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### PRACTICE POINT

# Stinging insect hypersensitivity: Evaluation and management in children and youth

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#### Abstract

There are two types of IgE-mediated reactions to stinging insects: large local reactions and systemic reactions. Acute management of large local reactions is symptomatic and a patient history of a large local reaction does not indicate need for an epinephrine auto-injector or venom immunotherapy. By contrast, acute management of systemic reactions requires intramuscular epinephrine. Long-term management includes prescribing an epinephrine auto-injector and consideration for venom immunotherapy by a paediatric allergist.

**Keywords:** Allergy; Anaphylaxis; Large local reaction; Stinging insect; Venom immunotherapy

Systemic allergic reactions to insect stings affect 0.4% to 0.8% of children [1]. This practice point reviews the different types of allergic reactions to stinging insects, how to evaluate such reactions, and both acute and chronic management. The focus is on stinging insects found in Canada (hornets, wasps, yellow jackets, honeybees). Imported fire ants are an important cause of anaphylaxis in the Southern United States but not yet in Canada [1]. Systemic reactions from bites, such as spider bites, are rare.

## Classification of IgE-mediated reactions to stinging insects

Two types of IgE-mediated reactions to insect stings can occur: large local reactions and systemic reactions. Large local reactions involve swelling of 10 cm or more in diameter around the sting site. Typically, the reaction increases in size for 1 to 2 days, then resolves over 3 to 10 days [1].

By contrast, systemic reactions present with a combination of cutaneous (urticaria, angioedema), gastrointestinal (vomiting, diarrhea), respiratory (wheeze, cough), or cardiovascular (hypotension, syncope) signs. Systemic reactions typically occur within 5 to 30 minutes after an insect sting <sup>[2]</sup>, and can occur without a history of reaction to stings in the past.

# Evaluating insect sting reactions

History-taking should include a detailed description of where the sting occurred (with nest location, if possible), the activity the child or youth was engaged in at the time, a positive identification of the insect species (if possible), organ systems involved in the reaction, and timing of both reaction onset and resolution. Large local reactions can be confused with cellulitis and streaking associated with lymphangitis may be present, but a diagnosis of cellulitis should only be considered when there are other systemic symptoms, such as fever [1].

Knowledge of the nesting patterns and life cycles for different stinging insects can sometimes help to identify the insect involved, which makes it easier to diagnose the reaction, prescribe follow-up therapy, counsel avoidance measures, and provide a prognosis prognosticate (Table 1) <sup>[1]</sup>. Of all the stinging insects, yellow jacket stings cause the most frequent insect reactions.

Species	Nest location	Aggression level	Stinger left at site	Additional comments
Yellow jacket*	In-ground	High	Sometimes	Stings often occur during yardwork or gardening
Wasp*	Grey, honeycomb-patterned nest in shrubs and under eaves of barns or houses	Moderate	No	Can also nest in fencing and playground equipment
Hornet* (yellow hornet, white faced hornet)	In trees or shrubs. May be large but well hidden	High	No	Rarely sting
Honeybee	Commercial beehives	Low	Yes	Not aggressive
* Scavenger attracted by	foods and drinks			

# Acute management of sting reactions

## Large local reactions

Treating large local reactions is symptomatic and may involve a combination of cold compresses, oral non-sedating antihistamines, oral analgesics or (should the reaction be severe) a brief course of oral corticosteroids [1].

#### Systemic reactions

As for all causes of anaphylaxis, any systemic reaction should be treated with intramuscular epinephrine. For first-aid management of anaphylaxis, an epinephrine dose of 0.01 mg/kg is injected intramuscularly, to a maximum of 0.3 mg in a prepubertal child and up to 0.5 mg in an adolescent, followed by observation in the emergency department (ED) for a minimum of 4 to 6 hours [3][4]. Epinephrine is the only life-saving intervention for systemic reactions to stings. Beneficial mechanisms of epinephrine include vasoconstriction (thus alleviating hypotension), bronchodilation and decreasing laryngeal edema [5]. Oral non-sedating antihistamines are an adjunct therapy and are not to be used in lieu of epinephrine [6][7]. While oral corticosteroids are often prescribed to prevent a biphasic reaction, evidence for their efficacy is lacking [6][7]. Bronchodilators can be used adjunctively with epinephrine, specifically for lower respiratory symptoms that are refractory [6]. A CPS statement on anaphylaxis provides a comprehensive list of medications and doses for acute treatment of anaphylaxis [4]. Longer monitoring in the ED may be considered for children at higher risk for a biphasic reaction, including cases of delayed presentation to the ED and individuals who require more than one dose of epinephrine, to whom a beta-agonist is administered in the ED or who present with wide pulse pressure [8].

Following treatment, children with a history of systemic reaction should be prescribed an epinephrine auto-injector and educated, along with family members and caregivers, in its use. Epinephrine auto-injectors are available in 0.15 mg and 0.30 mg doses. It is recommended that the 0.30 mg dose be used in children weighing  $\geq$  25 kg [3]. Children with a history of systemic reaction should also be referred to a paediatric allergist for further evaluation.

# Long-term management insect sting reactions

## Large local reactions

The risk for anaphylaxis with future stings is low in children with a history of large local sting reactions [9]-[11]. Allergy testing, venom immunotherapy (VIT) and prescribing an epinephrine auto-injector are not needed [1], but avoidance measures (Box 1) should be reviewed with the family.

#### Box 1. Stinging insect avoidance measures

Do not walk barefoot outdoors

Exercise caution when eating and drinking outdoors

Avoid drinking from opaque cans or straws outdoors

Wear gloves and long sleeves for gardening and a long sleeve shirt for play in high-risk areas

Remove all insect nests around the home and call a professional for insect control or nest removal in confined or hard-to-reach spaces

Information derived from reference 1

## Systemic reactions

Along with prescribing an auto-injector and family education [3][7], be sure to reiterate that there are no contraindications to epinephrine use to treat a systemic reaction. Recommend that children at risk have an anaphylaxis action plan posted for staff at their school/child care setting, that they wear a MedicAlert bracelet or other identifier, and periodically review avoidance measures with the family. Also refer these children to a paediatric allergist for intradermal skin testing because, when combined with a history of systemic reaction, a positive skin test indicates eligibility for VIT [1]. Intradermal testing is more sensitive and ideally the first-line investigation by paediatric allergists. If there is a convincing history of severe reaction and testing is negative, a serum-specific IgE and repeat skin testing to stinging insects is ordered: if both tests are negative, the chance of a future systemic reaction to a stinging insect is minimal [1].

VIT is an established and effective disease-modifying immunomodulatory treatment that can reduce risk for future systemic reactions in children from approximately 30% to an estimated 5% [11]. Typically, VIT is administered over 3 to 5 years [12]. Initially, subcutaneous injections of highly specific venom doses are usually administered once per week for several weeks (the increasing dose build-up phase), then once every 4 weeks over the next 1 to 2 years (the maintenance phase). Eventually, the dose is administered only once every 8 to 12 weeks. Several different protocols for VIT are available, with maintenance dosing levels being attained within a range of days to weeks of initiating VIT, with adjustments often being made at the discretion of the attending physician. Because there is extensive cross-reactivity between yellow jacket and hornet venom, VIT for just one of the three stinging insects (typically yellow jacket) provides coverage for all three [1]. Cross-reactivity is less evident for wasp venom and rare for honeybee venom. VIT has recently been impacted by a shortage of *Hymenoptera* venom for VIT, which will hopefully be resolved in the near future [13]. Carrying an epinephrine auto-injector is not necessary during the maintenance phase of VIT or for individuals who have completed the full course of treatment. However, carrying an epinephrine auto-injector is necessary for individuals undergoing VIT when there has been a history of near-fatal reaction or systemic reaction during treatment in cases with severe honeybee allergy, elevated baseline serum tryptase level or an underlying medical condition or for persons likely to experience more frequent unavoidable exposure [1].

A baseline serum tryptase should be drawn from children or youth with a history of severe anaphylaxis (especially if they experience hypotension or absence of urticaria). High serum tryptase levels have implications for prognosis, with higher risk for systemic reactions to stinging insects in future and failure to respond to VIT [1]. A serum tryptase level >20 ng/mL may also indicate a comorbid condition of systemic mastocytosis, which is a mast cell

disease [14].

One important exception to allergy testing and VIT in all age groups (including individuals over age 16 years, according to the latest literature) is in cases of isolated systemic cutaneous reaction (i.e., when the only body system involved is the skin, such as generalized hives), which carries a very low risk for a more severe systemic reaction in future [1]. For example, one study of 242 children aged 16 and under with a history of a cutaneous (only) reaction to stinging insects showed that although 9.2% had a systemic reaction when re-stung, no subsequent reaction was more severe than the initial reaction; in fact, 88.9% were less severe [15]. Consequently, epinephrine auto-injectors are not required for individuals in all age groups who experience isolated systemic cutaneous reactions.

## Conclusion

The two types of IgE-mediated reactions to insect stings have very different treatment courses and prognoses. Children who experience a large local reaction are at low risk for systemic reaction and require supportive therapy only. Children with a history of systemic reaction to an insect sting must carry an epinephrine auto-injector and be evaluated by a paediatric allergist as potential candidates for VIT. The sole exception to VIT is in cases of skin reaction alone (e.g., generalized hives), which signals low risk for more severe systemic reactions in the future.

- Clinicians encountering reactions to insect stings in any care setting should keep the following practice points in mind: Treatment of large local reactions is symptomatic, and may include use of oral non-sedating antihistamines, cold compresses, oral analgesics or a brief course of oral corticosteroid
- Large local reactions do not require prescribing an epinephrine auto-injector or referral for venom immunotherapy (VIT).
- Treatment of systemic reactions is with intramuscular epinephrine. Epinephrine is the only life-saving intervention for anaphylaxis.
- Evaluation of insect sting reactions causing severe anaphylaxis should include a baseline serum tryptase blood test.
- Children with a history of systemic reaction (except for those who experience isolated systemic cutaneous reactions) should be prescribed an epinephrine auto-injector, counselled appropriately, and evaluated by a paediatric allergist for VIT.

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