

Hymenoptera venom allergy How to minimize the risk of further stings?

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Systemic hypersensitivity reactions due to single or few Hymenoptera stings are reported by 0.8% up to 5.0% of the general population [1]. In most cases they are caused by IgE-mediated allergy to venom proteins, i.e. these are anaphylactic reactions. Stings by a honeybee (*Apis mellifera*) or by a wasp (*Vespula germanica*, *Vespula vulgaris*) are the most frequent elicitors, but also other species (in mediterranean countries particularly *Pollistes* spp) can be responsible. Symptoms are those of immediate type allergic reactions, ranging from mere skin involvement (generalized itching, flush, urticaria), minor to moderate cardiovascular, respiratory or gastrointestinal symptoms to full shock with a fatal outcome in some cases. Venom hyposensitization (immunotherapy) protects nearly all patients from further systemic sting reactions. Selection of patients for this treatment necessitates to assess the actual risk of re-stings in an individual.

The diagnosis of honeybee or wasp venom allergy is based on history and determination of immediate type skin reactivity and specific serum IgE antibodies to venoms. Neither skin test reactivity nor concentration of venom-specific IgE antibodies correlate positively with the severity of prior reactions. More importantly, sting challenge tests using living insects in patients with systemic

reactions who had not been on immunotherapy resulted again in systemic symptoms in only 14% to 58% [2], and for the individual patient there was found no reliable diagnostic parameter which would predict the outcome of such a re-sting. Thus it has been suggested that sting challenges should be performed routinely to identify those patients who need hyposensitization. However, a single negative challenge test seems not to be reliable, as the second such test, performed in subjects who tolerated a first challenge without clinical response, caused systemic reactions in 21% requiring sometimes epinephrine administration [3]. Sting challenge tests allow to identify only presence, but not absence of hypersensitivity.

Patients at risk of further anaphylactic sting reactions can be identified only by a history of prior systemic allergic symptoms, and hyposensitization is indicated in them if an IgE-mediated mechanism is apparent from skin or *in vitro* tests; some restrict this therapy to patients with severe sting reactions. Children with systemic sting reactions involving exclusively the skin developed systemic symptoms after re-stings in less than 20%, and as there was no increase of severity, hyposensitization is not necessary in most patients of this particular group [4]. Besides hyposensitization patients with systemic sting reactions are to be

instructed how to avoid further stings and how to use their emergency kit (antihistamine, corticosteroid, epinephrine) which they have always to carry with them [5].

There are certain patients in whom hyposensitization has to be performed with particular care and vigilance. Intense exposure to hymenoptera due to occupational or recreational activities poses some patients (e.g. beekeepers, farmers, gardeners, motocyclists) at an increased risk of re-stings. Threatening sting reactions are to be expected in patients with the following characteristics:

- history of prior severe sting reactions;
- older age of the patient;
- cardiovascular disease;
- asthma;
- mastocytosis;
- use of beta-blockers or ACE inhibitors (to be avoided by patients with systemic immediate type reactions);
- physical or psychical stress.

We have found constitutively elevated baseline serum levels of mast cell tryptase ($>13.50 \mu\text{g/l}$) and/or cutaneous mastocytosis in about 30% of the patients who had sting reactions with loss of consciousness. It is recommended to determine the mast cell tryptase concentration in the serum of patients with hymenoptera venom allergy, as about 80% of those with elevated levels have had very severe symptoms indicating a substantially increased risk also furtheron [6].

Patients with increased exposure to hymenoptera or with individual risk factors should be treated with hyposensitization in any case (definite contraindications are rare!). At least in

honeybee venom allergy the standard dose of $100 \mu\text{g}$ venom/four weeks should be increased to $200 \mu\text{g}$, as a single bee sting may deliver up to $200 \mu\text{g}$ venom. A sting challenge test should be performed after about 6 to 12 months of hyposensitization in order to identify patients still reacting systemically and needing an increase of the treatment dose to achieve full protection. Also, treatment longer than the usual three to five years has to be considered in patients with special risks. In the case of mast cell disease (elevated mast cell tryptase in the serum and/or mastocytosis) lifelong venom hyposensitization is indicated [7].

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