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ALLERGIC REACTIONS CAUSED BY VENOM OF HYMENOPTEROUS STINGING INSECTS AND THE ROLE OF HEALTH CARE WORKERS

By
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Abstract

The Hymenoptera are the third largest order of insects, comprising the sawflies, wasps, bees and ants. Worldwide, over 150,000 species are recognized, with many more remaining to be described. The name refers to the wings of the insects, but the original derivation is ambiguous. The Ancient Greek ὑμήν (*hymen*) for membrane provides a plausible etymology for the term because these insects have membranous wings. However, a key characteristic of this order is that the hind wings are connected to the fore wings by a series of hooks called hamuli. Thus, another plausible etymology involves, Hymen, the Ancient Greek god of marriage, as these insects have "married wings" in flight. Stinging insects and the medical risk associated with their venoms are complex topics, and presentation of information pertaining to them requires the use of technical terms. The most common reactions to these stings are transient pain and redness at the site lasting a few hours (local reaction), and exaggerated swelling lasting a few days (large local reaction). The most dangerous immediate reaction is anaphylaxis, which is potentially fatal.

Key words: Hymenoptera insects, Sting venom, Clinical pictures, Management, Infection control.

Introduction

The insects that are responsible for the majority of serious sting-related reactions belong to the order Hymenoptera. The Hymenoptera families of medical interest include the following (Goddard, 2003): The winged Hymenoptera: Apidae family (honeybees and bumblebees) Vespidae family (yellow-jackets, yellow hornets, white faced hornets, and paper wasps). The sociality phenomenon among insects is best developed among the aculeate Hymenoptera or could be called stinging wasps, though the group also contains the ants and the bees, where the structure originally used to lay eggs is modified instead to deliver venom (Campbell *et al*, 2014)

The wingless Hymenoptera: Formicidae family (fire ants, harvester ants, bulldog ants, and jack jumper ants). The clinical manifestations and treatment of fire ant stings are discussed in detail separately. The imported fire ants (IFAs) were aggressive, venomous ants that sting with little provocation and are difficult to avoid in endemic areas. Their venom causes painful local reactions and induces a high rate of allergic sensitization. The patients who become allergic to IFA venom could experience a range of reactions, including life-threatening anaphylaxis (Lofgren *et al*, 1975).

Different species of Hymenoptera show a wide range of feeding habits. The most primitive forms are typically herbivorous, feeding on leaves or pine needles. Stinging wasps are predators, and will provision their larvae with immobilised prey, while bees feed on nectar and pollen.

A number of species are parasitoid as larvae. The adults inject the eggs into a paralyzed host, which they begin to consume after hatching. Some species are even hyperparasitoid, with the host itself being another parasitoid insect. Habits intermediate between those of the herbivorous and parasitoid forms are shown in some hymenopterans, which inhabit the galls or nests of other insects, stealing their food, and eventually killing and eating the occupant (Davies *et al*, 2012).

Hymenoptera generally sting people in self-defense or to protect their nests or hives. Their stings are acutely painful and patients are aware that a sting occurred, although they might not have visualized the insect. Identification of responsible winged Hymenoptera species can be difficult since the resultant lesions are all similar. The culprit species could sometimes be identified based upon nest location and appearance, geographical location or setting in which the sting occurred (Vetter and Visscher, 1988).

Most people develop only minor local reactions, but patients with venom allergy are at risk for systemic allergic reactions (i.e., anaphylaxis), which could be mainly severe and led to anaphylaxis fatalities. Also several uncommon and delayed types of reactions that may develop after Hymenoptera stings, such as the serum sickness (Freeman, 2004)

Insect and stinger removal: Bees and occasionally yellow-jackets have a stinging apparatus lodged in the human skin and rips away, along with the venom sac, from the insect's body following a sting event. Stingers should be removed as rapidly as possible after a sting by any means possible, because venom can be released for several seconds. But, after the first few seconds, no special technique (e.g., flicking to avoid compressing the venom sac) is necessary, since the venom should be fully expelled already (Brown *et al*, 2003). The remaining stingers must be removed as they could occasionally cause foreign body reactions (Jain *et al*, 2007).

The local reactions consist of the characteristic symptoms confined to the tissues contiguous with the sting site. They are usually mild and transient, but some patients developed large local reactions or secondary bacterial infections. The uncomplicated local reactions are a typical local reaction to a sting is redness and an area of painful swelling (1 to 5 cm) at the site of the sting that develops within minutes and resolves within a few hours. Occasionally, swelling may last 1 to 2 days. Uncomplicated local reactions might be treated with cold compresses.

Imported fire ant stings typically cause pustule-like lesions at the site of the sting(s) within about 24 hours (Tracy *et al*, 1995). These pseudopustules are sterile and patients should be advised not to open them, as this can lead to infection. In the absence of this advice, patients tend to un-roof the lesions, either because of the intense pruritus associated with the fire ant stings or because draining the infection (Triplett, 1976).

Large local reactions: Approximately 10% of individuals develop exaggerated redness and swelling at the site of the sting that gradually enlarges over one to two days. This response is called a large local reaction (LLR). The LLRs peak at an approximately 48 hours and then gradually resolve over 5 to 10 days. The area of swelling typically measures about 10 cm in diameter (Severino *et al*, 2009). The large local reactions (LLRs) are IgE-mediated late-phase inflammatory reactions that can cause great morbidity but are associated with a relatively low risk of future anaphylaxis. Patients with LLR may benefit from consultation with an allergist to help clarify the relative risk, to plan the best treatment for future stings, and to determine whether or not to pursue testing or venom immunotherapy (VIT). Chance of anaphylaxis to future stings was <5%, so VIT was not re-commended to people who have had LLR. Whether to prescribe an epinephrine injector is often determined by the frequency of exposure, proximity to medical care, and the impact on quality of life. For people who have unavoidable exposure and need treatment almost every year for LLR, VIT could be re-commended with confidence that it would be significantly and safely reduce LLR severity to stings (Golden, 2015).

Most Hymenoptera stings do not become superinfected, although this can occur. An infected sting must be differentiated from a large local reaction. The stings of yellow-jackets and fire ants are more likely to become infected than those of other species. Yellow-jackets tend to scavenge around rotting food and presumably carry bacteria on their exterior. Fire ant stings cause sterile pustule-like lesions that can become infected if opened (Reisman, 2003).

Infection is suspected when redness, swelling, and pain become dramatically worse 3 to 5 days after the sting, when the typical large local reaction was beginning to regress. The presence of fever suggests infection, but lymphangitis streaks may be seen with either infection or an uncomplicated LLR. If the clinician is unsure, a course of oral antibiotics may be prudent.

Management of cellulitis and erysipelas should include elevation of the affected area and the treatment of underlying conditions. The elevation facilitates gravity drainage of edema as well as the inflammatory substances. The skin should be sufficiently hydrated to avoid dryness and cracking without interdigital maceration. Many patients with cellulitis have underlying conditions that predispose them to developing recurrent cellulitis (include *Tinea pedis*, lymphedema, and chronic venous insufficiency). In such patients, treatment should be directed at both the cellulitis and the predisposing condition. Patients with edema may benefit from treatment with compressive stockings and diuretic therapy (Siljander *et al*, 2008).

Patients with a history of a large local reaction often have the same response to subsequent stings (Mauriello *et al*, 1984). However, LLRs are believed to be IgE-mediated based upon the following evidence: Patients with large local reactions are more likely to have specific IgE demonstrated by skin test to the insect involved. Eosinophils, which are found in the late-phase of IgE-mediated allergic reactions, were demonstrated in biopsy specimens from fire ant-induced LLRs, but not in specimens from patients without LLRs. In one case within this report, the large local reactivity was transferred passively.

A total of 5 to 10% of patients with past the LLRs have subsequent systemic reactions. The reasons for this relatively low risk of subsequent anaphylaxis, despite the presence of venom-IgE, are not known. Most patients with LLRs are not treated with venom immunotherapy because the risk of anaphylaxis is generally low, as described previously. However, the immunotherapy can be con-sidered for patients who wish to lower the risk of future anaphylaxis further, and immunotherapy may also reduce severity of future LLRs. The indications for venom immunotherapy are reviewed in more detail separately (Golden, 2015).

The most dangerous immediate reaction to the Hymenoptera stings is a systemic allergic reaction, or the anaphylaxis. Anaphylaxis may be defined as a serious allergic reaction that was rapid in onset and might cause death (Sampson *et al*, 2006). The venom-induced anaphylaxis involves signs and symptoms in one or more anatomic systems distant from the site of the sting and was reported in 0.3 to 3% of stings (Tang *et al*, 2009).

A single sting is sufficient to precipitate a severe reaction in a venom-allergic individual, and insect stings are a leading cause of fatal anaphylaxis. Venom-induced anaphylaxis can be particularly severe, sometimes persisting despite multiple doses of epinephrine (Bilò and Bonifazi, 2008).

Hymenoptera stings caused 40 to 100 identified deaths annually in the US, and reported rates were similar in other parts of the world (Clark and Camargo, 2006). The true incidence may be higher because sudden deaths occurring outdoors may be mistakenly attributed to heart attacks or strokes. A high frequency of venom-specific IgE was found in post-mortem serum of individuals who died suddenly of unknown cause (Riches *et al*, 2002). Even more suspicious is the presence of elevated serum tryptase as well as venom IgE in deaths of unknown cause.

The prevalence of venom allergy in the general population is unknown. However, an American survey study of the general population found that approximately 3% of people reported experiencing some systemic symptom after a Hymenoptera sting. Since approximately 60 to 90% of patients with a suggestive clinical history have venom specific IgE upon evaluation, an estimated 2% of adult population and 0.5% of children could have venom allergy (Forrester *et al*, 2012).

About one-half of patients who die as a result of Hymenoptera-induced anaphylaxis did not know that they had an allergy. The majority of patients who reported past systemic symptoms had not sought medical attention. Thus, venom allergy was very likely under-recognized and under diagnosed (Muller, 2005). Venom allergy could develop at any age, but adults suffer more severe reactions and most deaths occur in this age group. Men are affected more often than women, probably due to a greater prevalence of outdoor occupations. Not surprisingly, beekeepers are at highest risk (Muller, 2007).

The patients with the concomitant cardiovascular disease and with the poor tolerance for biochemical and physiological stress are at particular risk for severe and fatal anaphylaxis. Fatal anaphylaxis has been described particularly following hymenoptera stings, but also occasionally after the intake of drugs such as the non-steroidal anti-inflammatory drugs, the opioids and drugs in the perioperative setting. However, data on the frequency of drug hypersensitivity in mastocytosis and vice versa are scarce and evidence for an association appears to be limited. Nevertheless, clonal MC disorders should be ruled out in severe anaphylaxis: basal serum tryptase determination, physical examination for cutaneous mastocytosis lesions, and clinical characteristics of anaphylactic reaction might be useful for differential diagnosis (Bonadonna *et al*, 2015). A total of 1 to 2% of patients with severe anaphylactic reactions after stings was subsequently found to have clonal mast cell disease; cutaneous and systemic mastocytosis, as well as other clonal mast cell disorders (Akin *et al*, 2007). These patients showed the known characteristic dermatitis called *urticaria pigmentosa*, or report the role of skin barrier abnormallities, as well as the modulatory effects of the innate and the adaptive immune responses, are major areas of the investigation (Sicherer and Leung, 2012).

When evaluating a patient with any symptoms of an allergic reaction, it is important to ask specifically about the different manifestations of anaphylaxis, as patients often focus on just one symptom and don't recognize other symptoms, or may not report sensations with which they are unfamiliar and cannot readily describe. Sudden illness on the golf-course or while working in the yard may be readily mistaken for a cardiovascular event or asthma attack, unless the patient is carefully questioned/ examined to reveal the full array of signs and symptoms (Shiue, 2015). There are over 40 signs and symptoms of the anaphylaxis. But, in the venom-induced anaphylaxis, the following are regularly reported: Skin symptoms, such as the generalized urticaria, flushing, and angio-edema, are common. This is the only manifestation of a systemic allergic reaction in the majority of children (about 60%), whereas in adults, this mild presentation accounts for only about 15% of cases. Respiratory symptoms include hoarse voice or upper airway obstruction due to edema of pharynx and epiglottis, and shortness of breath and wheezing due to bronchoconstriction. Cardiovascular symptoms, ranging from lightheadedness to hypotension, shock, and circulatory collapse, are features of severe sting anaphylaxis (Adkinson *et al,* 2009).

Adults tend to have more severe systemic reactions and the vast majority of deaths occur in adults as a result of circulatory collapse. Ninety percent of adults had reactions involving the respire-tory or cardiovascular system, whereas 30 percent of reactions in children suffered from cardiopulmonary symptoms (Pastorello *et al*, 2015). Most episodes of venom anaphylaxis develop rapidly, escalate, and then resolve in a uniphasic manner. However, a small percentage followed a biphasic course, in which the initial reaction was treated and resolved spontaneously, but there was a recurrence of symptoms hours later. The protracted anaphylaxis proved to be uncommon presentation (Shaker *et al*, 2013).

The diagnosis of anaphylaxis is clinical and based upon signs and symptoms in the setting of a suggestive history. Three diagnostic criteria have been proposed, each reflecting the different clinical presentation of anaphylaxis. Anaphylaxis is highly likely when any one criterion must be fulfilled. The diagnosis can be particularly challenging when the cardiovascular signs and symptoms existed in isolation (Lieberman, 2014).

The diagnosis of anaphylaxis can be further supported by the documentation of elevated concentrations of the mast cell and basophil mediator's histamine or total tryptase. Any elevation is consistent with anaphylaxis and indicates that these cells have been activated on a massive scale. These changes may be very transient, and normal levels do not exclude the diagnosis. It is critical to obtain blood samples for measurement of these mediators during specific windows of time after the onset of symptoms. Medical instructions for the proper timing and collection of samples must be followed (Simons, 2011).

Acute management of venom-induced anaphylaxis is similar to the treatment of anaphylaxis from other causes, with intramuscular injection of epinephrine into the anterolateral thigh being the initial drug of choice. Rapid overview tables of the initial assessment and treatment of anaphylaxis and dosing of epinephrine in adults and children were provided. These tables are intended to assist clinicians in emergency department and urgent care setting (Dinakar, 2012).

Prior to discharge from the acute care setting, patients should be informed that venom allergy is a potentially fatal disorder, further evaluation will be needed, and that venom immunotherapy is available to prevent anaphylaxis to future stings. They should receive: An epinephrine auto-injector(s) supplying at least two doses of epinephrine and how and when to use epinephrine (Salter *et al*, 2014).

The patients suspected of having a systemic allergic reaction following a Hymenoptera sting (of any severity) should be referred to an allergist/ immunologist, to determine if they are candidates for venom immunotherapy. Providing the patient with a prescription for the self-injectable epinephrine is an essential but not sufficient intervention, because patients often do not fill the prescription or have the epinephrine on hand when needed, and because severe venom anaphylaxis can be refractory even to the promptly administered epinephrine. Venom immunotherapy reduces the risk of recurrent life-threatening reactions from 30 to 60% to less than 5% and proved the definitive treatment for the venom allergy (Bilò and Bonifazi, 2011).

Rarely, toxic effects are seen with large numbers of simultaneous stings. Moreover, Hymenoptera stings occasionally cause the delayed-onset, immunologic or idiosyncratic reactions, such as serum sickness or nephritis. The venoms injected by Hymenoptera are toxic and have vasoactive properties that are associated with systemic symptoms. Symptoms include nausea, vomiting, diarrhea, headache, vertigo, syncope, convulsions, and fever. The hemolysis, cardiac complications, renal failure, and rhabdomyolysis have also been described (Betten *et al*, 2006).

Toxic reactions are uncommon since most stinging events involve one to a few stings and only a small amount of toxin is injected into the body. However, patients who disrupt a nest or hive can sustain massive envenomation as the insects swarm out for self-defense. Case reports of toxic reactions mostly involved patients who had sustained hundreds of stings, although renal failure was described after as few as 20 wasp stings. The number of stings associated with a potential 50% fatality rate due to direct venom effects (Morsy and Lashen, 1996). Africanized honey bees, found in South America and southern parts of Texas in United States, are no more toxic per sting than other bees. However, this species acquired the common name "killer bees" because they can sting in large numbers once provoked (Pinto *et al*, 2005).

Acute treatment of a patient with numerous Hymenoptera stings begins with rapid general assessment and prompt removal of any insects or stingers still attached to the skin or entrapped in the patient's clothing, without specific antitoxins available to treat the Hymenoptera stings. Some patients had concomitant anaphylaxis and required immediate epinephrine and other appropriate management. Otherwise, care was supportive. Patient should be kept under observation and monitored with serial chemistries, including hemoglobin and myoglobin.

The insect venom is highly sensitizing, and individuals who have sustained a toxic reaction after multiple stings may develop positive skin tests to venoms and are at risk for anaphylactic reactions in response to future stings. Referral to an allergy specialist is a must (Biedenbach *et al*, 2014).

Occasionally, other types of systemic reactions are reported after insect stings. These include serum sickness, vasculitis, neuritis, myocarditis, and encephalitis. Onset is typically delayed by days to weeks after the sting, as most of these reactions arise from the tissue deposition of antibody-antigen complexes, which precipitate only after sufficient antibody was formed (Quercia *et al,* 2007). The serum sickness was usually manifested as urticaria with joint pain, fever, fatigue, and lymphadenopathy, 7 to 10 days after bring stinged. The patients with serum sickness might demonstrate IgE and IgG anti-venom antibodies (Reisman, 2005).

The onset of cold-induced urticaria has also been noted in patients several weeks after Hymenoptera stings. Most patients had no adverse reaction to the sting itself (Hogendijk and Hauser, 1997).

In Egypt, huge numbers of stinging insects were encountered mainly rural areas. As to venom complications, Morsy and Lashen (1996) reported an unusually severe bee sting allergy in a son of a bee keeper. Nabil *et al*. (2002) studied solitary wasp venoms. They found that venoms affect different types of muscles (cardiac, skeletal, and smooth) in different ways. The effect of the venoms on the heart muscle was rapid and led to bradycardia, marked increase in R amplitude on ECG, and other cardiac disorders such as atrioventricular block. The effects were abolished by atropine, indicating mediated through peripheral nervous system. They concluded that all the venoms reversibly blocked nicotinic receptors of toad skeletal muscle and the muscarinic receptors of smooth muscles.

Sand *et al*. (2002) reported that patients with various degrees of skin allergy as well as children who spend the night sleeping on the floor and suffered from generalized lymphadenopathy, with or without fever were presented to Benha University Hospitals from the suburb of Benha City and some adjacent villages. The patients were treated with carbolic acid (1:25). Besides, oral anti-histamine (H1) and systemic antibiotics were given when indicated in the complicated cases. The parasitological field study to the patients who live in some adjacent villages in concrete houses, a huge number of the large ants (mainly *Catagliphus bicolar*) were found moving here and there, particularly in the indoors animal houses. Spreading or burning the dried leaves of camphor tree proved to an effective control measure for these aggressive ants.

Zalat *et al.* (2005) evaluated the effect of 19 venoms from the solitary wasps, solitary bees, social wasps and ants were investigated for their effects on nicotinic acetylcholine receptors (nAChR) and the ionotropic glutamate receptors (IGRs) of both the N-methyl-d-aspartate (NMDAR) and non-NMDAR type, using whole-cell patch clamp of human muscle TE671 cells to study nAChR, and of rat cortical and cerebellar granule cells for IGRs. They found that solitary wasp venoms caused significant voltage-dependent antagonism of nAChR responses to 10 microM ACh and NMDAR responses to 100 microM NMDA (+10 microM glycine) when co-applied at 1 microg/ml with the agonists. At positive holding potentials [V(H)] potentiation of these receptors was detected with some venoms. The solitary bee venoms only affected nAChR by causing either voltage-independent antagonism or potentiation of their responses to 10 microM ACh. Of four social wasp venoms, one acted on nAChR by potentiating responses to 10 ACh, while another generated an ACh-like response when applied alone. They had no effect on IGRs. Of the two ant venoms, one caused voltage-independent inhibition of nAChR, but neither affected IGRs.

Sayed *et al*. (2009) evaluated the potency of bee product-immunized rats to induce *Staphylococcus aureus* infection. They found that bee product-immunized rats could significantly challenge the induced *S. aureus* infection (P<0.01). The effects were severe pronounced in the rats received fennel honey solution.

Ebaid *et al.* (2014) evaluated whether Samsum ant venom (SAV) could influence the effects of carbon tetrachloride (CCL4) exposure, by treating mice with SAV in doses of 100, 200, 300 and 400µg /kg body weight and the effects on oxidative status and kidney function. Serum levels of the creatinine, malondialdehyde (MDA), and blood urea, together with the renal and hepatic levels of MDA, the glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT) were also quantified to evaluate antioxidant activity assessment. They found that mice injected with the CCL4 exhibited significantly higher levels of oxidative stress markers, MDA, and significantly lower concentrations of GSH, SOD and catalase and that SAV significantly improved the oxidative markers, occasionally, in a dose-dependent way. Also, treatment with SAV was associated with the same behavior in respect to kidney functions previously impaired by CCL4. Histopathologically SAV, in the different groups of mice improved the renal tissue damage induced by CCL4 and the histological scores confirmed that significant improvements were obtained after treatment with SAV, particularly with the lowest dose (100µg /kg body weight). They concluded that the SAV proved to have the potential capability to restore oxidative stability and to improve kidney functions after the CCL4 acute injury

Tantawy (2015) mentioned that in the ancient Egyptian traditional medicine the considerable evidence supported the theory of using the parasites (helminthes and insects), and their biproducts in the treatment of many diseases. He added that what was more important being the venomous of scorpions, bees, wasps, spiders, ants, centipedes, snail, beetles, and caterpillars. These venoms and toxins provided a promising source of natural bioactive compounds which could be employed in development of the many new active drugs with the potential anti-microbial, antiviral, and anticancer pro-perties. The possibility of using the active molecules in biotechnological processes could make these venoms and toxins a valuable and promising source of natural bioactive compounds. He added that the therapeutic use of helminthes and insects and their products would be of the critical value to the development of Biomedical Sciences.

Conclusion

For the majority of people, mainly the children an insect sting is a painful but transitory episode. Nevertheless, the sting can have fatal consequences.

The health care workers, mainly staff nurses must be aware of all the potential complications of insect stings and the management available options.

Recommendations for Nursing

Anaphylaxis is an emergency condition that requires immediate, accurate diagnosis by one or more of the following: 1- Difficulty/noisy breathing, 2- Swelling of lips, tongue, face or eyes, 3-Swelling/ tightness in throat, 4- Difficulty talking and/or hoarse voice, 5- Difficulty swallo-owing, 6- Pain distal from sting site, 7- Vomiting, 8- Abdominal pain, 9- Wheeze or persistent cough, 10- Signs of envenomation/neurotoxic paralysis as one or more of the following: a- Roping of eye lids (ptosis), b- Decrease/paralysis of eye movements (ophthalmoplegia), c- Limb weakness, and/or d- Respiratory abnormalities. Additional Full history of sting: a- Date and time, b- Location/size of injury, c- Possible perpetrator, d- First aid treatment prior to hospital administration, and e- Tetanus immunizations (Academy of Managed Care Pharmacy, 2014).

Management Principles: 1- Remove insect and stinger if still attached to skin, 2- To remove stingers, use a sideways scraping motion to avoid further envenomation, 3- Inspect patient's clothing and remove any other insects and stingers, 4- Apply a cold pack at 20 minute on/off intervals for pain relief and to reduce swelling, 5- Provide more analgesia as indicated according to pain scale-refer to any cause, 6- Consider administration of tetanus toxoid as per immunization history and tetanus toxoid standing order, and 7- Document assessment findings, interventions and outcomes (ECI's, 2015).

General Recommendations

To avoid stings by yellow-jacket and brown hornets, hymenopterans attracted to odors from food sources and garbage, special care should be taken when cooking, eating, drinking, and disposing of food, refuse, and human wastes while outdoors. Ground-dwelling vespids often nest in rotting tree stumps and fallen logs, which should be avoided. If repeatedly annoyed by bees or wasps protect man's head and neck with his hands and should move away slowly from the likely nesting area. Besides, never approach or agitate a displaced honeybee hive or swarm or an active hornet or wasp nest. Notify the proper authorities of the exposed hive or nest and caution all to avoid the area, including the domestic animals. Only an experienced beekeeper has proper personal protective equipment to remove and to transport a displaced honeybee hive or swarm.

Uncomplicated local reactions usually do not require treatment beyond the cold compresses application. But, large local reactions typically require symptomatic treatment to control itching (mainly with fire ant stings) or minimize swelling. The affected part should be elevated if possible. Anaphylaxis occurs in up to 3% of stings. Venom induced anaphylaxis can be particularly severe and is a leading cause of anaphylactic deaths.

Anaphylaxis is clinically diagnosed. Individuals with possible allergy should be questioned carefully about different symptoms of anaphylaxis, which may be unfamiliar to the patient and not readily reported. Choice initial treatment is epinephrine injected intramuscularly into antero-lateral thigh. Upon discharge, any patient with a systemic allergy or anaphylaxis should be: 1- Supplied with an epinephrine auto-injector and instructed in how and when to use it, and 2- Referred to an allergy specialist to determine if they are candidates for venom immunotherapy, which is the definitive treatment for the venom allergy. Some anaphylactic reactions are so severe that treatment is unsuccessful despite rapid recognition and treatment. Improving evidence base for various treatment modalities could minimize fatalities once recognizing anaphylaxis (Kemp and Kemp, 2014).

The anaphylaxis risky individuals must carry adrenaline in pre-loaded syringes, for self-administration. The medic alert bracelet or necklace would alert others to the need for rapid action.

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