Hymenoptera Envenomation: Bees, Wasps, And Ants

Imagine these scenarios:

Paramedics call your emergency department to inform you that they are transporting a 12-year-old boy who was stung several hundred times by a swarm of honeybees. The patient is agitated and has innumerable erythematous papular stings to his face and extremities. What are your immediate priorities, and what are your subsequent concerns for delayed toxicity?

A 7-year-old girl is brought to triage by her parents after she was stung a single time by a wasp. She is lethargic with facial swelling and a generalized urticarial rash. In addition, she has respiratory distress with bilateral wheezes on lung examination, and pulse oximetry demonstrates oxygen saturations of 87% on room air. How should this life-threatening situation be managed?

A 2-year-old male is transported to your emergency department after stumbling into a fire ant nest. He is crying, irritable, and tachycardic but has no respiratory distress. He has multiple erythematous papules on his legs that are beginning to form fluid-filled vesicles. What is the treatment for this envenomation?

Stinging insects have long been known to cause allergic reactions in humans. The earliest recorded death from an allergic reaction caused by a stinging insect was that of Pharaoh Menes of Egypt who died in 2641 B.C. after being stung by either a hornet or a wasp.1

Bees, wasps, and ants (Figure 1) are stinging insects belonging to the order Hymenoptera, which is Latin for “membrane-winged.” The 3 families of greatest medical significance within this order are Apidae (honeybees and bumblebees), Vespidae (yellow jackets, hornets, and yellowjackets), and Formicidae (ants) (Figure 2).

References


CME Objectives

Upon completing this article, you should be able to:

1. Describe the epidemiology and pathophysiology of Hymenoptera envenomation.
2. Identify and treat the immediate life-threatening complications of bee and wasp stings.
3. Understand and manage the delayed complications of Hymenoptera envenomation.
4. Describe the presentation and management of fire ant envenomation.

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and wasps), and Formicidae (fire ants). Hymenoptera stings cause a wide spectrum of illness ranging from benign nuisance to life-threatening toxicity and anaphylaxis. It is estimated that anaphylaxis to Hymenoptera species affects up to 0.5% of the U.S. population and is responsible for more than 40 deaths per year in the United States.1,2

Children are frequent victims of this important group of stinging insects, and very young children are at increased risk for significant toxicity due to their inability to escape from multiple envenomations and increased venom delivered per kilogram. This issue of Pediatric Emergency Medicine Practice will focus on the evaluation and management of the child with Hymenoptera envenomation.

Critical Appraisal Of The Literature

The literature review for this article included PubMed searches for articles related to bee, wasp, and ant envenomation. The search also included the terms “Hymenoptera” and “Solenopsis envenomation,” as well as “bee,” “yellow jacket,” and “Solenopsis venom.” Further manual searches of references from key publications and pertinent textbook chapters provided additional articles for review. Since most of the major morbidity and mortality from these envenomations result from allergic reactions and anaphylaxis, it is not unexpected that many of the references were published in allergy-immunology literature. However, it is important to note that there is also a growing body of literature documenting morbidity and mortality resulting from mass envenomations by Hymenoptera.

Part I. Apidae And Vespidae (Bees And Wasps)

Epidemiology

In 2005, 10,792 exposures to bees, wasps, and hornets were reported to U.S. Poison Centers. Over 4000 of these exposures were in children less than 19 years of age. Over 1200 exposures were treated at a health care facility and 1 death was reported.4 It is important to note that the true number of exposures and serious outcomes is much higher than these numbers would suggest because significant underreporting occurs.

Apidae

Honeybees

Apis mellifera, otherwise known as the honeybee, is originally a European and African species. Honeybees were introduced to North America by European settlers for their honey-making abilities. They are one of the few domesticated insects, and colonies are maintained in hives in many countries. Feral honeybee colonies usually nest in hollow trees or crevices in rocks and even in the walls of occupied buildings.3,5,6

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Figure 1. Taxonomy Of The Order Hymenoptera

Adapted from Goldfrank’s Toxicologic Emergencies, Eighth Edition
Honeybees are small, hair-covered insects with alternating tan and black stripes. They are relatively non-aggressive and generally sting only when threatened. Fatalities from honeybee stings are fortunately a rare event. Most fatalities are caused by Type I IgE-mediated anaphylactic reactions, but deaths are also reported following massive envenomation involving hundreds to thousands of stings.

Africanized Honeybees (AHBs)

Disease-resistant African bees were imported into Brazil in the 1950s in the hope of cross-breeding them with honey-producing domestic bees to increase productivity as well as disease resistance. However, in 1956, 26 imported queen bees and their colonies escaped and began interbreeding with local honeybees. The resulting Africanized bees (Apis mellifera scutellata) then proliferated and migrated through South and Central America. They eventually entered the United States in the 1990s and spread throughout the southwestern states.

The Africanized bee usually displays the same behavioral patterns as the European bee. However, when AHBs perceive that their hives have been threatened, they will attack more rapidly and in greater numbers than their European cousins. AHBs will also pursue and continuously sting their victims over greater distances than the domesticated honeybees with distances reported up to 0.6 miles. The primary risk to the victim is in the sheer number of stings that the AHB will deliver.

AHBs also differ from European honeybees by swarming several times a year compared to European honeybees, which swarm only once or twice a year. Swarming occurs when new queens are produced in a colony and part of the colony leaves with the old queen. This increases the number of colonies within a given area. Also, AHBs often colonize in unprotected areas where they are more easily disturbed by humans.

Africanized honeybees preferentially seek food, water, and shelter in metropolitan areas of the Southwestern United States due to the warmer climate. Africanized honeybees do not establish colonies well in freezing climates but have the potential to pose a threat during the warm season due to inadvertent transport by various forms of shipping.

The first reported mass envenomation involving AHBs in the United States occurred in the spring of 1991 in the lower Rio Grande Valley of South Texas and resulted in 350 stings. Since their arrival, there have been 4 deaths associated with attacks by AHBs in Texas and Arizona. Although there have been AHB mass envenomation incidents reported in California, no fatalities have been reported in that state.

Bumblebees

Bumblebees (Bombus terrestris) are found mostly in the Northern hemisphere and are large, slow-moving, noisy bees with hairy bodies and alternating yellow and black stripes. They usually reside in small colonies of no more than 200 insects and nest just under the surface of the ground, often in abandoned mammal burrows. They are non-aggressive and account for only a small fraction of stings. Bumblebees typically are not involved in mass stinging and will generally only sting if the nest is threatened or if they are captured or trapped between skin and clothing.

Bumblebees have long been used in North America and Europe to pollinate vegetable crops. Due to their increased use in the agricultural sector, the incidence of bumblebee stings and occupationally-related anaphylactic reactions to bumblebee venom has increased.

Vespidae

Wasp (Yellow Jackets, Hornets)

Wasps are a well-recognized medical concern in North America and Europe. Wasps often build their nests close to human dwellings under roofs, behind shutters, and in dryer vents. Yellow jackets and hornets are wasps belonging to the subfamily Vespinae.

Yellow jackets are usually 10-15 mm in length. They build and live in nests in the walls of occupied buildings or in the ground. Yellow jackets maintain colonies of several hundred to several thousand individuals. They are also strongly attracted to garbage and other rotting organic materials.

Hornets usually live in large paper-like nests built hanging in trees or under branches. Hornets are usually 15-40 mm in length. They also maintain colonies of several hundred to thousands of individual insects and are theoretically more dangerous due to greater venom injection capability and venom toxicity.

Etiology

Apidae

Venom Apparatus And Stinger Mechanism

Members of the Apidae family (bees) can only sting once because their stinger is a modified ovipositor that resides in the abdomen. The stinger is barbed and is attached to a venom sac. After the sting, the bee is disemboweled as the stinger detaches and takes along with it the distal segment of the bee’s intestinal tract including nerves, muscles, and venom sac. After it is detached, the stinger’s nerves and muscles continue to work the barb deeper into the flesh of the victim. A valve and piston pumps venom from the venom sac through the stinger and into the wound.
Vespidae

Venom Apparatus

Vespidae do not eviscerate after stinging their victims because their stinger is smooth instead of barbed. The venom apparatus consists of 2 acid glands: an alkaline gland and a venom sac, which is connected to a stinger. The distal part of the acid gland secretes the venom while the proximal part transports the secretions to the venom sac, which acts as a reservoir. The venom moves to the alkaline gland, which adds a mildly toxic substance. The venom is subsequently transported to the stinger apparatus, which is surrounded by muscle fibers from the alkaline gland that create a sphincter-like structure.14

Pathophysiology

Venom

Apidae

Honeybees and AHBs have very similar concentrations of the major components of their venom. The difference usually lies in the amount of venom delivered to the victim and whether it is an isolated sting or a mass envenomation.5

Melittin is the major component of honeybee and AHB venom. It accounts for 50% of the venom’s volume and is the major pain-inducing compound. It is theorized that melittin causes neurotoxicity by acting as a molecular mimic of an immunodominant peptide which induces an acute disseminated encephalomyelitis. Melittin, with the aid of phospholipase A2 (PLA2), inserts itself into the phospholipid layer of cell membranes, induces skeletal muscle necrosis, disrupts the vascular endothelium, and causes the breakdown of red blood cells, leukocytes, and platelets. Other venom components include the major allergen PLA2, hyaluronidase, and mast-cell degranulating protein.5, 6, 9, 15-17

Hyaluronidase is a secondary allergen known as a “spreading factor” because it causes the breakdown of connective tissue and increases the uptake and spread of melittin and PLA2. Hyaluronidase makes up about 1%-2% of honeybee venom. Hyaluronidase is also present in the venom of other animal species, including spiders and snakes, where it serves a similar function.6, 9, 18, 19

Apamin, another bee venom peptide, is a neurotoxin that primarily affects the spinal cord. Adolapin is a recently-described bee venom peptide and has anti-inflammatory effects. Adolapin may explain why apitherapy seems to be effective in treating some forms of arthritis.3, 20

Mast-cell degranulation protein makes up about 2% of honeybee venom and causes mast cells to break down, releasing histamine. Honeybee venom itself also contains small amounts of histamine. The exogenous and endogenous histamine contribute to localized inflammation and increased venom absorption.6, 8

Bumblebee (B. terristris) venom also contains the major allergen PLA2, proteases, and hyaluronidase. Bumblebee venom is chemically and antigenically related to honeybee venom and can have significant immunologic cross-reactivity.10, 11

Vespidae

Vespidae venom has similar protein compositions across different species and contains hyaluronidase and phospholipase. However, there are a few differences between Vespidae and Apidae venom that should be noted. For example, the intense pain that is caused by hornet and wasp stings is largely due to serotonin and acetylcholine, which make up 1%-5% of dry venom weight. Wasp kinins (venom peptides) contribute to pain production and can also produce significant hypotensive effects. Vespula venom also contains Antigen 5, which may function as a major allergen.3, 21

Allergic Reactions And Anaphylaxis

Bee and wasp venoms contain 9-13 different peptide antigens that all may trigger allergic reactions. The most well known allergic reaction is the Type I anaphylactic or immediate hypersensitivity reaction (Table 1). This reaction is mediated by immunoglobulin E antibodies, which trigger mast cell degranulation when they are cross-linked by the appropriate antigen. Symptoms usually occur distant to the sting site and include hives, pruritis,
dyspnea, hypotension, loss of consciousness, and heart palpitations (Table 2). Symptoms may start within 15 minutes after exposure but can be delayed for as long as 6 hours. It is important to note that upper airway obstruction is the leading cause of death, and intractable hypotension is the second leading cause of death in patients with anaphylaxis. Such patients require intensive supportive care including airway control and restoration of hemodynamic stability with aggressive fluid resuscitation and pressor support. Nearly all deaths caused by Hymenoptera envenomation occur by Type I immediate hypersensitivity. Other immune-mediated reactions to Hymenoptera envenomation include immune complex (Type III) and cell-mediated (Type IV) reactions. Type III (serum sickness) reactions occur 3-14 days after the sting and present with fever, headache, urticaria, lymphadenopathy, polyarthralgia, and polyarthralgias. Type II hypersensitivity reactions (antibody mediated) do not commonly occur following Hymenoptera envenomation.

Major local reactions are usually the result of a Type IV hypersensitivity reaction. The associated local edema and erythema can last up to a week.

Mass Stinging Events
Mass stinging events can be acutely life-threatening due to the toxic action of large amounts of injected venom. Toxicity from massive honey bee envenomation occurs directly from the systemic effects of the venom, as opposed to immune-mediated anaphylaxis (Table 3). Death may result from exposure to hundreds or thousands of stings.

Mass envenomations usually occur when stinging insects respond to an intruder as a threat to their colony. Most mass envenomation cases that are reported in the literature involve hundreds of stings and can result in toxic systemic reactions and renal failure. Mass bee envenomations usually number in the hundreds to thousands of stings while mass wasp envenomations usually involve tens to hundreds, reflecting hive size. Stings are predominately in the head and neck because the insects prefer to sting in these areas, but stings can also involve other exposed areas such as the arms and legs.

The very young and the very old may be at greater risk for morbidity and mortality from massive bee attacks. Children have smaller body mass and are exposed to a greater amount of venom per kilogram. However, the few docu-

| Table 2. Clinical Presentation Of Hymenoptera Envenomation (Hypersensitivity Reactions) |
|---------------------------------|---------------------------------|
| **System**                     | **Symptoms**                   |
| Prodomal                       | Pruritis                       |
|                                | Metallic taste                 |
|                                | Feeling of impending doom      |
| Vital Signs                    | Tachycardia                    |
|                                | Tachypnea                      |
|                                | Hypotension                    |
|                                | Hypoxia                        |
| Dermatologic                   | Flushing                       |
|                                | Warmth                         |
|                                | Urticaria                      |
|                                | Edema                          |
| Respiratory                    | Wheezing, bronchospasm         |
|                                | Bronchorrhea                   |
|                                | Cough                          |
|                                | Laryngeal edema                |
|                                | Angioedema of the tongue, upper airway |
| Cardiovascular                 | Syncope                        |
|                                | Tachydysrhythmias              |
|                                | ECG changes: ST and T wave     |
| Abdominal                      | Nausea                         |
|                                | Vomiting                       |
|                                | Diarrhea                       |
|                                | Bloating                       |
|                                | Crampy pain                    |

Adapted from Ford and Delaney “Clinical Toxicology” Chapter 114 Hymenoptera

<table>
<thead>
<tr>
<th>Table 3. Clinical Presentation Of Mass (Toxic) Envenomation</th>
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<tr>
<td><strong>Systems</strong></td>
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<td>Neurologic</td>
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<td>Respiratory</td>
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<tr>
<td>Metabolic</td>
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<td>Musculoskeletal</td>
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Adapted from Ford and Delaney “Clinical Toxicology” Chapter 114 Hymenoptera
mented cases of more than 1000 honeybee stings in children have resulted in recovery after hospitalization. Children are more likely to be stung due to carelessness and are less able to escape when stung. The elderly often have co-morbidities that increase their risk of severe outcome after mass envenomation.

The initial symptoms after massive envenomation include edema, fatigue, fever, nausea, vomiting, localized pain, and loss of consciousness. Rapid onset of diarrhea and urinary incontinence may be secondary to endogenous histamine release. Stings to the eyes can lead to corneal edema and ulceration. If bees are swallowed and internal envenomation occurs, life-threatening pharyngeal edema and respiratory obstruction may result. Systemic toxicity usually develops within 24 hours. Multisystem derangements include hemolysis, rhabdomyolysis, transaminosis, thrombocytopenia, and disseminated intravascular coagulation. Rhabdomyolysis may lead to oliguria, acute tubular necrosis, and renal failure. With excellent supportive care, the systemic toxicity is usually reversible. No specific antidotes are available. Death from mass envenomation has been reported in victims with 500-1000 stings. With aggressive supportive care, survival is possible in such situations.

Other Reactions
In general, most Apidae envenomations are characterized by transient local reactions of erythema, edema, and pain, but other unusual manifestations have been known to occur. Vasculitis, neuritis, and encephalitis have been reported several days to weeks after a bee sting. Thrombotic thrombocytopenic purpura has also been reported as a rare complication of bee stings.

Oropharyngeal stings can cause significant edema resulting in airway obstruction. The airway obstruction usually occurs early in presentation but may be somewhat delayed. These patients warrant close monitoring and may require aggressive airway management.

Allergy to honeybee body components has also been documented. Patients have reportedly developed inhalant allergy to whole bee body components, though the exact body component has not been identified. These patients usually also have a concurrent bee venom sensitivity and develop the allergy through occupational exposure.

Differential Diagnosis
In most cases, patients seeking medical attention are able to provide the specific history of being stung by a bee, wasp, or unidentified insect. The physical examination typically confirms the history. However, it may be impossible to obtain a history if the patient is nonverbal, such as a very young child, or if the patient presents in extremis. In cases where the etiology is not clear, the differential diagnosis should be expanded to include other considerations.

For example, local reactions may be mistaken for other envenomations or localized infections, such as abscess or cellulitis. In patients with anaphylaxis, allergic reactions to other allergens, such as foods or medications, should be considered. Causes of acute shock must be considered and differentiated. Physical findings such as warm, flushed skin can help differentiate between anaphylactic shock and other types of shock. Systemic mastocytosis and urticaria pigmentosa should also be considered because the mast cell degranulation in these patients may mimic anaphylaxis. Scombroid poisoning may also present in a similar fashion.

Although toxic systemic reactions from mass envenomations are usually not difficult to diagnose with the presence of multiple sting marks on the skin, other causes of progressive multi-organ failure, such as sepsis, should be considered.

Urticaria Pigmentosa And Mastocytosis
Patients with urticaria pigmentosa have focal salmon-colored to brown macules that produce a wheal-and-flare reaction when stroked. Biopsy of these lesions shows abnormally high numbers of mast cells. Patients can have acute episodes of mast cell degranulation that are clinically indistinguishable from allergic anaphylaxis. There have been reports of these patients having equivocal bee venom-specific IgE and still exhibiting full anaphylactic responses and mastocytosis.

Prehospital Care
Prehospital care of the patient with bee or wasp envenomation consists of excellent supportive care and transport to the nearest emergency department. The patient with anaphylaxis and respiratory distress must be treated rapidly and aggressively. The patency of the airway should be maintained while supplemental oxygen is provided. Nebulized albuterol may be considered for treatment of bronchospasm. Bag-valve-mask ventilation or endotracheal intubation may be required for severe respiratory compromise. Subcutaneous or intramuscular epinephrine should be administered quickly and intravenous access established. Intravenous doses of diphenhydramine and corticosteroids are also beneficial. Hypotension is treated with intravenous boluses of normal saline and pressors as needed.
ED Evaluation

As with all patients presenting to the emergency department, the initial evaluation of patients with bee or wasp envenomation consists of rapid identification and stabilization of any immediate life-threatening problems. This is followed by a more comprehensive history, physical examination, and diagnostic evaluation. After airway, breathing, and circulation have been evaluated and stabilized, a detailed history should be obtained for the following information: past medical history, medications, immunization status, and allergies (with special attention to prior history of bee or wasp exposure and reactions, since patients who have been previously sensitized to bee or wasp stings have a 30%-60% chance of developing anaphylaxis with future stings). It is also important to note the estimated number of stings, progression of symptoms since envenomation, and types of prehospital therapies performed. Tetanus status should be updated, if appropriate.

Diagnostic Studies

In the emergency department, the diagnosis of bee or wasp envenomation is clinically made after historical and physical examination data are evaluated. Although specific diagnostic testing for Hymenoptera envenomation is not available in the acute setting, other laboratory evaluations may be warranted, depending on the patient’s condition. For example, arterial blood gas analysis may be helpful in evaluating the patient with respiratory distress or hemodynamic compromise. Later, after the patient has been referred to an allergy-immunology specialist, further testing to determine the specific allergen may be undertaken as outlined later in this article.

Venom Allergy

A detailed history of the patient’s allergic reaction is essential in diagnosing venom allergies, including the specific insect involved, the symptoms experienced, and the sequence and timing of events. Accurate diagnosis is important due to its implications for management. Tests for venom-specific IgE antibodies can also be performed and are essential if desensitization is being considered as a treatment. Skin testing by an allergist should be performed with venom extracts rather than whole body extracts. Whole body extracts are less sensitive in diagnosing venom allergy.

Table 4. Classification And Treatment Of Reactions To Hymenoptera Envenomations

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Clinical Presentation</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Local (allergic and toxic)</td>
<td>Localized pain, pruritis, edema, erythema, warmth</td>
<td>Cold compresses, analgesics, oral antihistamines, large local reactions may benefit from oral steroids</td>
</tr>
<tr>
<td></td>
<td>Solenopsis (imported fire ants) envenomation characteristically results in pustule formation</td>
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<tr>
<td>Systemic Allergic Reaction</td>
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<tr>
<td>Mild</td>
<td>Generalized weakness, chest and throat tightness, nausea, vomiting, diarrhea, generalized angioedema</td>
<td>Oral antihistamines, steroids</td>
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<tr>
<td>Moderate</td>
<td>Wheezing, stridor, laryngeal and pulmonary edema, hoarseness, dyspnea, cyanosis, tachycardia, hypertension, cardiovascular collapse, confusion, coma</td>
<td>IV antihistamines, steroids and IM or IV epinephrine, IV crystalloid, vasopressors, inhaled beta agonists, inhaled racemic epinephrine for stridor</td>
</tr>
<tr>
<td>Severe</td>
<td>Vomiting, diarrhea, generalized edema, collapse, coma, confusion, headache, muscle spasms, seizures, tachycardia, hypotension, hemolysis, thrombocytopenia, disseminated intravascular coagulation, rhabdomyolysis, acute renal failure, hepatotoxicity</td>
<td>Supportive care (i.e., correcting hypotension, coagulopathy, renal dysfunction, etc.); no specific antidote or allergy treatment</td>
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<tr>
<td>Systemic toxic (mass envenomations)</td>
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<tr>
<td>Delayed allergic (serum sickness)</td>
<td>Fever, malaise, urticaria or other rashes, lymphadenopathy, myalgia, arthralgia, polyarteritis, headache, glomerulonephritis, nephrotic syndrome, necrotizing vasculitis</td>
<td>Oral analgesics, antihistamines, steroids</td>
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fingernail rather than being plucked or pinched out. It was reasoned that plucking or pinching the venom sac would cause injection of additional venom.\textsuperscript{2}

In \textit{vivo} studies have shown that nearly all the venom is injected into the victim within the first few seconds after the sting. By the time the patient presents for care, stinger removal by pinching the stinger does not increase the degree of envenomation.\textsuperscript{13, 14}

Delays in stinger removal cause more venom to enter the wound as opposed to inappropriate removal technique. Visscher et al used sting wheal bioassays to reflect the quantity of venom received and reported an increase in wheal size with increased time between sting delivery and removal. Therefore, it may be prudent to remove the stinger by the quickest technique available in order to stop further venom exposure.\textsuperscript{13, 41, 42}

**Local Reactions**

\textit{Apidae} and \textit{Vespidae} envenomation typically results in localized pain and erythema that resolve in a few hours. Cold compresses and analgesics are usually all that are needed.\textsuperscript{1}

Large local reactions may require the addition of antihistamines and corticosteroids to manage symptoms. Antihistamines, such as diphenhydramine, can be given by mouth or via IV depending on the severity of the reaction. Diphenhydramine 1 mg/kg IV up to 50 mg or hydroxyzine 0.5 mg/kg PO up to 50 mg are both suitable H\textsubscript{1} antihistamines. Hydroxyzine should not be given intravenously. H\textsubscript{2} blockers can also be administered and have been found to be just as efficacious as H\textsubscript{1} blockers in urticaria and anaphylaxis. H\textsubscript{2} blockers should be given when hypotension is prominent and if sedation and anticholinergic side effects are not desirable. The combination of H\textsubscript{1} and H\textsubscript{2} blockers appears to be superior to either agent alone and should be given in severe anaphylaxis. Acute severe urticaria may also benefit from a single dose of epinephrine, but this is usually not necessary since there is no acute threat to life. Adult dosages of famotidine 20 mg or ranitidine 50 mg IV can be used in situations of severe anaphylaxis. Famotidine and ranitidine dosages for children less than 12 years of age have not been well established. In the future, the patient should be instructed to take oral antihistamines as soon as possible if they are stung again to prevent the establishment of a local reaction.\textsuperscript{37}

**Systemic Reactions**

The most common symptoms of bee and wasp envenomation are dermal in nature and include generalized urticaria, flushing, and angioedema. The more severe but less common anaphylactic reactions may cause upper airway edema and circulatory collapse, ultimately resulting in death.\textsuperscript{1} Please refer to the “Special Circumstances” section for more detailed management of upper airway obstruction due to anaphylaxis.

Epinephrine is the most rapid-acting and effective medication to reverse the life-threatening complications of anaphylaxis and should be administered immediately for any patient with evidence of an anaphylactic reaction. The intramuscular route is preferable because it provides faster onset of action and more reliable blood levels than subcutaneous administration. The intravenous route should be reserved for patients \textit{in extremis} since it may be associated with cardiac ischemia or dysrhythmias. Epinephrine’s action on beta-adrenergic receptors promotes the synthesis of cyclic AMP in mast cells, thereby blocking further release of chemical mediators such as leukotrienes. The alpha-adrenergic effects of epinephrine are of therapeutic benefit by causing vasoconstriction with resultant improvement in blood pressure and decreased swelling in edematous tissue. Delays in administration of epinephrine may allow the airway obstruction or cardiovascular collapse to progress to the point of irreversibility and death.\textsuperscript{7} Patients should be treated with 0.01 mg/kg (maximum dose 0.5 mg) of the 1:1000 dilution of epinephrine intramuscularly, preferably in the lateral thigh. Epinephrine can be continued in a dose of 0.01 mg/kg IM at 20 minute intervals or an epinephrine drip can be considered (0.05-1 µg/kg/min; titrate to clinical effect).\textsuperscript{12}

In cases of hypotension and cardiovascular compromise associated with anaphylaxis, 1 or 2 IM injections of epinephrine and rapid saline infusions usually are efficacious. H\textsubscript{2} blockers seem to have a positive effect on hypotension as well. If the patient is refractory to these modalities, then IV epinephrine should be initiated. Fortunately, most patients with anaphylaxis will not require such intensive therapy and will respond well to 1 or 2 doses of epinephrine given intramuscularly at 15-20 minute intervals, along with IV fluid resuscitation.\textsuperscript{12}

Corticosteroids are recommended for all anaphylactic patients. Though corticosteroids have no immediate benefit, they are thought to speed the resolution of angioedema and urticaria. Corticosteroids block the formation of late phase reactants. It is theorized that corticosteroids may prevent recurrence of symptoms after the initial treatment of anaphylaxis. Dosages similar to status asthmaticus should be initiated for anaphylaxis, such as methylprednisolone 2 mg/kg IV bolus followed by 1 mg/kg every 6-8 hours. In milder cases, oral corticosteroids such as prednisolone or prednisone can be dosed at 1 mg/kg twice a day.\textsuperscript{7, 2, 12}

**Prevention**

Prevention of \textit{Apidae} stings is especially important in patients with an allergy to bees. Avoidance of bright clothing, flowers, scented deodorants, shampoos, and
perfumes helps to decrease attraction of these insects. Also, patients with known allergy to bees should wear long sleeves, shoes, and long pants when out of doors to further avoid being stung.2

Part II. Formicidae (Ants)

Epidemiology

The ant of greatest medical importance in the United States is the imported red fire ant (Solenopsis invicta) which belongs to the subfamily Myrmicinae and family Formicidae. The fire ant’s painful sting accounts for its name. In addition, the venom is more likely to produce hypersensitivity reactions than that of native North American ant species. The fire ant was introduced from South America to Alabama in the 1930s via shipments of infested nursery stock and other agricultural products and has since spread to the southern United States. It now ranges from southeastern Virginia to central Texas and Oklahoma, where it has largely displaced and eliminated native ant species. S. invicta has been reported to infest more than 310 million acres in 12 states and Puerto Rico. Other states at risk of being colonized with imported fire ants include: Arizona, California, New Mexico, Oregon, and Washington. There are other species of fire ants found in North and Central America as well as the Caribbean and Pacific islands. Allergic reactions to the venom of all of these species have been reported. Solenopsis richteri, the black imported fire ant, is found in areas of northeastern Mississippi and parts of Alabama.3, 36, 43-46

Fire ants measure 2-5 mm in length. They are reddish-brown to black, highly mobile, and very aggressive. They have powerful mandibles as well as a stinger at the end of its abdomen. Stings occur most frequently during the summer months. However, encounters with humans may occur at other times if the fire ants are actively seeking new sites for colony survival during periods of environmental stress.3, 43, 47

In endemic areas, 23%-58% of the population will experience a fire ant bite or sting in the course of a year. It has been estimated that approximately 24%-28% of the population in these endemic areas has hypersensitivity to fire ant venom via skin testing. Children younger than 15 years of age are the most likely to be stung.48, 49

Problems arise when fire ants come in direct contact with humans. In urban areas, fire ants build mounds in open areas such as playgrounds and lawns. They also can build colonies underneath pavement and buildings. In rural areas, fire ants are a hazard to humans and farm animals and can also damage farm equipment, electrical systems, irrigation systems, and crops.43, 47, 49-52

Fire ant colonies differ from bee and wasp colonies in that they have multiple queens in one colony. This allows for close approximation of colonies with the possibility of having more than 500 fire ant mounds per acre in some areas. Each colony can have up to half of a million individual insects.43, 46

The 2005 annual report of the American Association of Poison Control Centers documented 2101 exposures to ant species. Approximately 1100 of these exposures were in children less than 19 years of age with over 250 exposures treated at a health care facility and no deaths reported.4 Unfortunately, significant under-reporting occurs, making it difficult to estimate the true number of fire ant exposures.

In 1989, Stafford et al published the results of a survey conducted with the cooperation of the American Academy of Allergy and Immunology Fire Ant Subcommittee. They reported that over 20,750 patients are treated annually for significant reactions to fire ants in the southeastern United States. Of these patients, an estimated 63% experienced local reactions only, while 2% required medical intervention for life-threatening anaphylaxis.53

Etiology

Stinging Mechanism

Fire ants attack when their colony is threatened, and the ants appear to boil out of the dome-shaped nest to attack in huge numbers. Multiple stings are the rule rather than the exception. The ant uses its mandibles to attach itself to the victim’s skin and arches its back to inject venom through the stinger located at the end of its abdomen. Venom is released from the venom sac and injected over seconds to minutes through the stinger, which is usually 0.5-1 mm in length. The volume of the venom sac is approximately 40 nanoliters and the volume of venom delivered in a single sting has been estimated at 0.04-0.11 microliters. If not removed quickly, the ant will sting repeatedly by using its head as a pivot, withdrawing the stinger and reinserting it in multiple sites within one area.43, 46, 52, 54

Pathophysiology

Venom

Fire ant venom differs from that of other Hymenoptera due to its mostly water-insoluble alkaloid composition. Piperidine alkaloid accounts for 95% of the venom’s volume and causes histamine release as well as necrosis of human skin. The alkaloids do not result in IgE-mediated responses but have cytotoxic, hemotoxic, bactericidal, and insecticidal properties and also activate the complement pathway. Piperidines are responsible for the pain and other typical findings of fire ant stings.52, 54-56
Clinical Pathway For *Hymenoptera* Sting Management

**Patient with *Hymenoptera* envenomation**

- **Local or anaphylactic reaction?**
  - **YES**
    - Consider PO antihistamines and corticosteroids. (Class II)
  - **NO**
    - Consider IM epinephrine; PO, IM, or IV antihistamines; and corticosteroids. (Class II)

- **ANAPHYLACTIC REACTION**
  - **YES**
    - Life-threatening episode?
      - **YES**
        - Initiate IM epinephrine (consider IV if *in extremis*), antihistamines, and corticosteroids. Consider inhaled alpha- and beta-agonists, airway management, and IV fluids. (Class II)
      - **NO**
        - Good clinical response?
          - **YES**
            - Patient cleared for discharge home on antihistamines and corticosteroids.
          - **NO**
            - Admit and monitor for late phase reactants or delayed hypersensitivity. Admit patients with severe reactions to ICU.

- **NO**
  - Admit and monitor for late phase reactants or delayed hypersensitivity. Admit patients with severe reactions to ICU.

- Once symptoms resolve, discharge home on PO antihistamines, corticosteroids, and Epi-Pen®. (Class II)

- **Patient should consult with an allergist.**
The proteins in fire ant venom are highly allergenic but only make up 0.1% of the dry weight of the venom. To date, 4 protein allergens have been isolated: Sol i 1, Sol i 2, Sol i 3, and Sol i 4. All of these proteins have been shown to be important allergens. Patients have been found who react to every combination of these 4 proteins. These 4 allergens appear immunologically distinct when tested with human IgE antibodies. Sol i 1 is a venom phospholipase that exhibits immunologic cross-reactivity with vespid venom phospholipase. This is important because patients who are sensitized to vespid venom can present with significant allergic reactions after fire ant stings. Sol i 1 comprises 2%-5% of the venom protein. Sol i 2, 3, and 4 are not immunologically related to apid or vespid venom proteins. Sol i 2 accounts for two-thirds of the venom protein and has strong phospholipase A activity. Sol i 3 comprises 20% of fire ant venom protein and is a member of the antigen 5 family of venom proteins but does not exhibit immunologic cross-reactivity with vespid antigen 5. Sol i 4 accounts for 8%-10% of the venom protein and is related to but not immunologically cross-reactive with Sol i 2. Hyaluronidase is also present in fire ant venom.43, 50, 52, 55-58

**Mass Stinging Events**

Recently, mass sting attacks by fire ants have been reported in young children and infants as well as elderly residents of nursing homes. It is clear that immobilized individuals are at risk for mass envenomation when they encounter fire ants.43, 59

**Differential Diagnosis**

In most cases, patients or their caretakers are able to provide the history of being stung by fire ants. The characteristic formation of pustules within 24 hours typically confirms the clinical suspicion of fire ant envenomation. However, when the etiology is not clear, the differential diagnosis may include other considerations such as localized pustular infections or cellulitis due to *Staphylococcal* or *Streptococcal* bacteria. In the case of systemic reactions, including anaphylaxis, exposure to other allergens should be considered. A detailed history of recent foods, medications, and other exposures may reveal another etiology for the patient’s illness.

**Prehospital Care**

The prehospital care provider who is called to transport an individual with fire ant envenomation should make a rapid assessment of whether the patient is experiencing limited local effects or a life-threatening systemic reaction. The patient with respiratory distress, cardiovascular compromise, and anaphylaxis must be treated aggressively and transported rapidly to the nearest emergency department for further stabilization. In this situation, it must be recognized that early administration of subcutaneous or intramuscular epinephrine is essential to reverse the systemic effects of anaphylaxis, including upper and lower airway obstruction. Supplemental oxygen should be provided to all patients with respiratory distress, and nebu-
lized albuterol may be considered for treatment of bronchospasm. Bag-valve-mask ventilation may be required for severe respiratory compromise, while endotracheal intubation should be considered as a last resort due to anticipated difficulties with intubation secondary to upper airway obstruction. Establishment of intravenous access will allow administration of crystalloid fluids as well as pressors, diphenhydramine, corticosteroids, and other medications as needed.52

ED Evaluation

The first priority is to quickly identify and treat any life-threatening effects that develop following fire ant envenomation. After the initial stabilization, a more comprehensive physical examination and diagnostic evaluation may be completed. A detailed history should be obtained including past medical history, medications, tetanus immunization status, and allergies (with special attention to prior history of Hymenoptera exposures and reactions). It is also important to note estimated number of stings, progression of symptoms since envenomation, and types of prehospital therapies performed.

Diagnostic Studies

Local reactions typically do not necessitate diagnostic evaluation and should be treated symptomatically. However, in patients who have had systemic allergic reactions to imported fire ant stings, a thorough evaluation by an allergist is warranted. The clinical history should be correlated with the presence of fire ant specific IgE antibody by skin testing or in vitro testing (i.e., Radioallergosorbent test or RAST). Currently, only whole body extracts are available on the market, as opposed to fire ant venom extracts. Whole body extracts are manufactured by crushing and grinding whole fire ants. If the patient demonstrates fire ant specific IgE antibodies upon testing, then venom immunotherapy should be considered.52, 60, 61, 62

Treatment

Reactions to the imported fire ant may be classified into 4 categories: local, large local, systemic allergic, and systemic venom toxicity. Treatment is dependent on the type of reaction.52, 56 See Table 4 for more information.

Local

Local non-allergic reactions present with burning pain at the sting site. Within 20 minutes, a pruritic wheal-and-flare reaction evolves, which then turns into a pustule over the next 20-40 minutes. The pustular fluid initially contains lymphocytes and other leukocytes, but after 24-48 hours it mostly contains necrotic debris. Local reactions can be treated symptomatically, with analgesics and local measures such as cool compresses and frequent cleansings, to prevent secondary bacterial infection.57, 52

Large Local

Large local reactions initially present very similarly to local reactions except that they evolve into pruritic erythema and induration, which expands for the next 24 hours. This reaction may expand to involve an entire extremity before they subside after 48 hours. Typical pustules develop at the sting site, much like the local reaction, except that the fluid contains mostly eosinophils.52

Systemic Allergic Reactions

In addition to local reactions, previously sensitized patients may develop systemic allergic reactions in response to fire ant envenomation. As noted previously, people who are sensitized to wasp venom also demonstrate immunologic cross-reactivity with fire ant venom. Anaphylaxis is estimated to occur in 0.6%-6% of individuals who have been stung. The clinical presentation and treatment of such anaphylactic reactions are the same as for anaphylaxis caused by stings of other Hymenoptera.52

Systemic Venom Toxicity

Although rare, life-threatening systemic manifestations of direct venom toxicity have been reported in victims of mass fire ant envenomation, and infants, young children, and the immobile elderly are at particular risk. These patients may develop shock, metabolic acidosis, coma, hemolytic anemia, coagulopathy, and multi-organ failure, requiring aggressive supportive care. No specific antidotes are available. Cardiorespiratory arrest and death have also been reported.56

Prevention

Patients and their caretakers should be educated to recognize and avoid fire ant mounds so that future envenomation can be prevented. Shoes and protective clothing will also decrease the risk during outdoor activities. Young children must always be carefully supervised in areas where fire ants are known to exist. Fire ant surveillance and eradication should be undertaken near residences, daycare centers, and nursing homes or any place where infants, elderly, or other individuals with decreased ability to escape from multiple envenomations reside.
Risk Management Pitfalls For Bee, Wasp, And Ant Stings

1. “I didn’t think a single bee sting could be fatal.”
   In the setting of previous sensitization to *Hymenoptera* venom, a single sting can result in fatal anaphylaxis. A patient who has experienced *Hymenoptera*-induced anaphylaxis incurs a 30%-60% risk for anaphylaxis with subsequent stings.

2. “I should have used epinephrine earlier for that patient with the anaphylactic reaction.”
   Epinephrine should be administered immediately for patients with evidence of an anaphylactic reaction, upper airway obstruction, or cardiovascular collapse. The intramuscular route provides faster onset of action and more reliable blood levels than subcutaneous administration, while the intravenous route should be reserved for patients in extremis since it may be associated with cardiac ischemia or dysrhythmias. Delays in administering epinephrine may allow airway obstruction or cardiovascular collapse to progress to the point of irreversibility and death.

3. “I should have intubated that patient with upper airway obstruction sooner.”
   If epinephrine and other immediate interventions fail to improve respiratory distress from anaphylaxis-induced upper airway obstruction, early endotracheal intubation should be strongly considered. A delay in airway control may result in progressive angioedema, making it impossible to intubate the patient and, therefore, necessitating a surgical airway.

4. “I wish I had checked the patient’s blood pressure sooner.”
   Intractable hypotension is the second leading cause of death in anaphylaxis after laryngeal edema associated with upper airway obstruction. Early recognition is of key importance. Patients with such cardiovascular collapse require early treatment with epinephrine, aggressive volume resuscitation with intravenous crystalloid, and continuous infusions of vasopressors.

5. “I was so busy treating the other aspects of the envenomation that I forgot to ask about tetanus immunization status.”
   Although it is easy to focus on treating the more impressive local and systemic reactions to these envenomations, it is important not to forget the basic principles of wound care, such as tetanus prophylaxis.

6. “I thought that 24 hours of antihistamines and corticosteroids would be enough for that allergic reaction.”
   A 3-day course of antihistamines and corticosteroids should be prescribed for all patients who are discharged home after an episode of anaphylaxis in order to suppress the recurrence of symptoms due to the ongoing release of pharmacologically-active mediators of the allergic response.

7. “I didn’t think that patient would deteriorate at home after discharge from the ER.”
   Patients with life-threatening complications of anaphylaxis (such as respiratory distress or cardiovascular compromise) should be admitted to the hospital for observation and continued therapy, even if the symptoms improve in the first few hours of treatment. Patients with incomplete response to therapy, debilitated patients, and those with serious underlying cardiac or pulmonary illness should also be admitted. These patients are at increased risk for deterioration at home if discharged prematurely from the ER.

8. “I didn’t know that delayed reactions could occur over a week after envenomation.”
   Patients may present 1-2 weeks after envenomation with serum sickness, which is a type III hypersensitivity reaction mediated by immune complex formation. This unusual presentation is characterized by fever, arthralgia, myalgia, rash, and adenopathy.

9. “I forgot to prescribe an EpiPen® when I discharged the patient.”
   Patients who have experienced an episode of anaphylaxis secondary to *Hymenoptera* envenomation should always be discharged home with an EpiPen® (or other emergency epinephrine kit, such as Ana-Kit®). The risk of anaphylaxis for such a patient is estimated to be 30%-60% if the patient is stung by *Hymenoptera* in the future. It is important to educate patients on the correct use of the epinephrine kit and the importance of having it with them at all times.

10. “I didn’t know that I should have made a referral to an allergist.”
    Patients who have experienced an episode of anaphylaxis secondary to *Hymenoptera* envenomation should be referred to an allergist for further evaluation and management including education, skin-testing, and consideration for venom desensitization immunotherapy.
Part III. Hymenoptera Points Of Interest

Special Circumstances

Upper Airway Management
Upper airway obstruction secondary to anaphylaxis is a true medical, and possibly surgical, emergency. If massive angioedema of the tongue or larynx is present, then endotracheal intubation under direct or fiberoptic laryngoscopy may be impossible. In this situation, a surgical airway, such as a cricothyroidotomy, must be established to prevent a fatal outcome. The first important point to make is that of early recognition. When the gravity of impending upper airway obstruction is appreciated early, emergency interventions are more likely to result in a positive outcome. Endotracheal intubation may be lifesaving when performed early, before the airway obstruction becomes too severe. A second important principle is full mobilization of available resources. If your hospital has a rapidly available team to assist with the difficult airway, it should be mobilized early. For example, some hospitals have a “STAT Difficult Airway Team” including an anesthesiologist and an ENT surgeon, which can be paged to provide rapid assistance in situations such as upper airway obstruction. The emergency department’s difficult airway cart should be brought to the patient’s bed-side and the strategy for airway management as well as contingency plans should be reviewed with available staff members. Aggressive medical management should be undertaken immediately and should include intramuscular or intravenous epinephrine, antihistamines, and corticosteroids. Inhaled alpha-adrenergic agonists, such as epinephrine, can also be administered via nebulization to decrease supraglottic and laryngeal edema. Heliox can also be considered as a temporizing measure since it decreases airflow resistance and improves ventilation in upper airway obstruction.12

Cutting Edge

Apitherapy
Apitherapy is the medical use of honey bee products including the honey, bee pollen, royal jelly, and bee venom. The most highly visible application of apitherapy is bee venom therapy for autoimmune diseases and multiple sclerosis. Some preliminary animal studies demonstrate positive results in treating arthritis. However, further studies are needed to confirm such findings in humans. Adolapin, a bee venom peptide, has been shown to have anti-inflammatory activity and may be responsible for the beneficial effects of apitherapy. Adolapin also appears to inhibit the prostaglandin synthetase system and has been shown to decrease edema and polyarthritis in rats.20,66

Immunotherapy
Venom immunotherapy has been considered for patients with severe systemic allergic reactions. Venom immunotherapy has been shown to be effective and safe for preventing sting-induced anaphylaxis. It has been shown to be 97% effective in reducing anaphylaxis in adults with previous systemic reactions. It has been estimated that without venom immunotherapy, 30%-60% of adults with previous systemic allergic reactions will have systemic reactions if stung again. Venom immunotherapy in general carries around a 10% risk of inducing systemic allergic reactions and can potentially induce anaphylaxis. Fatalities are rare and are estimated at 1 per year.1,67-71

The indications for venom immunotherapy are the following: history of anaphylaxis due to Hymenoptera sting, cardiac or respiratory distress after sting, evidence of venom-specific IgE, likelihood of continued exposure to stings, and good likelihood of patient compliance. For example, children with dermal reactions only after a Hymenoptera sting are not candidates for venom immunotherapy. It is not meant for patients who have significant concurrent medical or immunological disease, concurrent treatment with medications (i.e., beta blockers) likely to impair possible treatment for anaphylaxis, and patients who are insufficiently willing or motivated to attend regularly and complete the prescribed course of treatment. Pregnant patients should not start immunotherapy but can continue maintenance if already in treatment. Venom immunotherapy is contraindicated for children less than 5 years of age and in patients with a history of chronic perennial asthma and severe dermatitis.72-75

Patients who are considered for venom therapy first undergo properly performed skin testing with venoms from honeybees, wasps, yellow jackets, yellow hornets, white-faced hornets, and paper wasps to diagnose Hymenoptera sensitivity. Whole body extracts of S. invicta are used for skin testing because S. invicta venom extracts are currently unavailable on the market. If the patient demonstrates positive skin tests, then immunotherapy is initiated. Venom immunotherapy is given once or twice a week for several months and patients should be premedicated with antihistamines to enhance the effectiveness of immunotherapy. The therapy is then spaced monthly or even longer for at least 3-5 years. When the skin test or in vitro tests for specific IgE become negative, then therapy can...
be discontinued.\textsuperscript{40, 67, 73, 76, 77}

Immunotherapy leads to marked changes in cytokine secretion patterns by changing the abnormal T-helper 2 cell cytokine responses to a normal T-helper 1 cell cytokine response. This leads to a long-term loss of IgE synthesis and increase in venom-specific IgG and a loss of the allergic reaction.\textsuperscript{1, 37, 67}

Though Apidae, Vespidae, and Formicidae contain similar allergenic proteins, the current problem in the clinical management of venom-allergic patients is due to the existence of multiple reactivity in a large fraction of patients. There does not seem to be any significantly reliable method to determine the primary insect which causes the patient’s sensitivity. Therefore, manufacturers of venom immunotherapy sera combine all of the important North American insect species in each batch of extract. This appears to be the most efficient course for the clinician to treat venom-sensitive patients.\textsuperscript{57, 78, 79}

\textbf{Disposition}

\textbf{Local Reactions}

Patients with local reactions to Hymenoptera stings can be discharged home from the emergency department after symptomatic treatment. Rare exceptions that require hospital admission would include: large local reactions near the airway that may cause respiratory compromise or large local reactions of an extremity that may cause vascular compromise. In addition to local wound care, oral antihistamines and corticosteroids may be prescribed for more significant local reactions. All patients should be educated to avoid Hymenoptera envenomation in the future.

\textbf{Mild Allergic Reactions}

Patients who present with mild allergic reactions to Hymenoptera envenomation are usually safely discharged home from the emergency department after a brief observation period. These patients may have generalized urticaria, pruritis, or skin flushing, but no respiratory distress or cardiovascular compromise. Their symptoms are typically controlled with oral antihistamines, often with the addition of oral corticosteroids.\textsuperscript{37} These patients should be warned to try to avoid these stings in the future.

\textbf{Moderate And Severe Allergic Reactions}

All patients with severe allergic reactions that cause respiratory distress or hemodynamic compromise should be admitted to the hospital, often to an intensive care setting. These anaphylactic reactions require aggressive supportive care and vigilant monitoring. Patients with moderate systemic al-

ergic reactions may also require hospitalization. If the symptoms improve after initial treatment in the emergency department and do not recur during a 4-6 hour observation period, it is reasonable to discharge the patient home on oral antihistamines and corticosteroids as well as a prescription for injectable epinephrine and a referral for outpatient allergy-immunology evaluation. However, if moderate symptoms persist, such as throat discomfort, chest tightness, or vomiting, it is prudent to admit the patient for continued observation. During hospitalization, allergy-immunology consultation can be obtained. In addition, the time in the hospital should be utilized for patient education and prevention of future envenomations. Patients should be discharged with a prescription for injectable epinephrine with specific instructions of how and when to administer the medication.\textsuperscript{80}

The patient should also be instructed to use antihistamines, such as diphenhydramine, as well as to obtain a medic-alert bracelet, which can alert emergency personnel to the presence of a sensitized individual. Patient education is extremely important to achieve compliance because patients perceive the injectable epinephrine as cumbersome or intimidating.\textsuperscript{37, 80}

\textbf{Systemic Toxic (Mass) Envenomation}

Patients with systemic toxic reactions secondary to mass envenomation should be admitted to the hospital for close monitoring and supportive care. Such patients with large numbers of stings are at risk for multi-system toxicity, which may occur on a delayed basis. Patients who have appeared stable in the emergency department have subsequently decompensated with severe complications.

\textbf{Summary}

Hymenoptera envenomation in the United States results in significant morbidity and mortality every year. The most common cause of severe or fatal outcome is anaphylaxis. Less commonly, direct toxic effects from mass envenomation may also result in severe consequences. It is therefore necessary for the emergency physician to be familiar with the clinical presentation, as well as the appropriate evaluation and management of these stings. Proper treatment and patient education will optimize outcome for the envenomation.

\textbf{Case Conclusions}

This 12-year-old boy sustained massive bee envenomation, likely the result of an aggressive swarm of Africanized honeybees. You observed that he had several...
hundred bee stings to his face, extremities, and torso, but no evidence of anaphylaxis. The immediate priorities of airway, breathing, and circulation were attended to. He was breathing comfortably without stridor, wheezes, or hypoxia. He had moderate tachycardia but no hypotension. Intravenous access was obtained, and the patient was treated with intravenous fluids, corticosteroids, antihistamines, and analgesia. Although he remained stable for several hours in the emergency department, you admitted him for observation due to your concerns that he may develop delayed toxicity secondary to the massive envenomation. In the hospital, the patient did indeed decompensate 12 hours after admission with vomiting, tachycardia, hypotension, and altered mental status. Laboratory evaluation revealed hemolysis, hemoglobinuria, rhabdomyolysis, renal insufficiency, and hepatic transaminase enzyme elevations. Aggressive supportive care measures in the intensive care unit were required to stabilize the patient. His condition gradually improved, and he was discharged home in good condition after 1 week in the hospital.

You immediately recognized that this 7-year-old girl was experiencing an anaphylactic reaction to the wasp sting and brought her to the resuscitation room for aggressive management of this life-threatening emergency. Oxygen and nebulized albuterol were administered, and the patient was given an intramuscular injection of epinephrine simultaneously. Intravenous access was obtained, and the patient received fluids, antihistamines, and corticosteroids. Her initial blood pressure was 72/40 mm Hg, and this improved to 90/64 mm Hg after 1 dose of epinephrine and 2 boluses of normal saline. Her wheezing and oxygen requirement resolved, and her mental status improved. She continued to have generalized urticaria, but the rash had faded considerably. You breathed a sigh of relief as you consulted the allergy-immunologist and made arrangements for hospital admission.

Your initial examination of the child revealed no respiratory distress or other signs of anaphylaxis, and the parents were not aware of the child having any prior exposure to fire ants. After confirming that the child had no significant compromise of vital signs, you felt comfortable that the child’s envenomation could be treated with good wound management and symptomatic care. The affected areas were gently cleansed with soap and water, and cool compresses were applied. The child’s tetanus status was confirmed to be current. The patient’s pain and itching were treated with oral ibuprofen and diphenhydramine. His irritability and tachycardia resolved as he stopped crying and became more comfortable. Prior to discharge home, you reassured the parents, who were thankful for the good care their child received.

References
Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.


55. Hoffman DR, Sakell RH, Schmidt M. Sol i 1, the phospholipase allergen of imported fire ant venom. J Allergy Clin Immunol. 2005;115(3):611-616. (Comparative study)


CME Questions

1) What is the most common cause of death following Hymenoptera envenomation?
   a. Severe local tissue damage
   b. Systemic toxicity following mass envenomation
   c. Anaphylaxis
   d. Delayed allergic reactions

2) What is the most important medication to administer when treating a patient with severe anaphylaxis?
   a. Prednisone
   b. Albuterol
   c. Diphenhydramine
   d. Epinephrine

3) What is the characteristic appearance of fire ant stings?
   a. Pustules
   b. Urticaria
   c. Macules
   d. Purpura
4) Which of the following Hymenoptera typically can only sting once?
   a. Fire ants
   b. Honeybees
   c. Wasps
   d. Yellow jackets

5) Which of the following Hymenoptera belongs to the Family Apidae?
   a. Wasps
   b. Yellow jackets
   c. Hornets
   d. Bumblebees

6) Compared to normal domestic honeybees, Africanized honeybees:
   a. Are more venomous
   b. Are more aggressive when the hive is threatened
   c. Are more widespread in cold as well as warm climates
   d. Are less likely to attack in large swarms

7) What type of allergic reaction is anaphylaxis?
   a. Type I, immediate hypersensitivity
   b. Type II, antibody-dependent
   c. Type III, immune complex
   d. Type IV, cell-mediated

8) Imported fire ants:
   a. Are not aggressive and usually do not sting when disturbed
   b. Only sting once because their stinger is barbed
   c. Have venomous stings but do not induce allergy
   d. Often sting the victim multiple times

9) Prevention of bee stings for sensitized individuals includes:
   a. Wearing bright-colored clothing
   b. Wearing strong perfumes
   c. Wearing long-sleeved shirts and long pants while outdoors
   d. Walking barefoot

10) The main cause of death from anaphylaxis is:
    a. Upper airway obstruction secondary to laryngeal edema
    b. Upper airway obstruction secondary to lip and tongue edema
    c. Local airway obstruction secondary to bronchospasm
    d. Refractory hypotension

11) Which of the following patients is the most appropriate candidate for venom immunotherapy?
    a. 3-year-old male with generalized urticaria after fire ant envenomation
    b. 20-year-old healthy female college student with marked hand swelling, redness, and pain after a bee sting
    c. 25-year-old healthy male landscaper with anaphylaxis to yellow jacket stings and a positive skin test for Hymenoptera sensitivity
    d. 50-year-old homeless male with a history of chronic asthma who presents with wheezing after a bee sting

12) The name “Hymenoptera” means:
    a. Honey producer
    b. Painful stinger
    c. Strong jawed
    d. Membrane-winged

13) Which of the following therapies is contraindicated in the treatment of anaphylaxis with respiratory distress?
    a. Epinephrine
    b. Beta-blockers
    c. Corticosteroids
    d. Antihistamines

14) Imported fire ants:
    a. Are more likely to cause hypersensitivity and anaphylaxis than native North American ant species
    b. Are less aggressive than native North American ant species
    c. Envenomate their victims via specialized poison glands in their mandibles
    d. Build their nests in trees

15) Bumblebees:
    a. Live in huge colonies containing many thousands of insects
    b. Are often involved in mass stinging events
    c. Account for a large majority of Hymenoptera stings
    d. Are non-aggressive

16) Which of the following is the best method for removing a bee stinger from the victim’s skin?
    a. Pinching with tweezers
    b. Grasping with fingers
    c. Scraping with a credit card
    d. Whichever method can be done the quickest
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Coming In Future Issues:

Evaluation of the Pediatric Cervical Spine
Initial Assessment and Management of Knee, Ankle and Wrist Injuries
GI Decontamination
Severe Brain Injury

Class Of Evidence Definitions

Each action in the clinical pathways section of Pediatric Emergency Medicine Practice receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with no exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful
- Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies; historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence

<table>
<thead>
<tr>
<th>Class</th>
<th>Case Series, Animal Studies, Consensus Panels</th>
<th>Occasionally Positive Results</th>
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<tr>
<td>Class I</td>
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Physician CME Information

Date of Original Release: June 1, 2008. Date of most recent review: May 10, 2008.

Termination date: June 1, 2011.

Accreditation: This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Mount Sinai School of Medicine and Pediatric Emergency Medicine Practice. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation: The Mount Sinai School of Medicine designates this educational activity for a maximum of 48 AMA PRA Category 1 Credit(s)™ per year. Physicians should claim credit commensurate with the extent of their participation in the activity.

ACEP Accreditation: Pediatric Emergency Medicine Practice is also approved by the American College of Emergency Physicians for 48 hours of ACEP Category 1 credit per annual subscription.

AAP Accreditation: This continuing medical education activity has been reviewed by the American Academy of Pediatrics and is acceptable for up to 44 AAP credits. These credits can be applied toward the AAP CME/CPD Award available to Fellows and Candidate Fellows of the American Board of Pediatrics.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals & Objectives: Upon completion of this article, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

Discussion of Investigational Information: As part of the newsletter, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration approval labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product. Disclosure of Off-Label Usage: This issue of Pediatric Emergency Medicine Practice discusses no off-label use of any pharmaceutical product.

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