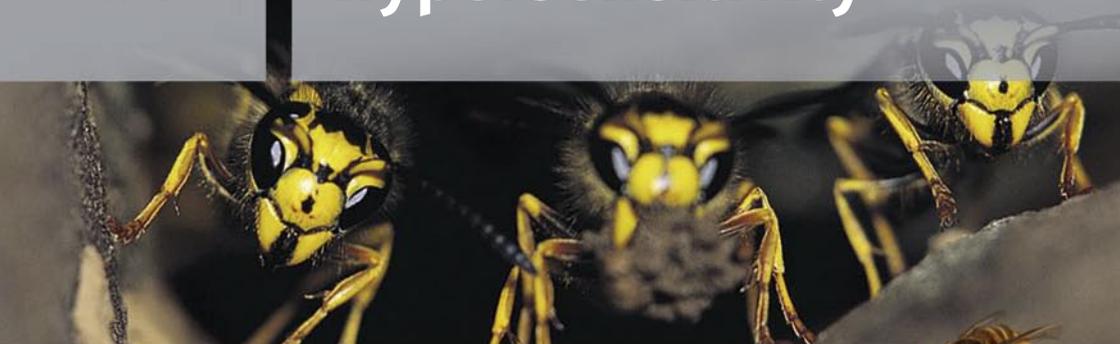




Insect venom hypersensitivity



THE UCB INSTITUTE OF ALLERGY

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Insect venom hypersensitivity

Despite the great variety of biting and stinging insects only wasps, bees and bumblebees and occasionally horseflies are able to cause severe allergic reactions in humans.

Bites from insects such as mosquitoes, ants and horseflies sometimes induce large itchy swellings which may result from a hypersensitivity reaction to the saliva introduced during the bite. Such local allergic reactions are unpleasant but rarely dangerous. Insects that are able to cause life threatening reactions belong to the Hymenoptera genus which do not bite but inject venom during a sting. In Belgium the majority of severe allergic reactions to stings are caused by classical wasps (yellow jackets) (*Vespula Germanica* or *vulgaris*) and to a lesser extent by honeybees (*Apis mellifera*), European hornets (*Vespa crabro*) and White face hornets (*Dolichovespula*). In other Western European countries such as Switzerland and Germany, honeybees seem to be the dominant offending insects. Bumblebees (*Bombus terrestris*) sting very rarely. With a few exceptions, bumblebee stings only occur in occupationally exposed people for example in bumblebee farms and in greenhouses.



Insect venoms can cause allergic reactions by their proteins which induce specific IgE antibodies as well as non-allergic reactions by low molecular weight substances that act directly on vascular structures and by peptides that directly degranulate mast cells in a non-specific way, causing an immediate local reaction. Consequently, after an insect sting, most people will develop an itchy swelling up to 5cm which may last for a few hours but does not need treatment. The situation is of course different when a sting occurs in the throat. In this case there is

a risk for upper airway obstruction and medical treatment may be necessary. Dangerous non-allergic reactions to insect stings and even to insect bites may on the other hand occur in patients with a particular susceptibility to these non-specific mast cell degranulating peptides in venoms and in saliva. This is the case in patients with cutaneous or systemic mastocytosis or in patients with an elevated basic serum tryptase. These patients must carry an emergency kit.



Insect venoms contain proteins, which induce the production of IgE-antibodies that then bind to receptors on the surface of mast cells and circulating basophils. Upon a next sting the injected venom will cross-link these cell bound IgE-antibodies at the injection site and, in case of intravascular absorption, also at distance. This results in degranulation of the mast cells which release different mediators that then cause either an immediate or delayed **large local** or a **systemic** allergic reaction.

The size of an allergic **large local** reaction varies but is often larger than 10 cm and usually lasts for several days. Sometimes the entire arm or leg is involved. Such large local reactions occur in 20% of the beekeepers at the start of the season.

In a general population the frequency of **systemic** allergic reactions to insect stings ranges from 0.5 to 3%. These reactions are characterized by allergic symptoms at distance of the sting site. The most frequent symptoms are generalized itching and redness, often followed by urticaria or angio-oedema and eventually by vomiting, abdominal pain, constriction in the chest, hoarseness, dizziness with or without a fall in blood pressure and feeling of impending disaster. Life threatening symptoms are abrupt shortness of breath, loss of consciousness and shock which may be fatal in patients with underlying cardiovascular or respiratory diseases and in patients with mastocytosis. The risk for a fatal reaction increases with the length of the interval between the onset of the systemic reaction and the administration of therapeutics.

It is impossible to predict the risk for developing a systemic allergic reaction to a next sting in the individual patient with a history of previous allergic sting reactions. However, studies have shown that the risk is approximately 10% in case of previous large local reactions, 25% in case of a previous systemic reaction to a wasp sting and 50% in case of a previous systemic reaction to a bee sting. The risk is lower in children and higher in patients with mastocytosis. There is little doubt that the more severe the previous systemic reaction was, the greater the risk for an even more severe reaction on a next sting. A first life threatening reaction is, therefore, an absolute indication for venom immunotherapy.



How to avoid stings?

Patients with a history of abnormal reactions to bee or wasp stings should be careful and should take the following preventive measures

1. Avoid picnics and barbecues.

Sweets and cakes, sliced cold meats, beer and other foods attract wasps. Never leave soft drinks open outside. Wasps can get into them unnoticed and sting in the mouth or throat of the person who is drinking.

2. Over-ripe fruit, dustbins and rubbish heaps attract wasps.

3. Avoid strong physical activities outside in hot weather.

Perspiration attracts bees and wasps.

4. Avoid mowing lawns, cutting hedges and working on balconies, in gutters, brushwood, abandoned houses or old attics.

All these places can hide wasps' nests. Ensure that there are none of them before starting to work.

5. Avoid hives and flower beds.

These places are often overcrowded with bees.

6. Do not wear bright coloured or black clothing.

White, green and brown are least attractive for insects.

7. Never walk bare-foot on lawns.

There is always a risk to step on a bee or a wasp or to end up in a wasps' nest.

8. Avoid strongly perfumed deodorants, after-shave lotions, hair sprays and sun creams.

Fragrant odours attract bees and wasps.

9. Avoid abrupt or zigzag movements when an insect is approaching.

It is most important to stay calm. Indeed, most insects do not sting spontaneously and will leave again unless threatened. If a wasp settles on you, approach it carefully with your hand and flick it away. Never hit it. You run the risk of not killing it and of getting stung.

10. Never kill a bee or wasp near its nest.

When they feel threatened, bees and wasps release volatile substances which attract other insects and incite them to sting.



What to do in case of a sting



1. General rule:

- If the sting is left in the skin, take it out as quickly as possible. Take care not to press on the venom sac because in this way the remaining venom will be injected. Use a sharp object or your nail and move it parallel to the skin to dislodge the sting as indicated in the diagram.
- Apply ice-cold compresses to the sting site.

2. For individuals with a history of hypersensitivity reactions:

- If possible place a tourniquet above the sting site
- Take an antihistamine as soon as possible.
- If symptoms appear at distance from the sting site, contact a doctor without delay.
- People with a history of generalized allergic reactions to insect stings should carry an emergency kit containing a dose of adrenaline ready for use.

Prevention of severe allergic reactions to insect stings.

Sting allergic reactions with severe symptoms at distance of the sting site are indications for venom immunotherapy on condition that a sensitization to the culprit venom has been demonstrated. The decision to start this treatment should be made on an individual basis, taking into account several risk factors such as age, degree of exposure, severity of the previous reaction and, not the least, anxiety that can seriously affect the quality of life.

The treatment aims at inducing tolerance to wasp or bee venom and mostly results in complete protection with wasp venom and in 75% protection with bee venom. During the «build-up» phase the dose of subcutaneously injected venom is progressively increased to a maximum dose, which is then further administered repetitively during the «maintenance» phase. Many different build-up regimens exist: from fast dosage increase schedules (ultra-rush, rush and semi-rush), that are carried out on in-patients, to slower ambulant regimens. During the maintenance treatment the interval between 2 injections is progressively increased to 6 or 8 weeks, and even more. In most European countries the treatment duration is 3 to 5 years. However in patients with very severe reactions and in patients with mastocytosis a life long treatment should be considered.

Bee and wasp venom differ considerably with regard to the allergenic proteins that are responsible for hypersensitivity reactions. If immunotherapy should be carried out, it is essential to identify the culprit insect.

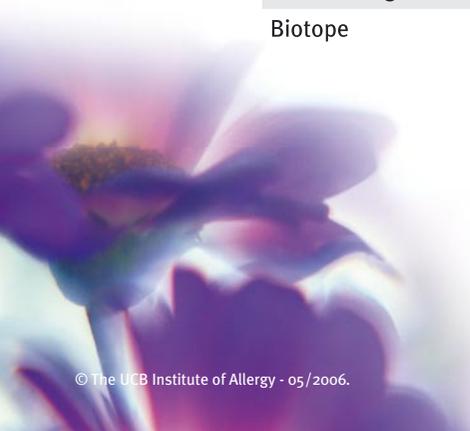


Identification of the culprit insect

The patient cannot positively identify the culprit insect when no insect was seen or recognized. The table shows some characteristics which can help to find which insect was the most probable cause.

Some characteristics of bees, wasps or bumblebees

CHARACTERISTICS	BEE	WASP	BUMBLEBEE
Hairy body	+	-	++
Colour	Brown-black	Yellow-black	Black-orange (yellow)-white
Spontaneous sting	-	+	-
Season	Spring, summer	Summer and autumn	Spring and summer
Loss of sting	+	-	-
Biotope	Hives Flower beds Clover-fields	Nests Fruit trees Foodstuffs Dustbins Thickets	Flower beds





The most important distinguishing features are the colour of the insect and the presence of a sting at the sting site. Bees frequently lose their sting, whereas wasps usually do not. Stings occurring early in spring are most frequently from bees. Allergic reactions to bee stings occur in particular in beekeepers, their family members and their neighbours. A spontaneous sting occurring in late summer, or in the neighbourhood of foods or fallen fruits, is almost certainly from a wasp. In Belgium, sting anaphylactic reactions are three times more frequently caused by a wasp than by a bee sting. Wasps are indeed much more aggressive than bees and therefore much more people are at risk to be stung.

In addition to the history, technical investigations such as venom skin tests and the determination of venom specific IgE antibodies can be very helpful to identify the culprit insect. Moreover, venom immunotherapy should only be performed if one of the two tests proves the presence of a sensitisation to bee or wasp venom. For both tests the degree of positivity is of no value in predicting the risk for- and the intensity of a reaction to a re-sting. On the other hand, in patients with very severe allergic reactions to insect stings or bites it is recommended to determine the basic tryptase level. If increased, the risk for a re-sting systemic reaction is indeed very high.



THE UCB INSTITUTE OF ALLERGY

Division of UCB S.A., The UCB Institute of Allergy (IOA) is an independent, European and not-for-profit organisation, created in 1987 to combat allergy.

In response to the international epidemic of this disease, the Institute's objective is to implement all the resources necessary to raise awareness of allergy as a major health issue amongst the general public, patients, health care professionals and public authorities.

Under the supervision of a Scientific Advisory Board made up of eminent European specialists in the field of allergy, IOA has initiated many actions. These aim to inform and educate about allergy, to improve prevention, to analyse the current situation and to define key actions to be taken over the coming years. Moreover IOA favours cooperation between various allergy related organisations. The Institute is present all around Europe with about 20 national sections and in South Africa.

The Institute's web site (<http://www.theucbinstituteofallergy.com>) provides patients and health care professionals with current relevant information and publications about allergy. For the general public, schools and children, IOA has produced videos (e.g. "Who's sleeping in your pillow?", "Allergic: to be or not to be?...Rhinitis"), educational games and other information material. IOA also organises and holds meetings, symposia, conferences, panel discussions.

As a result of these activities, The UCB Institute of Allergy hopes to forestall the sobering prediction of certain epidemiologists: In 30 years' time, everyone may be allergic... Unless we act now!



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The UCB Institute of Allergy thanks:

Prof. Anne-Marie Kochuyt, Afdeling Allergie en
Klinische Immunologie, Universitair Ziekenhuis
Gasthuisberg, Leuven, for her collaboration.

Head of Department: Prof. J. Ceuppens



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