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Hymenoptera Stings

Kevin T. Fitzgerald, PhD, DVM, DABVP and Aryn A. Flood, AAS, CVT

The medically important groups of Hymenoptera are the Apoidea (bees), Vespoidea (wasps, hornets, and yellow jackets), and Formicidae (ants). These insects deliver their venom by stinging their victims. Bees lose their barbed stinger after stinging and die. Wasps, hornets, and yellow jackets can sting multiple times. Most deaths related to Hymenoptera stings are the result of immediate hypersensitivity reactions, causing anaphylaxis. Massive envenomations can cause death in nonallergic individuals. The estimated lethal dose is approximately 20 stings/kg in most mammals. Anaphylactic reactions to Hymenoptera stings are not dose dependent or related to the number of stings. Bee and wasp venoms are made up primarily of protein. Conversely, fire ant venoms are 95% alkaloids. Four possible reactions are seen after insect stings: local reactions, regional reactions, systemic anaphylactic responses, and less commonly, delayed-type hypersensitivity. Clinical signs of bee and wasp stings include erythema, edema, and pain at the sting site. Occasionally, animals develop regional reactions. Onset of life-threatening, anaphylactic signs typically occur within 10 minutes of the sting. Diagnosis of bee and wasp stings stem from a history of potential contact matched with onset of appropriate clinical signs. Treatment of uncomplicated envenomations (stings) consists of conservative therapy (antihistamines, ice or cool compresses, topical lidocaine, or corticosteroid lotions). Prompt recognition and initiation of treatment is critical in successful management of anaphylactic reactions to hymenopteran stings. Imported fire ants *both* bite and sting, and envenomation only occurs through the sting. Anaphylaxis after imported fire ant stings is treated similarly to anaphylactic reactions after honeybee and vespid stings. The majority of Hymenopteran stings are self-limiting events, which resolve in a few hours without treatment. Because life-threatening anaphylactic reactions can progress rapidly, all animals stung should be closely monitored and observed. In the following review article, we will examine the sources and incidence, toxicokinetics, pathological lesions, clinical signs, diagnosis, treatment, and prognosis for dogs and cats suffering Hymenoptera stings.
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Each year a large number of companion animals fall victim to insect stings. The stinging insects are members of the order Hymenoptera of the class Insecta. These venomous insects possess the capability to sting using a modified ovipositor found on the terminal end of their abdomen. The three medically important groups are the *Apoidea* (bees with 20,000 species), *Vespoidea* (the wasps, hornets, and yellow jackets with 15,000 species) and *Formicidae* (ants with 15,000 species). The fire ants will be considered separately in this discussion.

The family Apoidae includes the social honeybees, the solitary bees, and bumblebees. Honeybees are herbivorous and live on nectar and pollen (Fig 1). Wasps, hornets, and yellow jackets (Vespoidae) are predacious carnivores and live on other insects and sweet substances, such as sap and nectar (Fig 2). Feeding cues for bees emanate from flowers among which they forage. The feeding cue for the vespids comes from flesh and the smell of sugars. There is often a great deal of misidentification between bees and their vespid cousins. However, the two groups differ tremendously in their behavior and body type and can be readily identified. Honeybees are social insects and build their nests (hives) in hollow trees or other cavities. Yellow jackets are usually ground dwellers, whereas the hornets and wasps live in shrubs and trees, and are not ground nesting. Unlike bees, vespids can be frequently found near open cans of soft drinks and sweet food and garbage.

The stinger of these insects is another method of identification.[1,2] Honeybees can only sting once; they possess a barbed stinger that stays behind in the victim's skin after they sting. The stinger and the venom sac are pulled out of the

Alameda East Veterinary Hospital, Denver, CO.
Address reprint requests to Kevin T. Fitzgerald, PhD, DVM, ABVP, Staff Veterinarian, Alameda East Veterinary Hospital, Denver CO 80231. E-mail: kfitzgerald@aevh.com

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Figure 1 Honeybee *Apis mellifera*. (Photographs courtesy of Dr. Michael Breed.) (Color version of figure is available online.)

bee's abdomen and soon after the insect dies. Wasp, hornet, and yellow jacket stingers are not barbed and each insect is capable of delivering multiple venom-injecting stings without dying.[3] Vespids are much more aggressive whereas bees are generally more docile. However, honeybees will vigorously defend their hives against intruders (Fig 3A, B). Typically, people and animals are stung accidentally when they step on bees or otherwise disturb the insects. An exception to this is the aggressive behavior of the more recently introduced Africanized honeybee. These bees attack more readily than their European and North American counterparts, potentially inflicting hundreds of stings.[4] If the offending specimen causing the sting is not available, learning the circumstances of the stinging incident, looking for the presence of a stinger in a victim, knowing the differences in body types, and understanding the behavioral differences between bees and wasps can be instrumental in correctly identifying the stinging insect.[5]

Lethal Dose

Death can result from insect stings in a few different manners. Most deaths related to Hymenoptera stings are the result of immediate hypersensitivity reactions causing anaphylaxis. However, death may also occur from severe local reactions, particularly if involving the airways with subsequent respiratory obstruction. Massive envenomation, as seen in swarm attacks, can likewise cause death in nonallergic individuals. In humans, the estimated lethal dose is about 500 stings for adults.[6] The estimated lethal dose is about 20 stings/kg in most mammals.[7]

It has been estimated that the European honeybee injects 147 μg of venom per sting, and most wasps about 17 μg of venom each sting.[8,9] It does not appear that stinging insects can meter their venom like some venomous snakes and spiders; each Hymenoptera sting delivers a relatively standard venom volume. Anaphylactic reactions are not dose-related and death can occur after a single sting.

Toxicokinetics

The venom of stinging insects contains several powerful allergens and pharmacologically active compounds. Hymenoptera venoms are composed of complex mixtures of allergic proteins, active antigens, and peptides.[10] Both bee and wasp venoms are made up primarily of protein. Bee venom is a complex mixture of biologically active components, primarily consisting of proteins, enzymes, and amines.

Bee Venom

The major component of honeybee venom is mellitin, which acts as a detergent to disrupt cell membranes and liberate biogenic animes, and potassium.[10] Mellitin is a protein that hydrolyzes cell membranes, alters cellular permeability, and causes histamine release. Mellitin is considered the agent most responsible for local pain. In addition, it induces catecholamine release, which acts with phospholipase A_2 to cause intravascular hemolysis.

Peptide 401 (or mast cell degranulating peptide) causes mast cells to degranulate, releasing histamine and vasoactive amines. Histamine release by bee venom is mainly mediated by mast cell degranulation peptide.

Phospholipase A_2 is the major allergenic component of bee venom and acts in concert with mellitin to cause intravascular hemolysis. Phospholipase A_2 appears to represent the major antigen and/or allergen in bee venom.

Hyaluronidase causes changes in cell permeability by altering cell membranes and disrupts collagen, allowing other

Figure 2 Yellowjackets *Vespula pennsylvanica* eating a dead bee. (Color version of figure is available online.)

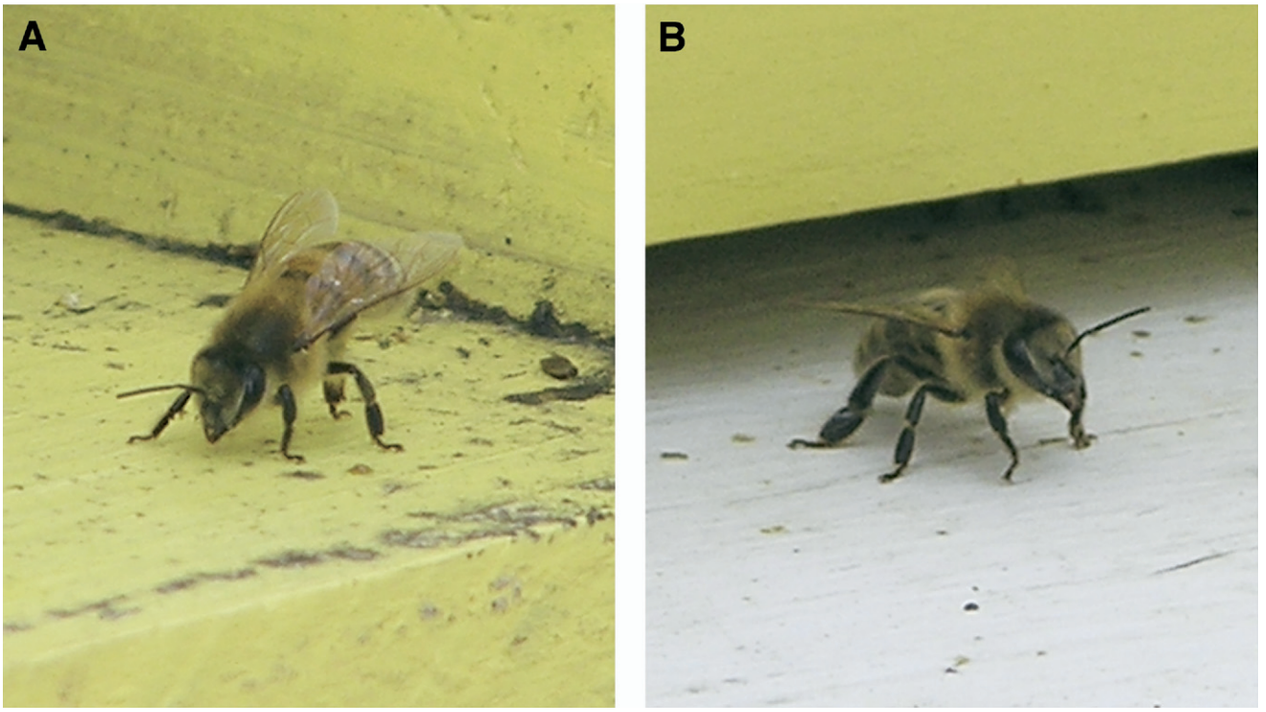

Figure 3 Honeybees defending their hives. (A, B) (Color version of figure is available online.)

venom components to penetrate into the victim's tissues; it is called the "spreading factor." Hyaluronidase is allergenic. The chief enzymes found in bee venom are hyaluronidase and phospholipase A.

The venom also contains vasoactive amines, such as histamine, dopamine, and norepinephrine, and other unidentified proteins.[6,11]

Apamin in bee venom is a neurotoxin that acts on the spinal cord. Adolapin inhibits prostaglandin synthetase and has anti-inflammatory actions, and it has been postulated that it may be useful in the treatment of arthritis.

Wasp and Hornet Venom

The venom of the vespids contains three major proteins that act as allergens and also a wide variety of vasoactive amines and peptides.[12] Mellitin is not found in vespid venom. The intense pain of vespid stings is because of serotonin, wasp kinins, and acetylcholine. The major allergen in vespid venom is called antigen 5. Its biological activity has not been fully determined. The mastoparans are similar to the mast cell degranulation peptide in bee venom, but its action is weaker. Phospholipase A may account for some of the coagulation abnormalities caused by wasp venom. A comparison of Hymenoptera venoms is included in Table 1.

Response to Envenomation

Four primary reactions may be seen after a Hymenoptera envenomation. First and most commonly seen is local pain and swelling. This reaction occurs in all envenomated (stung) individuals to some degree and is caused by vasoactive components of bee venom rather than by an allergic mechanism. Second is a larger, regional reaction, mediated by allergic mechanisms, involving parts of the body in continuity with the sting site. The third and more severe type of reaction is a systemic, anaphylactic response characterized by varying degrees of urticaria, angioedema, nausea and vomiting, hypotension, and dyspnea, caused by an immediate hypersensitivity reaction. This type of reaction occurs in individuals who have specific IgE antibodies to allergenic components of bee venom and occurs within a few minutes of the sting. The fourth possible reaction is uncommon and consists of skin rashes and serum sickness-like symptoms occurring within 3 days to 2 weeks after envenomation. This type of response is thought to be mediated by circulating immune complexes or a delayed hypersensitivity reaction.

The exact incidence of anaphylactic reactions to bee or vespid stings is unknown in companion animals. In humans the incidence is somewhere between 1 and 3%. Anaphylactic signs usually are apparent within 15 minutes of the sting. For

Table 1 Comparison of Hymenoptera Venom

Apids (bees)	
Phospholipase A	Biogenic amines
Hyaluronidase	Acid phosphatase
Mellitin	Mast cell degranulating peptide
Apamin	Minimine
Vespids (wasps, yellow jackets, hornets)	
Phospholipase A	Acid phosphatase
Hyaluronidase	Antigen 5
Biogenic amines	Mast cell degranulating peptide
Kinins	
Formicides (fire ants)	
Phospholipase	Piperidines
Hyaluronidase	
Biogenic amines	

dogs, if a severe systemic allergic reaction has not occurred within 30 minutes, it is unlikely to begin.

Anaphylaxis is IgE mediated.[11] In individuals who have previously been sensitized to bee venom, IgE antibodies attach to tissue mast cells and basophils. Once these cells are activated, the progression of the cascade reaction increases vasoactive substances, which stimulate release of leukotrienes, histamine, and eosinophil chemotactic Factor-A. Anaphylactic reactions are not dependent on the number of stings. Animals allergic to bee and vespid venom develop a wheal and flare reaction at the site of the inoculum. The shorter the interval between the sting and the onset of signs, the more severe the anaphylactic reaction will be. A fulminant cascade of reactions can quickly follow initial mild clinical signs. Death can occur within several minutes.

The accidental introduction of the native African bee *Apis mellifera scutellata* into Brazil in 1957 and its subsequent displacement and hybridization with the long-established European bee *Apis mellifera mellifera* has resulted in the highly aggressive Africanized honeybee.[13] The Africanized bees attack in larger numbers, are ready to sting much faster and with much less provocation, and are more persistent in their attacks than their European counterparts. The Africanized hybrids are better adapted to warmer climates than European bees and as a result have been very successful and have spread rapidly throughout Latin America. By 1992 the African hybrid bees crossed the border into the United States and are now found in Texas, Arizona, New Mexico, and southern California. Based on weather and seasonal temperatures, they are predicted to eventually be distributed as far east as North Carolina. Despite the Africanized bees' tendency to attack and sting more quickly and in much greater numbers (victims may be stung by dozens of these bees), the venom of the African hybrids is no more toxic than the venom of European varieties. In view of the almost identical nature of their venom, the greater toxic reaction seen in animals stung by Africanized hybrids is a direct result of the higher venom dose to the victim because of the greater number of stings inflicted.

Clinical Signs and Manifestations

Typically, honeybee stings are manifested as localized edema without a systemic reaction. Unlike venomous spider bites, venom of all Hymenoptera causes some degree of local swelling and pain, and victims know that they have been stung. Generally the small local reaction of erythema, edema, and pain at the site of the sting is a self-limiting, non-IgE-mediated condition, which spontaneously resolves within 24 hours. Occasionally, animals develop more extensive regional reactions. These more severe regional responses involve erythema and local edema and may involve an entire extremity. The regional reaction is thought to occur from local mast cell degranulation and may not develop until up to 24 hours after the envenomation. This reaction is often termed cellulitis; however, infection rarely follows insect stings. Less common reactions from envenomating stings is edema of the oropharynx, which can result in compromise of the airways. Fatalities can result from airway occlusion from stings inside the oral cavity.

Systemic anaphylactic signs caused by insect stings are no different from other anaphylactic reactions. Onset of life-threatening signs occurs rapidly (often within 10 minutes of the sting). Although it is not understood, signs of anaphylactic reaction may vary in severity.[14] Mild anaphylactic signs include urticaria, pruritis, and angioedema.[15] Other nonlife-threatening signs include vomiting and diarrhea. More serious signs of anaphylactic reaction include the respiratory and cardiovascular systems.[16] Wheezing, dyspnea, cough, and bronchoconstriction may occur and lead to hypoxia and respiratory arrest. Local upper airway edema can cause congestion of the larynx, epiglottis, and surrounding tissue. The majority of insect sting fatalities are the result of severe respiratory compromise.

The unusual delayed reactions reported include serum sickness, vasculitis, glomerulonephritis, neuropathy, disseminated intravascular coagulation, and arthritis.[17] Direct toxic effects of Hymenoptera venom independent of immune mechanisms are venom volume-dependent reactions. Animal victims of such multiple stings may demonstrate rhabdomyolysis, hemolysis, and acute renal failure from direct tubular toxicity.[15] Myocardial infarction has been documented in victims of insect stings.

Bee and wasp stings typically cause only local redness, erythema, and transient pain in dogs. Urticaria may or may not accompany the swelling. Dogs may cry out when stung, and they may rub their mouth and eyes on the ground. These cutaneous reactions appear quickly and will spontaneously regress.

Potential allergen mediators of anaphylaxis include phospholipase A, hyaluronidase, acid phosphatase, and mellitin.[1] Vespid venoms share much more similarity in allergens with other vespids than with bee venoms. This may explain the cross-sensitivity in allergic reactions seen in people stung by various vespids. Furthermore, cross-sensitivity to both bee and wasp venom has been documented in humans.

The signs of anaphylaxis in dogs include urination, vomiting, defecation, muscular weakness, depressed respiration, and finally seizures.[15] Signs typically are seen within 15 minutes of the sting and if a systemic reaction has not started within the first 30 minutes, it is unlikely to occur. Fatalities typically occur within 60 minutes of the initial sting. Anaphylaxis in cats is manifested by pruritis, salivation, incoordination, and collapse.[15] The signs of anaphylaxis are attributable to antigen-induced IgE release and formation of chemical mediators that target smooth muscle and blood vessels.

Animals receiving massive envenomations (many stings) are usually febrile and visibly depressed. Facial paralysis, ataxia, seizures, and neurological signs may be observed. Dark brown or red urine, bloody feces, bloody or dark brown vomitus may also be seen.[15] A complete blood count may reveal a leukocytosis. Animals may be thrombocytopenic, particularly if disseminated intravascular coagulation is imminent. Granular casts may be detected on urinalysis reflecting renal tubular damage as a result of the nephrotoxic nature of Hymenoptera venom. Acute renal failure can be caused by acute tubular necrosis (the result of hemolysis) or direct renal toxic effects of the venom.[15] Dogs suffering multiple stings may develop a secondary immune-mediated hemolytic ane-

Table 2 Clinical Signs of Insect Stings

Mild
Swelling
Urticaria
Erythema
Pruritis
Pain
Severe (anaphylaxis)
Vomiting
Defecation
Urination
Swelling
Muscle weakness
Respiratory depression
Seizures
Death

mia.[18] Animals suffering massive envenomations should be hospitalized and monitored closely. Clinical signs of insect stings are listed in Table 2.

Minimum Database and Diagnostics

Identification of insect stings is not difficult if human caretakers were with the animal. Accurate diagnosis of Hymenoptera stings stems from a history of potential contact with stinging insects and the clinical signs displayed by the victim. It has been reported that certain dog breeds (bull terriers, Staffordshire terriers, and boxers) have a higher incidence of severe reactions to insect stings.[15]

The circumstances surrounding the sting episode may reveal clues as to the offending insect. Yellow jackets are attracted to and are frequently found near open sweet soft drink cans. Bees usually are not. Honeybees are more commonly found foraging among flowers. They are often stepped on as they work through clover. Honeybees can sting only once, leaving their stinger behind in the victim. Wasps and other vespids can sting multiple times and do not lose the stinger. Thus, if the attacker is not seen or found, the presence or absence of a stinger, the conditions surrounding the sting incident, and knowing something of the different behavior between bees and wasps can be helpful in narrowing the index of suspicion and identifying the stinging insect.[5]

Other diagnostic aids include skin testing, isolation of specific IgE or IgG antibodies, assay for histamine release, and actual sting challenges. Most insect stings cause small, self-limiting local reactions and victims rarely are taken to veterinary hospitals for treatment. Dense fur may mask local clinical signs of Hymenoptera stings. The true incidence of insect stings in companion animals is unknown as many incidents probably go unrecognized.

Treatment

For most solitary stings the application of ice, cool compresses, and antihistamines is sufficient to halt swelling and to ease discomfort. The majority of small local reactions to honeybee and wasp stings resolve completely without treatment within a few hours. On account of their dense coats, time-consuming and meticulous searches for and removal of embedded stingers should not be attempted. Vespids do not leave stingers behind. Honeybee venom sacs continue to contract even after the stinging apparatus is torn from the bee's body and 100% of its contents is delivered within 60 seconds of the sting.[19] Victims should be watched closely because animals with anaphylaxis can deteriorate rapidly, without warning, and catastrophically. Access to cardiac monitoring, supplemental oxygen, crash cart drugs, and airway intubation equipment must be readily available in veterinary hospitals treating Hymenoptera stings.

More severe, regional reactions and those involving multiple stings should be initially treated as the small local reactions. However, the animal should be hospitalized and monitored closely for onset of more devastating progression of the envenomation syndrome. Corticosteroids may benefit these patients (prednisolone sodium succinate 10 mg/kg IV and followed by prednisolone orally at 1 mg/kg bid, then tapered over 3-5 days). An intravenous bolus of normal saline is indicated if hypotension is present. Continuous intravenous fluid infusion ensuring constant urine output is usually indicated for these animals. For severe reactions of this type, administration of fluids and electrolytes, correction of hypovolemia, and prevention of vascular stasis is a cornerstone of therapy. Toxic reactions to massive envenomations from multiple stings require early aggressive stabilization and therapy with fluids, corticosteroids, and topicals and may require vigilant monitoring of hemotologic, cardiac, respiratory, and renal parameters for several days. Animals suffering this type of insect attack may require hospitalization and supportive therapy until stable. Septicemia is a possible sequela of massive envenomations and administration of broad-spectrum antibiotics may be justified. Most single stings do not become infected.[15]

Because most anaphylactic deaths from insect stings occur within 1 hour of the initial sting, early aggressive monitoring, treatment, stabilization, and intervention are mandatory. Death may ensue quickly if the anaphylactic reaction is not managed expeditiously and appropriately. Anaphylaxis after insect stings has been reported in companion animals and when diagnosed, epinephrine 1:1000 (0.1-0.5 mL) should be given subcutaneously immediately.[15] Administration can be repeated every 10 to 20 minutes. When epinephrine must be given intravenously, it must be diluted to 1:10,000 and 0.5 to 1 mL is administered. Intraveous epinephrine must be administered cautiously and slowly infused while the patient is carefully scrutinized for signs of improvement or adverse effects (arrhythmia). Vigilant monitoring is required of heart rate, heart rhythm, and blood pressure. Epinephrine stabilizes mast cells and thereby terminates continued propagation of anaphylaxis. Intravenous fluids are crucial to prevent vascular collapse, and shock volumes of cystalloid solutions (90 mL/kg dog and 60 mL/kg cat) should be given rapidly in anaphylactic animals. Antihistamines and corticosteroids may need to be administered. Aggressive airway management may be necessary and intubation equipment and supplemental oxygen should be readily available.

Delayed reactions characterized by rashes, serum sickness, low-grade fever, general malaise, polyarthralgias, and lymphadenopathy can occur within 2 weeks of the sting.[16] Unless the initial sting is witnessed or identified, the actual cause of

Table 3 Prevention of Insect Stings

Avoid scented lotions, soaps, or perfumes
Avoid large areas of flowering plants
Do not leave open cat food or dog food dishes outside
Keep all garbage cans tightly closed
Do not leave open soft drink cans outside
Bees are attracted to dark colors
Keep picnic foods tightly covered
Quickly dispose of freshly fallen fruit
Have only professional exterminators remove hives and insect nests

the reaction may not be recognized, and the diagnosis of a delayed reaction is easily missed.

Because of their potential for anaphylaxis and subsequent rapid deterioration and life-threatening destabilization, all insect stings should be taken seriously. Any animal sustaining multiple stings (massive envenomations) and any animal exhibiting clinical signs of anaphylaxis should be hospitalized, treated aggressively, and kept for 24 hours after cessation of signs.

Certain protocols, products, and principles of immunotherapy for insect stings have been taken from human medicine and applied to dogs who have previously demonstrated severe systemic reactions.[20,21] At present this therapy regimen is not widely available in veterinary medicine.

Prevention and Prognosis

Bees are attracted to dark colors and strong fragrances. Mammalian sweat seems to agitate them, attacks can be triggered by CO_2 from the victim's breath, and they are defensively stimulated by dark colors.[11] Avoiding areas with flowering plants where bees are feasting on nectar and keeping outdoor eating areas and garbage cans clean (because wasps are attracted to food waste) lowers an animal's risk of being stung. Avoid scented shampoos and soaps for your dog. Truly an ounce of prevention is worth a pound of cure. Do not leave canned cat or dog food in dishes outside in warm weather because this may also attract hungry wasps. Antihistamines should be part of any animal first aid kit. Animals that have demonstrated severe or anaphylactic reactions after insect stings should be identified with bee anaphylaxis identification collar tags. A number of ways to decrease insect stings is included in Table 3.

When bees sting they deposit an alarm pheromone that triggers other bees to sting at the same site. The pheromone has an odor that smells like ripe bananas. The odor stems from isopentyl acetate, one of the chemical found in ripe bananas. The alarm pheromone signals other bees where to sting. As a result, keep bananas away from bee hives so as not to attract the insects.

The prognosis for most victims of insect stings is excellent. Most of these episodes are self-limiting and will resolve within the first hour, primarily from anaphylaxis. If anaphylactic signs are not apparent within 30 minutes of the sting they are unlikely to occur. Animals suffering from anaphylaxis or from severe reactions as a result of multiple stings may be successfully stabilized if aggressive therapy is instituted early and appropriately applied. These therapies would involve intravenous volume support, drugs, and intubation with supplemental oxygen. Many dogs do not seem to learn about insect stings and are repeatedly stung over multiple summers.

Gross and Histologic Lesions

The behavior or bees and wasps can help predict their stinging probability. Histopathological lesions following simple, single, nonreactive local stings are either absent, undetectable, extremely mild, or nonspecific. Even after fatal anaphylaxis, there are no pathognomonic findings on necropsy and pathological changes are very general.[1,7] In necropsy after suspected fatal anaphylactic reactions, particular attention must be paid to the larynx for the presence of hyperemia, edema, and hemorrhage.[17] Histology of the larynx can be helpful in confirming a diagnosis of anaphylaxis. In cases of mass envenomation, evidence of acute renal tubular necrosis; fatty degeneration of the kidneys, liver, and myocardium; presence of hyaline membrane disease, and splenic hemorrhage and infarction may be documented.[15]

Tryptase is a mast cell-specific enzyme that is released from mast cells on degranulation; in human victims it is almost 100% specific for anaphylaxis.[17] The peak of tryptase activity occurs 1 to 2 hours after anaphylaxis, and then declines fairly rapidly with a half-life of about 2 hours. Studies in postmortem human cases have demonstrated that venon-specific IgE and tryptase were elevated in anaphylactic death but not in other causes of death. Further studies are needed to establish the usefulness of a serum tryptase test in animals.

The majority of deaths related to insect stings are the direct result of the immediate hypersensitivity reaction mediated by IgE and resulting in anaphylaxis. However, death can occur from severe local reactions (regional) involving airways and resultant respiratory obstruction. The primary pathology in wasp and bee sting deaths is found in the respiratory tract, such as massive edema, obstructive secretions, and total collapse or severe reduction in functional airway diameter. Massive envenomation from swarm stings can also cause death in nonallergic individuals. Deaths from multiple stings result from three major mechanisms: direct venom toxicity, intravascular hemolysis mediated by mellitin, and the profound hypotension resulting from massive histamine release.[17] Together these mechanisms have a cumulative, cascading effect, resulting in multiorgan failure represented by acute tubular necrosis and renal failure, respiratory distress, rhabdomyolysis, myoglobinemia, myocardial cell damage, hepatocellular necrosis, disseminated intravascular coagulation, and hemorrhage.

In summary, even with catastrophic fatal systemic responses there may be little or very nonspecific histological evidence on necropsy. As a result, such causes of death are probably underreported in our companion animals. Insect stings must remain on the list of differentials for a variety of clinical presentations and more specific ways of documenting their actual incidence in companion animals need to be researched.

The incidence of infection after insect stings is extremely low. The abdomen of the honeybee is covered with numerous hairs, most of them branched and plume-like, to which pathogenic bacteria can attach. Vespids lack these hairs. It is

Table 4 Differential Diagnoses for Insect Stings

Infection	Allergy
Cat fight abscess	Abscessed tooth
Trauma	Foreign object
Neoplasia	

known that bees may be attracted to garbage, which may contaminate these hairs. Potentially, the act of stinging could inoculate either bacteria from the bee or bacteria from the victim's skin surface under the epidermis. In addition, scratching because of pruritus commonly associated with insect stings can cause further traumatic epidermal injury and lead to intradermal implantations of pathogenic bacteria. Nevertheless, infection after insect stings is rare.

Differential Diagnoses

Because the initial stinging incident is rarely witnessed, and the clinical signs can be notoriously nonspecific, a diagnosis of insect sting can be easily missed by both owners and clinicians. A correct diagnosis depends on a high index of suspicion for possible insect stings, presenting clinical signs, and attempts to understand the conditions surrounding the episode. A list of differential diagnoses and potential look-alikes for insect stings is included in Table 4.

Fire Ant

Reports of fire ant stings are becoming more widespread. Fire ants are members of the order Hymenoptera, family Formicidae, subfamily Myrmicinae and genus *Solenopsis*. There are native fire ants in the United States, but two imported species *Solenopsis richteri* (the black imported fire ant) and *Solenopsis invicta* (the red imported fire ant) are of major medical importance.[11] The black imported fire ant (*S. richteri*) is originally from eastern Argentina and Uruguay.[22] The red imported fire ant (*S. invicta*) is a native of the Mato Grasso region of Brazil, where its range extends into northern Argentina. Both species appear to have entered the United States on produce through the port of Mobile AL, the black imported fire ant in about 1918 and the red imported fire ant species about 1939. The black imported species (*S. richteri*) has been contained to a small area of Alabama and Mississippi. However, the red imported fire ant(*S. invicta*) has colonized more than 310 million acres in 12 southern states (Alabama, Arkansas, Florida, Georgia, Louisiana, Texas, and Virginia).[23] The red imported fire ant is also found in Puerto Rico. Populations have recently been found in California, Arizona, New Mexico, and up the eastern coast to Washington DC.[24] Highly adaptive insects, the red imported fire ant has both supplanted and interbred with local native ants. Red imported fire ants and their hybrids now account for more than 90% of ants in some parts of some southern states.

Initially, it was estimated that the spread of the ants would be limited by a minimum climatic temperature of −12.5°C (10°F).[25] However, it appears that the hybrids are more cold tolerant than the original species. Also the hybrids have been seen to use concrete and human habitations as heat sumps and successfully over winter. It is currently estimated that the ants could expand into areas with a minimum temperature of −17.8°C (0°F). If these predictions are accurate red imported fire ants and their hybrids could ultimately colonize at least 25% of the continental United States. These ants are very mobile and have a capacity to exploit diverse habitats in setting up new colonies, allowing a westward migration rate of approximately 120 miles per year. Because of their ability to interbreed with native species, it may take several years before the presence of the new ants is first detected.

Fire ants are aggressive and venomous. They have definite adverse effects on agriculture as their mounds can damage farming equipment and the ants can attack livestock and food crops. Reports of attacks on livestock and native wildlife (including the decimation of some ground-nesting birds, turtles, frogs, and arthropod species) are not uncommon. Accounts of attacks indoors on both companion animals and debilitated humans (nursing home patients) have become more frequent.

Fire ant workers range in size from 1.8 to 6 mm in length (average 3-4 mm).[26] Fire ants are similar in appearance to ordinary, native house and garden ant species. The life span of worker fire ants is 2 to 6 months. Queens are larger than workers and measure about 1 cm in length. Queens also have wings used during the nuptial flight. Fire ant mounds measure up to 1 meter in diameter and 0.5 meter in height. In heavily infested areas, mound density can range from 40 to 200 mounds per acre. Tunnels between mounds can extend more than 40 meters. A single queen mound may have more than 200,000 worker ants, whereas multiple queen colonies can have more than 500,000 workers. Queens are capable of producing 100 to 200 eggs per hour for up to 6 years.[27] Four castes of fire ants exist: fertile females (queens) with wings before mating, winged males, major workers, and minor (smaller) workers. They have efficient chemical tracking capability, which allows them to quickly locate food sources. It has been reported that fire ants get to injured and dead people at automobile accident scenes faster than rescue squads. In addition to finding food, the major (larger) ants also aggressively swarm and defend their nest and will sting anything unfortunate enough to disturb their mound. Workers have powerful mandibles with four teeth. Fire ants contain magnetite, which functions as a compass and orients them to a north-south axis. The magnetite senses other electric fields and fire ants have been shown to be attracted to underground power lines.

Imported fire ants are omnivorous and sting and kill invertebrates as their primary food source; they also scavenge dead animals and eat plants, ripe fruit, and seeds. Worker ants ingest sugars, fats, and oils and return solid food to be fed to the immature brood ants. Fire ants are fast and can move 1.6 cm per second. They accumulate on victims in large numbers before detection. They then sting simultaneously using chemical pheromone cues. The majority of sting encounters involve worker ants.

Fire ants are named for the burning paint they inflict. The sting of the fire ant is a two-stage maneuver. Before stinging prey or intruders, the fire ant latches itself on to the victim with its prominent mandibles and thus anchors by biting. It then tucks up its abdomen under its body and stings. The nonbarbed stinger of the imported fire ant is a modified ovipositor, with an associated venom gland at the posterior portion of the abdomen. After the first sting, while still secured to

the victim by its mandibles, the imported fire ant withdraws the stinger, rotates one step sideways, and stings again. Typically, they sting six or seven times in a circular pattern pivoting around the attached head. Unlike bees, wasps, and hornets, fire ants inject their venom slowly. Each sting takes 20 to 30 seconds. As a result, the onset of pain is delayed. Humans describe an initial burning sensation, but the majority of those stung by fire ants report it is less painful than a bee sting.

Lethal Dose

Imported fire ants represent a significant health hazard for people and animals living in endemic areas. Sting reactions range from local pustules to anaphylaxis. Anaphylaxis is the main cause of fatal response to fire ant stings. Anaphylactic reactions are not dose dependent and do not correlate with the number of stings.

Systemic toxic reactions to envenomations by fire ants have been reported after 50 to 100 simultaneous stings.[7] Fatal toxic reactions have been reported in dogs and other small animals after massive envenomation (multiple stings).[27] In humans, nonallergic subjects have survived hundreds of stings with only supportive therapy. However, there are reports of death related to direct venom toxicity. In general, death caused by direct venom toxicity after massive envenomations occurs greater than 24 hours after the stings, whereas death caused by anaphylaxis typically occurs a short time after the sting.

On stinging, each imported fire ant delivers about 0.11 μL of venom and they can deliver venom in 20 consecutive stings before depleting their venom store.[25] A lethal number of fire ant stings has not been reported for mammals. However, most fatalities after fire ant stings are thought to be caused by anaphylaxis and not dependent on the number of stings.

Toxicokinetics

The mechanism of toxicity of fire ant stings is fairly unique. Imported fire ant venom differs from the venoms of bees, wasps, and hornets, which are composed largely of protein-containing aqueous solutions. Fire ant venom is made up of 95% water-insoluble alkaloid.[28] The alkaloid portion consists primarily of 2,6 di-substituted piperidines, which have cytotoxic, hemolytic, antibacterial, and insecticidal properties. The alkaloids produce sterile pustules, but do not induce the IgE response that is the hallmark of anaphylaxis. The aqueous phase of fire ant venom contains four major allergenic proteins that are responsible for the specific IgE response of allergic animals. In addition, the small protein fraction contains hyaluronidase and phospholipase, which may explain why fire ant venom antigenetically cross-reacts with vespid venom (especially yellow jackets). Venoms from the two imported fire ant species are highly cross-reactive. The piperidine alkaloids found in fire ant venom have local necrotic and hemolytic effects and are responsible for pain.

The usual response to fire ant stings for most individuals is an immediate development of a 25 to 50 mm dermal flare. A wheal forms within 1 minute and papules within 2 hours. Vesicles develop within 4 hours; first filled with a clear fluid that is cloudy by 8 hours and then developing into sterile pustules by 24 hours.

The fire ant pustule results from tissue inflammation caused by the venom alkaloids. The presence of this pustule is almost pathognomonic for the sting of the imported fire ant. The superficial pustule is infiltrated with activated neutrophils and platelets, with necrosis at the base in 24 hours.

A small percentage of those bitten (17%) also develop extensive local reactions adjacent to the bite, with induration, erythema, and pruritis that may last up to 7 days.[22] Large, regional reactions to fire ant venom have been shown to be mast-cell dependent, IgE-mediated, late-phase reactions. Systemic reactions and direct toxic effects of massive envenomations have also been documented. It has been reported that systemic nonallergic responses (direct venom effects) often exhibit a large number of pustules, rhabdomyolysis, disseminated intravascular coagulation, and seizures.[25] Anaphylactic reactions to fire ant stings have been observed in both humans and animals. Anaphylactic reactions usually happen shortly after the sting occurs. Anaphylactic reactions may include general urticaria, cutaneous or laryngeal edema, bronchospasm, and/or cardiovascular collapse. Untreated, these anaphylactic reactions can become life-threatening. Secondary infection may follow imported fire ant stings, particularly those involving regional reactions.

Clinical Signs

Reactions to imported fire ant stings range from minor skin lesions to anaphylaxis and death. Typical stings cause an annoying burning sensation. Three types of local reactions may be present: a wheal and flare reaction, a sterile pustule, and a large regional reaction. Local reactions alone occur in nonallergic animals.

The typical local reaction to a sting, the wheal and flare, is followed by immediate pain, inflammation, and intense pruritis. The wheal and flare reaction usually resolves within 30 minutes to 1 hour. A papule forms and evolves into a fully developed sterile pustule at the site of the sting within 24 hours. These sterile pustules may last up to 2 to 3 weeks before spontaneously involuting. The pustules are usually accompanied by significant pruritis. Occasionally, the pustules become secondarily infected (usually from self-trauma by scratching) and can progress from cellulitis to sepsis. By 24 hours, the pustule contains necrotic tissue with cellular infiltration of lymphocytes, eosinophils, and polymorphnuclear cells. Usually after 72 hours, the epidermis covering the pustule sloughs and then healing takes place, leaving a scar or macule.

A smaller number of victims display regional reactions at the site of the sting. These lesions are erythematous, edematous, indurated, and extremely pruritic. Regional reactions to fire ant stings are mast cell-dependent, IgE-mediated, late-phase reactions. Regional reactions may lead to enough tissue edema to compromise blood flow to an extremity.

Systemic or anaphylactic reactions are IgE-mediated reactions that involve clinical signs occurring remote from the initial sting site. The signs include urticaria, cutaneous and/or laryngeal edema, bronchospasm, and vascular collapse. Most deaths resulting from imported fire ant stings are because of systemic anaphylaxis. However, it is possible that secondary

Table 5 Clinical Signs of Fire Ant Stings

Simple, local sting
Wheal and flare
Erythema
Warmth
Pain
Intense itching
Large, regional reaction
Erythema
Warmth
Pain
Itching
Anaphylactic reaction
Urticaria
Cutaneous edema
Laryngeal edema
Bronchospasm
Vascular collapse

infection of large reaction sites can also lead to death. The direct toxic effect of the venom of multiple fire ant stings can result in the death of the victim. In general, deaths caused by anaphylaxis occurs a short time after the sting, whereas deaths caused by venom toxicity occur greater than 24 hours after the sting. The exact incidence of fire ant anaphylaxis is unknown. The mechanism of anaphylaxis after fire ant stings is identical to the pathway of anaphylaxis from other causes. The systemic reaction to fire ant venom is similar to those experienced with other Hymenoptera venoms, except the pathognomonic pustule almost always enables identification of the imported fire ant as the stinging insect. Clinical signs following fire ant stings are listed in Table 5.

Minimum Database and Confirmatory Tests

Definitively establishing that fire ants are the cause of particular lesions can be difficult. Helpful clinical clues in determining a diagnosis of fire ant stings include development of a classic pustule after 24 hours, actual identification of the stinging insect, and the presence of typical fire ant mounds in the vicinity of the stinging incident. There are no laboratory tests to determine fire ant exposure. Veterinary clinicians should familiarize themselves with stinging insects found in their region.

Treatment

Currently no treatment has been shown to be beneficial in preventing or resolving location reactions, including the characteristic pustules. However, various therapies may provide symptomatic relief. Local sting reactions may benefit from antihistamines, topical corticosteroids, application of cool compresses (water or alcohol), ice, and topical treatment with camphor and menthol (Sarna lotion). Topical lidocaine preparations have also been suggested. Some dogs stung by fire ants appear to feel much better after warm baths. While widely proposed, topical application of aluminum sulfate and meat tenderizer (papain) is ineffective in relieving the pain and itching of imported fire ant stings.[29,30]

Severe, regional reactions are less commonly encountered, but these should be treated supportively and therapy may include antihistamines, corticosteroids, analgesics, and intravenous volume support. Secondary infections to fire ant stings should be treated with broad-spectrum antibiotics.

Anaphylactic reactions to fire ant stings have been documented both in humans and animals. They are typically seen not long after the initial sting incident. Anaphylaxis after a fire ant sting should be treated similarly to anaphylactic reactions seen after honeybee and vespid stings and may require epinephrine, endotracheal intubation, and the administration of oxygen, corticosteroids, antihistamines, and supportive fluid therapy. Prompt recognition and initiation of treatment is crucial in the successful management of anaphylaxis. Companion animals showing, severe, regional reactions or anaphylaxis after fire ant stings should be hospitalized until stable enough to be released for treatment and subsequent observation at home. Research is currently being done examining the merits of treating hypersensitivity to fire ant stings with immunotherapy regimens.

Prevention and Prognosis

Currently there are no effective insect repellants to protect companion animals from fire ants. Reaction to imported fire ant stings is best prevented by avoidance. Yards, exercise areas, and playing fields, must be routinely inspected for the presence of ant mounds. Many attempts have been made to eradicate fire ants from an area, but none have been shown to be completely successful. Basic methods currently used are broadcast applications of toxic baits that are carried back to the mound by workers and fed to the queen and/or individual mound treatments with chemicals to kill the queen and other ants.[25] The chemicals used are generally insecticides and formulated as drenches, granules, dusts, aerosols, or liquid fumigants. If the queen is not destroyed, she will continue to produce eggs and the treated mound will recover. Baits used usually contain slow-acting toxicants dissolved in an attractive food source like soybean oil. The toxicant-containing oil is then absorbed into corn grits, a carrier that permits easy handling and application. The slow reaction of the poison allows the workers to carry it back to the mound and feed it to the queen, to immature ants, and to other workers before they die. To be successful, the queen must be killed. Toxic bait eliminates the need to locate mounds because it relies on foraging workers who bring the bait back and feed the poison to the rest of the colony.

Baits using insect growth regulators are also marketed.[24] These growth-inhibiting substances are placed in baits to be carried back to the mound to prevent the development of adult worker ants. A major drawback of these growth regulators is that they act slowly over days to months. Additionally, they are not specific for fire ants and can have environmental consequences for other sensitive insects, some of which are beneficial to man. Other methods under study for more specific and effective control of fire ants include the use of various parasites, including nematodes and microsporideans that directly feed on ants and infect ant blood cells.[24]

The prognosis for animals stung by fire ants depends on the nature of the reaction displayed following the sting. Simple local reactions are painful and itch, but resolve with sup-

portive measures and time. Regional reactions require more aggressive therapy, but typically resolve. Anaphylactic reactions to fire ant stings can be fatal if untreated. Prompt recognition and initiation of treatment is critical in the successful management of anaphylactic reactions.

Finally, in endemic areas, companion animals should not be left outdoors unsupervised for long periods and should be examined often for signs of ant stings. Older, more debilitated animals and very young animals should be even more vigilantly observed. Particular attention should be paid to garbage containers, uncovered food dishes, and outdoor feeding areas, all of which may attract ants. Methods of prevention of imported fire ant stings are listed in Table 6.

Table 6 Methods of Prevention for Imported Fire Ant Stings

Companion animals must be closely supervised in endemic areas
Yards, exercise areas, and playing fields must be routinely inspected for ant mounds
Old, debilitated, and very young animals deserve particular attention in endemic areas
Garbage containers, outside feeding areas, and uncovered food dishes may attract ants
Ant mounds must be vigorously treated (the queen must be killed) for eradication attempts to be successful

Gross and Histologic Lesions

The intense inflammatory response and pustule that develops at the fire ant sting site has been shown to result from potent cytotoxins and hemolytics found in the alkaloid venom fraction. These toxins cause localized necrosis of the dermis and underlying connective tissue that creates the characteristic sterile pustule that develops within 24 hours of most stings.[28] In the continental United States, the pustule is only caused by imported fire ant stings. An erythematous flare follows the sting followed in minutes by a wheal. The wheal-flare resolves within 2 hours. A central vesicle containing clear fluid begins to form within 4 hours. The fluid becomes cloudy and the pustule appears generally surrounded by a red halo and an area of edema.

Histological studies have demonstrated that imported fire ant venom causes histamine release at the sting site.[28] Edema, painful necrosis, and infiltration of histiocytes, plasma cells, and lymphocytes occurs within minutes. By 24 hours, the pustule contains many polymorphonuclear cells, lymphocytes, and neutrophils. At 72 hours, plasma cells and cosinophils can also be found. The pustule's central core becomes obliterated, and the pustular infiltrate extends into surrounding necrotic tissue. At this point the pustule fluid is composed of primarily neutrophils and necrotic debris.

The pustule usually heals and resolves spontaneously; however, the intense pruritis may cause an animal to itch off the epidermal covering, establishing a microhabitat compatible with secondary bacterial infection, which can potentially become systemic. Undisturbed pustules resolve unremarkably in 3 to 10 days, leaving a small macule with little scarring. Secondarily infected stings may leave a significant scar.

Large regional reactions are not uncommon in many Hymenoptera stings. It has been shown that the size of the wheal-flare response at 20 minutes correlates directly with the size of the regional reaction at 6 hours. Pathologically the regional reaction resembles late-phase IgE-mediated reactions developing after intradermal injections of ragweed or insulin. These reactions are characterized by development of dense fibrin deposits, with trapping of edema in the reticular dermis around the pustule. Eosinophils are present in the pustular fluid. This is not the same as the systemic allergic (anaphylactic) reaction.

In the United States, fatal anaphylactic reactions to imported fire ant stings are less frequent than other Hymenoptera stings; however, this may change as the range of the ants increases.[28] Like other Hymenopterans, true anaphylactic reactions to imported fire ant envenomations are not dependent on the number of stings inflicted. Necropsy findings, although nonspecific, are typical of Hymenoptera-induced pathological changes. Primary findings include acute pulmonary changes and cerebrovascular congestion.[28] In many cases congestion can also be seen in the kidneys, liver, spleen, and adrenal glands.

Other histological changes after fire ant stings include serum sickness, nephrotic syndrome, and mononeuritis. Some animals have been reported to have seizures after multiple stings. It should be noted that cross-reactivity and similar sequences of histological reactions occur between imported fire ant venom and the venom of other Hymenopterans.

Table 7 Differential Diagnoses of Fire Ant Stings

Trauma
Infection
Allergy
Neoplasia
Self-trauma
Other causes of anaphylaxis

Differential Diagnosis

Potential differential diagnoses and possible look-alikes to imported fire ant stings are listed in Table 7. These include any conditions leading to immediate swelling, pain, and pruritis. Differential diagnoses include trauma, infection, neoplasia, allergy, self-trauma, or other causes of anaphylaxis.

References

1. Tunney FX: Stinging insects, in Haddad LM, Shannon MW, Winchester KF (eds): Clinical Management of Poisoning and Drug Overdose (ed 3). Philadelphia PA, WB Saunders Company, 1998
2. Reisman RE: Insect stings. N Engl J Med 321:523, 1994
3. Goddard J: Physician's Guide to Arthropods of Medical Importance (ed 3). Philadelphia PA, WB Saunders, 2000
4. Minton SA, Hechtel HB: Arthropod envenomation, in Averbach PS, Mosby CV (eds): Wilderness Medicine: Management of Wilderness and Environmental Emergencies. St. Louis, MO, CV Mosby, 1995
5. Degrondi-Hoffman G, Hoffman RF: Bee sting dysphagia. Ann Intern Med 130:943, 1999
6. Vetter RS, Visscher PK: Bites and stings of medically important venomous arthropods. Int J Dermat 37:481-496, 1998
7. Manoquerra AS: Hymenoptera stings, in Ling L, Clark R, Erickson T, et al (eds): Toxicology Secrets. Philadelphia, Hanley and Belfus, 2001
8. Franca FO, Benvenuti LA, Fan HW, et al: Severe and fatal mass attacks by "killer" bees in Brazil: Clinicopathological studies with measurement of serum venom concentrations. Q J Med 87:269-282, 1994
9. Winkler B, Bolwig C, Seppala U, et al: Allergen specific immunosup-

pression by mucosal treatment with recombinant Ves v 5, a major allergen of *Vespula vulgaris* venom, in a murine model of wasp venom allergy. Immonology 110:376-385, 2003
10. Banks BEC: The composition of Hymenoptera venoms with particular reference to venom of the honeybee, in Kornalik F, Mebs D (eds): Proceedings of the 7th European Symposium on Animal, Plant and Microbial Toxins, Prague, 1986
11. Hahn I, Lewin NA: Arthropods, in Goldfrank LR, Flomenbaum NE, Lewin NA, et al (eds). Goldfrank's Toxicologic Emergencies (ed 7). New York: McGraw-Hill, 2002
12. Lictenstein LM, Valentine MD, Sobotka AK: Insect allergy: The state of the art. J Allergy Clin Immunol 64:5-12, 1979
13. Jones RGA, Roth J, Spencer M, et al: A novel fab-based antivenom for treatment of mass bee attacks. M J Trop Med Hyg 61:361-366, 1999
14. Ludolph-Hauser D, Rueff F, Fries C, et al: Constitutively raised serum concentrations of mast-cell tryptase and severe anaphylactic reactions to Hymenoptera stings. Lancet 357:361-362, 2001
15. Cowell AK, Cowell RL: Management of bee and other Hymenoptera stings, in Bonagura JD, Kirk RW (eds): Kirks Veterinary Therapy XII: Small Animal Practice. Philadelphia, WB Saunders, 1995
16. Kocer U, Ozer Tiftikcioglu Y, Mete Aksoy H, et al: Skin and soft tissue necrosis following Hymenoptera sting. J Cutan Med Surg 133-135, 2003
17. Riches KJ, Gillis D, James RA: An autopsy approach to bee sting related deaths. Pathology 34:257-262, 2002
18. Noble SJ, Armstrong PJ: Bee sting envenomation resulting in secondary immune-mediated hemolytic anemia in two dogs. J Am Vet Med Assoc 214:1026-1027, 1999
19. Schmacher M, Treten M, Egen R: Rate and quantity of delivery of venom from honeybee stings. J Allergy Clin Immonol 93:831, 1994
20. Baker E: Small Animal Allergy: A Practical Guide. Philadelphia, Lea and Febiger, 1990
21. Weiss K: The Little Book of bees. New York, New York, Copernicus, 2002
22. Stafford CT: Hypersensitivity to fire ant venom. Ann Allergy Asthma Immunol 77:87-95, 1996
23. Kemp SF, deShazo RD, Moffitt JE, et al: Expanding habitat of the imported fire ant (*Solenopsis invicta*): A public health concern. J Allergy Clin Immunol 105:683-691, 2000
24. Hoffman DR: Fire ant venom allergy. Allergy 50:535-544, 1995
25. deShazo RD, Soto-Aguillar M: Reactions to imported fire ant stings. Allergy Proc 14:13-16, 1993
26. Stafford CT: Fire ant allergy. Allergy Proc 13:11-16, 1992
27. Prahlow JA, Barnard JA: Fatal anaphylaxis due to fire ant stings. Am J Forenic Med Pathol 19:137-142, 1998
28. Lockey RF: The imported fire ant: Immunopatholoical significance. Hosp Pract 109-124, 1970
29. Bruce S, Tschen EH, Smith EB: Topical aluminum sulfate for fire ant stings. Pharmacol Ther 23:211, 1992
30. Ross EV Jr., Badame AJ, Dale SE: Meat tenderizer in the acute treatment of imported fire ant stings. J Am Acad Derm 16:1189-1192, 1987