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Allergies to bees, wasps and co.
Clinical symptoms, diagnostics and therapy at a glance

Fig. 1: Swarm of bees

Image source: Dr Regina Wagner

Insect stings can trigger hypersensitivity reactions in dogs. Along with vaccines, medicines and feed, they are among the most frequent triggers of a generalised allergic reaction (anaphylaxis), and fatalities have also been described. In Central Europe, honey bees (*Apis mellifera*) and common wasps (*Vespula vulgaris* and *Vespula germanica*) are particularly significant in this respect. More rarely, paper wasps, hornets or bumblebees play a role. These insects belong to the order Hymenoptera within the class Insecta. The venom is released via stings. Bees lose their sting and die, wasps and hornets can sting several times. The prevalence of anaphylactic reactions to insect stings in dogs is unknown. In humans, it is 1 – 5 % according to studies (1, 2).

Aetiopathogenesis of allergic reactions

The venom of Hymenoptera contains a variety of allergens and biologically active components. It is a complex mixture of enzymes, amines, glycoproteins and peptides (3).

In most cases, insect venom allergies are hypersensitivity reactions of the immediate type (type I allergy). IgE antibodies against components of the insect venom, formed during the sensitisation phase, are attached to mast cells and basophilic granulocytes. They cross-link with the associated allergens on repeated contact. This triggers a degranulation of mast cells and basophilic granulocytes, resulting in the release of vasoactive substances and inflammatory mediators (histamine, leukotrienes, TNF-α, tryptase, etc.). Within seconds to a maximum of 30 minutes, allergic (in the worst case, life-threatening) symptoms occur. An anaphylactic reaction is independent of the dose, so it is not related to the number of stings (1 – 3). According to studies, some dog breeds seem to show more frequently anaphylactic reactions to insect stings. This concerns Rhodesian Ridgebacks, Boxers and Vizslas. Dogs suffering from atopic dermatitis are also overrepresented (4).

Clinical symptoms

Clinically, 3 types of reaction can be distinguished (1 – 5):

1. The local reaction with local pain, local swelling and redness: it is not life-threatening and selflimiting unless the sting is in the mouth/throat area and the swelling leads to airway obstruction.
2. The general allergic reaction: anaphylaxis (= acute, systemic, IgE-mediated hypersensitivity reaction), it develops within minutes after the sting. Anaphylactic reactions are classified into different degrees (degree 0 – 3) (Fig. 2). Several organ systems are involved (skin, gastrointestinal tract, cardiovascular system, respiratory tract, brain). Skin symptoms, especially angioedema (fig. 3), are present in more than 50 % of cases.
3. Intoxication: this occurs in case of swarm attacks and is dose-dependent (the lethal dose is estimated at 20 stings/kg). Rhabdomyolysis, haemolysis, disseminated intravascular coagulation, kidney, liver or brain damage may occur.

Diagnostics

The first diagnostic steps are the accurate history and assessment of the clinical symptoms to classify the severity of the allergic reaction or to distinguish anaphylaxis from intoxication (not allergic, but dose-dependent). It is often not easy to identify the site of the sting or (in the case of bee stings) the stinger that may still be present and to find out which insect was the trigger. Clues can be gathered by taking a detailed medical history. Honey bees are mainly found in flower meadows, while wasps are found near sweets, sweet drinks, open food and rubbish bins. If it is an allergic reaction, allergy tests can be performed. Allergy tests are available in the form of prick and intradermal tests as well as serological tests. Laboklin offers an allergen specific ELISA (Enzyme Linked Immunosorbent Assay). Assay using Fcε receptor technology, a highly specific serological test.

Organ	Strength of anaphylaxis			
	Skin symptoms only (Grad 0)	Mild (Grad 1) ≤ 1 clinical symptom of at least 2 organ systems	Moderate (Grad 2) ≤ 1 clinical symptom of at least 2 organ systems	Strong (Grad 3) ≤ 1 clinical symptom of at least 2 organ systems
Skin or eyes	- Urticaria - Angioedema - Erythema - Pruritus - Lacrimation - Unrest - Pain	as for grade 0	as for grade 0	as for grade 0
Gastrointestinal tract		- Abdominal pain - single episode of vomiting, diarrhoea, nausea, salivation	- Persistent vomiting and diarrhoea	- Persistent vomiting and diarrhoeal
Cardiovascular system			- Tachycardia - pale mucous membranes	-vasodilatory or vasoconstrictive shock - Arrhythmias - Collapse - Cardiac arrest
Respiratory tract			- Dyspnoea - Tachypnoea - Panting - Stridor	- Cyanosis - Bradypnoea - Respiratory arrest
Brain				- Weakness - Seizures - Unconsciousness

Fig. 2: Classification of general allergic reactions (1, 5) *Image source: Dr Elisabeth Reinbacher*

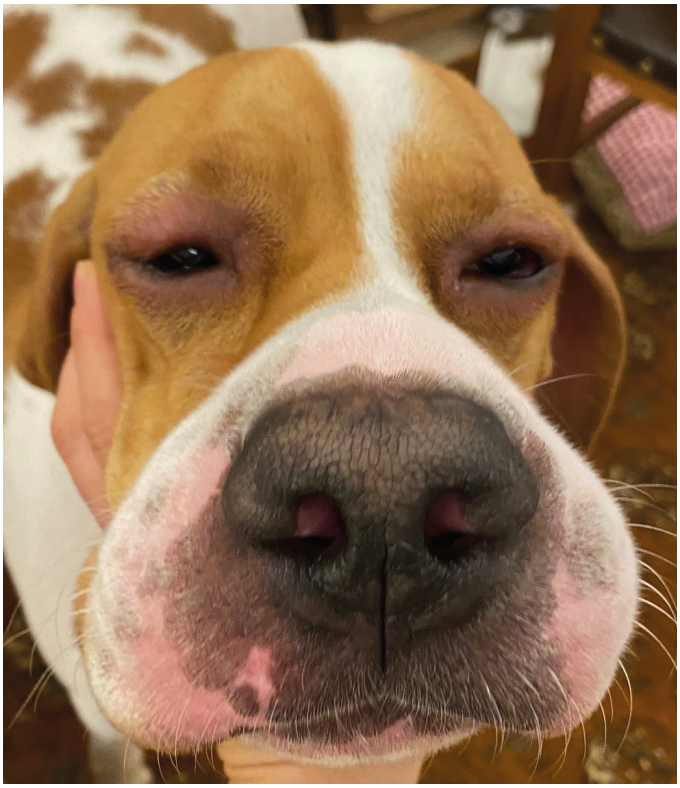

Fig. 3: Angioedema in the face of a dog
Photo source: Dr Ulrike Weiser

In addition, this serological test blocks the clinically insignificant crossreactive carbohydrate determinants (CCD) and thus only detects the clinically relevant IgE against hymenoptera venoms (bee, wasp, hornet and paper wasp).
When should be tested? The recommended timing is 2 – 4 weeks after the sting; if the result is negative, a repetition of the test is recommended after 4 – 8 weeks. Some studies even indicate a period of 3 – 6 months (1). Withdrawal periods with regard to therapy with glucocorticoids should also be considered (details can be found under https://laboklin.com/en/faq-allergy-general/).

Therapy of an anaphylactic reaction

Rapid diagnosis and grading of the degree of allergic reaction is the prerequisite for potentially life-saving therapy. Depending on the clinical severity of the anaphylaxis, different treatment regimens are recommended in acute cases. Local reactions can be alleviated by cooling. If the reaction is only skin symptoms (grade 0) or a mild anaphylactic reaction (grade 1), antihistamines and glucocorticoids are used to reduce the release of mast cell mediators and reduce their effect. The animal should be closely monitored for 24 – 72 hours, because it is known from human medicine (but not yet described in veterinary medicine) that a second anaphylactic episode can occur within the first 72 hours (biphasic reactions).
In moderate (grade 2) and severe (grade 3) allergic reactions with potentially fatal consequences, immediate and aggressive therapy is indicated. Epinephrine (= adrenaline) should be applied intravenously or intramuscularly and, if necessary, repeatedly after 15 – 20 minutes. Epinephrine leads to vasoconstriction and thus to an improvement in blood pressure and perfusion of vital organs. It also has a bronchodilator effect and reduces the production of inflammatory mediators. In addition, dogs with a grade 2 and 3 reaction should be treated with adequate intravenous continuous drip fluid therapy, oxygen administration, bronchodilators, antihistamines and glucocorticoids. Close monitoring of respiratory and heart rate, pulse quality and rhythm, blood pressure, oxygen saturation, blood gas parameters, haematocrit, liver, kidney and glucose parameters is recommended. Patients should be hospitalised until they are fully stabilised (1, 2, 4).

Prevention of further anaphylactic reactions

In general, the triggering allergen should be avoided. In the case of a bee allergy, this concerns flowering fields and trees, and in the case of a wasp allergy, picnic areas, fallen fruit and rubbish bins.
Owners of animals at risk of anaphylaxis should be given an allergy emergency kit consisting of an adrenaline injector, antihistamine and glucocorticoid tablets or suppositories.
As in human medicine, allergen specific immunotherapy (ASIT, hyposensitisation, venom immunotherapy, VIT) would be considered as a long-term therapy when a patient shows severe degrees (grade 2 or 3) of anaphylaxis. It is the only causal and also the most efficient treatment option to prevent or reduce further systemic reactions to insect venoms. The aim of VIT is to modulate the immune system, so that an allergic reaction of the organism to the insect venom is absent or milder. The efficiency of a VIT is very good in humans, in veterinary medicine however, there is little scientific

data available. There is no approved VIT for dogs on the market, which is why ASITs have to be carried out off-label. That means that the human allergens have to be mixed by the treating veterinarian. The information available from the literature suggests that the high efficiency of a VIT from human medicine could also apply to dogs. Rostaher, 2018 summarised the information from a total of 71 dogs that were hyposensitised: In 19 patients, there was no or a mild reaction after a new (not intentionally provoked) sting. Similar results were reported by Ewing et al., 2021 and Rostaher et al., 2021. The control of the efficacy of VIT can only be performed by sting provocation, repeated allergy tests are not suitable.
An ASIT is carried out in two phases: initiation phase and maintenance phase. Numerous treatment protocols have been described regarding the speed of the initiation phase (= dose increase of immunotherapy up to the maintenance dose): ultra-rush protocol, rush protocol, cluster protocol and conventional protocol. The faster the increase, the more often side effects are observed. For this reason, it is advisable to use an antihistamine for pre-medication during (ultra) rush immunotherapy, to insert a vein catheter and to monitor the patient intensively. Patients should stay in the practice for monitoring after the injection, although the exact period of this monitoring is not uniformly defined. Rostaher, 2018 describes side effects in 15% of 71 dogs treated with VIT, mainly gastrointestinal symptoms, but also urticaria and collapse are reported. In the study by Ewing et al, 2021, side effects occurred in only 2.8 % of the 82 patients, the majority occurred in the initiation phase. In the latter study, mainly gastrointestinal side effects, rarely urticaria, lethargy, pruritus, erythema and head oedema were described; no life-threatening side effects occurred.
The maintenance dose for VIT is 100 µg, which can be increased to 200 µg if therapy fails. The treatment interval using aqueous solutions is 4 – 6 weeks, which can be extended to up to every 8 weeks from the 3rd year onwards. Depot preparations with aluminium hydroxide are injected every 6 – 8 weeks. Extending the dose interval to 3 months seems to be possible in the future (1). In some VIT products, human albumin is used as a stabiliser; hypersensitivity reactions in dogs to human albumin have been described, which is why VIT products without human albumin should be used (6, 7).
The recommendation for the duration of treatment of VIT in dogs is not uniformly defined in the literature. According to data from human medicine, VIT may be discontinued after 5 years if a new sting does not lead to an anaphylactic reaction, otherwise the therapy is continued for life (1). Ewing et al., 2021 generally recommend lifelong therapy.

In summary, studies to date indicate that VIT in dogs allergic to insect venoms is a successful form of therapy with few side effects to protect against recurrence of anaphylactic reactions.
Currently, there is no VIT approved for the dog, which is why hyposensitisation against insect venoms can only be performed off-label using human allergens.

Dr Elisabeth Reinbacher

Further reading

1 Rostaher A. Bienen- und Wespengiftallergien bei Hunden – Von der Akutbehandlung bis zur Desensibilisierung. Kleintier Konkret. 2018;21(S03):13-19.
2 Fitzgerald KT, Flood AA. Hymenoptera stings. Clin Tech Small Anim Pract. 2006 Nov;21(4):194-204. doi: 10.1053/j.ctsap.2006.10.002. 3
3 Boord M. Venomous insect hypersensitivity. In: Noli C, Foster AP, Rosenkrantz W eds. Veterinary Allergy. Chichester, UK: John Wiley&Sons; 2014. p 191-4.
4 Rostaher A, Hofer-Inteeworn N, Kümmerle-Fraune C, Fischer NM, Favrot C. Triggers, risk factors and clinicopathological features of urticaria in dogs - a prospective observational study of 24 cases. Vet Dermatol. 2017 Feb;28(1):38-9. doi: 10.1111/vde.12342.
5 Turner K, Boyd C, Stander N, Smart L. Clinical characteristics of two-hundred thirty-two dogs (2006-2018) treated for suspected anaphylaxis in Perth, Western Australia. Aust Vet J. 2021 Dec;99(12):505-512. doi: 10.1111/avj.13114.
6 Ewing TS, Dong C, Boord MJ, Fang Y. Adverse events associated with venomous insect immunotherapy and clinical outcomes in 82 dogs (2002-2020). Vet Dermatol. 2022 Feb;33(1):40-e14. doi: 10.1111/vde.13016.
7 Rostaher A, Mueller RS, Meile L, Favrot C, Fischer NM. Venom immunotherapy for Hymenoptera allergy in a dog. Vet Dermatol. 2021 Apr;32(2):206-52. doi: 10.1111/vde.12931.