

Identifying and managing Hymenoptera venom allergy

Kane P *et al* (2016) Identifying and managing Hymenoptera venom allergy.

Nursing Standard. 30, 39, 44-51. Date of submission: June 2 2014; date of acceptance: November 10 2014.

Abstract

Hymenoptera venom allergy is an immunoglobulin E (IgE)-mediated hypersensitivity to the venom of insects from the Hymenoptera order and is a common cause of anaphylaxis. A diagnosis of venom allergy is made by taking an accurate medical, family and social history, alongside specific allergy testing. Systemic reactions to Hymenoptera venom occur in a small proportion of the population; these range from mild to life-threatening in severity. Treatment for local reactions involves the use of cold packs, antihistamines, analgesia and topical corticosteroids to help alleviate swelling, pain and pruritus. Venom immunotherapy is the treatment of choice for reducing the incidence of future anaphylactic reactions in individuals who have signs of respiratory obstruction or hypotension. Venom immunotherapy is the most effective treatment in reduction of life-threatening reactions to venom, and can improve quality of life for individuals. Treatment should only be provided by experienced staff who are able to provide emergency care for anaphylaxis and life-threatening episodes. A risk assessment to deliver treatment should be undertaken before treatment is commenced.

Authors

Patricia Kane Matron, Children's Allergy Service, St Thomas' Hospital, Guys and St Thomas' NHS Foundation Trust, London, England.

Victoria Timms Deputy clinical nurse specialist, Children's Allergy Service, St Thomas' Hospital, Guys and St Thomas' NHS Foundation Trust, London, England.

Roisin Fitzsimons Nurse consultant, Children's Allergy Service, St Thomas' Hospital, Guys and St Thomas' NHS Foundation Trust, London, England.

Correspondence to: victoria.timms@gstt.nhs.uk

Keywords

allergy, anaphylaxis, Hymenoptera, immunoglobulin E-mediated hypersensitivity, immunotherapy, systemic allergic reactions, venom allergy

Review

All articles are subject to external double-blind peer review and checked for plagiarism using automated software.

Online

For related articles visit the archive and search using the keywords above. Guidelines on writing for publication are available at: journals.rcni.com/r/author-guidelines.

HYMENOPTERA VENOM ALLERGY is an immunoglobulin E (IgE)-mediated hypersensitivity to the venom of insects. This hypersensitivity can cause local or systemic reactions that can vary in severity (Krishna *et al* 2011). When a person is stung by a venomous insect, they typically experience intense burning and pain at the site of the sting, followed by erythema and oedema. This usually resolves within a few hours, with or without antihistamine medication.

Hymenoptera venom primarily consists of aqueous solutions containing proteins, peptides and vasoactive amines. Some individuals have an immune response to Hymenoptera venom and produce IgE antibodies. In these individuals, subsequent stings can trigger a rapid systemic inflammatory response. The insects that are important medically belong to three families of the Hymenoptera order: the Apidae family that includes honey bees and bumble bees; the Vespidae family that includes wasps, hornets and paper wasps; and the Formicidae family that includes ants, harvest ants, bulldog ants and jack jumper ants. This article focuses on identifying and managing allergies to Apidae and Vespidae (bee, hornet and wasp) venom. Only the females of each species are able to sting (Krishna *et al* 2011).

Epidemiology

In Europe and the US, 56-94% of the population are stung by an insect of the Hymenoptera family at least once in their lifetime (Krishna *et al* 2011); 0.3-7.5% develop a systemic reaction to being stung. In high risk groups, for example bee keepers and their families, 14-32% develop a systemic reaction (Krishna *et al* 2011). Children appear to be stung more often than adults. However, it is estimated the incidence of systemic reactions is only 1% in children under the age of 17 years (Krishna *et al* 2011, Matysiak *et al* 2013).

Venom allergy is a significant cause of anaphylaxis. There is uncertainty in data collection, resulting from poor reporting and classification of anaphylaxis. For information on criteria and treatment of anaphylaxis, refer to

guidance from the National Institute for Health and Care Excellence (NICE) (2011, 2016), Royal College of Paediatrics and Child Health (2011) and the Resuscitation Council UK (RCUK) (2008).

Insect stings are the second most frequent cause of anaphylaxis outside a medical setting in the UK, second to drug allergy and two to three times more common than food allergy (Boyle *et al* 2012). Fatal anaphylaxis to venom accounts for 20% of anaphylaxis fatalities worldwide; however, anaphylaxis to venom is said to be lower in the UK population (Ludman and Boyle 2015). Systemic reactions to wasps are more common than to bees in the UK general population. Systemic reactions to bees are prevalent in beekeepers and their household members (especially during the early years of beekeeping) and individuals with an occupational risk (Bilò 2011, Matysiak *et al* 2013). The risk of severe reactions is increased by 5-15% if preceded by a large local reaction within a short interval, even if the first sting was well tolerated (Bilò *et al* 2005). This was more evident in individuals sensitised to bee venom than to wasp venom. For individuals who have experienced an anaphylactic reaction, the risk of having a recurrent episode is estimated to be between 57% and 75% (Bilò *et al* 2005).

Vespids usually do not lose their stings after stinging; hence they are capable of stinging individuals multiple times, whereas bees typically lose their barbed sting (Bilò *et al* 2005, Ludman and Boyle 2015). The honey bee is said to deliver more severe stings than insects in the Vespidae family (Ludman and Boyle 2015).

There appears to be no clear association with other allergy conditions and only 3% of individuals who have venom allergy were atopic (Krishna *et al* 2011). Venom allergy can develop at any age and usually manifests after several uneventful stings.

Data suggest that men are twice as likely as women to develop a Hymenoptera venom allergy (NICE 2011). This may result from male risk-taking behaviour around insects.

Published data on venom allergy are mostly from the US and mainland Europe. However, Pumphrey (2004) reported that in the UK, between the years 1992 and 2001, 47 out of 214 deaths due to anaphylaxis were caused by bee or wasp stings and the average age of death was 50 years. Bees release a large amount of venom, 50-140 micrograms, in comparison to wasps, which release 2-17 micrograms. At least one sting is required to sensitise a person to insect venom. Once sensitisation has occurred, a sting can cause mast cell and basophil degranulation. This results in the release of histamine and other inflammatory mediators, which can give rise to allergic reactions, and at the severe end of the allergic spectrum, anaphylaxis (Krishna *et al* 2011).

It is important to use consistent and reproducible methods to classify and identify the signs and symptoms of allergic reactions, and to record and report them. Using a standardised grading for allergic reactions ensures consistent recording of their severity, which enables accurate diagnosis and guides management and treatment options. Brown (2004) proposed a three-tier grading system (Table 1) that describes the significance of features in terms of the probability of developing hypoxia and/or hypotension (Hedde and Golden 2015).

It appears that the sooner the symptoms occur the more severe the allergic reaction. Some large local reactions are caused by a late-phase IgE-dependent reaction, where the reaction appears initially to be mild and then progresses after 12-24 hours to a more severe response. The risk of developing a severe reaction following a sting is estimated to be 5-15%, but the individual should be aware that a

TABLE 1

Grading system for generalised hypersensitivity reactions

Grade	Defined by	
1. Mild	Skin and subcutaneous tissues only.*	Generalised erythema, urticaria, periorbital oedema or angioedema.
2. Moderate	Features suggesting respiratory, cardiovascular or gastrointestinal involvement.	Dyspnoea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain.
3. Severe	Hypoxia, hypotension or neurologic compromise.	Cyanosis or oxygen saturation SpO ₂ <92% at any stage, hypotension (systolic blood pressure <90mmHg in adults), confusion, collapse, loss of consciousness or incontinence.

*Mild reactions can be further sub-classified into those with and without angioedema.
(Reproduced with permission from Brown (2004))

further sting within two months may manifest in a severe reaction (Krishna *et al* 2011). The presence of comorbidities which affect cardiac or respiratory function may increase the severity of a severe allergic reaction. The majority of serious reactions in children are cutaneous, but cardiorespiratory compromise is common in adults (Rueff *et al* 2013).

Fatal reactions are rare, but are thought to be often unrecognised, and therefore under-reported as a cause of death. Approximately one quarter (47/214) of all anaphylactic deaths in the UK in the years 1992 to 2001 occurred from a sting (Pumphrey 2004), with death occurring on average 10-15 minutes after a sting (RCUK 2008). Krishna *et al* (2011) reported that rare toxic reactions can occur as a result of multiple simultaneous stings, usually over 50, manifesting as delayed haemolysis, nephropathy, coagulopathy and neurological symptoms and Guillain-Barré syndrome. These reactions do not appear to be IgE-mediated, but the mechanisms are unknown.

Diagnosis of Hymenoptera allergy

It is recommended that an individual suspected of venom allergy, identified with a grade one to three (Table 1) allergic reaction to an insect sting, is referred to an allergy specialist for further investigation (Krishna *et al* 2011, NICE 2011).

The basis of the diagnosis involves taking a detailed medical, family and social history. This should take into account the symptoms and progression of the allergic reaction, with particular attention to the timing of events, number of stings and location of the affected area on the body. It is important to establish the pattern of previous stings and severity of reactions, as well as the treatments given and responses to medication and management.

Baseline serum tryptase should be measured after a reaction to a sting, ideally within two hours post-sting. Tryptase is a specific marker for mast cell and basophile degranulation in type 1 (immediate or anaphylactic) hypersensitivity reactions. About 10% of patients with Hymenoptera venom allergy present with an elevated baseline tryptase concentration >11.4 microgram/L (Krishna *et al* 2011, Rueff *et al* 2013). Baseline tryptase is elevated in 10% of patients experiencing anaphylaxis to venom (Rueff *et al* 2013). Therefore, baseline tryptase levels should be measured in all individuals following a severe systemic reaction to insect stings, since those with raised levels have an increased risk of future severe systemic reactions. When an abnormal elevation of tryptase is identified, a diagnosis of mastocytosis should be considered. Mastocytosis is characterised by a proliferation and accumulation of mast cells in several organs and tissues (Bonadonna *et al* 2010). This predisposes individuals to severe anaphylaxis and to exaggerated responses to exogenous triggers such as medication and insect stings.

Test results

Positive test results in the form of skin-prick testing (Figure 1a) and intradermal testing (Figure 1b) or blood tests for venom-specific IgE are helpful in the diagnosis and management of Hymenoptera venom allergy. Identification of the insect responsible for the sting can be difficult. It is a common error for patients to state that the insect was a bee when it was a wasp. Therefore, all patients should be tested for bee and wasp venom to assist in appropriate management. Venom-specific IgE testing does not predict the likelihood and severity of a future reaction, and false negative results are not uncommon (Golden 2005).

Skin-prick testing gives an immediate result, provides greater reliability than serum IgE and shows clearer discrimination between bee and wasp sensitisation than serum IgE. It is the gold standard investigation for venom allergy, together with taking a comprehensive history. Skin-prick testing should ideally be performed two to eight weeks after a sting, since the refractory period can produce false negatives (Biló *et al* 2005, Ludman and Boyle 2015). Intradermal testing is recommended if skin prick testing is negative in patients with a strong clinical history (Biló *et al* 2005, Krishna *et al* 2011, Ludman and Boyle 2015).

Intradermal testing is particularly useful in clarifying double-positivity to wasp and bee venoms. It is important to titrate the solution strengths for skin prick testing and intradermal

FIGURE 1

(a) Skin-prick testing and (b) intradermal testing

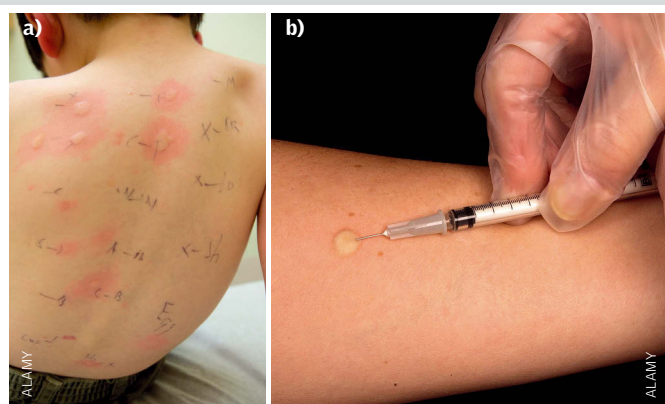
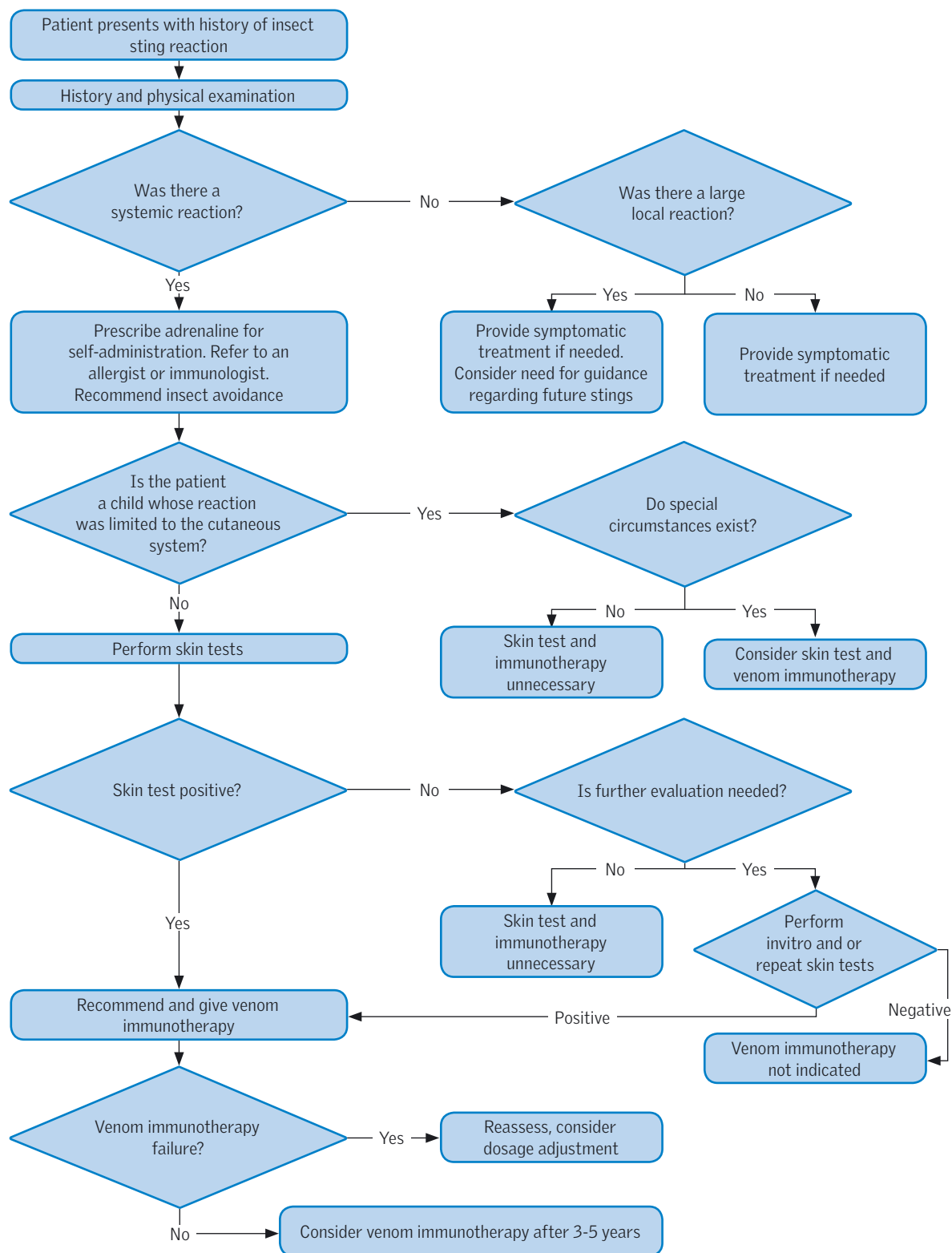


FIGURE 2**Algorithm: management of stinging insect reactions**

(Moffitt *et al* (2004); reproduced with permission)

testing according to the severity of venom reactions, since there have been cases reported of severe reactions during testing. Therefore, emergency equipment should be available and testing should be carried out only by experienced staff (Boyle *et al* 2012).

Skin prick testing results are considered positive with a wheal of at least 3mm greater than the positive control. Positive results of intradermal testing should display an increase of bleb diameter of 3-5mm. Venom-specific IgE blood levels are considered positive if equal to or greater than 0.35kU/L. Total serum IgE of >250 kU/L is generally thought to be a non-specific marker, but may indicate asymptomatic sensitisation (Krishna *et al* 2011). If there is uncertainty, specific recombinant allergens can be tested in the serum to identify Api m1 (bee) and Ves v5 (wasp) antibody levels (Erdmann *et al* 2004).

No single test can detect all patients with Hymenoptera venom allergy, so all forms of testing should be considered. However, standardisation is recommended, since variations in testing can be confusing in the diagnosis and management of venom allergy (Diwakar *et al* 2008).

Treatment and management

Local reactions to insect stings are usually treated with cold packs, oral antihistamines, analgesia and topical corticosteroids, to alleviate swelling, pain and pruritus. A short course of oral corticosteroids may be necessary for larger local reactions, and the possibility of infection should be considered and managed appropriately. Individuals with any associated signs of upper and lower airway obstruction or hypotension should

be treated with adrenaline intramuscularly and require urgent assessment by emergency services.

Muraro *et al* (2007) and NICE (2012) describe anaphylaxis as 'a severe, life-threatening, generalised or systemic hypersensitivity reaction'. This is characterised by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes. Early treatment with intramuscular (IM) adrenaline is the intervention of choice for patients having an anaphylactic reaction (Box 1) (RCUK 2008).

The risk of future systemic reactions to venom is affected by the sequence of events and the severity of signs and symptoms as a result of previous stings. Future management of venom stings should be discussed. An adrenaline auto-injector device should be prescribed and training on its use should be given. It is important to ensure that these devices are used within their expiry date.

Health education

Emergency kits are given to individuals with venom allergy. These kits include adrenaline auto-injector devices, antihistamines and an inhaled bronchodilator. They should be available during venom immunotherapy and following its completion, especially in those who continue to be at risk of multiple stings. A written emergency management plan should be developed for each individual. How to use the emergency kit should be demonstrated and discussed with the individual, family, and school or college personnel (Krishna *et al* 2011). Box 2 includes recommended measures for individuals and their school, college or workplace to take to reduce or avoid stings. The Anaphylaxis Campaign (2016) has a useful website for schools for further guidance on the management of Hymenoptera venom allergy.

The case study (Box 3) considers important aspects in the recognition, treatment and management of Hymenoptera venom allergy.

Venom immunotherapy

Venom immunotherapy aims to reduce the risk of future severe systemic reactions and is thought to be highly efficacious in preventing recurrent anaphylaxis in venom allergy patients (Oude Elberink and Dubois 2003). The efficacy of venom immunotherapy is 95% for wasp venom and approximately 80% for bee venom (Krishna *et al* 2011). Therefore, venom immunotherapy is the most effective treatment for preventing severe reactions to future stings (Boyle *et al* 2012).

Venom immunotherapy should only be performed in a specialist allergy service, with skilled personnel delivering and assessing the

BOX 1

Doses of intramuscular (IM) adrenaline

Adrenaline IM dose – adults

0.5mg IM (500 micrograms = 0.5mL of 1:1000 adrenaline)

Adrenaline IM dose – children

The scientific basis for the recommended doses is weak.

The recommended doses are based on what is considered to be safe and practical to draw up and inject in an emergency. (The equivalent volume of 1:1,000 adrenaline is shown in brackets.)

>12 years: 500micrograms IM (0.5mL), the same as adult dose.

300microgram (0.3 mL) if child is small or prepubertal.

>6-12 years: 300micrograms IM (0.3mL).

>6 months to 6 years: 150micrograms IM (0.15mL).

<6 months: 150micrograms IM (0.15mL)

Repeat the IM adrenaline dose if there is no improvement in the patient's condition.

Further doses can be given at five-minute intervals according to the patient's response.

(Reproduced with the kind permission of the Resuscitation Council (UK) 2008)

patient and in an environment that can instigate emergency treatment for anaphylaxis. Selection for venom immunotherapy treatment is based on history taking, results of baseline serum tryptase, skin-prick testing and/or intradermal testing and specific IgE to Hymenoptera venoms or recombinant specific allergens. Preparation of the patient is essential before commencing treatment, so that an informed choice and consent to proceed with venom immunotherapy is assured (Guy's and St Thomas' NHS Foundation Trust 2015). Venom immunotherapy is an invasive form of treatment that requires commitment and concordance from patients for between three and five years.

The criteria for offering venom immunotherapy to individuals usually include those who have reported severe systemic reactions or anaphylaxis, or have additional risk factors identified. Among these risk factors are a high baseline tryptase level, people whose quality of life has been significantly affected by anxiety regarding future stings, and those who have a high risk of future stings or live far from emergency medical care (Oude Elberink and Dubois 2003, Bonifazi *et al* 2005, Brown and Stone 2011, Krishna *et al* 2011, Simons *et al* 2011, 2012).

Venom immunotherapy treatments are recommended over a three to five-year programme in the UK. Treatment consists of an initial phase of either:

- ▶ Conventional: one injection every three to seven days.
- ▶ Modified rush: two to four injections given weekly at intervals of 30 minutes.
- ▶ Ultra-rush: four injections at 30-minute intervals, then one injection after 60 minutes.

Once the maintenance phase of treatment is reached the patient receives 100micrograms (equivalent of two venom stings) every four weeks for the first year, every six weeks for the second year and every eight weeks for the remaining years. Individuals may still develop large local reactions to the maintenance dose of 100micrograms over the three to five-year treatment programme.

The treatment is delivered subcutaneously in the upper deltoid region of the arm. The individual is assessed before each treatment to ensure that their vital signs are within safe parameters and that they are well to proceed with treatment. Signs of respiratory compromise before administration would contraindicate treatment. Prophylactic dosing with antihistamine is recommended once the maintenance stage is reached. This should be taken on the evening before and the morning of treatment. However, during the initial up-dosing the aim is to limit antihistamine cover

so that the body can gradually offer its own defence to the venom. Data suggest that venom immunotherapy provides immunity from severe systemic or anaphylactic reactions for 10-15 years (Rueff *et al* 2013).

Rueff *et al* (2013) and Madsen (2007) identified the contraindications for commencing or continuing venom immunotherapy. These include:

- ▶ Patients taking beta blockers, tricyclic antidepressants, monoamine oxidase inhibitors and angiotensin-converting enzyme inhibitors, since they may not respond to treatment with adrenaline.
- ▶ Pregnancy when commencing treatment. Therapy should not be initiated during pregnancy but can be continued during pregnancy if the patient has shown a good level of tolerance to previous maintenance injections.
- ▶ Mastocytosis – this results in a proliferation of mast cells in different tissues. In patients with venom allergy there is an increased risk of IgE and mast cell activation that causes allergic reactions. This increases the likelihood of fatal reactions and anaphylaxis (Niedoszytko *et al* 2009).
- ▶ People with malignancies, severe chronic or uncontrolled seasonal severe asthma and immunological conditions. This is because their immune system might be compromised, which may cause a severe allergic reaction.

Reactions during therapy can occur at any stage of treatment. These usually indicate long-term

BOX 2

Hymenoptera sting avoidance measures

Measures to avoid Hymenoptera stings:

- ▶ Wear light-coloured clothing.
- ▶ Avoid strong fragrances, perfumes and highly scented shampoos.
- ▶ Wear shoes while outdoors and cover your body with clothing, and a cap or hat while gardening.
- ▶ Avoid picking fruit from the ground or trees. Exercise caution in gardens and picnic areas, outdoors where food is served and near refuse.
- ▶ Try to avoid drinking from an open can or bottle that has been left unattended.
- ▶ Wash hands after eating or handling sticky or sweet foods outdoors.
- ▶ Keep uneaten foods covered, especially when eating outdoors.
- ▶ Avoid high-risk hobbies if possible.
- ▶ Always contact a professional to remove bee nests and nests of wasps that sting.
- ▶ Always wear full protective clothing if handling bees.
- ▶ Beehives should be located away from the family home to reduce the risk of family members of beekeepers being stung. Beekeepers should change their clothes before entering the family home.
- ▶ If prescribed, carry your adrenaline auto-injector device at all times, and check that this is in date. Ensure that others around you know how to recognise an allergic reaction and how to use the auto-injector device.
- ▶ Wear a medical alert bracelet.

(Brown and Stone 2011)

BOX 3

Case study

Oliver, a 12-year-old boy, developed anaphylaxis after a single bee sting. He was taken to the local emergency department, where he was given intramuscular adrenaline (x2), fluid replacement, oral antihistamines and oral steroids. The result of his baseline serum tryptase test was 8.2microgram/L.

Oliver recovered fully in six hours. On discharge, he was prescribed two auto-injector adrenaline devices and trained in their use, and instructed on the use of oral antihistamines. He was referred to the paediatric allergy service.

Oliver was seen within six weeks of referral and his history confirmed anaphylaxis to an insect sting. His history revealed two previous occasions where he was stung by an insect, each identified as a bee. The first sting resulted in mild inflammation at the site of sting. The second sting involved angioedema of the lips. These self-resolved in 24-72 hours.

He had no medical or family history of atopy; however his family owned a fruit and flower farm and kept bees for commercial use. Oliver was becoming more involved and interested in the family business.

A skin-prick test to bee and wasp venom was unclear, with a 2mm wheal in response to each venom. Intradermal testing was performed: this identified a wheal and bleb of 8mm to bee venom and was negative to wasp venom. Specific IgE to wasp antigen was negative and to bee antigen 0.45Ku/L. Bee venom allergy was confirmed.

Oliver was recommended for bee venom immunotherapy. Oliver and his family were given information regarding the venom immunotherapy regime, potential side effects and long-term aims of the therapy. The family were prepared for the long-term commitment to venom immunotherapy and acknowledged the invasive nature of the treatment. Informed written consent was obtained.

Oliver commenced ultra-rush venom immunotherapy three months later. Oliver received five gradually increasing subcutaneous injections until a dose of 50micrograms (one sting) was achieved. Oliver developed widespread pruritus and hives in addition to mild difficulty breathing after the third injection, which was 0.2mL (20micrograms). These symptoms were not treated and self-resolved in two hours. Oliver was continually monitored to ensure there was no escalation of respiratory compromise.

We continued with the final two injections, one hour apart, and no further reactions occurred. Oliver was discharged and emergency training was given to him and his family. The next two injections of 50micrograms, then 100micrograms, were uneventful.

Oliver attended every four weeks for injections during the first year with no adverse events. In the second year Oliver reacted after his second injection at the six-week interval, developing a rash, hives and widespread wheeze. This was treated with nebulised salbutamol (x4), oral steroids and antihistamine, and all symptoms resolved within one hour. Adrenaline did not need to be administered. Oliver's treatment schedule was changed back to 50micrograms/mL every four weeks for six months then 100micrograms/mL for six months. The nursing team supported Oliver and his family during this experience to reduce future anxiety.

In years three to five, Oliver came for his injections every eight weeks with no adverse events. At each visit there was localised swelling and pruritus at the site, as would be expected from one or two bee stings. Oliver did not experience any bee stings throughout the course of his venom immunotherapy.

After five years, Oliver was discharged. He was advised to carry his adrenaline auto-injectors and take note of the precautionary measures (Box 2). He was also advised that if he was unwell he should limit his exposure to bees.

Oliver is now studying farming at agricultural college. He has had no further anaphylactic reactions to bee stings, but has experienced several moderate or severe reactions to bee stings, which he treated successfully with high-dose antihistamines.

efficacy of treatment. Studies indicate that adverse reactions to venom immunotherapy vary from 5-15% of people reported mostly in the initial stage, to 0.26% in the maintenance phase, and are more likely to occur in patients receiving honeybee venom (Paschall 2012).

Changes in a person's medical condition or medication regimen and adverse reactions from previous injections should be established before treatment is given. Treatment will not be administered if the patient has an infection, particularly one affecting the respiratory tract, or with evidence of sepsis, so that a risk-benefit assessment analysis can be undertaken. The patient should be observed for a minimum of one hour after each administration of the venom to monitor for adverse reactions. On discharge the patient's vital signs should correspond to their initial baseline observations, and the site of injection should be observed and recorded for the appearance of local reactions.

A Cochrane review emphasised two studies which included data on health-related quality of life (Boyle *et al* 2012). These studies concluded that venom immunotherapy was associated with an improvement in quality of life compared with supplying adrenaline auto-injector devices alone, and that it provided less disruption to daily activities. Oude Elberink and Dubois (2003) observed that some Hymenoptera venom allergy patients were continuously preoccupied with the sting event, which had an effect on their emotional and social functioning and in some cases professional functioning. As mortality in Hymenoptera venom allergy is low, improved quality of life is an important therapeutic target of treatment (Oude Elberink and Dubois 2003).

Conclusion

Venom allergy is an immune response and an established trigger for anaphylaxis. Insect stings are common, and reactions can vary in severity. The identification of life-threatening events in response to insect venom is hindered by inconsistencies in the definition of anaphylaxis, as well as its recording and recognition. This can result in delays in investigation, treatment and health improvements for individuals.

A detailed history is the basis of individual diagnosis and management. All forms of specific allergy testing should be considered alongside this information in the diagnosis of venom allergy. Health education on preventing stings should be regularly provided to individuals with venom allergy, together with an emergency plan outlining treatment in the event of an allergic

reaction. The literature and allergy guidelines state that venom immunotherapy is the treatment of choice for prevention of future anaphylaxis to insect venom.

Venom immunotherapy is an intense and long course of treatment requiring commitment and concordance from patients. However, its efficacy is well documented, and patients who have

received venom immunotherapy report a better quality of life than those who solely carry an adrenaline auto-injector device. Further work is required to improve the identification of individuals who are at risk of life-threatening reactions to insect stings or bites. Venom immunotherapy needs to be investigated further to determine its long-term efficacy **NS**

References

- Anaphylaxis Campaign (2016) *Frequently Asked Questions: Schools*. tinyurl.com/h8xgg46 (Last accessed: May 17 2016.)
- Bilò MB (2011) Anaphylaxis caused by Hymenoptera stings: from epidemiology to treatment. *Allergy*. 66, Suppl 95, 35-37.
- Bilò BM, Rueff F, Mosbech H *et al* (2005) Diagnosis of Hymenoptera venom allergy. *Allergy*. 60, 11, 1339-1349.
- Bonadonna P, Zanotti R, Müller U (2010) Mastocytosis and insect venom allergy. *Current Opinion in Allergy and Clinical Immunology*. 10, 4, 347-353.
- Bonifazi F, Jutel M, Bilò BM *et al* (2005) Prevention and treatment of hymenoptera venom allergy: guidelines for clinical practice. *Allergy*. 60, 12, 1459-1470.
- Boyle RJ, Eiremeli M, Hockenhull J *et al* (2012) Venom immunotherapy for preventing allergic reactions to insect stings. *The Cochrane Database of Systematic Reviews*. Issue 10. CD008838.
- Brown SG (2004) Clinical features and severity grading of anaphylaxis. *The Journal of Allergy and Clinical Immunology*. 114, 2, 371-376.
- Brown SG, Stone SF (2011) Laboratory diagnosis of acute anaphylaxis. *Clinical and Experimental Allergy*. 41, 12, 1660-1662.
- Diwakar L, Noorani S, Huisson AP, Frew AJ, Krishna MT (2008) Practice of venom immunotherapy in the United Kingdom: a national audit and review of literature. *Clinical & Experimental Allergy*. 38, 10, 1651-1658.
- Erdmann SM, Sachs B, Kwiecień R, Moll-Slodowy S, Sauer I, Merk HF (2004) The basophil activation test in wasp venom allergy: sensitivity, specificity and monitoring of specific immunotherapy. *Allergy*. 59, 10, 1102-1109.
- Golden DBK (2005) Insect sting allergy and venom immunotherapy: a model and a mystery. *Journal of Allergy and Clinical Immunology*. 115, 3 439-447.
- Guy's and St Thomas' NHS Foundation Trust (2015) *Immunotherapy treatment with Pharmedgen wasp or bee venom* tinyurl.com/hdk2e8p (Last accessed: May 17 2016.)
- Hedde R, Golden BK (2015) *Allergy to Insect Stings and Bites*. tinyurl.com/jnycunn (Last accessed: May 17 2016.)
- Krishna MT, Ewan PW, Diwakar L *et al* (2011) Diagnosis and management of hymenoptera venom allergy: British Society for Allergy and Clinical Immunology (BSACI) guidelines. *Clinical and Experimental Allergy*. 41, 9, 1201-1220.
- Ludman SW, Boyle RJ (2015) Stinging insect allergy: current perspectives on venom immunotherapy. *Journal of Asthma and Allergy*. 8, 75-86.
- Madsen F (2007) EAACI 'standards for practical allergen-specific immunotherapy'. *Allergy*. 62, 3, 332.
- Matysiak J, Matysiak J, Breborowicz A, Kokot ZJ (2013) Diagnosis of hymenoptera venom allergy - with special emphasis on honeybee (*Aphis mellifera*) venom allergy. *Annals of Agricultural and Environmental Medicine*. 20, 4, 875-879.
- Moffitt JE, Golden DB, Reisman RE (2004) Stinging insect hypersensitivity: a practice parameter update. *Journal of Allergy and Clinical Immunology*. 114, 4, 869-886.
- Muraro A, Roberts G, Clark A *et al* (2007) Position Paper: The management of anaphylaxis in childhood: position paper of the European Academy of Allergy and Clinical Immunology. *Allergy*. 62, 857-871.
- National Institute for Health and Care Excellence (2011) *Anaphylaxis: Assessment and Referral After Emergency Treatment*. www.nice.org.uk/guidance/cg134 (Last accessed: May 19 2016.)
- National Institute for Health and Care Excellence (2012) *Pharmedgen for the Treatment of Bee and Wasp Venom Allergy*. NICE technology appraisal guidance No. 246.
- National Institute for Health and Care Excellence (2016) *Anaphylaxis*. Quality standard No. 119. www.nice.org.uk/guidance/qs119 (Last accessed: May 17 2016.)
- Niedoszytko M, de Monchy J, van Doormaal JJ, Jassen E, Oude Elberink JN (2009) Mastocytosis and insect venom allergy: diagnosis, safety and efficacy of venom immunotherapy. *Allergy*. 64, 9, 1237-1245.
- Oude Elberink JN, Dubois AE (2003) Quality of life in insect venom allergic patients. *Current Opinion in Allergy and Clinical Immunology*. 3, 4, 287-293.
- Paschall VL (2012) *Hymenoptera Venom Allergy*. The Cleveland Clinic Foundation, Center for Continuing Education, Lyndhurst OH.
- Pumphrey RS (2004) Fatal anaphylaxis in the UK, 1992-2001. *Novartis Foundation Symposium*. 257, 116-128; discussion 128-132, 157-160, 276-285.
- Resuscitation Council (UK) (2008) *Emergency Treatment of Anaphylactic Reactions: Guidelines for Healthcare Providers*. Annotated with links to NICE guidance July 2012. RCUK, London.
- Royal College of Paediatrics and Child Health (2011) *Allergy Care Pathways for Children: Anaphylaxis*. tinyurl.com/z2w277v (Last accessed: May 19 2016.)
- Rueff F, Przybilla B, Bilò MB *et al* (2013) *Clinical effectiveness of Hymenoptera venom immunotherapy: a prospective observational multicenter study of the European Academy of Allergy and Clinical Immunology Interest Group on insect venom hypersensitivity*. *PLOS One*. 8, 5, e63233.
- Simons FER, Arduoso LRF, MB *et al* (2011) World Allergy Organization Guidelines for the assessment and management of anaphylaxis. *Journal of Allergy and Clinical Immunology*. 127, 3, 587-593.
- Simons FE, Arduoso LR, Bilò MB *et al* (2012) 2012 Update: World Allergy Organization Guidelines for the assessment and management of anaphylaxis. *Current Opinion in Allergy and Clinical Immunology*. 12, 4, 389-399.