# Allergic reactions to insect bites and stings

**Although sensitisation to insect stings is common, serious life threatening reactions are not. Initial treatment of patients with allergies to insect stings may involve intramuscular adrenaline, oxygen and intravenous fluids; ongoing management depends on an assessment of risk of future reactions for each individual.**

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## Extent of the problem

Overall, 15 to 25% of a population exposed to insect stings shows serological and/or skin test evidence of sensitisation (i.e. detectable venom-specific IgE). However, only 1 to 5% of the population will give a history of immediate systemic allergic reaction to the prevalent stinging insects, and only half of these people will have experienced life threatening reactions.

The exact prevalences of sensitisation and clinical allergy depend on annual sting exposure rates.[1] Because deaths caused by insect stings can be difficult to identify at postmortem, we do not know the precise death rate from this cause. Data from South Australia and Tasmania suggest that it is less than one per million people per year.[2,3]

## Which insects are implicated?

Australia has one of the most diverse and potentially confusing arrays of stinging insects in the world. Detailed epidemiological data on Australian insect species are currently available only for Tasmania. In this State the prevalence of clinical systemic sting allergy within the general population is 4.5%, broken down as follows:

- 2.7% for *Myrmecia pilosula* (the jack jumper ant, a type of jumper ant or hopper ant)
- 1.4% for *Apis mellifera* (the honey bee)
- 0.6% for *Vespula germanica* (the European wasp, also known overseas as the yellow jacket)
- 0.3% for *Myrmecia forficata* (the inchman ant).[1]

### Ants

In mainland Australia, there are 89 species of *Myrmecia* ants. *M. pilosula* (Figure 1) accounts for most mainland ant venom allergy, with several larger *Myrmecia* species (Figure 2) accounting for much of the rest.

Ant sting allergy is a major problem in country Victoria,[4] although recognised deaths have been

**IN SUMMARY**

- **Sensitisation to local stinging insects is extremely common, immediate systemic allergic reactions are less common, and deaths following insect stings are very uncommon.**
- **Adrenaline, oxygen and intravenous fluids are the main therapies likely to be effective acutely for a systemic allergic reaction.**
- **Beware delayed and progressive reactions – a period of observation is essential.**
- **The prognosis of patients with purely cutaneous reactions to insect stings is usually favourable, but deteriorates progressively in those with a history of anaphylaxis of increasing severity.**
- **The automated adrenaline syringe is a major asset to first aid in the community and has wide acceptance; provision of a written action plan is also important.**
- **Patients with a history of immediate systemic allergic reactions with respiratory or hypotensive features should be referred to a clinical immunologist or allergist for advice regarding venom immunotherapy.**



Figure 1. *Myrmecia pilosula* (the jack jumper ant) is a type of 'jumper ant' or 'hopper ant'. About 10 to 12 mm long, it moves in short jerky movements, jumping to attack, sometimes out of surrounding bushes. Serological data suggest that it is responsible for about 90% of ant venom allergy in south-eastern Australia. It has well developed vision, is attracted to movement and is extremely aggressive.



Figure 2. A variety of larger (15 to 22 mm) *Myrmecia* ants such as this one (*Myrmecia forficata*, known in Tasmania as the 'inchman') are often referred to as 'bull', 'bulldog' or 'inch' ants. Common names can be confusing (some people also refer to jack jumper ants as bull ants), so it is important to record a description of the insect rather than a name. Expert identification is important when a specimen is available because most species are almost impossible to differentiate by the amateur.

confined largely to Tasmania.[2] Anecdotally, *M. pilosula* is also a significant problem in the Adelaide Hills of South Australia and around Canberra. The paucity of reported deaths due to *M. pilosula* allergy is likely to be due in part to a lack of awareness of the potential for ant sting allergy to cause death.

Other species of ants implicated in severe allergic reactions include:

- *Solenopsis invicta* (the imported fire ant) around Brisbane[5]
- several other ant genera in Queensland, including *Rhytidoponera metallica* (the greenhead ant).

**Insect bites and stings**



Generally, allergic reactions to insect bites and stings can be considered mild if they are confined to the skin (erythema, urticaria, angioedema), moderate if associated with gastrointestinal or mild respiratory disturbance, and severe if associated with collapse, hypotension or severe respiratory compromise.



## Bees

*A. mellifera* (the honey bee; Figure 3) is found throughout the continent, particularly in agricultural areas; however, a disproportionate number of deaths due to *A. mellifera* stings occur in South Australia.[3]

*Bombus* spp. (bumble bees) have become established in Tasmania and have a venom similar to *A. mellifera*, but cases of anaphylaxis to this



Figure 3. *Apis mellifera* (the honey bee). The presence of a retained stinger in the skin is diagnostic. In very hot weather honey bees seek out water and may be encountered accidentally in open drink bottles (leading to oropharyngeal stings and airway obstruction).



Figure 4. *Vespula germanica* (the 'European wasp' or 'yellow jacket') is found mainly in cooler regions. It is characterised by a waist part that becomes rapidly thicker at the abdomen and by its way of holding its legs close to the body during flight. These insects are particularly attracted to rotting meat, fallen fruit and sweet drinks (leading to oropharyngeal stings and airway obstruction).



Figure 5. Paper wasps are found mainly in warmer areas of the continent. They are characterised by the long thin waist and tapered abdomen, and by their 'spider like' dangling of legs during flight (pictured here; *Ropalidia gregaria*). These insects feed on agricultural pests and generally attack humans only when their nests (often found under the eaves of houses) are disturbed.

new arrival have yet to be documented in this State, probably because of its nonaggressive nature.

*Lasioglossum* spp. (native sweat bees) have been implicated in severe allergic reactions in South Australia.

### Wasps

*V. germanica* (the European wasp; Figure 4) is found mainly in cooler regions, and *Polistes* spp. and *Ropalidia* spp. (paper wasps; Figure 5) are important in warmer areas. *V. germanica* does not appear to have been responsible for deaths thus far, as all recognised wasp sting deaths have been confined to warmer areas of New South Wales and Queensland where paper wasps are presumed to be the culprits.[6]

*Diamma bicolor* has been implicated in severe allergic reactions in southeastern coastal regions. Known as the 'blue ant', it is a solitary, ground-dwelling, native flower wasp.

### Cross-reactivity

There is minimal cross-reactivity between wasp, bee and ant venoms, but frequent cross-reactivity between various species of wasps, between honey bees and bumble bees, and betweendifferent *Myrmecia* ant species. Thus, skin and serum venom-specific IgE testing alone may be unhelpful in diagnosis. Clinical correlation based on knowledge of local species is required.

### Insect bites

Despite the high frequency of local reactions to mosquito bites, anaphylaxis to insect bites (as opposed to venom) is very uncommon, but has been reported after March fly bites and tick bites. Anaphylaxis has also been reported after exposure to caterpillar spines.

## Managing the acute reaction

### Accurate documentation

Accurate documentation is essential for the management of patients presenting with an acute reaction. The following basic measurements are critical to further management:

- skin perfusion
- conscious state
- pulse, blood pressure
- respiratory rate
- oxygen saturation (if available)
- clinical evidence of upper airway obstruction and/or bronchospasm.

These measurements will be used to assess the need for immunotherapy and decide whether an adrenaline autoinjector must be provided (see below).

Generally, reactions can be considered mild if they are confined to the skin (erythema, urticaria and angioedema), moderate if associated with gastrointestinal or mild respiratory disturbance, and severe if associated with collapse, hypotension or severe respiratory compromise.

When initial management has been started, it is also useful to document a description of the causative insect while the patient's memory is fresh (not just a colloquial name, which may be inaccurate or confusing). In addition, key historical features, particularly the occurrence of collapse, presyncope, unconsciousness or breathing difficulty before being seen, should be noted. The presence of these features suggests a severe reaction, which may have resolved before the patient was seen due to endogenous compensatory mechanisms or self-administration of adrenaline.

### Severe reactions

#### Mainstays of treatment

Vasodilatation (distributive shock), fluid extravasation (hypovolaemic shock), upper and lower airway oedema and bronchospasm are the most important pathophysiological features of anaphylaxis. Thus adrenaline (which physiologically

antagonises the process at all points), volume resuscitation and high flow oxygen are mainstays of the management of patients with severe reactions to insect stings. Placing the patient in a supine position is also important to maintain cerebral and coronary perfusion until the adrenaline begins to work (see the box on this page).

If airway obstruction occurs, adrenaline is still the most important intervention before attempting advanced airway manoeuvres such as intubation. Reactions can progress rapidly to complete airway obstruction and cardiac arrest. Thus additional assistance may be required; activate the emergency medical system (phone the emergency number for an ambulance; 000 in Australia) as soon as possible.

### Adrenaline and IV fluids: administration and dosage

In most emergency situations, adrenaline will start being absorbed from an intramuscular injection before intravenous access can be obtained; use the anterior thigh, through clothing if needed. Subcutaneous injections and injections into the arm are absorbed unreliably.

The initial dose of intramuscular adrenaline is 0.3 to 0.5 mg (0.3 to 0.5 mL of a 1:1000 solution) in adults. In children, 0.01 mg/kg is the recommended dose. Alternatively, a simple approach is to use 0.15 mg for children under 6 years of age and 0.3 mg for older children (dosages that correspond to paediatric versus adult EpiPen dosages). Such doses can be repeated in 5 minutes if the initial response is inadequate, or earlier if the patient deteriorates.

For patients with severe reactions with severe and/or sustained hypotension, intravenous adrenaline and volume resuscitation (20 mL/kg normal saline or Hartmann's solution, repeated as required) may also be needed. Thus secure wide-bore (≥16 gauge) intravenous access as soon as possible and monitor the patient until an ambulance arrives. The fluid infusion rate needs to be brisk; a subject with severe hypotensive anaphylaxis may need as much as 60 mL/kg infused under pressure over 5 to 20 minutes.

Note that intravenous adrenaline boluses (in small aliquots, e.g. in an adult 0.2 to 0.5 mL of a 1:10,000 solution) should be used only if cardiorespiratory arrest is imminent.

In an emergency department environment, where intravenous access and infusion preparation can be achieved within minutes, we favour administration of an infusion of adrenaline at 1:100,000 (1 mg in 100 mL). This is administered using an infusion pump, starting at a rate that will give an appropriate intramuscular dose by the intravenous route over 30 to 60 minutes (e.g. 30 to 100 mL/hour in an adult). Close monitoring is required and the infusion should be adjusted according to responsiveness and/or occurrence of any untoward events (hypertension tachycardia, tremor, pallor and nausea).

### Other medications

Inappropriate intense bradycardia is an occasional feature of serious sting reactions, and intravenous atropine may sometimes be required.[7,8]

Injectable promethazine should be avoided as this is an alpha blocker and can aggravate hypotension and cause respiratory depression.

Because antihistamines are unlikely to have any useful clinical effect in the presence of many other anaphylactic mediators, we do not advocate their use.

Corticosteroids are very unlikely to have an effect acutely, but may have a role (although unproven) in protracted, severe reactions.

### Mild reactions

We use adrenaline for patients with mild systemic reactions to obtain rapid symptom relief. Antihistamines are an alternative and can provide some symptomatic relief for mild reactions. Nevertheless, for any reaction with more severe features (gastrointestinal, respiratory or cardiovascular features), give adrenaline and refer the patient to the nearest emergency department.

### Beware delayed and progressive reactions

Beware the patient with ongoing or progressive anaphylaxis that initially appears mild and/or is masked by an intial dose of adrenaline that will wear off before the underlying reaction does. All patients should be observed until it is clear that the reaction is resolving without treatment and until the adrenaline (if administered) has been given time to wear off. Patients with moderate to severe reactions should be transferred by ambulance to the nearest emergency department for ongoing management and observed until they have been symptom-free for at least four hours after the last dose of adrenaline has been given. They should be instructed to seek help immediately should symptoms recur after discharge.

**Insect stings: managing severe allergic reactions**

- Call for help
- Place the patient in a supine position with feet elevated, unless this increases respiratory distress
- Give intramuscular adrenaline into the anterior thigh
- Commence high flow oxygen
- Obtain intravenous access; consider fluid resuscitation and additional adrenaline if initial response is poor, and atropine if the patient has bradycardia

## Diagnosis and predicting risk

### Identifying the insect involved

The circumstances, season, insect prevalence, nature of the bite or sting, presence of recognisable insect and/or stinger and previous sting history are all

important for diagnosis of the insect involved. The presence of a stinger indicates a higher probability of the insect being a honey bee. If immunotherapy is contemplated for a patient, the presence or absence of specific IgE to likely insects needs to be assessed. Skin sensitivity tests and RAST need to be ordered and interpreted by someone with specific training in the area. This is because of the complexities regarding species (including confusing colloquial names), insect distribution, and sensitivity/specificity of the assays. A positive skin test or RAST alone does not prove clinical reactivity.

Although a gold standard in clinical trials, deliberate sting challenges are of limited use in individual cases. Reasons for this include the need for critical care facilities, variability in venom delivery in a sting, and the potential for increasing sensitisation. Thus subjects who report a life threatening reaction to a previous sting but then tolerance of a further sting (either deliberate or accidental) from the same insect cannot be reassured that they are no longer at risk.

## Natural history of stinging insect allergy

The often-heard comment that 'you have had a serious sting and the next sting will probably be lethal' is inaccurate. In deliberate sting challenges and prospective studies of accidental field stings, a significant number of people who give a history of an allergic reaction do not react when stung again.[1,9] Overall, the percentage of people with a history of systemic reactions who will react to a subsequent sting is 70% for *M. pilosula* (the jack jumper ant), 50% for *A. mellifera* (the honey bee) and 25% for *V. germanica* (the European wasp).

The risk of a reaction of any grade is higher in those with a history of severe reactions.[1,9] Furthermore, subsequent reactions are usually of either similar or lesser severity. In the case of children experiencing mild reactions to bee and wasp stings, the occurrence of subsequent severe reactions is exceptionally uncommon and most will lose their sensitivity.[10]

Conversely, a fluctuating course is common, with some people experiencing a near lethal reaction followed by no reaction to a subsequent sting, and then a near lethal reaction when stung yet again. We do not fully understand this phenomenon, but it may relate to:

- spontaneous variation in reactivity
- variability of the amount of venom injected with a sting
- venom allergenicity
- incorrect insect species identification.

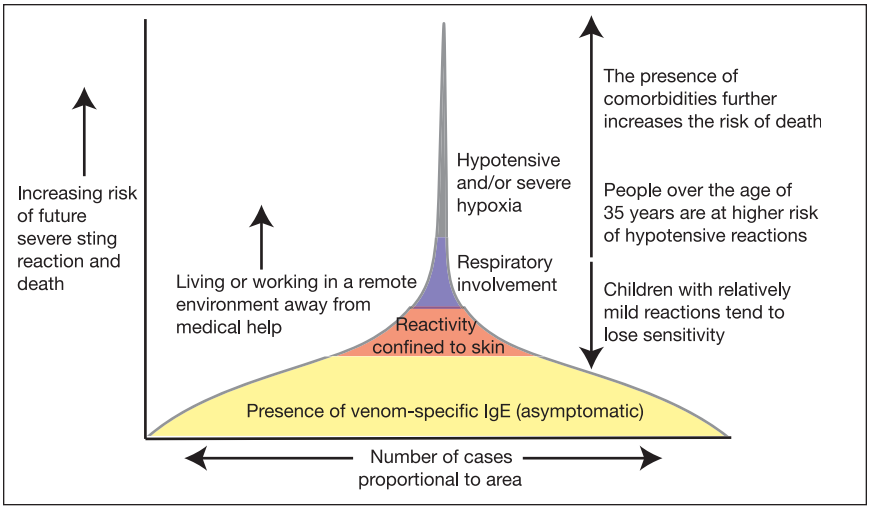


Figure 6. Level of risk versus population prevalence of sensitisation and sting reaction history.

This reinforces the concept that reaction risk is best related to the severity of the worst previous reaction rather than to the severity of reaction following the most recent sting.[1]

No one can be totally reassured as a significant proportion of deaths from stinging insects occur in individuals with no known history of insect hypersensitivity. Prospective studies of the natural history of untreated insect sting allergy have also been limited in their timeframe. We know that older people tend to have more severe reactions[1,9] and that people can have more severe reactions than previously when they are stung deliberately.[7] Thus, for people who frequent remote areas away from emergency medical care, we often provide adrenaline and immunotherapy even if their previous reactions have been relatively mild.

## Underlying disease and regular medications

In some series of sting deaths, subjects with underlying cardiovascular disease and receiving treatments for this appear to be over-represented. The pathophysiology of anaphylaxis suggests that it is likely to be aggravated by:

- pre-existing chronic respiratory illness or cardiovascular disease
- treatment with beta blockers and/or agents that inhibit the renin–angiotensin system or have negative inotropic effects on the heart.

Beta blockers, in particular, inhibit natural sympathomimetic activity and the beta effects of adrenaline whether endogenous or exogenous. Alpha blockade may result in treatment with adrenaline having a paradoxically hypotensive effect due to unbalanced beta stimulation. ACE inhibitors may aggravate angioedema, and there is evidence from several studies that the renin–angiotensin system is an important endogenous rescue system in anaphylaxis. Thus, when deciding on medications for such patients, the potential major

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## Action plan for patients highly allergic to insect stings

1. Honey bee sting – flick out any stinger immediately using a fingernail. Even after the stinger comes away from the insect, the venom sac contracts and continues to inject venom.
2. As soon as there are any local symptoms – i.e. significant pain, swelling and/or itching around a sting from an insect that normally causes a life threatening reaction:
   - Get help – make sure that someone nearby knows of your potential problem.
   - Find your adrenaline (EpiPen) and get ready to use it.
3. As soon as there are generalised symptoms – i.e. symptoms beyond the local sting site, such as an all-over rash, itch, nausea, face swelling or a feeling of impending disaster, or any of the more severe symptoms listed below, proceed as above plus:
   - Dial the emergency number for an ambulance immediately (000 in Australia). Make sure that the ambulance communications officer is told that you have a known serious sting allergy and are having an allergic reaction.
4. If you have severe symptoms – i.e. symptoms affecting swallowing, voice or breathing, or symptoms of light-headedness, impaired vision or threatened collapse, proceed as above plus:
   - Inject yourself with EpiPen immediately. Do not wait for an ambulance to arrive before using your EpiPen.
5. To use your EpiPen:
   - Remove the device from its container.
   - Remove the grey safety cap.
   - Using a fist-like grip, which allows the barrel of the device to move freely, push the black nose of the device hard against the front outer thigh.
   - You will hear and feel the device click, and should leave it in position for a count of 10 and then remove the device.
   - The EpiPen can be used through clothes.
   - Take care to minimise the risk of needlestick injury to other persons (e.g. by pushing the exposed needle into a cork), and give it to ambulance or medical staff for safe disposal.

Dialling the emergency number is the surest way of getting help quickly, even in remote areas because the ambulance service co-ordinates all available emergency resources and/or can direct you to the nearest emergency care available. Ambulances carry adrenaline if for some reason you do not have your EpiPen or if additional doses are required.

If you have any generalised symptoms or need to use Epipen, seek medical care immediately.

### General measures

- Do not engage in vigorous physical exertion, hot showering or bathing, or insert the wound in hot water. All of these will increase blood flow and thus absorption of inflammatory substances into the circulation.
- Application of an ice pack may help to reduce pain and swelling.
- Some people advise using a pressure-immobilisation bandage for sting allergy. There is no evidence supporting this approach, which in some situations can be harmful. Therefore, do not waste time doing this.
- Do not rely on antihistamines or corticosteroids. In most cases these will not help, apart from providing symptomatic relief for minor and local symptoms.

### Care for and renewal of your EpiPen

Keep an EpiPen near you at all times. The EpiPen is stable at any tolerable room temperature, but is best not refrigerated (many domestic refrigerators freeze intermittently). It should not be stored in the car, where damagingly high temperatures are often reached.

Your EpiPen should be renewed before its expiry date. However, if marginally over the expiry date and the contents are clear and not discoloured (look through the viewing window in the pen), it is likely to be effective still in an allergic emergency.

Adapted from the action plan devised and written by Dr Simon Brown and used by the Royal Hobart Hospital's Department of Emergency Medicine.

benefits on general cardiovascular morbidity need to be carefully balanced against the particular risk from insect stings in a given individual.

## Ongoing management

A key step in deciding an appropriate course of action for the individual patient is an assessment of risk (Figure 6). As risk increases, the thresholds for providing self-injectable adrenaline and immuno - therapy reduce.

### Avoidance measures

Relocating to a different geographic area may be effective for patients allergic to stings from insects with limited distribution (e.g. *M. pilosula* or the various paper wasps). However, subjects need to be warned about potential venom cross-reactivity (e.g. with other *Myrmecia* ants or wasps, respectively).

Activities at particularly high risk for being stung by insects involve visiting

apiaries, pest control activities, failure to wear shoes and accidentally driving into the insects without protection (on a motorcycle or with a car window open). Wearing shoes and long, light coloured, clothing and avoiding the use of perfumes (for honey bees) or accumulating protein-rich garbage (wasps) may assist. Care should be taken when drinking from cans and bottles, which may attract bees and wasps.

### A written action plan

All individuals with a history of immediate systemic allergic reaction to an insect sting need a written action plan with which they and their family and close associates need to be familiar. Even simple measures such as the contacting of another responsible adult and emergency care need to be preplanned, and regular reinforcement is needed.

The action plan on the use of the adrenaline autoinjector EpiPen, given in the box on page 22, has proven acceptable and usable in a large group of Tasmanian subjects highly allergic to insect stings. EpiPen is widely available, but patients must understand that this is only a temporising measure; higher doses of adrenaline and other measures may be required. Subjects at high risk, often those with a history of hypotensive anaphylaxis, should probably carry two EpiPens or be trained to use adrenaline ampoules for injection if cost is a problem.

### Immunotherapy

Venom immunotherapy is of proven value for *A. mellifera* (honey bee), wasp and *M. pilosula* (jack jumper ant) venom allergy.[7,11] However, *M. pilosula* and other native *Myrmecia* ant venoms are not generally available, with issues of production and distribution to be overcome. Venoms of *A. mellifera*, *Vespula* and *Polistes* paper wasp are available and subsidised by the PBS, but concerns have been expressed that overseas-sourced *Polistes* venom may not be appropriate to all local species.

The efficacy of venom immunotherapy appears to be at least 95% for wasp and *M. pilosula* allergies. Efficacy in studies of *A. mellifera* venom immunotherapy varies from 60 to 100%, but probably is about 80 to 90%.

Immunotherapy is a major undertaking with its own morbidity. It is intrusive of subjects' time and consuming of medical resources. In one very large representative study of honey bee and wasp venom immunotherapy, 12% of subjects experienced one or more systemic reactions during venom immunotherapy.[12] It is best that such therapy be initiated by those experienced in the procedure. The presence of a significant failure rate means that it is prudent that subjects on immunotherapy continue with their action plan incorporating EpiPen or other injectable adrenaline.

Venom immunotherapy is appropriate for subjects who have had respiratory compromise or hypotension (or symptoms suggestive of these) after an insect sting and evidence by *in vitro* test and/or skin test of specific IgE reactivity to the venom. Specialist opinion should be sought before initiating immunotherapy, and any underlying cardiorespiratory disorder and its therapies reviewed.

Venom immunotherapy is not appropriate for people with positive skin tests or RAST results alone in the absence of any history of immediate systemic allergic reaction. It has no proven value in subjects with local reactions. Unless special risk factors are present (e.g. a subject who is intellectually challenged, a rural and remote worker, or a subject who has

### Consultant's comment

The authors of this article are to be congratulated on producing a timely and lucid account of an important problem in Australia. They have made a major contribution to the subject by bringing to our attention the problem with jack jumper ants, and by conducting the first trials of immunotherapy (desensitisation). Insect stings evoke great fear especially in those unfortunate individuals who have had a major reaction to them.

There are several very important 'take-home' messages in this article:

- In Australia we have as big a diversity of stinging insects as that of any overseas country.
- It is sobering to reflect that, despite excellent Australian work characterising the venom of the jack jumper ant, and despite intensive lobbying, there is still no support in Australia for producing life saving therapeutic preparations of the venom.
- What happens with subsequent stings is unpredictable – there's no neat evolution to more severe reactions.
- Overall management of patients requires advice to minimise the risk of stings in the future and first aid measures should a sting occur.
- Primary management of anaphylaxis requires adrenaline as soon as possible; in almost all circumstances this should be given by the intramuscular (not the intravenous) route.
- Immunotherapy is a serious undertaking, very effective in the right setting, but appropriate selection of subjects requires many factors to be taken into account, and its prescription should be undertaken only by those with appropriate experience.

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continued

underlying cardiovascular comorbidities), the prognosis in individuals who have reactions confined to the skin is such that provision of an emergency plan and EpiPen may be sufficient.

Discontinuing immunotherapy is a risky decision that should be shared with a specialist. Limited evidence suggests that most subjects who have tolerated venom immunotherapy and any intervening stings can discontinue treatment after three to five years with reasonable prospects, irrespective of skin or blood test results at the end of therapy. Adverse prognostic factors appear to be a history of hypotensive anaphylaxis and/or systemic reactions to venom immunotherapy or interim stings while on immunotherapy. Subjects with hypotensive anaphylaxis, in particular, may merit indefinite immunotherapy.

## Summary

In patients who are allergic to insect stings, sensitisation is very common, clinical reactions are less common and death or severe permanent disabilities are very uncommon outcomes. The clinical challenge is to place patients who are allergic to stings in a hierarchy of risk, which has a very broad base and a very narrow peak. Management should then be matched to the patient's level of risk in the context of a disrupted lifestyle due to fear of a random, potentially lethal event. A powerful management tool for many insect stings is venom immunotherapy (hypo - sensitisation), but this is intensive and demanding of resources. MT

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