VENOM ALLERGENS
Bees release large amount of venom, 50–140 mcg/sting. 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.

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).

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.

Venom 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
syndrome, myasthenia gravis and coagulopathy following multiple bee stings. 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. This should be tested in adjunct to the skin tests and result interpreted in relation to the clinical history.

- **Serum specific IgE:** Serum specific IgE antibody is assayed by solid phase enzyme immunoassay. Level ≥0.35 KU/mL is considered 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.

- **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 mani-festations 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 epi...
Chapter 92  Indian Guidelines and Protocols: Bee Sting

Section 12

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

Patient presents with history of bee sting

Assess airway, breathing, circulation
Remove stinger

Mild local reaction
Ice pack, oral antihistaminics, analgesics

Large local reactions
Antihistaminics, (oral or IV), analgesics, oral prednisolone 1 hydrocortisone

Severe systemic reaction
Administer epinephrine, antihistaminics, crystalloids isotropes, IV steroids. Plan VIT

(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 β₂ 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 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.13,14 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

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

Section 12

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.  

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.

REFERENCES


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<tr>
<th>Clinical reaction, IgE status</th>
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<tr>
<td>Severe systemic reaction and positive specific IgE</td>
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<td>Severe systemic reaction and negative specific IgE</td>
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<td>Moderate systemic reaction and positive specific IgE</td>
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<td>Mild systemic reaction + positive specific IgE and evidence of psychological affection</td>
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<td>Large local reaction and positive specific IgE, or unusual reaction</td>
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