



# **The efficiency of immunotherapy to the subjects with allergy to bee venom and its influence in pollen allergy**

**Abstract author:**

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**Many thanks to  
USA, NATO, EU**

## Introduction:

Hymenoptera venom allergy is an **immunoglobulin E (IgE)- mediated hypersensitivity** to the venom of insects in the insect order Hymenoptera.

- This allergic reaction may be caused by stings from a number of species in this insect order, occurring only in persons who have previously been sensitized to Hymenoptera venom.
- Insect sting allergy can develop at any age and usually manifests after several uneventful stings.
- The incidence of **systemic reactions** to Hymenoptera venom is approximately **3% in adults**. Although **children are stung more often than adults**,
- **Systemic reactions** occur in only about **1% of children younger than 17 years**, and many of these reactions are relatively mild.
- **Large local reactions** to Hymenoptera stings are more common **in children**, with an estimated incidence of **20% and 10%**, respectively, for children and adults. The prevalence of insect sting allergy is **twice as high in male as in female** patients and may be a result of increased exposure rather than inherent susceptibility.
- Normally there is no clear association with other allergies, and **only 30% of patients with venom allergy are atopic**.
- In addition, insect sting allergy is statistically not more likely to occur in persons with a family history of sting reactions.



## History

The first reports of **stinging insect allergy** came from the **Middle East** thousands of years ago.

Even at that time, **people understood** that a small insect, such as a bee or a wasp, had **the potential to cause serious illness or even death.**


## • **Hymenoptera Stinging insects**

- All the stinging insects belong to the insect order Hymenoptera, of which there are **16,000 species** in North America.
- Less than **1% are responsible for human stings**.
- All the species that are medically important belong to three families:
  - **Apidae**,
  - **Vespidae**, and
  - **Formicidae**.
- Only the **females** of each species have **stingers**, which are **ovipositors** that have lost their egg-laying function and have been modified for stinging and **envenomization**. Most species sting in defense of themselves and their nests, although some species also sting as a means of capturing their prey.

## •SIGNS AND SYMPTOMS

- Most Hymenoptera stings cause ***small local reactions*** of no significant medical consequence.
- These normal sting reactions are characterized by **pain, itching, redness, and swelling** at the sting site that resolve within several hours and are caused by the pharmacologic properties of the venom.
- Some ***large local reactions*** are caused by a **late-phase IgE-dependent reaction** that is mild initially but progresses after **12 to 24 hours** to a **diameter of more than 5 cm**; these usually **peak in intensity at 48 to 72 hours**.
- These reactions are contiguous with the sting site and occasionally involve an entire extremity. In rare cases, massive swelling causes local anatomic compression.
- **Large local sting reactions** typically resolve gradually **over 5 to 10 days**.  
Virtually all patients with large local reactions continue to have similar reactions with subsequent stings.
- This tendency is not modified with venom immunotherapy; therefore, patients with large local reactions are not candidates for further diagnostic evaluation .



- 
- **Systemic reactions** cause signs and symptoms in one or more organ systems and are almost always **IgE-mediated**.
  - Systemic reactions cause a spectrum of manifestations, ranging from
    - **cutaneous signs** (*pruritus, flushing, urticaria, angioedema*) to
    - **respiratory involvement** (*cough, throat and/or chest tightness, dyspnea, wheezing*) and
    - **cardiovascular compromise** (*dizziness, hypotension, unconsciousness*), depending on the severity of the reaction.
    - **Gastrointestinal manifestations** (*nausea, vomiting, diarrhea*) and
    - **uterine cramping** also occur occasionally.
    - **Cardiac anaphylaxis** with manifestations of **coronary vasospasm, arrhythmias, or bradycardia** can also occur following stings, even in persons with no underlying cardiac disease.
  - **Systemic reactions** usually cause signs and symptoms **starting within minutes** following a sting. In general, the sooner the symptoms occur, the more severe the reaction.



## PATHOPHYSIOLOGY

- Both **systemic and large local reactions** to stinging insects are usually caused by **IgE-mediated** reactions to Hymenoptera venom.
- At least one prior sting is required to sensitize a person to venom, and sensitization is more likely to occur following multiple simultaneous stings or subsequent stings occurring over a relatively short period of time.
- Once **sensitization has occurred**, a sting can cause **mast cell and basophil degranulation**, resulting in **release of the histamine and other inflammatory mediators responsible for the signs and symptoms of anaphylactic and some large local reactions**.



• **Family: Apidae**

**Scientific name: Apis mellifera**

• **Common name: Bee**

• ***Apis mellifera***, commonly known as the bee, is a very common insect.

Believed to have originated in Africa, most likely this primitive species spread from France throughout Central Europe, north of the Alps, the British Isles, southern Scandinavia, down to the Ural mountains.

• Worker bees can have a length between 1.1 and 1.5 cm with a light orange and dark brown coloring.

• You can often see bees on flowering plants, on sources of sugar (honeydew, etc.) or on pools of water during hot days.

• Bees build nests in beehives or sometimes in hollow trees or cracks in the walls of buildings.

• Bees can attack en masse if not too far from their hives.

A peculiar characteristic of the *Apis mellifera* is the serrated stinger. The stinger is barbed so that it lodges in the victim's skin, tearing loose from the bee's abdomen and leading to its death in minutes.

Distribution: Throughout Italy.

• ***Period of exposure to allergens:*** All year round.

• ***Allergy testing:*** IDR testing, skin PRICK testing, determination of specific Ig-E

• Allergic reactions to bee venom can be severe enough to **cause anaphylactic shock, which can be fatal.**

## •Efficacy of VIT(Venom immunotherapy)

- Venom immunotherapy** is extremely **efficacious** in preventing subsequent systemic reactions in patients with stinging insect allergy.
- Efficacy** is highest with mixed vespid venom; it is **98% effective** in preventing subsequent systemic reactions with a maintenance dose of 300 µg (100 µg per venom).
- For **therapy with individual venoms** (i.e., honeybee, yellow jacket, or wasp) at a dose of 100 µg per venom, immunotherapy is **75% to 95% effective** in preventing systemic reactions to future stings.
- Those few patients who continue to have systemic reactions usually have milder reactions than before beginning treatment.
- Increasing the maintenance dose of immunotherapy to 200 µg provides full protection for most patients who have had systemic reactions while receiving treatment with single venoms at a dose of 100 µg.

- **In Kosovo** as in the other parts of the globe, allergy diseases are very often presented in medical institutions. Also the percentage is almost same as in Europe, or in the other parts of the world.
- In general, approximately **1/4 or 1/5 of inhabitants** is presenting **different kinds of allergy**, starting from mild symptoms to severe life threatening allergy reactions.
- As a certified specialized allergologist – immunologist, while living and working in the small city of Gjakova in Kosovo, in my everyday experience, I meet different kind of allergies to my patients like: pollen allergies, food allergies, medication allergic reactions, contact allergies, and insect sting allergies such as bites: bee, wasp etc.
- **In one case**, of my observed patient, I verified that the **subject 12 years old; gender: female** was **allergic in: pollens and bee venom with anaphylactic allergic reaction**.
- **Specific Ig- E detected with POLYCHECK (Bio-Check) first analysis are shown below:**

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**First Name:** PRENKAJ  
**Date of Birth:** Invalid  
**File Name:** c:\BIS\_20\Datenbanken\Temp.bio  
 Scan of 2/4/2012 5:05:30 PM (V2.19cv5) , chip # 1

**Test:** Mediterran-II  
**Order #:/Origin:** / ELIT-LAB  
**Date of Order:** 2/4/2012  
**Print Date:** 2/4/2012 (V. 2.19cv5)  
 c:\BIS\_20\Tmp\Chip1.bmp

Allergenes	Class	Concentr. [kU/l]	0,15	0,35	0,7	3,5	17,5	100
t02 Alder pollen	1	0.52	[Bar chart showing 0.52 concentration]					
t03 Birch pollen	2	0.97	[Bar chart showing 0.97 concentration]					
t04 Hazelnut pollen	2	0.97	[Bar chart showing 0.97 concentration]					
t05 Beech pollen	2	1.1	[Bar chart showing 1.1 concentration]					
t07 Oak pollen	2	1.1	[Bar chart showing 1.1 concentration]					
t09 Olive pollen	0	0.15	[Bar chart showing 0.15 concentration]					
t12 Willow pollen	0	0.25	[Bar chart showing 0.25 concentration]					
t16 Pine pollen	2	2.0	[Bar chart showing 2.0 concentration]					
m01 Pen.notatum	0	<0.15	[Bar chart showing <0.15 concentration]					
m02 Cladosp.herbarum	0	<0.15	[Bar chart showing <0.15 concentration]					
m03 Asp.fumigatus	0	<0.15	[Bar chart showing <0.15 concentration]					
m06 Alt.alternata	0	<0.15	[Bar chart showing <0.15 concentration]					
m11 Rhizopus nigricans	2	1.3	[Bar chart showing 1.3 concentration]					
g02/g05/g06 Grass mix	3	5.8	[Bar chart showing 5.8 concentration]					
h01 House dust	2	2.1	[Bar chart showing 2.1 concentration]					
i01 Bee venom	5	87	[Bar chart showing 87 concentration]					
i03 Wasp venom	0	<0.15	[Bar chart showing <0.15 concentration]					
e81 Sheep epithelia	0	<0.15	[Bar chart showing <0.15 concentration]					
w06 Mugwort pollen	0	<0.15	[Bar chart showing <0.15 concentration]					
w07 Ox-eye Daisy pollen	0	<0.15	[Bar chart showing <0.15 concentration]					

Concentr. [kU/l]	Class	Explanation
<0,35 kU/l	0	No specific antibody detection.
0,35 - 0,7 kU/l	1	Very weak antibody, frequently no clinical evidence, in case of an existing sensibilization.
0,7 kU/l - 3,5 kU/l	2	Weak antibody detection, existing sensibilization, frequently a clinical evidence in the upper range of this class.
3,5 kU/l - 17,5 kU/l	3	Clear antibody detection, clinical evidence is mostly present
17,5 kU/l - 50 kU/l	4	Strong antibody detection, nearly always with existing evidence.
50 kU/l - 100 kU/l	5	Very strong antibody detection.
> 100 kU/l	6	Extreme high antibody titer.

+355



**BIO-CHECK**  
 Diagnostic Center  
 K81728026N  
 2.427.025/026

99 355



# Polycheck®

Name: LAURETA  
 First Name: PRENKAJ  
 Date of Birth: Invalid  
 File Name: c:\BIS\_20\Datenbanken\Temp.bio  
 Scan of 4/12/2013 12:28:44 PM (V2.20) , chip # 1


Test: Mediterran-II  
 Order #:/Origin: / ELIT LAB  
 Date of Order: 4/12/2013  
 Print Date: 4/12/2013 (V. 2.20)  
 c:\BIS\_20\tp\Chip1.bmp

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t02 Alder pollen	0	<0.15							
t03 Birch pollen	0	0.16							
t04 Hazelnut pollen	1	0.41							
t05 Beech pollen	0	<0.15							
t07 Oak pollen	1	0.35							
t09 Olive pollen	0	<0.15							
t12 Willow pollen	0	<0.15							
t16 Pine pollen	0	0.29							
m01 Pen.notatum	0	<0.15							
m02 Cladosp.herbarum	0	<0.15							
m03 Asp.fumigatus	0	<0.15							
m06 Alt.alternata	0	<0.15							
m11 Rhizopus nigricans	0	<0.15							
g02/g05/g06 Grass mix	1	0.66							
h01 House dust	0	0.22							
i01 Bee venom	4	20							
i03 Wasp venom	0	<0.15							
e81 Sheep epithelia	0	<0.15							
w06 Mugwort pollen	0	<0.15							
w07 Ox-eye Daisy pollen	0	<0.15							

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50 kU/l - 100 kU/l	5	Very strong antibody detection.
> 100 kU/l	6	Extreme high antibody titer

Signature:



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- This **patient** has started **initial treatment** in “**Mother Theresa**” **University Hospital Center of Tirana in Albania**, 2 years ago with rush method.
  - After this process, the treatment was **continued** by me in “**Isa Grezda**” **Regional Hospital of Gjakova**.
  - Until now I’m performing by **schematic regimen SCIT** and every time the patient is under my **observation for 30 minutes**.
  - **During** the period of **two years of immunotherapy**, the treatment has indicated **very well** to the patient, with **moderate local reaction** in the beginning and now without any possible clinical adverse reactions.
  - Every **application** of vaccine was performed **deep subcutaneously in the upper external side of the arm**.





•After **one year** of venom immunotherapy with **Anallergo vaccine**, the patient has repeated Specific Ig-E on pollens and hymenoptera venoms, with the parameters of:

- Bee venom has fallen down from 5-4;**
- Alder pollen from 1-0;**
- Birch pollen from 2-0;**
- Hazelnut pollen from 2-1;**
- Beech pollen from 2-0;**
- Oak pollen from 2-1;**
- Pine from 2-0;**
- Rhizopus nigrans from 2-0;**
- Grass mix from 3-1**
- and house dust from 2-0.**
- **And concomitantly parameters of bee venom and parameters on pollens began to fall down without etiological treatment, it means without S.I.T on certain pollens.**

## • **Material and methods:**

- The patient was receiving\_
- L-Tyrosine-adsorbed subcutaneous immunotherapy (SCIT) for hymenoptera venom
- **ANALLERGO vaccine ( Apis mellifera)**

L-tyrosine delayed subcutaneous immunotherapy for hymenoptera venom consists of two initial vials of L-tyrosine delayed extract of purified venom, respectively one 5 ml vial containing 1 mcg/ml and one 5 ml vial containing 10 mcg/ml.

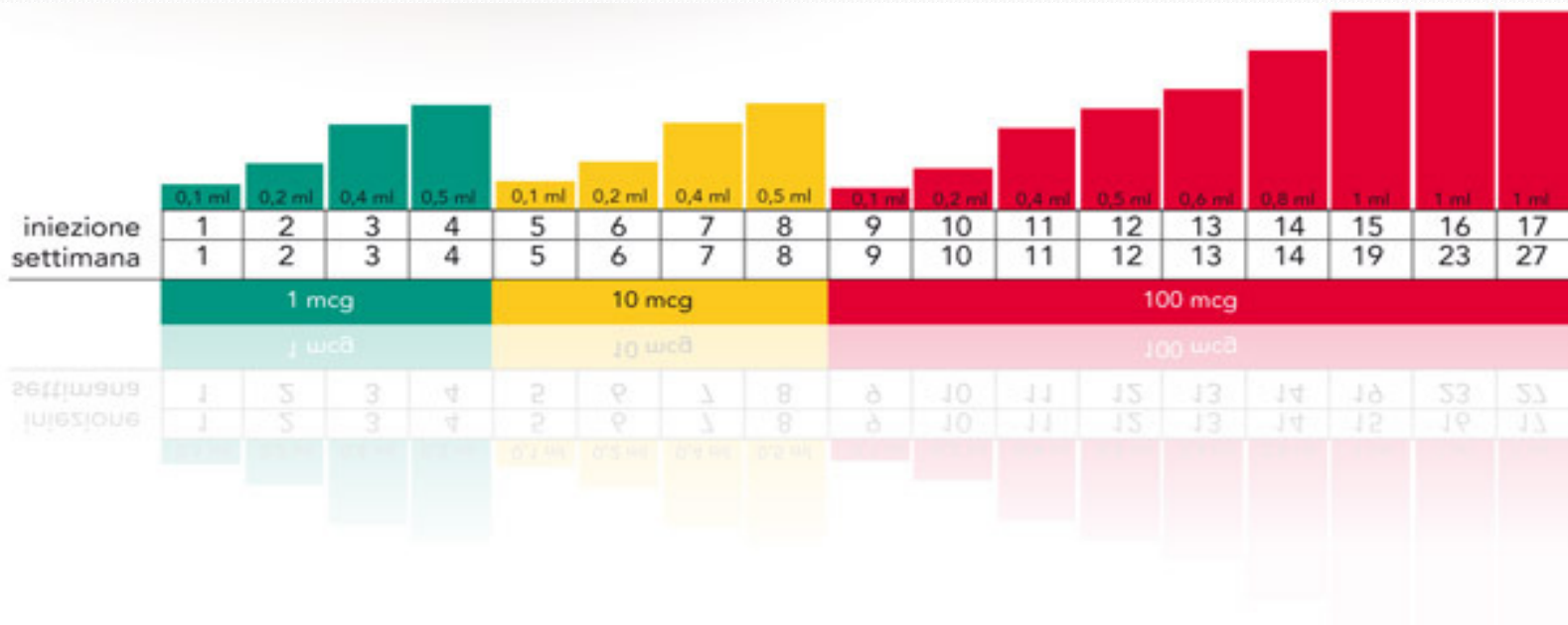
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## STARTING TREATMENT PLAN

- N. 1 - 5.0 ml green label vial containing 1 mcg / ml of hymenoptera venom.
- No. 1 - 5.0 ml yellow label vial containing 10 mcg / ml of hymenoptera venom.
- No. 1 - 5.0 ml red label vial containing 100 mcg / ml of hymenoptera venom.

## MAINTENANCE THERAPY

- No. 1 - 5.0 ml red label vial containing 100 mcg / ml of hymenoptera venom. Vials are packed in a protective rigid plastic container.



## CONCLUSION

- **The patients which are allergic to bee venom which are most of the time allergic to pollens too, by obtaining VIT can present a decrease of parameters in pollen allergy too.**
- **So, I need to follow one year more, the patient analysis, in order to make a definitive conclusion about the efficiency of VIT and its correlation of positive influence to pollen allergy?**



# SPONSORS:

A special thanks to:

- **MINISTRY OF HEALTH KOSOVO**

- **“ISA GREZDA”**

**REGIONAL HOSPITAL  
GJAKOVA, KOSOVO**

& Pharmaceutical supporters:

- **ANALLERGO**

- **GSK**

- **OMICS-Group**



**Thank You!**  
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