

Section 12 Toxicology

Chapter 92

Indian Guidelines and Protocols: Bee Sting

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INTRODUCTION

Bee sting is a common emergency in tropical countries, management of which requires a basic knowledge of the insect stinging mechanism, its varied clinical presentations and approach to treatment. Allergy testing is helpful to identify those who are at high risk of systemic reaction following exposure to bee sting. The incidence of anaphylaxis caused by insect sting has been estimated to be 1% in children and 3% in adults.¹ Immunotherapy reduces the risk of anaphylaxis in the allergic individuals.

ENTOMOLOGY OF BEES

Bees belong to the order Hymenoptera and family Apidae, which includes Honey bees (*Apis mellifera*) and Bumble bees (*Bombus terrestris*). Characteristically, the adult worker female honey bees have a barbed stinging apparatus attached to its abdomen. A sting is delivered by a tapered, needlelike structure located posteriorly on the abdomen which is designed to inject the venom (**Figure 1**). The bees sting defensively, when a human intrudes into its colony. Alarm pheromones are released by the stinging bee, which attracts other bees to the location. Honey bees die after a single sting because the sting and the venom apparatus get avulsed from its abdomen. In contrast to this, bumble bees can sting repeatedly as its sting is not barbed. Africanized honey bees are hybrids of domestic and African honey bee, found in South America. They are hostile, attack in swarms and pursue their victim aggressively.



Figure 1: Honey bee with its sting (posteriorly placed) embedded in the patient's skin

VENOM ALLERGENS

Bees release large amount of venom, 50–140 mcg/sting.² Allergens constituting the venom include vasoactive amines, small polypeptides and enzymes. Histamine, mast cell degranulating peptide, phospholipase A2 (PLA2), hyaluronidase, acid phosphatase and melittin are the important constituents.^{2,3} Bumble bee venom is antigenically and chemically similar to honey bee venom.²

ALLERGIC REACTIONS TO HYMENOPTERA VENOM

The spectrum of allergic reactions to bee venom ranges from normal (mild) local reactions to large local reactions to systemic anaphylactic reaction (mild, moderate and severe).² Systemic toxic reactions are seen in cases of mass envenomation by large number of bees. The usual effect of a sting is intense local pain, erythema and mild edema around the sting site. An area of induration with a diameter of 10 cm or more; which peaks between 24 hours and 48 hours and then subsides, is referred to as a large local reaction (LLR).² The symptoms are limited to the site of sting without any systemic involvement. Stings in the mouth may cause serious airway obstruction even in people who are not hypersensitive to venom. Systemic manifestations include hypotension, bronchoconstriction, respiratory distress, syncope, laryngeal edema and death. It is classified according to severity as given in **Tables 1 to 3**.

Systemic allergic reactions are IgE mediated Type 1 hypersensitivity reaction. Toxic reactions in mass bee envenomation are not allergic, but are due to the direct action of large amount of venom. Common clinical presentation of patients in India is normal (mild) local reaction surrounding the site of sting. However, severe anaphylaxis and multiorgan dysfunction after bee sting have been reported. There are several reports from India and abroad, of patients developing rhabdomyolysis, acute renal failure, Guillain-Barré

TABLE 1 | British Society of Allergy and Immunology classification of allergic, systemic reaction to bee sting²

Severity	Symbol	Reactions
Mild	+	Pruritus, erythema, urticaria, nausea, angioedema, rhinitis
Moderate	++	Mild asthma, moderate angioedema (Figure 2), abdominal pain, vomiting, diarrhea, mild and transient hypotensive symptoms
Severe	+++	Laryngeal edema, collapse or loss of consciousness, hypotension, rarely incontinence, seizures

TABLE 2 | Mueller grading system for systemic reaction to insect sting⁴

Grade 1	Systemic reaction is characterized by generalized urticaria or erythema, itching, malaise or anxiety
Grade 2	Reactions may include symptoms associated with grade I reactions as well as generalized edema, tightness in the chest, wheezing, abdominal pain, nausea and vomiting, and dizziness
Grade 3	Reactions may include symptoms associated with grade I or II reactions as well as symptoms of dyspnea, dysarthria, hoarseness, weakness, confusion and a feeling of impending doom
Grade 4	Reactions may include symptoms associated with grade I, II or III reactions as well as any two of the following—fall in BP, loss of consciousness, incontinence of urine or feces, or cyanosis

TABLE 3 | Investigation in hymenoptera venom allergy²

Aimed result	Description of test
Demonstration of specific IgE to bee and wasp venom	Skin prick test (10–100 mcg/ml) standardized venom extract Intradermal test (0.001–1 mcg/ml) standardized venom extract Serum specific IgE standardized enzyme immunoassay (Radio Allergo Sorbent Test)
<i>Serum total IgE</i>	
Baseline serum tryptase	If baseline tryptase is elevated (>20 mcg/L), consider follow-up investigation for systemic mastocytosis

syndrome, myasthenia gravis and coagulopathy following multiple bee stings.^{5–8} Authors encountered two cases of acute renal failure following bee sting, probably due to acute tubular necrosis.

Investigations for Venom Allergy

Systemic allergic reactions to bee sting are more often seen in those with an occupational risk, like bee keepers and their family members. Skin tests are needed for those individuals who are candidates for immunotherapy. British Society for Allergy and Clinical Immunology recommends following allergy tests:

- **Skin prick test (SPT):** Immediate hypersensitivity to allergen is tested using SPT. It involves pricking the epidermis through a drop of standardized bee venom extract (1–100 mcg/ml). A positive control with histamine and negative saline control should be done for comparison. A wheal measuring 3 mm more than the negative control is suggestive of presence of specific IgE antibody against bee venom.
- **Intradermal test:** If SPT is negative in a patient with a strong clinical history, intradermal test is done using allergen concentrations between 0.001 mcg/ml and 1 mcg/ml. A volume of 0.03 mL of the extract is injected intradermally to raise a bleb of 3–5 mm. An increase in the wheal diameter of 3 mm at 20 min is considered positive. A positive skin test in response to venom concentrations below 1 mcg/ml demonstrates the presence of serum specific IgE antibodies.
- **Serum specific IgE:** Serum specific IgE antibody is assayed by solid phase enzyme immunoassay. Level ≥ 0.35 KU/mL is considered

**Figure 2: Bee sting with angioneurotic edema**

positive. This should be tested in adjunct to the skin tests and result interpreted in relation to the clinical history.

An elevated serum tryptase level and mastocytosis are risk factors for severe reaction to bee sting. Baseline tryptase level (normal <11.4 mcg/L) should be checked in all patients who develop a systemic reaction. An elevated serum tryptase level reflects abnormal proliferation of mast cells. Patients with baseline tryptase level >20 mcg/ml should be investigated further for systemic mastocytosis by doing a bone marrow biopsy.

- **Serum total IgE:** Total serum IgE >250 KU/mL indicates asymptomatic sensitization and such patients may be protected from severe anaphylactic shock.
- **Basophil activation test:** This involves flow cytometric analysis of whole blood. It is a research tool and currently has no clinical role.

Treatment and Prevention for Venom Allergy

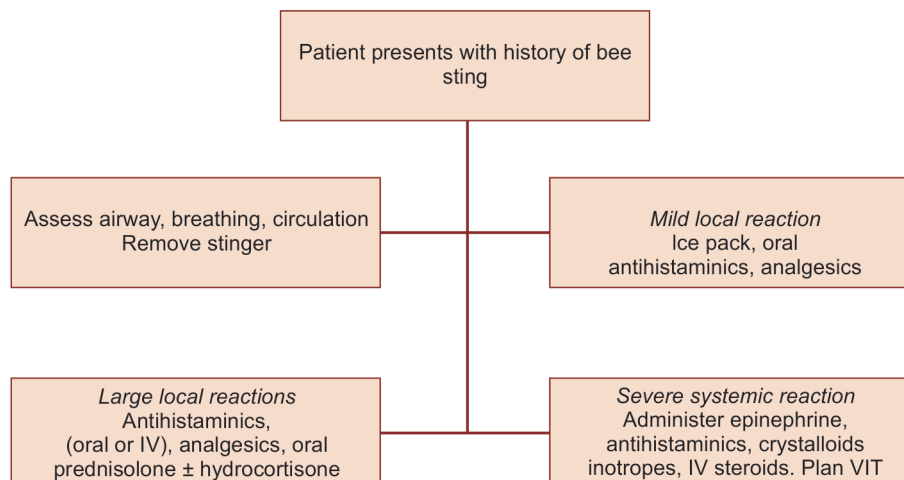
Anaphylaxis is diagnosed in a patient with suspected exposure to allergen bee venom, if there is an acute onset of illness with skin or mucosal involvement with one of the following:

- Respiratory compromise (dyspnea, bronchospasm, wheezing, hypoxemia, stridor)
- Hypotension (Systolic BP <90 mm Hg or 30% decrease from the baseline), syncope or evidence of end organ damage.

Management

- **Out of hospital:** At the first signs of any clinical manifestations of anaphylaxis, the patient should self-administer epinephrine, if available (adult dose, 0.3 mL of 1:1000 intramuscular; pediatric dose, 0.01 mL/kg of 1:1000 intramuscular). Susceptible patients may even use aerosolized epinephrine from a metered-dose inhaler (10–20 doses) to counteract the effects of laryngeal edema, bronchoconstriction, and other manifestations of anaphylaxis
- **In-hospital management (Flow chart 1):**
 - Assess airway patency, breathing and circulation. Establish intravenous (IV) access
 - Aqueous epinephrine (1:1000), in a dose of 0.3–0.5 mL is for adults and 0.01 mL/kg (not exceeding 0.3 mL) for children should be given. In case of profound hypotension, skin perfusion is hampered. In such cases, 2–5 mL of epinephrine

Flow chart 1: The management of a patient of bee sting



(1:10,000) should be given slow IV or an IV infusion can be set up by mixing 1 mg of epinephrine in 250 ml saline and be given at the rate of 0.25–1 mL/min. If IV access cannot be established, epinephrine can be given through endotracheal tube, intralingually or intramuscularly.⁹

- In case of hypotension, intravenous crystalloids should be given. Vasopressors like dopamine and norepinephrine may be needed for persistent hypotension
- Antihistaminics should be used in addition to epinephrine and not as its substitute. Diphenhydramine in a dosage of 50 mg IV can be given
- Nebulized β_2 agonist, salbutamol (2.5 mg diluted to 3 mL saline) can be used to relieve bronchospasm
- Methylprednisolone (125–250 mg IV) or intravenous hydrocortisone can be used
- Patients on beta blockers may respond poorly to epinephrine; glucagon is given to such patients to counteract the beta blockade. Dose: 1–5 mg IV over 5 min followed by 5–15 mcg/min infusion
- Rapid removal of stinger is advocated. It should not be squeezed out as it will release more venom from the venom sac (**Figure 3**)
- For mild reactions, application of ice pack or diluted vinegar to the site of sting may be sufficient. Oral and topical antihistaminics can also be used
- Multiple bee stings causing massive envenomation should be treated more aggressively with epinephrine, antihistaminics, steroids and calcium gluconate (10 mL of 10% solution slow IV) for hyperkalemia. Patient should be observed for 12–24 hours for coagulopathy, renal and neurological damage.

Venom Immunotherapy

Venom immunotherapy (VIT) is a highly effective and specific form of treatment to prevent life threatening reactions in hymenoptera allergy. It should be given to all bee keepers who have had a severe systemic reaction and want to continue the same occupation. It is contraindicated in pregnancy, asthma and those on beta blockers. The VIT is not generally necessary for patients 16 years of age or younger who have experienced cutaneous reactions without other systemic manifestations.^{10–12} Indications for the VIT based on clinical status and presence of specific IgE are given in **Table 4**.

Dosage schedule for VIT: VIT consists of subcutaneous injections of increasing amounts of purified bee venom extract. It has two phases: (a) build-up phase (b) maintenance phase. In build-up phase, tolerance



Figure 3: Technique of scraping off a bee stinger from the forearm using a card

to the allergen is gradually induced. To start with, the lowest dose of the most dilute allergen extract, i.e. 0.1 cc of 1:10,000 dilutions is given subcutaneously using 1 cc syringe in the upper arm. Patient is observed for 30 min and the size of the local reaction recorded and graded. The dose is increased weekly, until a maximum tolerated dose is achieved (0.5 cc of 1:1 concentration). This is given weekly as maintenance dose, till 1 year. Subsequently, the interval between maintenance doses is increased to two, three and 4 weeks, provided no large local reactions occur. Injections should be continued for 2–5 years after allergic reactions are controlled. Patients of immunotherapy must follow-up yearly with the doctor after completion of injections.^{11,12} Accelerated schedules of VIT are called as rush and ultrarush VIT.

Preventive Measures

- Frequent cleaning of surroundings, garbage cans and decaying fruit makes it less attractive for bees. Cracks in ceilings and walls should be sealed off as they are potential nesting sites for colonies
- Best defense, when attacked by bees, is to run to a place which can be sealed off, leaving the bees outside
- While rescuing a victim of massive bee sting, protective gear should be worn. Remove the victim to a safe area, remove the stinger and shift to hospital

TABLE 4 | Indications for hymenoptera immunotherapy in patients with clinical reaction after a bee sting¹⁰

Clinical reaction, IgE status	Candidate for immunotherapy
Severe systemic reaction and positive specific IgE	Yes
Severe systemic reaction and negative specific IgE	No
Moderate systemic reaction and positive specific IgE	Yes
Mild systemic reaction + positive specific IgE and evidence of psychological affection	Yes
Large local reaction and positive specific IgE, or unusual reaction	No

- To kill bees, 1–3% foam or detergent water mixture can be sprayed on the swarm of attacking bees. Insecticide should be sprayed around the nests at night, when they are less active
- Abandoned bee nests should be removed by bee keepers
- Individuals allergic to insect sting should carry emergency kit containing epinephrine autoinjectors and also carry identification tags.⁹

SUMMARY

The incidence of anaphylaxis caused by insect sting has been estimated to be 1% in children and 3% in adults. Repeated episodes of bee sting are often seen in bee keepers and their family members. Allergic reaction to bee sting can be classified as local and systemic. Further, local reactions can be normal (mild) and large local reactions, depending on the size of wheal surrounding the sting site. Systemic anaphylaxis can be further classified into mild, moderate and severe. Severe systemic reactions include bronchoconstriction, laryngeal edema, cyanosis, hypotension and death following a bee sting. Local reactions are treated with oral or intravenous antihistaminics and analgesics. Oral prednisolone has been tried for large local reactions. Epinephrine is the most important drug to be administered to a patient with systemic anaphylaxis. Intravenous hydrocortisone and methylprednisolone are the other drugs which

need to be considered. Hypotension, in such cases, should be corrected with intravenous fluids and, if necessary, inotropes should be added. Bronchodilators may be used to control bronchospasm. Patients who have had a previous systemic reaction to bee sting are candidates for VIT and allergy testing. VIT reduces the risk of a life threatening allergic reaction in case of recurrent sting. In case of stings by a large swarm of bees causing mass envenomation, patient should be treated aggressively and observed for 12–24 hours for the development of coagulopathy, renal and neurological damage.

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