to older age. No relationship could be established between SA and comorbidities, concurrent cardiovascular medication, concentration of venom-specific IgE, threshold of skin tests or the
severity of the systemic reaction during the buildup phase of venom immunotherapy (bpVIT).

**Conclusion**
Apart from BST and older age, male sex, short TI (<5min) and absence of U/A are also indicators of SA. Cardiovascular concomitant diseases in general are not correlated with the SA. Future studies should examine the association of specific severe cardiovascular diseases (e.g. coronary heart disease, cardiomyopathy) with SA. Moreover, absence of U/A after field sting in combination with elevated BST constitutes a highly significant indicator of SA, presumably because of the high risk of concurrent presence of an indolent mastocytosis. Finally, patients with a SA after field sting do not have an elevated risk for systemic reactions during the bpVIT in comparison to the patients with mild anaphylaxis and therefore, they do not require additional preventive measures.

**P02 - Systemic Mastocytosis In A 5 Year Old Child Presenting With Hypovolemic Shock, Succeeded By Severe Anaphylaxis To Fentanyl**

**Inger F Bocca-Tjeertes**, Hanneke N Oude Elberink, Bouwe Molenbuur, Aline B Sprikkelman

**UMCG, Groningen, The Netherlands**

**Background**
Mastocytosis is characterized by the clonal expansion and accumulation of mast cells (MCs) in different tissues and organs. In children, cutaneous mastocytosis, or typical maculopapular cutaneous lesions (TMCL/urticaria pigmentosa), is the most common form of mastocytosis, with a prevalence of 13 in 100,000, and resolution in many in puberty. Systemic mastocytosis (SM) is very rare in children. However, it is more likely in children with a persistent serum tryptase level of >20ng/mL, or those with symptoms of explosive diarrhea, syncope, as well as recurrent anaphylaxis reactions. Precautions are taken for procedural anesthetics if SM is suspected. In these cases, histamine releasing opioids, like morphine, are preferably replaced by fentanyl or any other synthetic opioid.

**Case report**
A 5 year old boy was referred to our hospital. At age six months, the patient was referred to a dermatologist for lesions on his forehead, consistent with TMCL, confirmed by a skin biopsy. During his entire life, he frequently suffered from diarrhea. At age three he was seen by a pediatrician for failure to thrive. At this point, serum tryptase was 42.6ng/mL. The consulted gastro-enterologist concluded there was no SM. Tryptase was 47.1ng/mL. At age five, the patient suffered from an anaphylactic shock following diarrhea for which he had to be resuscitated. During transfer to pediatric intensive care, morphine was administered intravenously, which triggered severe hypotension. Therefore, renewed intubation was performed using fentanyl provoking again severe hypotension. Tryptase rose to >200ng/mL. A few weeks later, without any complication, bone marrow biopsy (BMP) was performed under general anesthesia using propofol and ketamine after administration of H1 and H2-blockers intravenously. BMP revealed abnormal morphology of MCs (>25% spindle shaped), an activating mutation at codon 816 of
KIT, and the expression of CD25 in MCs, but no aggregates of >15 mast cells (major criterion). Hereby, meeting all minor criteria for SM. In follow-up the patient is doing well with H1 and H2-blockers combined with nalcrom.

Conclusion
SM should be considered in all children with a persistent serum tryptase >20ng/mL. In this case, severe delay was most likely due to lack of knowledge. Anaphylaxis to synthetic opioids is rarely seen, but possible and all anesthetics should be administered in a highly controlled setting in children with SM, preferably after premedication.

P03 - Insect-Venom Elicited Anaphylaxis, A Prospective Cohort Study From The European Anaphylaxis Registry.

Wojciech Francuzik¹, Sabine Dölle-Bierke¹, Franziska Ruëff², Claudia Pföhler³, Kathrin Scherer Hofmeier⁴, Margitta Worm¹

1. Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany
2. Department of Dermatology and Allergology, Klinikum der Universität München, München, Germany
3. Department of Dermatology, Saarland University Hospital, Homburg / Saar, Germany
4. Department of Dermatology, University Hospital Basel, Basel, Switzerland

Background
Insect-venom elicited anaphylaxis is a common hypersensitivity reaction which may be life-threatening.

Materials and methods
Using the data from the European Anaphylaxis Registry (11596 cases in total) we identified insect-venom elicited anaphylaxis cases (n = 4482) and analyzed these in comparison to anaphylaxis elicited by other elicitors (n = 7114).

Results
The data show that 68.57% of all insect elicited cases were elicited by yellow jackets, followed by bees (21.86%). The insect venom elicited cases occurred mostly in outdoor places (44.65%) patients' homes (12.87%) or urban places (9.616%). Skin, gastrointestinal and respiratory symptoms occurred less frequently in insect elicited cases of anaphylaxis, whereas cardiologic symptoms (with hypotension, collapse, and loss of consciousness) were more frequent. Intramuscular adrenaline (as a first-line therapy) was administered significantly less often in insect venom elicited cases (4.04%, p < 0.0001). The mortality rate in insect anaphylaxis was comparable (0.156%) to other cases (0.295%, p = 0.174). Patients who experienced insect-venom anaphylaxis were older (p < 0.0001), more often had concomitant mastocytosis (p < 0.0001) and cardiologic conditions (p < 0.0001) and females more often had concomitant thyroid diseases and less often suffered from a food allergy or atopic dermatitis.
Conclusion
Symptoms of insect venom anaphylaxis are distinctively different from other
reactions, indicating that the therapy of insect elicited cases of anaphylaxis should
be considered separately. Indeed we observed different therapeutic patterns in
insect elicited cases of anaphylaxis (more antihistaminics but fewer corticosteroids,
bronchodilators, and surprisingly - adrenaline). This indicates that the management
of insect-venom induced anaphylaxis may be improved and is especially required in
patients with concomitant cardiologic conditions and these with hyperreactive mast
cells.

15 P04 - Do We Need Premedication With Omalizumab In Patients With
Systemic Mastocytosis Having Venom Immunotherapy?
Osman Ozan Yegit¹, Semra Demir¹, Derya Unal², Bahauddin Colakoglu¹, Suna
Buyukozturk¹, Asli Gelincik¹

1. Istanbul University, Istanbul Faculty of Medicine, Department of Internal
Medicine, Division of Immunology and Allergic Diseases, Istanbul, Turkey
2. Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital,
Immunology and Allergic Disease Clinic, Istanbul, Turkey

Background
In systemic mastocytosis (SM) insect stings are one of the most important causes
of anaphylaxis. Recent literature presented that the use of omalizumab as a
premedication may decrease adverse effects occurred during venom
immunotherapy (VIT) although consensus statement is needed.

Materials and methods
In this case series, we reported demographic and clinical characteristics of 9
patients diagnosed as SM and Hymenoptera venom allergy and presented seven VIT
receiving patients with or without omalizumab premedication.

Results
4 patients were female (44.4%) and the mean age was 49.6±10.7 years. Bone
marrow biopsies of all patients were compatible with SM. The median tryptase level
was 25.8 µg/L (16-150) and c-Kit D816V mutation was positive in 8 patients.
Culprit insect types in the history were bee, wasp and both in 5, 1 and 2 patients,
respectively and one patient was unaware of the insect type. All patients had grade
4 systemic reactions. Seven patients underwent VIT (4 for bee, 1 for wasp and 2
for both venoms) and two patients refused to receive VIT. Four patients received
monthly 150 mg of omalizumab three months before VIT and during the updosing
period while in 3 patients VIT started without omalizumab. Among the patients who
received omalizumab, one patient (Patient no:7) experienced anaphylaxis during
skin prick tests and the other (Patient no:6) during the first dose of VIT and both
had to receive adrenaline (Table 1). Therefore, VIT was postponed and three doses
of omalizumab was administered prior VIT in patient no 6. The other two patients
were diagnosed as mastocytosis prior to VIT and therefore received omalizumab.
The remaining three patients were diagnosed as mastocytosis after the updosing
period of VIT and did not receive omalizumab and had no reactions during VIT. Six
patients received clustered schema in updosing and one patient had conventional
VIT (Patient no:6). In one patient (Patient no:6) who was pretreated with
omalizumab before VIT, a grade 4 reaction occurred in the 6th week of VIT.
However, in the 3rd year of treatment a trouble-free bee sting was witnessed.

**Conclusion**

Omalizumab may be considered as a premedication in patients who experience reactions during skin tests and VIT but systemic reaction may develop in patients under omalizumab premedication and precaution should be considered during VIT in every systemic mastocytosis patient.

**Characteristics of the patient**

<table>
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<th>No of patients</th>
<th>Age</th>
<th>Gender</th>
<th>Types of venom in history</th>
<th>Grade of reactions in history</th>
<th>VIT</th>
<th>Side effects during VIT</th>
<th>Prick tests</th>
<th>Total IgE kU/L</th>
<th>Specific IgE kU/L</th>
<th>Tryptase µg/L</th>
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<td>Wasp:0,04</td>
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<td>24</td>
<td>+</td>
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<td>-</td>
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<td>Bee + Wasp +</td>
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P05 - Omalizumab In Immunotherapy With Hymenoptera Venom

Cristiana Ferreira, Patricia Barreira, Joana Lopes, Jose P. Moreira Da Silva, Ines Lopes

Centro Hospitalar Vila Nova de Gaia-Espinho, Vila Nova De Gaia, Portugal

Background
Specific immunotherapy (VIT) is the established therapeutic option in patients who experience allergic reactions due to hymenoptera stings. Sistemic reactions may occur with VIT, preventing its progression. Omalizumab (OMZ) can be used in combination with VIT, in order to prevent systemic adverse reactions.

Materials and methods
We report 4 successful cases of tolerance to bee VIT after pre and concomitant treatment with OMZ.

Results
All patients are beekeepers, had normal basal tryptase levels, started VIT using an ultrarush schedule with antihistamine pre-treatment and had severe systemic reactions during VIT. The first case is a 43-year-old female, healthy, with a history of a grade II reaction according to Mueller's classification; the second and third patients are first patient’s children: a 16 year-old male and a 19 year-old female, both healthy, that experienced a grade IV and III reaction; the fourth patient is a 33-year-old male, with hypertension under Irbesartan and had a history of a grade III reaction. Omalizumab doses were calculated based on weight and total IgE level. In the first two patients, OMZ was initiated 1 week before VIT in the first administration and 1 hour before in the subsequent ones. In patient 3, OMZ was administrated every 2 weeks during 2 months (1 week before first VIT´s administration) and was maintained 1 week before subsequent ones. In patient 4, OMZ was administrated 1 week before every VIT administrations. These approaches were applied for 6 months. In all patients, VIT tolerance to 100µg was accomplished and no severe systemic reactions occurred after several months of OMZ discontinuation. Patient 3 just recently initiated VIT administration without OMZ and more time is needed to evaluate the result. We started the first administration of pre-treatment with OMZ in a fifth patient: a 39-year-old female, beekeeper, healthy, with a history of a grade III reaction who also developed an anaphilaxis reaction with VIT ultrarush.
Conclusion
Omalizumab seems to be a secure and effective option for those patients who do not tolerate VIT. More studies are needed to establish doses, frequency and duration of treatment.

P06 - Evaluation Of Systemic Mastocytosis With 3 Cases

Nilay Orak Akbay¹, Hakan Yesil¹, Atilla Uslu², Günsah Kaygusuz³, Selami Koçak Toprak², Aylin Okçu Heper³, Günhan Gürman², Yavuz Selim Demirel¹, Betül Ayse Sin¹

1. Ankara University, School of Medicine, Department of Pulmonary Diseases, Division of Immunology and Allergy, Ankara, Turkey
2. Ankara University, School of Medicine, Department of Hematology, Ankara, Turkey
3. Ankara University, School of Medicine, Department of Pathology, Ankara, Turkey

Background
Systemic mastocytosis (SM) is a heterogeneous disease which is characterized by the abnormal proliferation of mast cells. It can be divided into various subtypes and phenotypes with different prognoses. Systemic mast cell activation results with anaphylaxis in these patients. Here, we report the clinical characteristics of three SM patients, presenting with anaphylaxis.

Case report
Case 1 was a 40 years old man who was referred to our clinic due to 10 years old history of flushing episodes. The episodes are characterized with generalized redness of the body, headache, weakness, and the last episode was accompanied by syncope. Tryptase level was elevated to 23.8 ng/ml (normal <11.5 ng/ml). KITD816V mutation was identified in blood sample. The bone marrow biopsy was hypercellular, and focal paratrabecular infiltration of atypical mast cells was seen. Case 2 and case 3 (female-35 yo, and female-56 yo) had anaphylaxies several times in their history, without describing any particular trigger. Case 3 physical examination revealed macular pigmented lesions distributed mainly on the trunk. Serum basal tryptase levels were 38.2 ng/ml and 191 ng/ml, respectively. Skin biopsy was reported as cutaneous mastocytosis for the latter one. Hepatosplenomegaly was detected in case 3. The average time to diagnosis for the patients were average two years.

Conclusion
SM includes a wide spectrum of signs and symptoms and atypical presentation can delay the diagnosis substantially. Skin involvement, anaphylaxis attacks and unexplained osteoporosis should alert physician for mastocytosis. A normal serum tryptase does not exclude the diagnosis of SM and it should be considered in the differential diagnosis of patients presenting with recurrent anaphylaxis without a clear cause.
P07 - Risk Factors In Hymenoptera Venom Allergy

Svetlana Shvets, Natalia Ilyna

National Research Center – Institute of Immunology Federal Medical-Biological Agency of Russia., Moscow, Russia

Background
Increased serum tryptase and/or mastocytosis has been linked to the severity of the reaction after Hymenoptera stings. The aim of the study was to analyse Hymenoptera venom-allergic patients with regard to basal tryptase relation to the severity of sting reactions. Mastocytosis and/or elevated basal serum tryptase may be associated with severe anaphylaxis.

Materials and methods
Of the 93 patients included in this study (Group A), 34 were allergic to Bee venom (BV) and 59 were allergic to Vespula venom (VV) (Table 1). All patients gave a history of systemic allergic reactions to Hymenoptera stings. Based on clinical symptoms, the reactions of the patients were divided into 4 grades of severity according to Mueller classification. Basal serum tryptase was measured in all patients (34 Honey Bee, 59 Vespula). Levels of the mast cell-specific enzyme tryptase and of venom-specific IgE (sIgE) were estimated by ImmunoCAP.

Results
Basal serum tryptase levels were elevated in 16 (17.2%) of the 93 patients. Evidence of cutaneous mastocytosis as documented by skin biopsy was present in 3 of 16 patients (18.8%) – all with a history of severe shock reactions. All patients with elevated tryptase had a history of severe systemic allergic reactions to Hymenoptera stings; no significant correlation, however, between basal serum tryptase and sting reaction severity was observed (r = 0.174; p = 0.099). There was a correlation of the grade of the initial allergic reaction and venom-specific IgE to Bee venom (r= 0.296, p=0.0114), but not Vespula venom (r=0.063, p=0.562).

Conclusion
These results corroborate the elevation of basal serum tryptase as well as mastocytosis as the risk factors for severe or even fatal shock reactions to Hymenoptera stings. Although the efficacy of venom immunotherapy in these patients is slightly reduced, most of them can be treated successfully. Based on currently available data, lifelong venom immunotherapy treatment for these patients is typically considered.

Demographic, clinical and laboratory data on 93 Hymenoptera venom-allergic patients.

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Allergic to Bee venom (n=34)</th>
<th>Allergic to Vespula venom (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>18/16</td>
<td>26/33</td>
</tr>
<tr>
<td>Grade of reaction</td>
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P08 - Contribution Of Component Resolved Diagnosis In Hymenoptera Venom Allergy

Ayse Engin¹, Betul Oktelik¹, Asli Gelincik², Aytul Sin³, Betul Sin⁴, Adile Berna Dursun⁵, Sengul Beyaz², Begum Gorgulu⁴, Esin Cetin¹, Gunnur Deniz¹

1. Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Immunology, Istanbul, Turkey
2. Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Immunology and Allergic Diseases, Istanbul, Turkey
3. Ege University, Faculty of Medicine, Department of Internal Medicine, Division of Immunology and Allergic Diseases, Izmir, Turkey
4. Ankara University, Faculty of Medicine, Department of Internal Medicine, Division of Immunology and Allergic Diseases, Ankara, Turkey
5. Recep Tayyip Erdogan University Faculty of Medicine, Training and Research Hospital, Department of Immunology and Allergy Diseases, Rize, Turkey

Background
In Hymenoptera venom allergy, difficulties in diagnosis can be seen in daily life practice and new practical diagnostic methods seems to be promising. In this study, the contribution of component resolved diagnostics (CRD) were evaluated in patients who had a systemic reaction due to a Hymenoptera.

Materials and methods
81 patients from four different centers were included in the study. Prick, intradermal skin test with venom extracts were performed and serum specific IgE levels for whole venoms were measured. sIgEs for Api m1, Api m2, Api m10, Ves v1 and Ves v5 were also evaluated (Euroline DPA-Dx Venom kit 2, Euroimmun, Lubeck, Germany).

Results
Seventeen out of 33 patients with bee venom allergy revealed a positive skin test result and/or a high sIgE level to honeybee venom whereas 16 patients had positivity with both venoms. In 11 out of 17 patients with bee venom allergy, the diagnosis was confirmed with CRD whereas CRD was negative in the remaining 6 patients. In 13 of the bee allergic patients with double positivity to both venoms (13/16), double sensitivity was confirmed with CRD. CRD revealed a sensitivity of 73% in bee venom allergic patients. Seven of 18 patients with wasp venom allergy demonstrated sensitivity only to Vespula spp according to skin tests and/or sIgE levels whereas 11 patients revealed double positivity. Total sensitivity of Ves v1 and Ves v5 was calculated as 88%. Eight of 20 patients with a history of hypersensitivity to both venoms showed double sensitivity with CRD, one patient...
revealed cross-reactivity, seven patients was found sensitive only to bee venom, and finally one patient was sensitive only to Vespula spp. 10 patients were uncertain for the culprit insect type, half of them had double sensitivity and one had cross-reactivity according to CRD.

**Conclusion**
CRD seems to be more helpful in diagnosing wasp venom allergy than bee venom allergy. It is also promising to differentiate double sensitivity from cross-reactivity and it is valuable in cases where the culprit insect is unknown.

**P09 – SENSITIZATION TO BEE VENOM IN NON-ALLERGIC BEEKEEPERS**

Ana Margarida Mesquita, Ricardo Coutinho, Luís Amaral, José Luís Plácido, Alice Coimbra

Centro Hospitalar de São João, Serviço de Imunoalergologia, E.P.E., Porto, Portugal

**Background**
Hymenoptera venom allergy is a major cause of anaphylaxis and beekeepers are at particular risk.

OBJECTIVE: To evaluate sensitization to bee venom in beekeepers without any history of systemic reactions to bee stings.

**Materials and methods**
This cross-sectional study used a questionnaire, skin prick tests (SPT) with common aeroallergens and intradermal tests (IDT) with bee venom (0.1 and 1 mg/mL) on beekeepers who volunteered to participate during a beekeeping meeting. Written informed consent was obtained.

**Results**
A total of 64 beekeepers without any systemic reactions to bee stings agreed to participate; 52 (81%) males with median age of 46 (±15) years. Four (6%) reported asthma and 9 (14%) rhinitis. Duration of beekeeping activity was as follows: 5 (8%) under 1 year, 10 (16%) 1 to 2 years, 18 (28%) 2-5 years, 13 (20%) 5-10 years and 18 (28%) longer than 10 years.

Of the total, 38 (59%) had positive IDT. In beekeepers under 1 year, 3 (60 %) had positive IDT and in those longer than 10 years, 9 (50%) had positive IDTs. In this group, there was no significant association between the estimated mean annual number of stings and sensitization to bee venom.

The beekeepers who wore totally protective suits had less sensitization to bee venom (p=0.011). Individuals with more years of beekeeping had a higher number of positive IDT with 0.1 mg/mL (p <0.05). In addition, sensitization to cultivated grass pollen and wild grass pollen was associated with a higher number of positive IDT with 0.1 mg/mL and 1 mg/mL (p=0.001; p=0.048; p=0.007; p=0.028).

**Conclusion**
In this group, 59% of the beekeepers were found to be sensitized to bee venom. This is possibly due to the greater exposure to stings. We would infer this could occur with greater number of stings, when no protective suit is worn and a longer period of beekeeping. Regular exposure to bee venom in these individuals may
confer greater tolerance and thus reduce the risk of systemic allergic reactions due to stings. More extensive studies with larger samples and follow-up may help to clarify these issues.

**P10 - MOLECULAR DIAGNOSIS AND BEYOND UNMET NEEDS IN RUSH IMMUNOTHERAPY FOR HYMENOPTERA VENOM- SINGLE CENTER EXPERIENCE IN ALBANIA**

Mehmet Hoxha, Eralda Lekli, Erina Lazeri, Arieta Sherri

UHC Mother Theresa, Tirana, Albania

**Background**

Component resolved diagnosis (CRD) as a novel tool is helping in providing correct selection of venom immunotherapy treatment (VIT) formulations and monitoring of such lifesaving treatment. Despite significant number of patients requiring emergency care due to hymenoptera sting allergy in Albania, few undergone VIT. This is first study performed in Albania since CRD availability which limitations mainly include diagnosis and treatment related cost.

**Materials and methods**

Retrospective analytical-descriptive study providing data from patients records treated with VIT at the Allergology Service at Mother Theresa UHC, Tirana.

**Results:** 25 cases (56% male), mean age 37.83 years (SD ± 16.52) received VIT for APIS 21 (84%), Vespu 3 (12%); Polister 1 (4%). IDR (Intra Dermal Reaction) sensitization at concentration 0.1 mcg/ml showed Apis 84%, Ves 16% and Pol 12%. CRD performed incidences of sensitization for antigens were: honeybee i1-75%; rApi m1-25%; rApi m2-33,3%; rApi m10-41,7%; common vasp i3-58,3%; rVes v1- 25%; rVes v5-58,3%. CDD was positive in 25% of cases indicating cross reactivity. Previous VIT patients had an average of 2.69 episodes of generalized systemic reactions (SR) classified according Mueller grading system: 44% - grade 4; 40% - Grade 3; 16% Grade 2. In 12(48%) SR happened on initial phase of VIT; 58% (Mueller Grade 3-4); 5 (20%) had SR during maintenance phase of VIT (dose I-VIII) with 3 cases of anaphylaxis. Natural sting challenge during VIT happened in 20% cases resulting in SRs 1-grade Mueller lower than prior VIT initiation. There was no statistically significant correlation (p> 0.05) between Mueller grading of SR and size of papules/ erythema in IDR test).

**Conclusion**

Our experience with the molecular components of the hymenoptera venom has been limited, but remains a key to successful treatment and follow-up for VIT. Fully reimbursement of molecular diagnosis and VIT treatment in near future will help decreasing burden of venom allergy disease and improvement in patients quality of life in Albania.
P11 - Contribution Of Molecular Diagnosis Of Bee Venom Allergic Patients With Systemic Reactions During Venom Immunotherapy

Tatiana Lourenço1,2, Mara Fernandes1,3, Anabela Lopes1, Elisa Pedro1, Manuel Pereira Barbosa1,4, M.Conceição Pereira Santos2,4

1. Serviço de Imunoalergologia, Hospital Santa Maria - Centro Hospitalar Lisboa Norte, Lisboa, Portugal
2. Laboratório de Imunologia Clínica, Faculdade de Medicina/ Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal
3. Unidade de Imunoalergologia, Hospital Dr. Nélvio Mendonça, SESARAM, EPE, Funchal, Funchal, Portugal
4. Clínica Universitária de Imunoalergologia - Faculdade de Medicina, Universidade Lisboa, Lisboa, Portugal

Background
Bee venom (BV) allergy is one of the most common causes of severe anaphylaxis in adults. Venom immunotherapy (VIT) is considered the most effective treatment, but systemic reactions (SR) can occur during it. Molecular diagnosis can improve diagnostic accuracy, but no correlation was identified with SR during VIT. **Aim:** Characterize the sensitization profile by molecular components of pts with anaphylactic reactions to BV under VIT and investigate if SR during VIT are related to different patterns of sensitization.

Materials and methods
Prospective study including 30 pts under VIT for at least 1 year. We considered a group of pts reacting during the ultra-rush (Group A) that was compared with the group with no reactions (Group B). Serum specific IgE (sIgE) for BV (i1) and recombinants: rApi m1, rApi m2, rApi m3, rApi m5 and rApi m10 were evaluated before and after 1 year of VIT by ImmunoCAP (Termofisher Scientific, Uppsala, Sweden). A value>0.35kUA/l was considered positive. All statistical tests were performed with Graph-Pad Prism v5.01.

Results
80%-male, mean age-45 years old (14-70). Group A -10 pts; Group B-20 pts. 4 pts (2 -group A and 2-group B) were drop out during first year of VIT. Before VIT, sIgE to rApi m1 was detected in 86.7%, rApi m2-46.7%, rApi m3-16.7%, rApi m5-43.3% and rApi m10-70%. Positive results to at least one bee venom allergen were detected in 100%. 80% of pts were sensitized to >1 allergen and 13.3% to all allergens. Characterization profile of both groups - median and interquartile range (IQR25/75) before and 1 year after VIT are represented in table 1. There was no statistically significant differences in the profile of both groups before VIT, however we found a significant decrease: p=0.045, p=0.017, p=0.021 to i1, Api m3, Api m10 respectively, in group B 1 year after VIT.

Conclusion
These data showed that 1 year after VIT there was a significant decrease of Api m3 and Api m10 in pts without reactions during VIT, however there was not found association between pts with SR during VIT and there sensitization profile. Nevertheless is important to study a greater number of pts.
### Table 1. Characterization of sensitization profile of group A and B before and 1 year after VIT (\(^{+}\) before VIT; \(*\) 1 year after VIT)

<table>
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<tr>
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<th>Group A</th>
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<tr>
<td></td>
<td>Median(^{+}) IQR25/75(^{+})</td>
<td>Median(^{+}) IQR25/75(^{+})</td>
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<td>Median(^{+}) IQR25/75(^{+})</td>
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<tr>
<td>i1</td>
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<td>2.52/26.68</td>
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<td>0.02/1.14</td>
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<td>rApi m5</td>
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<tr>
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<td>0.20/2.80</td>
<td>1.116</td>
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P12 - OMALIZUMAB IN IMMUNOTHERAPY WITH HYMENOPTERA VENOM-CASE REPORT

Mara Fernandes\(^{1,2}\), Tatiana Lourenço\(^{1}\), Anabela Lopes\(^{1}\), Joana Caiado\(^{1}\), Ana Mendes\(^{1}\), Elisa Pedro\(^{1}\), Manuel Pereira Barbosa\(^{1,3}\)

1. Serviço de Imunoalergologia, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal
2. Unidade de Imunoalergologia, Hospital Dr. Nélio Mendonça, SESARAM, EPE, Funchal, Portugal
3. Clínica Universitária de Imunoalergologia, Faculdade Medicina da Universidade de Lisboa, Lisboa, Portugal

**Background**

In Europe the prevalence of systemic reactions with hymenoptera sting varies between 0.3-7.5\%, being higher in beekeepers. Hymenoptera venom immunotherapy (VIT) provides protection in 80-100\% of the cases. Allergic reactions may occur with VIT especially during the initiation with ultra-rush, preventing its progression. Omalizumab can be used in combination with ITV, in order to reduce allergic reactions.

**Materials and methods**

A 53-year-old man, beekeeper in his free time, goes to the emergency room with nasal obstruction, rhinorrhea, dyspnea and facial erythema beginning 10 minutes (min) after a bee sting on the right index finger. At the emergency room, 3 hours after the sting, he was hemodynamically stable, eupneic, without bronchospasm, with nasal obstruction and facial erythema. He was treated with systemic steroids, clemastine, and ranitidine, with improvement. The tryptase was 16.6 ug/L.
Immunoallergology workup revealed bee venom specific IgE > 100 kUA/l and positive intradermal skin test for bee venom extract at concentration of 0.01 µg/mL. Bee venom ultra-rush was started with pretreatment with clemastine and montelukast but it was interrupted by anaphylactic reaction 30 min after administration of 10 µg of bee venom. He was treated with made adrenaline, methylprednisolone and bronchodilators, with improvement. He repeated new ultra-rush with pretreatment with montelukast and antihistamine for 15 days and had a new reaction 30 min after administration of 10 µg of venom: erythema on the face and neck, that regressed after corticosteroid and ranitidine ev. On the same day he repeated the administration of 10 µg, with reappearance of skin complaints and edema of the uvula on observation. He made hydrocortisone, ranitidine and aminocaproic acid ev, with improvement. A new ultra-rush was performed under omalizumab, maintaining antihistamine and daily montelukast. Initially, he did 2 administrations of omalizumab, 7 days and 1 hour before the ultrarush, with onset of erythema of the face and nasal obstruction. He subsequently performed 4 doses of 300 mg omalizumab with a 15-day interval. On the 7th day he restarted ultra-rush with good tolerance.

Conclusion
Omalizumab has been used in association with IT in the control of allergic reactions with good results. The authors describe a clinical case in which the use of omalizumab successfully allowed the progression of ultra-rush with hymenoptera venom.

P13 - Precision Medicine And The Tryptase Framework Of Wasp Venom IgE-Sensitization In Mastocytosis

Douwe De Boer¹, Marjan C. Slot², Huub P. Willems³, Judith A. Bons¹, Chris M. Nieuwhof²

1. Maastricht University Medical Center+, Central Diagnostic Laboratory, Maastricht, The Netherlands
2. Maastricht University Medical Center+, Department of Internal Medicine, Immunology and Allergology, Maastricht, The Netherlands
3. Máxima Medical Center, Department of Internal Medicine, Eindhoven, The Netherlands

Background
Mastocytosis patients are at high risk if they are IgE-sensitized to insect venom, while tryptase measurements are very useful or even required to perform a clinical follow-up of both the status of mastocytosis and anaphylaxis. One of the challenges is to distinguish a chronically elevated tryptase level (TL evl) due to mastocytosis from an anaphylactic TL evl. As a decreased tryptase level (TL dcr) below the basal level (TL bas) may follow an anaphylactic TL evl and the long-term TL bas may vary in time, the challenge is to distinguish a TL evl and TL dcr from the TL bas. The goal of this study is to establish the TL bas and the individually biological variation (CVi) of tryptase in mastocytosis patients as well as to identify abnormal tryptase fluctuations in general and the provoking IgE-sensitization in particular.

Materials and methods
Tryptase data of mastocytosis patients, which were obtained routinely for their
follow-up, were collected retrospectively and included if > 6 data points were available. Iterative polynomial regression fitted the patients’ data points in a model, each time adjusted after outlier exclusion. Outlier exclusion was based on using the Median Absolute Deviation set at 4.5. Using the model, the combined total correlation of variation (CVt) of the CVs of each observed data point was calculated. The analytical CV (CVa) was set at 5.7% and the unforeseen CV (CVu) at 0%. The CVi was defined as CVi = square root of [(CVt)² – (CVa)² – (CVu)²]. All tryptase measurements and those for IgE sensitizations were performed by the ImmunoCAP assay.

Results
Median number of datapoints per patient was 10 and the period of follow-up 7.1 yr. The range of CVi of the mastocytosis patients (n = 47) was 0.6-16.6% (95% CI 4.9-6.9%; median 5.1%). Although the CVi was stable and small in general, the range within the group was broad and abnormally distributed; As in some patients the TL bas significantly varied in time also, the use of a grouped TL bas and CVi was not justified. Personalized TL bas and CVi were needed to recognize abnormal fluctuations. Based on outlier calculation single or multiple abnormal fluctuations were identified in 13 patients, which at least in one case could be attributed to wasp venom IgE-sensitization.

Conclusion
Personalized TL bas and CVi are required to recognize abnormal fluctuations in tryptase levels. Therefore, precision medicine should be part of the tryptase framework in mastocytosis in general and of IgE-sensitization in mastocytosis in particular.

P14 - Soluble FcεRI Is A Potential Biomarker Of IgE Mast Cell Desensitization During Chemotherapy Treatment Of Allergic Cancer Patients

Sherezade Moñino Romero1,2, Leticia De Las Vecillas Sánchez3,4, Leila A Alenazy4, Marina Labella4, Zsolt Szépfalusi1, Edda Fiebiger2,5, Mariana C Castells4,5

1. Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria
2. Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, United States
3. Department of Allergy, Marqués de Valdecilla University Hospital-Instituto de Investigación Marques de Valdecilla, Santander, Spain
4. Division of Rheumatology, Immunology, and Allergy, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, United States
5. Department of Medicine, Harvard Medical School, Boston, United States

Background
IgE-desensitization to chemotherapy in allergic cancer patients inhibits mast cell (MC) activation and protects against anaphylaxis in a high proportion of patients but no biomarkers exist to predict at risk candidates and there is little understanding of the events leading to successful desensitizations. A soluble isoform of the high affinity IgE receptor (sFcεRI) has been identified in atopic
individuals and its role is thought to protect against anaphylaxis, and it is not
known whether sFcεRI could modulate the desensitization process. We sought to
understand the effect of desensitization on sFcεRI production in vitro and monitor
serum sFcεRI titers in vivo in cancer desensitized patients.

Materials and methods
Murine MCs expressing the human IgE-binding FcεRIα were sensitized with serum
from platin allergic patients and stimulated with anti-human IgE. β-hexosaminidase
and sFcεRI were measured after activation and desensitization. Ovarian and colon
cancer patients (n= 14) with severe allergic reactions to oxaliplatin and carboplatin
were evaluated at the time of rapid desensitization and serum sFcεRI, IgE, and
tryptase titers were measured before and after desensitization.

Results
Desensitization significantly inhibited β-hexosaminidase release and sFcεRI
production in humanized MCs, in contrast to activation. Two groups of patients were
identified based on their baseline sFcεRI titers. Patients with sFcεRI titers > 2
ng/mL (n= 5) presented increased sFcεRI and IgE titers, and a significant decrease
in tryptase levels following successful desensitization. In contrast, patients (n=9)
with sFcεRI titers < 2 ng/mL showed increased IgE and tryptase levels, whereas
sFcεRI remained unchanged. One patient reacted during desensitization in that
group.

Conclusion
Desensitization inhibited sFcεRI production in humanized mast cells in vitro, which
correlated with inhibition of β-hexosaminidase release, providing novel insight into
the mechanism of IgE-desensitization. In cancer desensitized patients higher serum
sFcεRI was associated with decreased tryptase and protection from allergic
reactions. Measurement of sFcεRI may provide a new biomarker of protection
against drug-induced reactions during desensitization.

P15 - The Need Of Bee Venom Immunotherapy Reintroduction Due To
Unsuccessful 5-Year-Lasting Treatment In Adolescent Boy

Ewa Cichocka-Jarosz, Urszula Jedynak-Wasowicz, Beata Kusak, Grzegorz Lis

Department of Pediatrics, Jagiellonian University Medical College, Krakow, Poland

Background
Venom immunotherapy (VIT) in children rarely requires reintroduction.

Case report
The 12-years-old boy was accepted for the reintroduction of bee venom
immunotherapy (B-VIT). In the past, due to anaphylactic shock after bee sting in V
2011, he was treated according to the guidelines with B-VIT (Pharmalgen for 1-
year, next Alutard) from March 2012 to October 2017. In the course of B-VIT in I-V
2017 large local reactions (LLR) and late mild systemic reactions due to venom
injections were observed, while natural four subsequent bee stings were tolerated
well. After detailed work-up, in June 2017, Giardia lamblia infestation was
diagnosed and treated with metronidazole with recovery. Within further course of
VIT till October 2017 he tolerated well both subsequent venom injections, and three
natural field stings. After 5 years of treatment, in October 2017, we decided to stop B-VIT. In 2018 he was stung three times by bee: in V and in VII in thumb with the normal reaction, without necessity of symptomatic treatment. For the third time he was stung by bee in the left cheek in VIII 2018. Fifteen minutes later, despite taking immediately oral antihistamine and glucocorticosteroid, he presented with vomiting, general urticaria, somnolescence. In GP office massive urticaria, facial edema, dysartia, BP 100/60, HR 50/min, exacerbated vesicular sound over the lungs were observed. He was given dexamethasone, phenazolinum iv. Ambulance staff found RR 16, BP 90/60 (regularly 100/60), HR 80/min, Sat 99%, normal vesicular sound; they refused to transport the boy to the hospital. Patient stayed under GP’s supervision for three hours, and then he was transported by parents to the clinic. At the admission he presented well, with normal vital signs and parameters. Only oral antihistamines were ordered. Since that time he was not stung by bee. There are still bee-hives in the house vicinity. In subsequent diagnostics in August 2018 laboratory results were as follows: 1. sIgE to: BV extract 24.1 kU/l, Api m 1 7.75 kU/l, Api m 10 12.1 kU/l, 2. baseline serum trypase 4.79 kU/l. In November 2018 he restarted B-VIT with Pharmalgen given as ultrarush protocol by Birnbaum. At the dose of 30 mcg (cumulative dose 61 mcg) he reacted with general urticaria and pruritus, with no other general symptoms. Double dose of cetirizine and one dose of dexamethasone i.m. were introduced.

**Conclusion**
Now, B-VIT is continued according to cluster protocol with up-dosing of 10-20 mcg every two weeks to achieve maintenance dose of 150 mcg. No immediate or late reactions were observed, though each medical visit is stressful for the patient.

**P16 - Multicenter Study Of Clinical Relevance Of Recombinant Allergen Api M 1 And Ves V 5 Determined By IgE Multiplex Test ImmunoCAP ISAC**

**Urska Bidovec-Stojkovic**, Martina Vachova, Mira Silar, Ziga Kosnik, Mitja Kosnik, Petr Panzner, Jasna Volfand, Matjaz Homsk, Vojko Berce, Peter Korosec

1. University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia
2. Department of Immunology and Allergology, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic
3. Diagnostic Centre Bled, Bled, Slovenia
4. Private Pediatric Practice, Lenart, Slovenia
5. University Medical Centre Maribor, Maribor, Slovenia

**Background**
ImmunoCAP ISAC (ISAC) is an advanced diagnostic tool for the assessment of complex cases. Two major venom components honeybee rApi m1 and yellow jacket rVes v5 are also included on this microarray. We evaluated ISAC results for those two components and its possible clinical relevance.

**Materials and methods**
Specific IgE to rApi m1 and rVes v5 were analyzed in all subjects, which were routinely tested with ISAC from 2012 to 2017 at University Clinic Golnik, Slovenia or at Faculty of Medicine Plzen, Czech Republic. Results were compared with singleplex ImmunoCAP (CAP) assay and evaluated weather they are clinically
Results
Positive results for rApi m1 and/or rVes v5 were observed in 342 (11.4%) out of 3001 ISAC tested subjects. 232 (67.8%) of 342 subjects were sensitized for rVes v5, 83 (24.3%) for rApi m1 and 27 (7.9%) for both allergens. Positive ISAC results from 93 (27.2%) subjects were clinically evaluated and compared with CAP. Honeybee venom allergy was confirmed in 5.4% (5/93) subjects, yellow jacket venom allergy in 23.7% (22/93), and both in one subject. Twelve of those patients (43%) experienced anaphylactic reactions while 16 (57%) had large local reaction. Concordance between ISAC and CAP results was 90.3% (84/93) for rApi m1 and 97.8% (91/93) for rVes v5. Discordance for rApi m1 was present in 9 subjects; 8 were negative with ISAC, but positive with CAP, one was positive with ISAC, but negative with CAP. Discordance for rVes v5 was demonstrated only in 2 subjects; in both ISAC was positive and CAP negative. There was a significant correlation between semi-quantitative ISAC and quantitative CAP measurements, both for rApi m1 (R=0.79, p<0.0001) and rVes v5 (R=0.69, p<0.0001).

Conclusion
In ISAC microarray, positive rApi m1 and rVes v5 results are frequent, reaching approximately 10-15% in the Middle Europe geographic region. The results were confirmed with standard CAP assay, both according to the positivity/negativity and semi-quantitative/quantitative levels, with higher matching for rVes v5 than for rApi m1. The sensitization was relevant in one third of the subjects (half with anaphylactic sting reactions), what obviously suggests that every positive subject should be clinically evaluated.

P17 - Systemic Mastocytosis With Low Serum Tryptase: A Challenging Diagnosis

Tiago Azenha Rama¹, Luís Delgado², André Moreira³, José Luís Plácido¹

1. Serviço de Imunoalergologia - Centro Hospitalar Universitário de São João; Serviço de Imunologia Básica e Clínica, Porto, Portugal
2. Departamento de Patologia, Porto, Portugal
3. Faculdade de Medicina da Universidade do Porto, Porto, Portugal

Background
Mastocytosis are a heterogenous group of diseases, characterized by clonal mast cell (MC) accumulation on several organs and systems. Serum tryptase (sBT) is mostly used as a MC proliferation marker and not as an activation marker. In the past, a normal sBT was used as a surrogate marker to exclude systemic mastocytosis (SM), in patients with mastocytosis in the skin (MIS). We aim to show how challenging the diagnosis and staging of SM may be in patients with a normal sBT, while showing that quite different clinical presentations may be seen in patients with similar sBT.
Case report

Clinical case 1.
A 21 years old female patient with persistent allergic rhinitis, with a onset of MIS at 2 years of age, was referred to us due to severe diarrhea starting 2 months before. The patient had a recent endoscopic study in which mastocytosis lesions were found. She had no history of anaphylaxis and her only trigger for MC mediator release symptoms was emotional stress. Blood tests showed an iron deficiency anemia and sbT rounding 8 ng/mL. Bone marrow (BM) study did not show MC aggregates, and MC were negative for CD25, CD2, and c-KIT D816V mutation. She was started on sodium cromoglycate and her gastrointestinal symptoms started improving a few weeks later. Diarrhea ceased completely after three months.

Clinical case 2.
A 44 years old female non-atopic patient with morbid obesity, depression, with onset of MIS at 35 years of age, was referred to us due to multiple anaphylactic episodes (1-2 yearly), starting 12 years before. The patient also complained of frequent pyrosis and sporadic diarrhea. Triggers for anaphylaxis included NSAIDs, several antibiotics and emotional stress. Blood tests showed sbT rounding 11 ng/mL. BM study showed atypical MC that did not form aggregates, immunophenotypically positive MC for CD25 and CD2 with c-KIT D816V mutation restricted to MC. Previous medication was suspended and she was started on sodium cromoglycate and proton pump inhibitors. She has not had anaphylaxis ever since.

Conclusion
Both cases were diagnosed with indolent MS with low BM MC burden. This diagnosis is often quite difficult, due to the histologically absent/low number of MC aggregates. Despite their similar good response and prognosis, these cases showed rather different clinical presentations and daily life impairments.

P18 - Kounis Syndrome: A Thought-Provoking Case Report

Francesca Rizzo¹, Franco Borghesan¹, Giampaolo Pasquetto², Carlo Agostini¹

1. Scuola di specializzazione in allergologia ed immunologia clinica, università degli studi di Padova, Padova, Italy
2. Unità operativa complessa di cardiologia, ospedali riuniti Padova sud, Padova, Italy

Background
Kounis syndrome is defined as the co-incidental occurrence of an acute coronary syndrome with hypersensitivity reactions following an allergic event, which could be triggered by many mediators, including hymenoptera venom. Three different variants have been defined: type I in patients without risk factors or coronary lesions, in which the allergic event may induce either coronary artery spasm without increased cardiac enzymes or coronary artery spasm progressing to acute myocardial infarction; type II in patients with pre-existing atheromatous disease previously quiescent or symptomatic, in whom acute hypersensitive reactions may induce coronary artery spasm with or without plaque erosion or rupture, culminating in acute myocardial infarction; type III has been defined in patients
with preexisting coronary disease and drug eluting coronary stent thrombosis.

Materials and methods
A 61 years old male, affected by mild hypertension, was brought to the Emergency Room (ER) with symptoms of anaphylactic shock after a wasp sting. Five minutes after the sting, the patient experienced tachycardia, rash, abdominal pain, dyspnea, chest pain and visual blurring, briefly followed by syncope; when the medical aid arrived at the scene a few minutes later, the patient was half-conscious and both epinephrine and methylprednisolone were administered. During the medical assistance in the ER, a significant elevation in cardiac enzymes (troponin I blood level was eight times the upper limit of normal) and ECG nonspecific repolarization were shown. Immediate coronary angiography was anyway performed and revealed an 80% stenosis in the left circumflex artery and the patient underwent coronary angioplasty. In addition, to exclude neurological causes of syncope, a brain CT was performed and didn’t show any pathological findings.

Results
One month later, the patient underwent allergologic examination, which showed: level of serum tryptase at the upper limit of normality, presence of specific IgE against wasp venoms and positivity for wasp in intradermal tests. Therefore, the patient started venom immuno-therapy for wasp (Polistes).

Conclusion
This case report describes a probable case of type II Kounis syndrome, in which the allergy workup has been performed with a significant delay; although it is not a rare disease, Kounis syndrome diagnosis is easily overlooked. The prescription of VIT in these cases is mandatory, also to avoid cardiac or cardiological effects of epinephrine injections.

P19 - Anaphylaxis Related To Hymenoptera Sting: The Relevance Of Laboratory Testing And Bone Marrow Biopsy

Margherita Deidda¹, Davide Firinu¹, Maria Pina Barca¹, Francesca Losa¹, Giovanni Caocci², Giovanna Piras³, Stefano Del Giacco¹

1. Department of Medical Sciences and Public Health, University of Cagliari, Monserrato Campus, Cagliari, Italy
2. Hematology, Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
3. Hematology Department, San Francesco Hospital, ASSL Nuoro, ATS Sardegna, Nuoro, Italy

Background
Hymenoptera venom anaphylaxis may be related to a mast cell disorder.

Case report
A 40-year-old man in June 2012 presented sudden loss of hearing and vision and marked hypotension one hour after a wasp sting He was given intramuscular adrenaline with prompt benefit. Over the following years until the summer of 2018 he reported frequent bites by unspecified hymenoptera without either cutaneous or
systemic manifestations, as he promptly took antihistamine and corticosteroid therapy at each episode. In September 2018, following a wasp sting, despite the usual therapy, he had general malaise with chills and subsequent loss of consciousness, and it was admitted to the nearest hospital and the symptomatology regressed only after having practiced therapy with epinephrine. He was referred to our allergy clinic and prick, intradermal tests were performed with Bee venom, Wasp, Polistes and Hornet. A local skin reaction was documented only for Wasp and Polistes that occurred after a few minutes from the tests and regressed after 48 hours, but no systemic symptoms were observed specific IgE for Bee, Wasp and Horsefly and their respective recombinants confirmed hypersensitivity to Wasp with slight positivity for Yellow Jacket 0.21 KU/l, Dolichovespula maculata 0.11 KU/l and Polistes 1.54 KU/l, rVespv5 and rPold5 respectively of 0.23 and 1.35 KU/l, and the remaining negative.

Conclusion
Should this be the case for other investigations? Yes, in the diagnostic hypothesis of an underlying mast-cell disorder. In fact, despite the patient did not report a wide range of mast-cells mediator symptoms, he had a syncope without urticaria and angioedema, moreover the specific IgE did not show particularly high titers. Therefore, his the assay of the serum tryptase 44.90 µg/L and the RT-PCR for c-KIT mutation D816V in peripheral blood gave a positive result. Finally, the bone marrow biopsy confirmed our suspicion of indolent systemic mastocytosis, showing nodular lymphocyte aggregates with CD117+, CD25+ and CD30+ mast cells at the periphery and scattered eosinophilic granulocytes.

P20 - Three Is A Charm!

Toon Ieven1, Esther Noë2, Anne-Marie Kochuyt3, Erna Van Hoeyveld4, Dominique Bullens5,6, Rik Schrijvers3,6, Christine Breynaert3,6

1. University Hospitals Leuven, Department of Internal Medicine, Leuven, Belgium
2. University Hospitals Leuven, Department of Dermatology, Leuven, Belgium
3. University Hospitals Leuven, Department of General Internal Medicine (Allergy and Clinical Immunology), Leuven, Belgium
4. University Hospitals Leuven, Department of Laboratory Medicine, Leuven, Belgium
5. University Hospitals Leuven, Department of Pediatrics (Pediatric Allergology), Leuven, Belgium
6. KU Leuven Department of Microbiology, Immunology and Transplantation, Allergy and Clinical Immunology Research Group, Leuven, Belgium

Background
Patients with mastocytosis have an increased risk for severe anaphylactic reactions after hymenoptera stings.

Case report
A 42-year old female patient was admitted to the ER due to loss of consciousness and hypotension (85/40 mmHg) 4 hours after a honeybee sting and 15 minutes after eating a cake and drinking alcohol. An acute serum tryptase, one hour after the event, was 59.6 µg/L (basal serum tryptase (SBT) 12.0 µg/L). Specific serum
IgE (sIgE) for honeybee venom (HBV) (Phadia Thermofisher) was 3.77 Ua/ml two months after the sting and intradermal skin testing with HBV was positive at 1 µg/ml. During the next months, the sIgE for HBV decreased. No immunotherapy for HBV was started due to the low sting risk and long interval between sting and reaction. Eight months later, the sIgE for HBV was 0.38 Ua/ml, and again 1 year later, sIgE for HBV was < 0.10 Ua/ml. SBT decreased to a semi-normal level of 10.8 Ua/ml. The reaction was considered as a non-specific mast cell release and an adrenalin auto-injector was prescribed.

In 2017, 8 years later, this patient presented again immediately after a honeybee sting with dizziness. Parameters were stable and rescue medication was administered. Acute serum tryptase was 8.6 µg/L. Allergologic work-up 14 days later showed following results: SBT 10.8 µg/L, sIgE HBV 6.63 kU/L (Api m1 0.46 kU/L, Api m10 < 0.10 kU/L), sIgE yellow jacket venom (YJV) < 0.10 kU/L. A D816V KIT-mutation was detected in peripheral blood (0.015%). Mastocytosis work-up revealed a diagnosis of indolent systemic mastocytosis (3 minor criteria (CD25+, spindle shaped and D816V KIT+ mast cells)). Bone densitometry showed osteoporosis (T-score -2.2 and -2.7 for L2-L4 and femur respectively). Two months later, patient had a YJ sting: she experienced a large local reaction and presyncope, with recovery after taking antihistamines. Three weeks later, during hair bleaching, she experienced dizziness, dyspnea and loss of consciousness with hypotension (60/40 mmHg) and an acute tryptase level 34 µg/L. Two weeks later, sIgE for YJV was 0.40 kU/L (Ves v1 0.45 kU/L, Ves v5 < 0.10 kU/L), HBV 2.40 kU/L (Api m1, Api m2, Api m5 and Api m10 <0.10 kU/L, Api m3 1.00 kU/L, Bromelain <0.10 kU/L). Venom immunotherapy (VIT) for YJV was started and 6 months later, VIT for HBV was associated.

Conclusion
This case illustrates the need to rule out an underlying mastocytosis in patients with severe and atypical reactions after hymenoptera stings and shows the rapid decrease of sIgE in these patients.

P21 - Hymenoptera Species: Who’s Eating And Stinging?

Arantza Vega1, Berta Ruiz León2, Francisco Carballada3, Leopoldo Castro4, Teresa Alfaya5

1. Hospital Universitario de Guadalajara, Guadalajara, Spain
2. Hospital Universitario Reina Sofia, Córdoba, Spain
3. Hospital Lucus Augusti, Lugo, Spain
4. I.E.S. Vega del Turia, Teruel, Spain
5. Hospital General Universitario de Ciudad Real, Ciudad Real, Spain

Background
Vespula, Vespa and Polistes behaviour differs in their habits and feeding source. The knowledge of the feeding habits of vespids could help to identify the insect responsible of the sting in a food environment. This could provide an important support in Hymenoptera venom allergy diagnosis.

Materials and methods
A prospective observational study was performed in Spain, from June 2017 to January 2019. Pictures of Hymenoptera species in a food environment were
collected and identified by an entomologist. Insect, kind of food and place were recorded.

**Results**

One hundred and three images corresponding to 50 insects were analysed. The identified insects were 37 *Vespula* (*germanica* and *vulgaris*), 5 *Vespa* (*crabro*, 4 *velutina*), 4 *Polistes* (*dominula*, 2 *gallicus*), 2 *Cerceris* spp., 1 *Bombus terrestris* and 1 *Apis mellifera*. Foods associated with the insects were carbohydrates in 20 cases (7 of them were alcoholic beverages) and proteins in 30. Only vespine species were found on proteic food (meat, fish, seafood). Most of the insects were in restaurant or home terraces (64%). Other places were countryside (7), swimming pool (3) and indoor (4).

All *Vespa* species were found in north-west Spain. There were no differences concerning *Vespula* and *Polistes* in the rest of regions.

**Conclusion**

*Vespula* was the hymenopteran mainly associated with food environments in our country (74%). Though *Polistes* spp. were present, they only were found in connection with carbohydrates (alcoholic beverages or fruit).

**P22 - Pit Latrines And Latrodeictism: An Additional Risk Factor For Spider Bites In Rural South Africa.**

Sipho Duncan Ntshalintshali

Port Shepstone Regional Hospital; University of KwaZulu Natal, University of Cape Town, Durban, South Africa

**Background**

The incidence, prevalence and the entire epidemiology of spider bites by the *latrodeictus* species has been well studied in South Africa (SA) in the early 1990’s and later reviewed in the early 2000’s. Risk factors that were found to be directly linked with cases involving *latrodeictus* species included occupations such as construction workers, agricultural workers, municipal and utility workers, domestic workers, and entomologists.

**Case report**

According to the SA nationwide census of 2011, it was discovered that in SA 57% of the population used flush toilets (16 million people), 31% pit toilets (16 million people), 3% chemical toilets (1.5 million people), and 2% bucket toilets (1 million people). The dark, moist, filthy and insect predominant nature of pit toilets serves as an ideal habitat for spiders. We report 3 cases of *latrodeictus* spider bites that occurred while using a pit latrine in the rural South Eastern part of SA, with one case resulting in a severe case of latrodeictism requiring antivenom administration.

**Conclusion**

In view of the above, pit latrines should be considered as a potential risk factor for spider bites in rural South Africa. Although rare, but some cases may be severe, with a potential of leading to death; hence government officials need to be informed, and an intervention strategy be put in place.
O04 - Sting-Challenge Demonstrated Tolerance In Patients Undergoing Ant Venom Specific Immunotherapy, Validating New Centre Approach.

Kymble Martin Spriggs¹,², Elizabeth Leahy¹, Nicole Weibel¹, Amber Frost¹, Emily Heke¹, Sara Barnes¹,³

¹. Monash Health, Clayton, Australia
². The University of Melbourne, Parkville, Australia
³. Monash University, Clayton, Australia

Background
Native ant Myrmecia pilosula [Jack Jumper Ants (JJA)] are responsible for a significant burden of hymenoptera-associated allergic disease in south-eastern Australia. In some areas a population sensitisation prevalence of ~3%; with a 12-month exposure and sting rate ~50% higher than that of honeybees; and significantly more severe anaphylactic phenotype. Although randomised clinical trial (RCT) data has established clear efficacy for venom specific immunotherapy, until recently it had not been used significantly outside of the state of Tasmania. Our state venom immunotherapy centre in Victoria is the first institution to implement this program at scale outside Tasmania. We report on the validation of our service by successful live-sting challenge of our initial cohort of patients.

Materials and methods
M pilosula venom-allergic patients were established on allergen specific immunotherapy according to a locally adapted 6-week modified-semi-rush protocol to a 50 mcg per month maintenance dose of standardised Tasmanian M pilosula venom (Royal Hobart Hospital, Tasmania). After 12 months of therapy patients underwent sting challenge with live, locally collected, mainland ants - with two sequential stings being applied to the forearm over a 30min period followed by 2 hours observation. Antihistamines were avoided prior, but were provided 30mins after second sting (in line with likely real-world behaviour) to treat residual symptoms.

Results
55 participants with prior history of clinically severe systemic JJA allergy, and demonstrable sensitisation, who completed > 12months of venom specific immunotherapy.
Baseline Tryptase ranged from 1.0 - 23.3 mcg/L
Following dual sting challenge:
0/55 (0%) experienced severe objective systemic reactions.
No adrenaline or other treatment for severe systemic reactions were required.
All participants (55/55, 100%) experienced local erythema, pain & swelling at the sting sites.
9/55 (16%) experienced mild subjective systemic symptoms.
3/55 (5%) experienced mild objective distal cutaneous symptoms.
All non-local symptoms resolved within the 2 hour observation period.
Conclusion
Our state centre processes are validated, replicating efficacy shown in prior RCTs. Tasmanian sourced M pilosula venom is effective in inducing profound clinical tolerance and protecting against severe allergic reactions in patients previously severely allergic to the geographically distinct mainland M pilosula ants.

O05 - Absence Of Th2 Cell Suppression After Induction Of Venom Immunotherapy In Wasp-Venom Allergic, Indolent Systemic Mastocytosis Patients.

Dries Van Hemelen, Martijn C. Nawijn, Merel C. Onnes, Joanna N. G. Oude Elberink
UMCG, Groningen, The Netherlands

Background
Wasp venom allergy (WVA) is a frequent manifestation of indolent systemic mastocytosis (ISM). In the general WVA population venom immunotherapy (VIT) induces a long-term clinical tolerance to wasp venom (WV) that lasts after cessation of VIT. However, in ISM patients this protection after cessation of VIT is absent, suggesting a different underlying immunological response to VIT in ISM patients.

Materials and methods
Specific IgE (sIgE) for WV, Ves v 1, and Ves v 5, as well as WV IgG4 were determined in serum of ISM and non-ISM WVA patients before and after induction of VIT. WV-specific Th cell responses were analysed by characterizing CFSE labelled PBMCs cultured in the presence of dialyzed, heat inactivated wasp venom (dhiWV) extract. Ex vivo expression of IL-4, IFNγ, IL-10, FOXP3, IL-9 and IL-17 in WV-activated Th cells was analysed by flow cytometry.

Results
WV-specific IL-4 producing Th cells were detected in both WVA patient groups. ISM patients show significantly lower serum levels of WV- and Ves v 5-sIgE. During VIT both patient groups showed induction of Ves v 5-sIgE, and WV-sIgG4. In WVA patients without ISM numbers of WV-specific IL-4 and IL-9 positive Th cells are suppressed by VIT. Remarkably, this Th2 cell suppression was not observed in WVA patients with ISM.

Conclusion
This is the first study on an underlying WV-specific Th2 response in WVA ISM patients. ISM patients remarkably show no Th2 cell suppression after induction of VIT, which stands in contrast to the non-ISM WVA population. This difference may either be a potential explanation for the lower clinical effectiveness of VIT in ISM patients or may be the result of a delayed Th2 cell suppression in this population. To further explore these observations data on the long-term immunological effect of VIT in this population are required.
006 - Predictors Of Severe Cardiovascular Honey-Bee Sting Reaction With Absence Of Skin Symptoms In Patients With Normal Baseline Serum Tryptase Levels

Peter Kopac, Nissera Bajrovic, Mihaela Zidarn, Mitja Kosnik, Renato Erzen, Julij Selb, Urska Bidovec Stojkovic, Peter Korosec

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

Background
Severe sting reactions (Muller grade III and IV) are often accompanied with urticaria and angioedema. However, some patients develop prompt cardiovascular symptoms in the absence of skin symptoms. Those high risk patients are suspected for the underlying clonal mast cell disease, regardless of baseline tryptase levels. Therefore, we sought to investigate the predictors of severe HB sting reactions in patients with normal baseline serum tryptase levels.

Materials and methods
We analyzed clinical factors (age, sex, use of beta blocker agents and angiotensin-converting enzyme inhibitors) and immunological factors (sIgE to HBV, JYV), rApi m 1 and rApi m 10, baseline tryptase levels and basophil CD63 expression to HBV) in 38 patients with severe honey-bee sting reaction with cardiovascular symptoms and absence of skin symptoms and compared it to 225 patients with Muller reaction grade III and IV with skin symptoms. In all patients baseline tryptase was < 11.4 ug/ml. We ascertainment predictors of anaphylaxis without skin symptoms using penalized logistic regression.

Results
Patients with absence of skin symptoms were older in comparison with patients with skin symptoms (median 50 years vs 47 years respectively, P:0.038), and had moderately higher baseline tryptase levels (median 4.76 ug/ml vs 3.93 ug/ml respectively, P:0.002) and basophil response at and 1 mcg/ml (median 86.4% vs 76.4% respectively, P:0.007). There was no difference in sex, use of beta blocker agents and angiotensin-converting enzyme inhibitors. However only baseline tryptase levels was independent predictor for anaphylaxis without skin symptoms (P:0.015; OR (95% CI) 1.237 (1.042-1.471)).

Conclusion
Minor increase in baseline serum tryptase is independent predictor for severe HB sting reaction without skin symptoms. The mechanistic background for this minor but clinically important tryptase changes are currently unknown and thus further studies are urgently needed.