FOGLIO DI ISTRUZIONI PER L’USO DI ADRENALINA AUTOINIEBBILE (FASTJEKT) NELLA PREVENZIONE DELLO SHOCK ANAFILATTICO:

ANAFILASSI:

Definizione di anafilassi: secondo il recente Position Paper della European Academy of Allergy and Clinical Immunology (EAACI) essa può essere definita come una “grave reazione allergica sistemica o generalizzata, pericolosa per la vita”. In base alla severità clinica l’anafilassi può essere:

– **lieve**: (solo cute e sottocutaneo) Eritema generalizzato, orticaria, edema periorbitario o angioedema;
– **moderata**: (sintomi suggestivi di interessamento respiratorio, cardiovascolare o gastro-intestinale) Dispnea, stridore, wheezing, nausea, vomito, stordimento (presincope), sudorazione, senso di costrizione alla gola o al torace o dolore addominale;
– **grave**: (ipossia, ipotensione o interessamento neurologico) Cianosi o sat. O₂ ≤ 92%, ipotensione, confusione, collasso, perdita di coscienza o incontinenza.

A chi va prescritta l’adrenalina auto iniettabile?

Ad ogni bambino che ha presentato un episodio di anafilassi può essere opportuno la prescrizione del Fastjekt. Tuttavia, in accordo a quanto raccomandato dall’American Academy of Allergy Asthma and Immunology, si suggerisce di inviare ad una consulenza allergologica ogni bambino affetto da un episodio di anafilassi, sospetta o conclamata, per un approfondito inquadramento diagnostico e terapeutico. Questo sia perché l’anafilassi è un evento potenzialmente grave e mortale, sia per evitare una ingiustificata prescrizione di un farmaco (la adrenalina autoiniettabile), costoso e non del tutto privo di effetti collaterali.

La diagnosi di anafilassi si riterrà accertata in presenza di entrambi i seguenti criteri:

a) una storia clinica compatibile
b) dimostrazione della presenza di IgE specifiche (con positività del Prick test o Rast) per l’alimento o il veleno di insetti (nelle forme di anafilassi IgE-dipendenti).

**Indicazioni Assolute**

L’adrenalina deve essere prescritta ad ogni bambino con pregresso episodio di anafilassi grave.

**Indicazioni Relative**

In bambini con precedente episodio di anafilassi lieve-moderata

La presenza dei seguenti fattori che in alcuni casi aumentano di rischio di avere reazioni più gravi:

- **Età>5aa**
- Affetti da asma grave.
- Con pregresso episodio da arachidi, noci, pesci e crostacei
- Con pregresso episodio verificatosi con minime quantità
- Con pregresso episodio con sintomi respiratori
- Affetti da allergia al grano e/o anafilassi da sforzo
- Residenti lontano da un PS
- Affetti da Dermatite atopica
- In terapia con Beta bloccanti o inibitori dell’angiotensin converting enzime
- Con valori di IgE > 10 000 UI/ml

**Effetti collaterali e rischi della somministrazione di adrenalina:**

Effetti collaterali più comuni: ansietà, agitazione, cefalea, vertigini, palpitazioni, pallore e tremori. Raramente, soprattutto in caso di sovradosaggio, aritmie ventricolari, angina, infarto miocardio, edema polmonare, improvviso brusco aumento della pressione sanguigna ed emorragia endocranica.

Il rischio di effetti collaterali può essere aumentato nei soggetti con malattie cardiache preesistenti o con problemi neurologici o con malattie tiroidee, in soggetti che utilizzano inibitori della monoaminoossidasi che bloccano il metabolismo dell’adrenalina o in quelli che usano antidepressivi triciclici o cocaina in cui la durata di azione dell’adrenalina è prolungata.

Per una lettura più approfondita può essere utile consultare il seguente link: [http://www.siaip.it/upload/933.pdf](http://www.siaip.it/upload/933.pdf)
FOGLIO DI ISTRUZIONI PER L’USO DI ADRENALINA AUTOINIEKTABILE (FASTJEKT) NELLA PREVENZIONE DELLO SHOCK ANAFILATTICO:

Adrenalina intramuscolare = farmaco di prima scelta nel trattamento dello shock anafilattico

Dose = 0.01 mg/kg di peso corporeo in sol. 1:1000 (1 mg/ml) con dose massima di 0,5 mg in adulti e 0,3 mg in bambini.

Attualmente l’adrenalina è disponibile in forma autoiniettabile (Fastjekt)

iniettore pre-riempito, costituito da siringa ed ago, che consente di somministrare una singola dose di soluzione (0.30 ml) 2 formulazioni:

Fastjekt  Adulti  330 mg indicato per soggetti di peso pari o superiore a 30 Kg
Fastjekt  Bambini  165 mg per pazienti di peso inferiore a 30 Kg.

La singola dose, in caso di necessità, è ripetibile dopo 5-15 minuti.

Istruzioni per l'uso:

FASTJEKT* è pronto all’uso e può essere utilizzato, ove possibile, previa disinfezione del punto di iniezione:

1- Togliere il tappo grigio.
2- Prendere in mano FASTJEKT® tenendo l'estremità in plastica nera a contatto con la coscia (anche attraverso i vestiti) e premere con forza sulla pelle: si sentirà lo scatto dell'ago.
3- Tenere FASTJEKT® in detta posizione per almeno dieci secondi, fino a quando cioè l'ago è penetrato nella pelle ed è stata iniettata l'adrenalina. In nessun caso allontanare FASTJEKT® dalla coscia prima della fine dell'iniezione.
4- Allontanare quindi FASTJEKT® dalla coscia e massaggiare il punto di iniezione per circa 10 secondi. Recarsi al più presto da un medico portando il FASTJEKT® utilizzato.

N.B. Per il suo corretto funzionamento l’iniettore viene riempito con una quantità di liquido (2,05 ml) nettamente superiore a quella da iniettare (0,30); quindi è del tutto normale che dopo l’utilizzo la maggior parte della soluzione rimanga nell’iniettore.

AVVERTENZE E PRECAUZIONI PER L’USO:

La confezione di Fastjekt deve essere utilizzata una volta solamente; accertarsi ogni 15 giorni che la soluzione di adren alina sia incolore e che non contenga precipitati di alcun tipo: in tali casi, non utilizzare e sostituire il prodotto; la soluzione contiene Sodio Metabisolfito, che in soggetti sensibili può scatenare reazioni allergiche ed attacchi asmatici anche gravi.

Per le mamme: può essere utile vedere il video al seguente link http://www.youtube.com/watch?v=Wvk1KibTs_4
Hymenoptera-Sting Hypersensitivity

Thomas B. Casale, M.D., and A. Wesley Burks, M.D.

A 24-year-old woman reported that a “bee” stung her upper lip while she was drinking from a can of soda at a picnic. Within 5 minutes, her lips swelled, and she became hoarse and light-headed and had difficulty swallowing. Diffuse flushing and urticaria also developed. She was taken to a local emergency department and received intramuscular epinephrine and intravenous fluids along with H₁-antihistamines. Her symptoms resolved, and after 3 hours of observation she was discharged with an epinephrine auto-injector. How should her case be managed from this point forward?

THE CLINICAL PROBLEM

Although anaphylaxis due to an insect bite has been reported in a small number of cases, stings from insects belonging to the order Hymenoptera are among the most important causes of systemic allergic reactions. The Hymenoptera insects whose stings cause allergy are generally from three families: Apidae (honeybees and bumblebees), Vespidae (hornets, wasps, and yellow jackets), and Formicidae (fire ants) (Table 1 and Fig. 1).

The sting apparatus of hymenoptera is a modified ovipositor (no longer used for egg-laying), and therefore only the female insects can sting. Although the venom from stings can be used to disable and capture prey, most insects sting to defend themselves and their nests. Hymenoptera deliver between 50 ng (fire ants) and 50 μg (bees) of venom with each sting.²,³ The venoms in hymenoptera contain vasoactive amines, including histamine and dopamine, as well as norepinephrine and kinins, which account for the painful, erythematous swelling and itching at the site of the sting.⁴,⁵ The major allergens leading to systemic reactions in allergic persons are primarily protein enzymes (phospholipase, hyaluronidase, and acid phosphatase).⁶ The venom from fire ants contains small amounts of proteins but substantial amounts of toxic alkaloids, which are responsible for the characteristic vesicles (Fig. 2). The molecular characteristics of the venoms from the three families of Hymenoptera are sufficiently different that there is very little antigenic cross-reactivity. Within families (e.g., vespids), there can be substantial cross-reactivity among the allergens present in the venoms; however, honeybee and bumblebee allergies are distinct.⁵,⁷

In sensitized persons, a sting can cause the injected venom to bind to venom-specific IgE on mast cells, cross-linking high-affinity IgE receptors and subsequently leading to the rapid release of mast-cell mediators, including histamine, leukotrienes, prostaglandins, and platelet-activating factor. The released mast-cell mediators can cause a spectrum of allergic reactions, from local reactions (affecting small or large [≥10 cm] areas) or urticaria to anaphylaxis and even death. Patients with large local reactions usually do not have a systemic reaction to subsequent stings (with systemic reactions occurring in <10% of these patients), nor do chil-

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Caren G. Solomon, M.D., M.P.H., Editor

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An audio version of this article is available at NEJM.org
dren with isolated urticaria. However, a previous systemic reaction in a patient with venom-specific IgE is associated with a high risk of subsequent systemic reaction, which may occur in 30 to 60% of these patients. Anaphylaxis due to a hymenoptera sting causes at least 40 deaths per year in the United States, although this number is probably an underestimate. Severe systemic allergic reactions occur in approximately 0.4 to 0.8% of children and 3.0% of adults. Although honeybees are more docile than yellow jackets, the honeybee sting is more likely to lead to a systemic allergic reaction. The venom from Africanized honeybees (so-called killer bees) does not differ substantially from that of other honeybees, but Africanized honeybees tend to attack in swarms, and life-threatening or fatal toxic reactions may result when hundreds of these honeybees sting. In rare instances, delayed reactions to stings of unknown mechanism can occur, including serum sickness-like reactions, encephalitis, peripheral and cranial neuropathies, glomerulonephritis, myocarditis, and the Guillain–Barré syndrome.

**Local Reactions**
Most hymenoptera stings cause acute pain and transient, localized swelling. These local reactions usually require no treatment other than symptomatic therapy with cold compresses or ice, analgesic agents, oral H₁-antihistamines, or topical glucocorticoid creams or ointments to reduce pruritus and local pain and swelling. Honeybees (but not bumblebees) often leave their stingers, and these can be removed by scraping the skin with a fingernail or credit card. However, unless the stinger is removed within 20 to 30 seconds, the venom sac is typically emptied. The intense local inflammation from a sting may cause the appearance of lymphangitic streaks in the first 24 to 48 hours, but this manifestation should not be mistaken for cellulitis.

Large local reactions are not usually dangerous, unless they are on the face and compromise the airway, which may occur especially in the case of a sting on the tongue or pharynx. If a local reaction is very large or the associated inflammation results in substantial problems, clinical experience suggests that oral glucocorticoids may be helpful.

Infections at the site of stings are very rare (especially in the first 2 days), and antibiotic agents are not typically indicated. In the case of fire ants, sterile pseudopustules (Fig. 2) may occur 1 to 2 days after a sting. The vesicles should be kept clean and left unperturbed to minimize the risk of secondary infection.
Table 1. Characteristics of Hymenoptera.*

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Taxonomic Classification</th>
<th>Size</th>
<th>Nesting Habits</th>
<th>Feeding Habits</th>
<th>Aggressiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honeybee</td>
<td>Apis mellifera</td>
<td>15–20</td>
<td>Tree cavities and artificial hives</td>
<td>Nectar and pollen</td>
<td>Nonaggressive</td>
</tr>
<tr>
<td>Africanized honeybee</td>
<td>Apis mellifera</td>
<td>15–20</td>
<td>Natural hives</td>
<td>Nectar and pollen</td>
<td>Aggressive</td>
</tr>
<tr>
<td>Bumblebee</td>
<td>Bombus species</td>
<td>12–25</td>
<td>Underground tunnels</td>
<td>Nectar and pollen</td>
<td>Nonaggressive</td>
</tr>
<tr>
<td>Fire ant</td>
<td>Solenopsis invicta</td>
<td>4–6</td>
<td>Mounds in disturbed soil</td>
<td>Omnivorous</td>
<td>Nonaggressive</td>
</tr>
<tr>
<td>Paper wasp</td>
<td>Polistes species</td>
<td>15–20</td>
<td>Single layer, hanging from eaves, porches</td>
<td>Nectar and arthropods</td>
<td>Aggressive</td>
</tr>
<tr>
<td>Yellow jacket</td>
<td>Vespula species</td>
<td>15–20</td>
<td>Multilayered, usually in open areas</td>
<td>Nectar and arthropods</td>
<td>Aggressive</td>
</tr>
<tr>
<td>White-faced hornet</td>
<td>Vespa crabro</td>
<td>25–35</td>
<td>Multilayered, usually in open areas</td>
<td>Nectar and arthropods</td>
<td>Aggressive</td>
</tr>
<tr>
<td>White-faced or bald-faced hornet</td>
<td>Dolichovespula maculata</td>
<td>25–35</td>
<td>Multilayered, usually in open areas</td>
<td>Nectar and arthropods</td>
<td>Aggressive</td>
</tr>
<tr>
<td>European hornet</td>
<td>Vespula species</td>
<td>25–35</td>
<td>Multilayered, usually in open areas</td>
<td>Nectar and arthropods</td>
<td>Aggressive</td>
</tr>
</tbody>
</table>

* Adapted from Freeman.1

Table 1

Acute systemic reactions typically occur very rapidly after a hymenoptera sting but may be delayed for several hours or be biphasic. Biphasic reactions occur in less than 20% of episodes and are defined as an initial reaction followed by a recurrence of symptoms (typically in ≤8 hours) after the resolution of the initial episode.6,7,14-21 The factors associated with an increased risk of severe reaction include being stung by a honeybee (greater risk than with other hymenoptera), underlying mast-cell disorders with elevated serum-tryptase levels at baseline, a previous severe reaction, preexisting cardiovascular disease, and concomitant treatment with a beta-blocker, angiotensin-converting–enzyme (ACE) inhibitor, or both.1,6,7,21 Beta-blockers potentiate the negative inotropic and chronotropic effects of mast-cell mediators and inhibit the beta-agonist effects of epinephrine used to treat anaphylaxis. ACE inhibitors prevent the breakdown of neuropeptides and bradykinin, which are released as a result of mast-cell degranulation.

Anaphylaxis can present with a spectrum of signs and symptoms affecting multiple organ systems, including the skin, gastrointestinal tract, cardiovascular system, nervous system, and both the upper and lower respiratory tracts (Table 2); hallmarks of anaphylaxis are the development of hypotension or the involvement of more than one organ system.7,21 Overall, the more rapid the onset of symptoms of anaphylaxis, the more severe the reaction tends to be.7,21 Death from anaphylaxis typically results from upper-airway obstruction or cardiovascular collapse.

The treatment of hymenoptera-induced anaphylactic reactions is the same as the treatment for anaphylaxis caused by any other triggers and depends on the manifestations of the reaction.7,21 At the earliest signs of an anaphylactic reaction, either the patient or a companion should administer injectable epinephrine, if available, into the muscle of the mid-anterolateral thigh, and the patient should be transported promptly to an emergency department. The dose of epinephrine is 0.01 mg per kilogram of body weight in a 1:1000 (1 mg per milliliter) solution, with a maximum dose of 0.5 mg in an adult and 0.3 mg in a child. There are no contraindications to the use of epinephrine for the immediate treatment of anaphylaxis, including preexisting cardiovascular...
lar disease, hypertension, or the concomitant use of beta-blockers. Delays in administration are associated with more severe reactions and an increased risk of death.

The administration of epinephrine should be repeated (at intervals of 5 to 15 minutes) if the patient has persistent or refractory symptoms or a recurrence of symptoms. Most patients require only one or two doses. In children, a cutaneous reaction with diffuse urticaria is not indicative of anaphylaxis and, in the absence of other manifestations of anaphylaxis, typically does not require the use of epinephrine. Treatment with H₁-antihistamines is recommended in this context and also as adjunctive therapy in patients treated with intramuscular epinephrine.

The treatment of anaphylaxis in the emergency department should include epinephrine for any patient who has more than cutaneous symptoms; epinephrine should also be considered in adults with urticaria alone. H₁-antihistamines can help relieve cutaneous signs and symptoms. For respiratory symptoms, supplemental oxygen and inhaled beta₂-agonists should be used. For patients with hypotension, volume resuscitation is indicated, with 1 to 2 liters of 0.9% (isotonic) saline infused rapidly (e.g., a dose of 5 to 10 ml per kilogram in the first 5 to 10 minutes in an adult, and 10 ml per kilogram in a child). Glucocorticoids are often used also, although evidence is lacking to support their effectiveness in patients with hypotension. Patients who have received epinephrine and have a resolution of symptoms should be observed for at least 2 hours for a possible recurrence and, at discharge, should be given instructions about the possibility of a late-phase allergic reaction.

LONG-TERM THERAPY

AVOIDANCE OF EXPOSURE

It is prudent for persons with a history of systemic allergic reaction to avoid areas with a high risk of exposure (e.g., yards, gardens, trash containers, and outdoor areas with uncovered food and drink), to refrain from walking outside barefoot or while wearing sandals, and to wear long sleeves, long pants, a head covering, and gloves when working outside. All patients who have had a systemic reaction to an insect sting and those who have frequent, unavoidable exposure to stinging insects (e.g., beekeepers) should receive a prescription for an epinephrine auto-injector (Auvi-Q, available in doses of 0.15 mg and 0.3 mg, Sanofi; EpiPen, available in a dose of 0.3 mg, and EpiPen Jr, available in a dose of 0.15 mg, Mylan Specialty; or
Adrenaclick, available in doses of 0.3 mg and 0.15 mg, Amedra Pharmaceuticals). Patients (or, for children, their caregivers) should be instructed to carry an auto-injector with them whenever there is a chance of a sting, and they should be educated regarding how and when to use the auto-injector. In some cases, the treatment for an anaphylactic reaction requires more than one injection; therefore, a prescription for more than one auto-injector should be considered. Patients at relatively low risk for anaphylaxis are those who have a history of only large local reactions to stings or strictly cutaneous systemic reactions, those receiving maintenance venom immunotherapy, and those who have completed more than 5 years of venom immunotherapy. For patients at relatively low risk for anaphylaxis, the decision to obtain an epinephrine auto-injector can be made on an individual basis, after discussions between the physician and the patient.

EVALUATION

Patients who have had a systemic reaction to an insect sting should be referred to an allergist–immunologist for skin testing and possibly in vitro testing for insect-specific IgE, since persons who have a positive test result may benefit from subcutaneous immunotherapy (see below). A large local reaction without a systemic reaction is generally not considered to be an indication for such testing unless exposures are frequent or unavoidable.

The extracts available for skin testing include venom from honeybee, yellow jacket, white-faced hornet (also called bald-faced hornet), yellow hornet, and wasp. For fire ants, venom extract is not available commercially, but whole-body extract is. If patients have a negative response to skin testing but a convincing history of anaphylaxis after an insect sting, in vitro testing for IgE antibodies or repeat skin testing should be considered before immunotherapy is ruled out, especially if the patient’s systemic reaction included upper-airway obstruction or hypotension.

False negative skin or serum venom-specific IgE testing may occur within the first few weeks after a systemic reaction to an insect sting; patients with a negative early test should be retested 6 weeks later. Waiting 6 weeks for initial testing is not advisable, because some patients may need to initiate venom immunotherapy immediately for safety reasons. It is possible for persons with negative venom skin tests to have systemic reactions to subsequent stings. Some cases of anaphylaxis due to sting may be non-IgE-mediated or may be attributable to subclinical (indolent) mastocytosis. Expert guidelines recommend that patients with a severe reaction to an insect sting undergo a workup for mast-cell disorders consisting of a baseline measurement of the serum-tryptase level and, in some instances, a bone marrow biopsy.

In the United States, a sting challenge is not part of the standard management of insect-sting hypersensitivity. Sting challenges can result in systemic reactions, and a negative challenge does not preclude a subsequent systemic reaction to stings.
IMMUNOTHERAPY

Subcutaneous immunotherapy should be considered in all patients who have had a systemic allergic reaction to an insect sting and who have a positive skin test (Table 3) or a positive result on an in vitro test for venom-specific IgE antibodies. With respect to adults who have had only a cutaneous reaction, there is not a consensus regarding the use of venom immunotherapy, although a joint task force from the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology generally recommends this therapy. Children 16 years of age or younger who have had isolated cutaneous systemic reactions to insect stings have a very low risk of subsequent reactions and do not require venom immunotherapy.29,30

Venom immunotherapy is also generally not necessary in patients who have had only a large local reaction, because their risk of subsequent systemic reactions is relatively low. However, patients with unavoidable or frequent exposures (e.g., beekeepers) may benefit, because observational data indicate that, after immunotherapy, local reactions are reduced in size and duration.31,32

Controlled trials of subcutaneous immunotherapy have shown a significant reduction, to less than 5%, in the risk of a subsequent systemic reaction to an insect sting. In cases in which patients have systemic reactions to subsequent stings despite immunotherapy, these reactions are generally milder than pretreatment reactions.33 Venom extracts for honeybee, yellow jacket, white-faced hornet, yellow hornet, and wasp are available for immunotherapy, as is whole-body extract from fire ants. In the United States, a commonly used extract for therapy is the mixed vespid-venom preparation (100 μg each of venoms from yellow jacket, yellow hornet, and white-faced hornet).

The duration of venom immunotherapy should be at least 3 to 5 years.34,35 Approximately 80 to 90% of patients who undergo immunotherapy for 3 to 5 years do not have a systemic reaction to a future insect sting.36-44 Studies have shown that treatment for 5 years is associated with a greater suppression of allergic sensitivity and a lower risk of relapse than treatment for 3 years.42,45 There are no reliable means of discerning which persons will have a relapse after stopping venom immunotherapy; however, the risk of relapse is higher among patients with a history of severe anaphylaxis with shock or loss of consciousness than among those without such a history. In the patients at higher risk, venom immunotherapy may be continued indefinitely, although the added benefit and cost-effectiveness of indefinite therapy are unclear.

The recommendations for immunotherapy with whole-body extract from fire ants are generally the same as those for immunotherapy with venom extracts.4 However, data are lacking to guide the duration of fire-ant immunotherapy. Survey data indicate that therapy is commonly continued for 3 to 5 years; some physicians discontinue therapy when results of skin testing or in vitro testing become negative.46

<table>
<thead>
<tr>
<th>Table 2. Clinical Features of Anaphylaxis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ System</td>
</tr>
<tr>
<td>Nervous system</td>
</tr>
<tr>
<td>Eyes, nose, and mouth</td>
</tr>
<tr>
<td>Respiratory system</td>
</tr>
<tr>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
</tr>
<tr>
<td>Cutaneous system</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3. Criteria for Positive Skin Tests.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venom or Extract</td>
</tr>
<tr>
<td>Venom from honeybee, yellow jacket, white-faced hornet, yellow hornet, or wasp</td>
</tr>
<tr>
<td>Whole-body extract from fire ant</td>
</tr>
</tbody>
</table>

AREAS OF UNCERTAINTY

Research is needed to improve the identification of patients at risk for relapse after stopping venom or extract immunotherapy in order to better understand which patients might benefit from ongoing treatment. The current guidelines for
the testing of allergies to venom are based on a history of systemic reaction, but half the deaths from insect stings occur with a first sting; research is needed to identify patients at risk for such reactions before one has occurred.

GUIDELINES

In 2011, the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma, and Immunology; the American College of Allergy, Asthma, and Immunology; and the Joint Council of Allergy, Asthma, and Immunology published updated guidelines regarding the recommended treatment of hypersensitivity to insect stings. The recommendations in this article are generally consistent with these guidelines (Table 4).

**CONCLUSIONS AND RECOMMENDATIONS**

In patients with Hymenoptera allergy, such as the patient described in the vignette, venom immunotherapy is the standard of treatment and can prevent life-threatening anaphylactic reactions. Epinephrine is the mainstay of treatment for patients who have a severe reaction to a hymenoptera sting; patients with a history of a systemic allergic reaction should be instructed regarding the need to carry an epinephrine auto-injector and to use it as needed — including possibly more than one injection per reaction.

Dr. Casale reports receiving consulting fees from Stallergenes and consulting fees to his institution from Genentech and Novartis; grant support from Novartis, Genentech, ALK-Albello, Merck, and Stallergenes; and lecture fees from ALK-Albello. Dr. Burks reports receiving consulting fees from Abbott Laboratories, McNeil Nutritional, and Gerson Lehrman Group Research; serving as an unpaid consultant for Dow AgroSciences, Merck, Novartis, Schering-Plough, Unilever, ExploraMed Development, Nordic Biotech Advisors, Nutricia North America, Perrigo, Portola Pharmaceuticals, Regeneron Pharmaceuticals, and Porphos; owning stock in Allertein Therapeutics and Mast Cell Pharmaceuticals; and giving an unpaid lecture for Mylan Specialty. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

### Table 4. Type of Sting Reaction and Recommended Subsequent Management.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Children</th>
<th>Older Adolescents and Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large local reaction</td>
<td>Further workup not recommended routinely‡</td>
<td>Further workup not recommended routinely¶</td>
</tr>
<tr>
<td>Cutaneous systemic reaction</td>
<td>Further workup not recommended routinely‡</td>
<td>Diagnostic testing and immunotherapy§</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Diagnostic testing and immunotherapy§</td>
<td>Diagnostic testing and immunotherapy§</td>
</tr>
</tbody>
</table>

* The recommendations for children apply to those younger than 16 years of age. For adolescents 16 years of age or older, the recommendations for adults apply.
† The risk of anaphylactic reaction is extremely low among these patients.
‡ Further workup is not recommended routinely because of the low risk of clinically significant allergic reactions.
¶ The risk of anaphylaxis is more than 60% in these patients. However, if appropriate immunotherapy is started, the risk of anaphylaxis decreases to less than 5%. If indicated, skin-prick testing and serum-specific IgE testing should be performed to determine appropriate venom allergens. Immunotherapy is indicated for patients with a positive skin-prick test or positive serum-specific IgE testing. Obtaining a baseline serum-tryptase level is recommended for patients who have had a severe anaphylactic reaction.
§ The testing of allergies to venom is based on a history of systemic reaction, but half the deaths from insect stings occur with a first sting; research is needed to identify patients at risk for such reactions before one has occurred.

### REFERENCES