

# Guideline for Hymenoptera Allergy in Children and Adults

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## Key Points

- Hymenoptera stings cause a wide spectrum of reactions, from localized pain and swelling to life-threatening anaphylaxis.
- Insect-sting anaphylaxis accounts for a large number of cases of anaphylaxis seen in emergency departments.
- Venom skin prick and/or venom-specific IgE are the tests of choice to confirm Hymenoptera allergy for those with history of a systemic sting reaction.
- Venom immunotherapy can prevent future systemic allergic reactions in up to 95% of patients with Hymenoptera allergy.

## Definition, Assessment, Diagnosis

### Definition

- Hymenoptera accounts for the largest order of insects, including yellowjackets, hornets, wasps, bees, and ants. Although commonly associated with human stings, these insects play an important role in crop pollination and reduction of insect pest populations.
- The Hymenoptera insects that cause most human stings are in the Vespidae (wasp) family and include yellowjackets (*Vespula*), aerial yellowjackets (*Dolichovespula*), hornets (*Vespa*), and paper wasps (*Polistes*). Other important families include bees (*Apidea*) and imported fire ants and harvester ants (*Formicidae*).
- Hymenoptera anaphylaxis is defined as a systemic allergic reaction following a Hymenoptera sting.
  - Systemic allergic reactions occur in 0.15% to 0.8% of children and 0.3 to 8.9% of adults following a Hymenoptera sting<sup>2</sup>
  - Between 40 and 100 people die each year from insect-sting anaphylaxis

## Assessment

- Hymenoptera insect characteristics and behavior
  - Honeybees and bumblebees
    - Typically not aggressive but will sting if their hives are threatened. Hives are constructed from beeswax in combs and hexagonal cells.
    - Bumblebee nests are typically found in concealed locations constructed of loose, fibrous materials such as grass clippings.
    - Honeybee stings are characterized by the stinger that is left behind in the skin.
  - Paper wasps, yellow jackets, and aerial yellow jackets
    - Commonly confused due to similar coloring and appearance, but can be differentiated based upon their nests.
    - Paper wasp nests are often found under eaves of homes and have a single paper comb with no protective envelope.
    - Yellow jackets make their nests in concealed locations such as wall cavities or stumps.
    - Aerial yellow jackets live in large colonies near human dwellings and can be aggressive.
  - Imported fire ants (IFA)
    - Build large mound colonies connected by deep tunnels made of loose soil often found in yards, fields, or pastures and can contain more than 200,000 ants
    - IFA stings are characterized by sterile pustules that form within 24 hours.
- Reactions following Hymenoptera sting
  - Mild local reaction
    - The most common reaction following a Hymenoptera sting
    - Characterized by pain, swelling, and erythema at the site of the sting
    - Typically resolves within 1-2 hours
  - Large local reaction
    - Characterized by pain, swelling, and erythema at the site of the sting, but involves a much larger area of skin, at least 10 cm in size.
    - Symptoms of nausea and vomiting may also be present.
    - Peaks at 48 hours and may last for up to 1 week
    - Less than 5% of patients with large local reactions will have a systemic allergic reaction following future stings.
  - Systemic allergic reaction
    - Cutaneous, systemic allergic reactions
      - Cutaneous manifestations alone (i.e., generalized urticaria, flushing, erythema, and/or pruritus) without involvement of other organ systems
      - Ten percent (10%) of children <16 years of age with this presentation will have systemic allergic reactions upon re-sting, but most of these are limited to the skin.
    - Anaphylaxis
      - Involves more than one organ system and typically includes the skin, gastrointestinal, respiratory, and/or cardiovascular systems
      - Anaphylaxis is a life-threatening reaction and should lead to prompt medical attention.
      - There is often no warning that this type of reaction will occur; however, patients with a history of systemic allergic reaction following Hymenoptera sting are at risk for a similar reaction with future stings.

## Diagnosis

- Known exposure to Hymenoptera insects is the most useful historical factor to diagnose Hymenoptera allergy.
- Correct identification of the offending insect is useful but can be difficult. An appropriate

medical history should also include relevant details regarding the type of reaction that occurred.

- There are few laboratory tests that can be performed at the time of presentation to confirm the diagnosis of a systemic allergic reaction to a Hymenoptera insect.
  - An elevated serum tryptase following a Hymenoptera sting can help confirm a systemic allergic reaction; however, a normal serum tryptase does not rule it out. Serum tryptase peaks 1-2 hours following a systemic allergic reaction and has a half-life of 2 hours; thus, tryptase must be drawn within 6 hours to be helpful.
- Referral to an allergist/immunologist is ideal to confirm a diagnosis of Hymenoptera allergy as well as to initiate treatment to prevent future systemic allergic reactions.
  - In general, pediatric patients with a history of a local or large local reaction following Hymenoptera sting do not require further testing.
    - In adults with large local reactions, venom immunotherapy is effective in reducing the size of these reactions.
    - Testing and venom immunotherapy should be considered in those at risk for frequent occupational and/or recreational exposure.
    - No studies have been completed analyzing the use of venom immunotherapy in children with large local reactions.
  - Patients with a history of systemic allergic reaction following Hymenoptera sting should undergo further testing.
  - Appropriate skin testing should be delayed for 3 to 6 weeks following a sting due to a higher risk of false negative results. Venom-specific IgE may be present within several days of a sting but may take up to 6 weeks to become detectable.
  - Testing for family members of Hymenoptera allergic patients without a history of systemic allergic reaction is not recommended due to the poor predictive value of skin testing for future reactions.
- Diagnostic testing
  - Skin prick and intradermal testing are the most reliable tests to confirm Hymenoptera allergy. Skin testing with venoms is safe with a <2% chance of systemic allergic reaction during testing. Reactions that do occur are usually mild.
  - Venom-specific IgE testing can be performed in patients who cannot undergo skin testing, but is not as sensitive nor specific as skin testing
    - Negative venom-specific IgE tests obtained within the first few days following a sting should be repeated 3-6 weeks later to confirm negativity.
    - Venom-specific IgE testing can be performed in patients with negative skin testing and a convincing clinical history of a systemic allergic reaction.
      - Approximately 5-10% of Hymenoptera-allergic patients will have positive venom-specific IgE and negative skin tests.
      - Similarly, 20% will have positive skin tests, but negative IgE tests.
  - Serum tryptase levels should be obtained in patients with a history of systemic allergic reaction following a Hymenoptera sting.
    - Approximately 8% of patients with Hymenoptera allergy will have a mast cell disorder (i.e. systemic mastocytosis, mast cell activation syndrome, etc.)
    - Baseline serum tryptase levels >11.4 mg/L are associated with a higher risk of a severe systemic allergic reaction with future Hymenoptera stings.

## Management and Treatment Recommendations

- Acute management of Hymenoptera stings
  - Local reactions
    - Local reactions can be treated symptomatically with ice packs. Many local reactions will require no treatment.

- Secondary infection is the most common complication and should be treated with appropriate antibiotics
  - Large local reactions: Application of ice packs, elevation of the affected limb, and use of oral antihistamines and/or systemic corticosteroids may be helpful
  - Systemic allergic reactions
    - Patients with systemic allergic reactions should immediately be placed in the recumbent position with the lower extremities elevated. When necessary, emergency medical services should be contacted.
    - Epinephrine is the drug of choice for the treatment of anaphylactic reactions
      - In children, 0.01 mg/kg up to 0.3 mg should be given intramuscularly (IM) in the anterior-lateral thigh.
      - In adults, 0.3 to 0.5 mg IM should be given in a similar manner.
      - Repeat doses of epinephrine can be given every 5 to 15 minutes as required to control the systemic allergic reaction.
    - H1/H2-antihistamines, corticosteroids, oxygen, bronchodilators, intravenous fluids, and vasopressors can also be used, when necessary, as adjunctive therapies but should not delay the use of epinephrine in the treatment of systemic allergic reactions.
  - All patients with a history of a systemic allergic reaction following Hymenoptera sting should be prescribed a self-injectable epinephrine device (Auvi-Q®, Epi-Pen®, etc.) as well as instruction for its proper use. Patients should also be instructed regarding avoidance of future stings as well as be prescribed a MedicAlert® bracelet. (<http://www.medicalert.org>)
- Long-term management of Hymenoptera stings – Venom immunotherapy
  - VIT is indicated in patients with a history of a systemic allergic reaction following Hymenoptera sting with evidence of venom-specific IgE antibodies (through skin testing or specific IgE testing)
    - VIT is recommended in adults with systemic sting reactions confined to generalized cutaneous symptoms only if quality of life is impaired.
    - VIT prevents future systemic allergic reactions in 75-95% of patients; 40-60% of patients that do not receive VIT will have a systemic allergic reaction with future sting.
    - When systemic allergic reactions following re-sting do occur in VIT-treated patients, most are mild and non-life-threatening.
    - VIT induces long lasting protection; more than 80% of patients who complete 3 years of therapy will be protected against systemic allergic reactions for an additional 7 years after therapy is stopped.
  - In children <16 years of age, VIT is not indicated for those whose reaction includes only cutaneous manifestations, such as generalized urticaria, flushing, erythema, and/or pruritus.
    - Ten percent (10%) of children with cutaneous reactions will have a systemic allergic reaction upon re-sting and most of these will be mild and limited to the skin.
    - VIT is indicated in children with cutaneous reactions following stings by imported fire ant as these patients are at higher risk for future systemic allergic reactions. VIT should be initiated for patients with underlying mast cell disorders and a history of systemic allergic reaction following a Hymenoptera sting.
  - VIT typically requires 8 to 15 weeks to reach maintenance, the dose at which the patient is considered to be protected from future systemic allergic reactions. Maintenance can be achieved earlier with rush or ultra-rush therapy, although there is a higher risk of side effects.
  - VIT is recommended for at least 3 to 5 years, although some patients may require life long therapy
    - There are no consensus recommendations for discontinuing VIT but it could be considered in patients whose venom-specific IgE decreases to insignificant

- levels, conversion to negative skin testing, or completion of a specific time.
- For patients who complete 3 to 5 years of therapy less than 10% will have a systemic allergic reaction upon re-sting and those are usually mild.
- Caution should be exercised in discontinuing VIT in patients with a history of life threatening systemic allergic reaction, particularly in those with continued positive skin tests after 3-5 years of VIT; such patients are at higher risk of systemic allergic reaction with future sting.
- Life-long VIT should be considered in patients with mast cell disorders.
- Risks of VIT
  - Local reactions at the site of injection can cause pain, swelling, redness, and/or pruritus.
  - Systemic allergic reactions occur in up to 12% of patients receiving VIT, although most are mild.
  - VIT is safe to utilize during pregnancy if the patient has already reached maintenance therapy.
  - VIT should not be initiated during pregnancy, unless the benefit of such outweighs the risk.
  - Patients receiving beta-adrenergic blocking medications may not be responsive to treatments instituted for a systemic allergic reaction.
    - Therefore, beta-adrenergic blocking medications, where possible, should be discontinued before VIT is initiated.
    - If they cannot be discontinued, extra caution should be exercised when administering VIT.
  - Patients with mast cell disorders and poorly-controlled asthma are at higher risk of adverse reactions while receiving VIT; extra caution should be used in these populations.
  - Caution should be exercised using VIT in patients with multiorgan autoimmune disorders. Organ-specific autoimmune disorders, including Hashimoto's thyroiditis, type 1 diabetes mellitus, Crohn's disease, ulcerative colitis, and rheumatoid arthritis, are not considered a contraindication only when the underlying disease is stable or in remission.

## Prevention and Education

- Avoidance of stinging insects is the best preventative measure, although this may be difficult for some patients.
- Understanding of the nesting and behavior patterns of Hymenoptera insects is also important:
  - Honeybees protect their hives and frequently sting in defense, but otherwise are not typically aggressive.
  - Yellow jackets are a common cause of insect stings in North America.
    - They are naturally aggressive and are attracted to food, especially meat and fruits.
    - Yellow jackets will commonly sting in pursuit of food; thus, food garbage should be placed in a closed container.
    - Wasps and hornets sting humans less often than yellow jackets; stings that do occur are typically the result of provocation, usually in the area of their nests.
  - If a Hymenoptera nest is discovered and is a threat for human stings, removal by a trained professional is the best option.
  - Insect repellants are not useful to prevent Hymenoptera stings.
  - Avoid going barefoot to prevent IFA stings; recognition of their mounds and prompt treatment with bait chemicals is also effective to reduce IFA populations.
  - Clean, white clothing is less attractive to stinging insects.
    - Long sleeves and pants worn while outdoors may also be protective.
    - Going barefoot or wearing sandals is not advisable.

*This guideline was developed to improve health care access in Arkansas and to aid physicians and other health care professionals in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may*

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