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## **CARE FOR PATIENTS WITH HYPERSENSITIVITY TO HYMENOPTERA VENOM CHALLENGE FOR THERAPEUTIC TEAM**

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### **Abstract**

This insect venom allergy is a special form of allergy because it carries a high risk of developing Anaphylaxis, the most severe, life-threatening form of allergic reaction. This is one of the most dangerous allergies. It is a major problem in modern allergy because it is still under-diagnosed in its pathomechanism, diagnosis and treatment.

In the care of this group of patients, it is important to treat, educate patients, teach them the Principles of prevention, use drugs for immediate intervention, and most of all, the adrenaline. These tasks should cover all staff Responsible for the care of the patient both physicians, psychologists and nurses.

**Key words: venomous insects, venom allergy, care, patient**

### **Admission**

Allergy to Hymenoptera venom allergy is a special form because it carries a high risk of anaphylaxis, serious, life-threatening form of allergic reaction. It is therefore one of the most

dangerous allergies. At the same time it is a very significant problem in modern allergy, because the phenomenon is still poorly understood in terms of its pathomechanism, diagnosis and treatment. Until recently it was believed that allergy to stings by the insect species is caused by allergens insect whole body, hence the name "allergy to Hymenoptera." Only the development of knowledge on the pathogenesis of this form of allergy and finding the factors responsible for allergic reactions to insect venom only allowed to specify the name, which now takes into account the venom as the main source of allergens, allergens. Venom is also used to treat the allergy. The first attempts to "desensitize" the venom, or specific immunotherapy in patients with allergic sting reactions have already been conducted 50 years ago. Currently, this method is the mainstay of treatment for people with severe allergic reactions after Hymenoptera sting by ensuring their safety during subsequent stings and increasing the quality of life of these patients. Immunotherapy comprising administering to a patient uczulonemu increasing doses of the allergen, so that the immune system learns "tolerance" of its components [2].

In the care of a group of people with an allergy to Hymenoptera venom is very important not only treatment, but a large role is played here adequate patient education, to teach them the principles of prevention to protect against stings, the proceedings in the case of stings, use of drugs of the "package of drugs for immediate intervention "autostrzykawkami mainly with adrenaline. In these activities should be involved all personnel responsible for the care of the patient at risk of an allergic reaction to the venom, both doctors, a psychologist and a nurse. [4]

Hymenoptera are very high, and was divided into many species, a systematic cluster of insects (Insecta). They differ in terms of physiological and morphological generally biological other arthropods. Among the Hymenoptera bees can be distinguished: honey bees and bumblebees and a group osowatych: wasps ordinary klecanki (typical of the Mediterranean region), with wasps and hornets Dolichovespula species.

Hymenoptera (Hymenoptera) are equipped with a stinging apparatus, which is a defensive tool. Sting is connected to the venom-producing glands, which inter alia contains ingredients of an allergen [25].

The insect venom, 88% of water content. Dry matter venoms are three types of components:

- Substances of low molecular weight
- peptides

- Proteins with enzymatic properties (ie. Those which are of enzymes).

Low molecular weight components of the venom include amino acids, biogenic amines and phospholipids. They are responsible for the spread of the venom in the body of the victim and for the pain and burning that occurs in people użądłonych by an insect.

In terms of the content of low-molecular components of wasp venom is different from bee venom, that it contains more histamine and it is adrenaline and acetyliodiolina. Venom both species also includes serotonin, dopamine and noradrenaline. The main component of dry venom of both species are peptides which are responsible for most of the toxic reactions sting. The bee venom peptides are the following: melittyna, apamina, mast cell degranulating peptide (MCD), and Skopin terciapina. venom, hair and also other peptide antigen 5 [8].

Melittyna damages the cell membrane resulting in the release of lysosomal enzymes from leukocytes, platelet serotonin or histamine from mast cells. Apamina is one of the most powerful neurotoxins of animal origin. In apamina toxic doses causes severe seizures clonic-tonic seizures. Enzymes present in the venom of insects include. Phospholipase and hyaluronidase. These are the main factors responsible for the allergenic properties of the venom.

The following table lists the individual components of the venom of insects along with their percentage share.

Table 1. Components of bee and wasp venom (according to Edery). [18]

<b>Ingredients venom of bees and wasps</b>		
<b>type of substance</b>	<b>representation ingredients</b>	<b>Dry weight [%]</b>
low molecular weight substances	Biogenic amines, sugars, amino acids, oligopeptides, phospholipids	20 to 25
peptides	Melittyna (only in bees), apamina factor deregulujący mast, kinins	50 to 60
proteins	Phospholipase A1 and A2, hyaluronidase, phosphatase, esterase, antigen 5 (only in osowatych)	15 to 30

### ***What is allergy to insect venom***

Allergy (i.e., immune hypersensitivity reactions) indicates the presence of disease symptoms after contact with a very small amount of the substance, which do not react allergic individual's predisposition, i.e. not sensitive [1].

Allergy to insect venom is excessive, usually fast growing response (local or general, that is, on the whole body) occurring after an insect sting. Particularly severe, violent, life-threatening allergic reaction called anaphylaxis.

Allergy to Hymenoptera venom (Hymenoptera) is a big problem in the practice of allergy. In Central Europe, the majority of allergic reactions poużądleniowych is caused by honey bees (*Apis mellifera*), rarely by wasps (*Vespula vulgaris*, *Vespula germanica*), hornets (*Vespa crabro*), bumblebees (*Bombus* spp.) And ants (*Formicidae*). The incidence of allergic reaction to the sting and the severity of which may vary. This depends primarily on the level of human exposure to stings, climatic variations, insect species, insects differences between individuals such as the composition of venom and degree of aggressiveness in man [14].

In patients with hypersensitivity to insect venom allergic reactions can be very dangerous and life threatening. In addition, a history of severe systemic reactions, increases the level of fear and anxiety for his life before the next stings. This has a very negative impact on the comfort and quality of life. Therefore, these patients should be properly diagnosed in order to provide them with adequate care, medication and immunotherapy selected cases. All of these patients should be instructed on the principles of prevention against stings and, therefore, subject to a careful, systematic education on the subject.

Studies show that the symptoms of allergies to the venom of stinging insects occur in a substantial portion of the population. The most common are excessive local reactions sting which can apply 3.1 to 17, or even 28% of the population [15]. Generalized reactions are less frequent and on low 0.3 ÷ 5, and according to some authors, up to 8% of the population [17]. Even more common than the symptoms of this allergy are positive skin test results and / or the presence of specific IgE antibodies against the venom, which occurs in almost 25% of the people [20]. Vulnerable groups in the occurrence of this allergy include persons performing certain professions such as beekeepers and their families, gardeners, farmers, foresters, confectioners, vendors of sweets, ice cream. The studies say that even a 17 ÷ 43% of the beekeepers are allergic to bee venom [22]. Additional risk factors identified in beekeepers are allergic symptoms of

upper respiratory tract occur while working in the apiary and the number of stings per year. More severe reactions are mainly beekeepers rarely żądlonych ie. Less than 10 to 25 times a year.

Of the remaining patients, with an average degree of exposure to the severity of allergic reactions to drugs, insect stings may affect certain predisposed patients. These include the patient's age (More severe reactions are observed in adults, particularly > 50 years of age than in children), coexisting diseases of the vascular and circulatory medication, especially beta-blockers and ACE inhibitors [23]. The greatest risk patients are also suffering from mastocytosis, and those who have elevated levels of tryptase in serum [19].

In the course of an allergic reaction can occur after the sting deaths. Their frequency is not exactly known, but according to data from Europe seems to include several dozen cases per year [31]. The following table shows demographic data 29 deaths sting by Sasvwarý and Muller. Sasvwarý i Muller analyzed 29 cases of fatal sting [7].

Table 2. Demographics 29 deaths sting by Sasvwarý Müller and [7].

<b>Age</b>	60 years (36 ÷ 89)	
<b>Women / Men</b>	7/22	
<b>Insect - perpetrator</b>	Bee	11 (38%)
	Wasp	23 (45%)
	Hornet	2 (7%)
	Unknown	3 (10%)
<b>The number of stings (24 patients)</b>	1	17 (71%)
	2-9	3 (12%)
	> 10	4 (17%)
<b>A history of positive (24 patients)</b>	atopy	3 (13%)
	Venom allergy	10 (42%)
	Cardiovascular disease	11 (46%)
	Respiratory diseases	7 (29%)

### *Symptoms non-allergic reaction*

In people who are not allergic to the venom in the sting site may appear redness, soreness and swelling. The diameter of the swelling should be less than 10 cm and should not last longer than 24 hours. This reaction may be called physiological ie. The one that is appropriate for the event. Swelling and pain may be greater in the case of the sting around the loose subcutaneous tissues such as the eyelid, fingertips, lips or oral mucosa.

### ***Toxicities (sting cluster)***

After repeated stings by bees, wasps and hornets, and therefore in patients undergoing żądleniu-gromadnemu by several dozens of insects, according to their number may appear high temperature, joint pain, inflammation of the nerves, lymph node enlargement in the vicinity of żądlenia. Toxic effects of the venom can also cause impaired and damage to the kidneys, liver, disintegration of red blood cells (hemolysis), and cerebral edema, muscle breakdown fringe (mioliza) [24].

### ***The symptoms of local allergic reaction (called LLR. Large local reaction)***

Big, local allergic reactions that occur after żądleniu call local reactions. According to the classification HL Mueller excessive local reactions (LLR: large local reaction) is defined as the swelling with a diameter of over 10 cm of erythema and itching at the site żądlenia continued over 24 hours [28].

The reaction LLR most are mild, but severe local reactions may affect the entire limb or cause swelling of the entire face but usually these symptoms disappear within 48 ÷ 72 hours without complications. But is dangerous occurrence LLR after the sting in the neck, head and especially the inside of the mouth and tongue, which can cause swelling of the throat, larynx and as a consequence of acute respiratory failure. The pain felt in place żądlenia it is caused by the action of peptides and enzymes venom.

The majority of patients with allergic local reaction reveals the presence of specific IgE antibodies against the venom, which indicates that it is the immediate reaction (Type I according to Gell and Coombs). Symptoms occur in tissues where they are present a plurality of mast cells (ie. Mast cells), which are degranulation upon contact venom allergens to IgE antibodies on the surface anchored mestocytów [21].

### ***Symptoms of generalized (SYS called. Systemic)***

Symptoms of generalized have very different severity, and their symptoms are very diverse. SYS reaction can proceed mildly and moderately or heavily, which ostanowi the basis of the distribution of the reaction SYS in two classifications used in medical practice, a scale and a scale Mueller Ring Messmer (Table 3.4). SYS on the signs of the various organs: skin, mucous membranes, gastrointestinal tract, respiratory or cardiovascular. Mildest general symptoms in patients użądlnych which can be encountered most often skin reactions [13].

Skin manifestations are in the form of extensive swelling, urticaria, and pruritus. With the swelling of the deeper layers of skin angioedema. Allergy symptoms of the gastrointestinal tract are known. difficulty swallowing (dysphagia) cramps (colic), abdominal pain, nausea and vomiting. Symptoms of the respiratory system are: swelling of the throat, larynx (hoarseness, wheezing breath), bronchospasm (wheezing, prolonged exhalation) and shortness of breath. The most severe symptoms are usually classes of cardiovascular hypotension and shock, which poses a direct threat to life and requires swift and comprehensive action [20].

Table 3. Classification of systemic reactions poużądleniowych according to their gravity

<b>Classification of systemic reactions poużądleniowych according to their gravity</b>	
<b>reaction type</b>	<b>symptoms</b>
I - smaller	Generalized urticaria, pruritus, edema, malaise, anxiety
II - generalized	Any of the above symptoms and at least 2 of the following: chest tightness, nausea, diarrhea, vomiting, hoarseness, abdominal pain, dizziness, angioneurotic edema
III - severe	Any symptom of the above, and at least two of the following: shortness of breath, wheezing, stridor, dysarthria, dysphagia, lethargy
IV - anaphylactic shock	Any of the above symptoms, and at least two of the following: fall in blood pressure, collapse, loss of consciousness, cyanosis, incontinence or incontinence.

Evaluation systems intensification of reaction formed to help decide on the intensity of the patient's treatment early enough, before the full development life-threatening symptoms [21].

Table 4. The intensity of anaphylactic reaction (acc. J. Ring, Messmer K.)

<b>The severity of an anaphylactic reaction (Acc. J. Ring, Messmer K.)</b>				
<b>Degree</b>	<b>Skin</b>	<b>Digestive tract</b>	<b>Respiratory system</b>	<b>Cardiovascular system</b>
AND	Pruritus, erythema, urticaria, angioneurotic edema	No symptoms	No symptoms	No symptoms
II °	None or as above	Nausea, abdominal cramps	Runny nose, hoarseness, dyspnoea	Tachycardia, drop in blood pressure to >20mmekg
III °	None or as above	None or as above	Glottal edema, bronchial obstruction	Shock
IV °	None or as above	None or as above	respiratory arrest	cardiac arrest

Diagnosis of insect venom allergy is based on the study, including subject, object, and additional studies.

### ***Physical examination***

Physical examination is to collect very detailed interview about the circumstances and symptoms of the sting. It is intended to determine the insect species that caused the symptoms and the cause of allergies, assessing whether the definition described symptoms of allergies and what was their severity.

Patients who show a reaction after the SYS żądleniu wasps can also be allergic to hornet venom. Sometimes, unfortunately, we can not accurately determine which insect (bee or wasp) żądliła patient. This is called "unidentified insect" [16].

### ***physical examination***

Physical examination is a detailed physical examination, patients with anaphylaxis. They should be carried out during the period of acute symptoms. You can then determine the severity of the allergic reaction by accepted international classification. One must take into account the changes in skin, subcutaneous tissue, respiratory, cardiovascular, abdominal and central nervous system.

Patients should be monitored following parameters: blood pressure, heart rate, respiratory rate [22].

### ***Diagnostic tests***

Patients with large local reactions LLR not require further in-depth diagnostics. The possibility of systemic reactions is small.

In the case of systemic reactions SYS I ° and II °, which are generalized reactions perform detailed diagnostics. The main diagnostic test in vivo are dot-and intradermal skin test [29].

### ***In vivo tests***

Test point of the venom is a simple and safe embodiment of the method of diagnosing allergy. It serves assessing whether a patient is described by the reaction to the venom allergy is a subsidiary of IgE antibodies. When the test point out a negative intradermal test was carried out with 0.05 ml of a solution using the venom of the concentrations **od  $10^{-8}$  do  $10^{-4}$ ,  $10^{-4}$ ,  $\frac{10^{-3} \text{ g}}{1}$**  Every 20 minutes until the first positive test. The test is



read after 20 minutes. A positive result is a bubble diameter  $\geq 5$  mm with the surrounding erythema.

Using the concentration of the venom of this test is positive in about 75 to 100% of the venom allergy, and at a concentration of up to 100 in 90% [32]. The tests are evaluated only when applied with the solvent control is negative and histamine prick test positive. This shows

the correct skin reactivity.  $\frac{10^{-4} \text{ g}}{1 \frac{10^{-3} \text{ g}}{1}}$  It should also be noted that patients taking antihistamines and drugs from the group of neuroleptic phenothiazines may give false negative results.

Positive test result in a patient with a history confirms the diagnosis of allergy to the venom.

### **In vitro assays**

Performs tests to assess the presence of specific antibodies in serum specific IgE class of patients. This method is less sensitive as from approx. 15 to 20% of the positive test is negative  $\acute{s}$ ródskórnymi [32]. In contrast, 10% of negative  $\acute{s}$ ródskórnymi tests showed the presence of sIgE in serum. As in the case of intradermal tests specific IgE testing should be performed after 4  $\div$  6 weeks episode  $\acute{z}$ ądlenia. A negative result of the test must be repeated at 3  $\div$  4 months after  $\acute{z}$ ądlenia [23].

Patients with severe course of an allergic reaction to the sting should be indicated concentration of tryptase.

Tryptase is an enzyme released by mast cells only in the process of degranulation of the cell. Mast cells are stimulated to secrete a substance of granules under the influence of a number of stimuli of physical, chemical and immunological reactions in the dependent and independent from the presence of IgE antibodies.

Tryptase concentration in serum is elevated in diseases characterized by rozplemem mast cells (mast cell) and during systemic anaphylaxis. Tryptase is an important and sensitive indicator of systemic allergic reactions. After about 15 to 20 minutes after the onset of clinical signs SYS enzyme concentration in the serum rises and is maintained at elevated values of up to three days (including autopsy) [24].

### **TREATMENT - Immunotherapy**

Treatment of patients with symptoms of venom allergy is divided into drug treatment, which is taken immediately after the onset of symptoms and treatment of allergy

"desensitization" that is a kind of venom immunotherapy, which is recommended in patients with the most severe symptoms of allergy to the venom. Drug therapy helps control poużądleniowych symptoms, but does not prevent further symptoms after subsequent stings when venom immunotherapy can cause permanent cure, ie. To prevent the occurrence of allergic symptoms at each successive insect sting [29].

***Indications for insect venom immunotherapy rightful (VIT called. Venom immunotherapy)***

Venom immunotherapy to eligible patients who after the sting had a severe allergic reaction and have a positive skin tests with venom or anti-venom serum IgE. The severity of the reaction poużądleniowej should be determined based on the classification Muller. All patients who had systemic allergic reaction of III and IV according to the classification Muller regardless of their age must be subject to insect venom immunotherapy (VIT) [6]. In children who are under 5 years of age does not begin with VIT. The study shows that an allergic reaction when re sting in this age group is very unlikely.

Venom immunotherapy is carried out for 3 ÷ 5 years. Women who during immunotherapy become pregnant there is no need to interrupt it. It has never been reported to continue the vaccination had a negative effect on pregnancy. While the beginning of the immunotherapy in pregnancy is risky and should not be the start [7].

Table 5. Indications for hymenoptera venom immunotherapy.

<b>Reaction by Muller</b>	<b>Skin test or serum specific IgE</b>	<b>The decision to treat</b>
SYS IV: All ages	positive negative	Yes no
SYS III: All ages	positive negative	Yes no
SYS I and II: Adults Children All ages	positive positive negative	usually do not no no
LL: All ages	positive and negative	no
UNUSUAL SYMPTOMS	positive and negative	no

### ***Contraindications to VIT***

You can not say that there are absolute contraindications to take immunotherapy.

The relative contraindications for immunotherapy is the age of the children under 5 years of age, tumor diseases and autoimmune diseases, severe forms of systemic diseases and chronic organ failure, pregnancy, treatment with beta-blocking adrenergic receptors and receptor for enzyme (ACE-blockers). Also, patients who do not have self-discipline and do not cooperate with the medical staff in the process of treatment should not receive immunotherapy [13].

Immunotherapy venom should be postponed, discontinued (temporarily) or preceded by a consultation with specialists when patients develop acute febrile illness or a contagious disease (eg. Tuberculosis), in the case of exacerbations of chronic diseases (eg. Asthma, orifice pressure), deterioration of the diseases neurological, psychiatric and endocrine. You should also verify the decision to continue VIT in patients with bleeding diathesis, perioperative, and when there are complications to vaccination.

Admission to the center immunotherapy is a therapeutic center and has appropriately trained staff who knows the principles of VIT and in case of any complications knows how to master it. Some substantive skills of staff are not enough. Dana facility must have the appropriate hardware and laboratory equipment [22].

### ***The choice of venom to VIT***

It plays an important role identification of the insect, which is responsible for the reaction poużądleniową. The decision also facilitates a positive test result confirming allergic to a particular insect venom.

Sometimes, however, that by the end, we can not say whether anaphylaxis was caused by a bee or wasp, and diagnostic tests are positive for venom bees and wasps. In the medical literature this phenomenon is termed "double positivity" (called. Double positivity). This situation triggers the need for a parallel vaccination venom bees and wasps. Immunotherapy starts from this type of venom which the next possible contact is more likely to [31].

The similarity of venoms of individuals from families Vespidae allows the use of wasp venom immunotherapy for patients who are allergic to the venom of hornets. No bumblebee venom vaccine and antigenic similarity to bee venom decides that the desensitization of patients allergic to the venom used bumblebee bee venom.

### ***Methods for VIT***

At present, several methods are used to carry out immunotherapy. There are three ways the initial phase of VIT: ultrafast (ang. "Ultrarush"), high-speed and conventional. The methods differ in growth rate of doses and the time to achieve full maintenance dose - 100 mg venom, which is used for the duration of the so-called. the maintenance phase of treatment lasting 3 ÷ 5 years [9].

In the method of ultrafast maintenance dose is reached after 3 ÷ 5 hours (six injections every 30 minutes), the method of rapid about four days (4 injections at 30 minutes for the next 3 days) in the conventional method after a few weeks (1 to 2 injections every 7 days).

Immunotherapy regardless of the type of method always starts at the first dose of the venom, which is 0,001 ÷ 0,1 mg, and further grow by the method used to achieve the maintenance dose, ie. 50 to 100 mg of venom (u beekeepers 200 mg). This corresponds to the injection of venom by two bees and some wasps.

After receiving a maintenance dose the patient in the first year should report every 4 weeks for another dose of maintenance. In subsequent years, the treatment period between doses is extended to six weeks, especially for 8 weeks [22].

Extending the vaccination more than 5 years it is recommended that patients who, during VIT have the side effects of an allergic (until a negative skin test), patients who are still sting allergic symptoms (if you need to change the maintenance dose of vaccine), and patients with mastocytosis.

### **Summary**

The prevalence of allergy to hymenoptera venom is not yet completely understood. Allergy to insect stings can occur in people of all ages, especially after multiple previous stings.

Advances in modern medicine, especially in the field of allergy pose new challenges for the team holding the therapeutic care of the man allergic to insect venom. The nurse in this team plays an important role in the diagnosis of the patient. She gets the materials for diagnostic tests. It also performs all kinds of tests confirming the presence of allergy. Since its professionalism, competence and accuracy of tests depends on the patient's qualification for further treatment (immunotherapy).

The nurse is also involved in the treatment process. By the doctor givessubcutaneously injections of venom. Following patient monitors basic parameters of life. Documents the results

of these measurements. If you experience side effects inform your doctor and take part in the healing process of any irregularities.

Very much inazny is also its participation in the process of patient education. To communicate professionally and expertly knowledge it must constantly update, expand and improve. People working with sensitive patients must have medical knowledge beyond the basic messages in entomologii.

Most of the therapeutic team is dependent on the patient's life that well-educated situations. "sam the same "with żądłącym insect can shake injection of adrenaline. His chances of survival increase with this skill.

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