

Anaphylaxis: Evidence-Based Long-Term Risk Reduction in the Community

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Anaphylaxis, defined clinically as a serious allergic reaction that is rapid in onset and may cause death [1], now occurs more frequently in community settings than in health care settings [2]. As with other allergic diseases, the rate of occurrence seems to be increasing in many countries [3]. Continued vigilance in preventing anaphylaxis, and in assessing and treating it promptly when it occurs, are critically important. Health care professionals also need to focus on long-term management of those individuals who have experienced anaphylaxis, specifically on risk assessment and risk reduction [2]. Allergy/immunology specialists and their allied health colleagues are uniquely trained for this task. The expertise they provide in this area is underutilized; for example, many individuals treated in emergency departments for anaphylaxis triggered by foods or insect stings who might benefit from the risk assessment and risk reduction measures instituted by an allergist do not get referred to an allergy/immunology specialist [4,5].

The fundamental basis of long-term risk reduction in anaphylaxis is accurate risk assessment, on which personalized long-term preventive measures depend [2]. The diagnosis of anaphylaxis should be confirmed by taking or retaking a detailed history of the acute episode, all antecedent events or exposures that occurred during the hours before the episode, and the response to treatment. In addition, the results of any laboratory tests, such as serum tryptase levels, that may have been obtained during the acute episode should be reviewed [2,6]. Comorbidities and the need

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for concurrently administered medications to control them should be evaluated [2].

Most individuals who have anaphylaxis have an insect venom, food, or other allergen trigger acting through a mechanism involving allergen-specific IgE and the high-affinity IgE receptor on mast cells and basophils [2,7]. Others have anaphylaxis triggered by non-IgE-mediated immunologic mechanisms; for example, intravenous immunoglobulin occasionally triggers anaphylaxis through immune aggregates, and the cellular elements in transfused blood can trigger anaphylaxis through cytotoxic mechanisms [7]. Some have anaphylaxis from nonimmune triggers, such as exercise or cold exposure, and others have idiopathic anaphylaxis [8–10]. Trigger avoidance in anaphylaxis is necessarily trigger-specific; therefore, trigger factors suggested by the history of the episode should be confirmed by allergen skin testing or measurement of allergen-specific IgE in serum. Positive skin tests or elevated allergen-specific IgE levels only document sensitization to allergens, and need to be interpreted in the context of the history in order to determine causality of the episode [2]. Depending on the history, additional tests (eg, an exercise challenge test) may be needed [2,8,10].

The main elements of risk reduction involve prevention of future episodes, emergency preparedness, and anaphylaxis education (Box 1) [2]. Each of these areas is discussed in detail. The level of evidence for the recommendations is graded using the following system [11]:

Grade A: based on a meta-analysis, or at least one randomized, controlled trial.

Grade B: based on at least one well-designed, but not necessarily controlled, study, including case control and comparative studies.

Grade C: based on expert reports or opinions.

Evidence-based medicine is extremely helpful in the management of common diseases such as asthma, in which there are many potential interventions and thousands of prospective, randomized, masked, controlled clinical trials of these interventions that are eventually summarized in evidence-based reviews and national and international guidelines [12]. When the principles of evidence-based medicine are applied to anaphylaxis, however, some limitations become apparent. For several reasons, anaphylaxis is a disease in which it is difficult (or, for epinephrine, almost impossible) to conduct prospective, randomized, double-masked, placebo-controlled trials. These include unpredictability of episodes, episodes commonly occurring in community settings rather than health care settings, and variability in symptoms and signs with regard to time of onset after exposure to trigger, pattern, severity, and duration. In addition, it may be difficult or impossible to obtain baseline measurements before a therapeutic intervention such as epinephrine, because it is unethical to delay treatment in a condition that may be acutely life-threatening. Consequently, most of the current evidence for long-term risk reduction in anaphylaxis, as summarized in Boxes 1 and 2, is based on consensus and opinion (Grade C), or at best

Box 1. Risk reduction in anaphylaxis*Risk reduction through prevention*

Trigger avoidance (Grade^a C)

Specific measures: immunomodulation and other approaches (Grade A^b, C)

Management of comorbidities (Grade C)

Risk reduction through emergency preparedness

Self-injectable epinephrine (Grade B)^c

Personalized Anaphylaxis Emergency Action Plan (Grade C)

Medical identification (Grade C)

Anaphylaxis education

At-risk individuals and their families (Grade C)

Health care professionals (Grade C)

General public (Grade C)

^a Grade for level of evidence.

^b Allergen-specific immunotherapy with Hymenoptera venom [15,16].

^c Epinephrine [35,36].

on well-designed studies that are not actually randomized, masked, controlled trials (Grade B).

Risk reduction through prevention*Trigger avoidance*

Written, personalized, specific information on trigger avoidance should be provided, and reviewed at regular intervals with those at risk and their caregivers [2,8,10,13–16]. Long-term avoidance is necessary for many triggers. Web site resources that consistently provide credible, accurate, and up-to-date information include the Food Allergy and Anaphylaxis Network (www.foodallergy.org), the American Latex Allergy Association (www.latexallergyresources.org), the American Academy of Allergy, Asthma, and Immunology (www.aaaai.org), and the American College of Allergy, Asthma, and Immunology (www.acaai.org).

Complete avoidance of exposure to a confirmed trigger (eg, food, stinging or biting insect, or natural rubber latex) for prevention of anaphylaxis is easier said than done, and is easier to initiate than to maintain for years or decades. Trigger avoidance can necessitate lifestyle changes that potentially impair the quality of life for the individual who has anaphylaxis and his or her family [17–19]. One example of this involves individuals who have

Box 2. Prevention strategies for anaphylaxis in community settings

Allergen avoidance (trigger-specific) based on history of exposure and confirmation of sensitization (Grade C)

Food

Insect stings and bites

Natural rubber latex

Medications^a (eg, β -lactam antibiotics)

Biologics^a (eg, allergens, vaccines, hormones)

Spices and other food additives

Inhalants (eg, horse dander)

Seminal fluid

Occupational allergens

Novel allergens^b

Avoidance of or modulation of exposure to nonimmune triggers (Grade C):

Exercise^c

Cold

Heat

Sunlight/radiation

Medications (eg, opiates)

Ethanol

Immunomodulation

Insect venoms: allergen-specific immunotherapy (Grade A)

Medications, (eg, nonsteroidal anti-inflammatory drugs):
desensitization (Grade B)

Seminal fluid: desensitization (Grade C)

Idiopathic anaphylaxis^d (Grade C)

Oral glucocorticoid (eg, prednisone). H₁-antihistamine
(eg, cetirizine)

^a "Safe" medications or biologics should be substituted.

^b Save the allergen (eg, food or insect) and save serum from the individual.

^c Avoidance of relevant co-triggers, such as cold air, food, or medication is critically important. Exercise itself should not be avoided.

^d Personalized prophylactic medication regimen for individuals who have frequent episodes.

Data from [2,8–10,13–16].

insect sting- or bite-triggered anaphylaxis, who may avoid outdoor sports or leisure and vacation activities in order to avoid exposure to insects. Another example involves individuals who have food-triggered anaphylaxis who require special food substitutes, with consequent potential economic, social, and cultural burdens [19]. For individuals who have confirmed anaphylactic sensitivity to foods, consultation with a licensed dietician can provide relevant information about the minimal daily requirements for essential nutrients, the basic food groups, any food substitutes or recipe adaptations that may be required, and food product allergen labeling interpretation [19]. Although improved food labeling should reduce the occurrence of anaphylaxis in at-risk individuals, it may also mean that those who have not been avoiding foods containing traces of allergen or allergens of doubtful relevance face additional ambiguity and unnecessary dietary restrictions [20].

Optimal management of comorbidities and wise selection of concurrent medications

Individuals who have mastocytosis, whether or not they have any symptoms of this disease, are at increased risk for anaphylaxis [21]. Some atopic individuals who have raised baseline total tryptase levels in serum may also be at increased risk for anaphylaxis.

Other at-risk individuals have comorbidities that can interfere with recognition of anaphylaxis triggers and symptoms. These include vision or hearing impairment, neurologic disease, or psychiatric disease, including depression, substance abuse, attention deficit hyperactivity disorder, behavior problems, and developmental delay [2,22,23].

Comorbidities can also affect the response to anaphylaxis treatment; indeed, most individuals dying from food-related anaphylaxis have concurrent asthma [24,25]. Cardiovascular disease can affect treatment in several ways, including reluctance to use self-injectable epinephrine because of fear of potential increased risk for adverse effects. Neuromuscular diseases and arthritis potentially place individuals at increased risk if they cannot self-inject epinephrine rapidly or correctly because of lack of coordination or strength.

In addition, concurrent medications used to treat comorbid diseases can place individuals at increased risk for anaphylaxis and for fatality from anaphylaxis. Some medications, such as first-generation sedating H₁-antihistamines, hypnotics, and other sedatives, potentially interfere with an individual's ability to recognize anaphylaxis triggers or symptoms, as do ethanol and recreational drugs.

Other concurrent medications can affect an individual's response to anaphylaxis treatment. α - and β -adrenergic blockers, especially nonselective β -blockers, regardless of the route of administration, potentially decrease epinephrine efficacy by interfering with α - and β -agonist effects at adrenergic receptors. Angiotensin-converting enzyme inhibitors, and to a lesser extent angiotensin II receptor blockers, potentially interfere with endogenous

compensatory responses in anaphylaxis. Although less commonly used now than in years past, tricyclic antidepressants and monoamine oxidase inhibitors potentially increase the adverse effects of epinephrine because of prevention of epinephrine uptake at adrenergic receptors [2,26–28].

Some medications (eg, those used for treatment of attention deficit hyperactivity disorder) can lead to side effects that are similar to those produced by epinephrine; amphetamines and methylphenidate release intracellular stores of epinephrine and also block monoamine oxidase, preventing epinephrine uptake at adrenergic receptors [2].

Specific preventive measures

Exercise-induced anaphylaxis

Strategies for preventing exercise-induced anaphylaxis are focused on avoiding relevant co-triggers, such as cold or dry air, food, or medication. Foods, including common triggers (eg, seafood) and less common triggers (eg, wheat) or medication, (eg, nonsteroidal anti-inflammatory medications) should be avoided for 4 hours before strenuous exercise. If no specific co-trigger can be identified, the at-risk individual should refrain from ingesting anything at all within 4 hours of exercise. General precautions include discontinuing exercise at the earliest hint of development of symptoms, such as itching, dizziness, or respiratory symptoms; never exercising alone; and always carrying self-injectable epinephrine. Warm-up and premedication are often recommended, although these measures seem to be less effective in prevention of exercise-induced anaphylaxis than they are in prevention of exercise-induced bronchospasm [8,10].

Idiopathic anaphylaxis

Idiopathic anaphylaxis, currently a diagnosis of exclusion, is more common in adults than in children and likely has an autoimmune cause. It is a glucocorticoid-responsive disease [9]; therefore, individuals who have frequent episodes of idiopathic anaphylaxis, defined as two episodes in 2 months or six in 12 months, benefit from prophylactic glucocorticoid treatment (eg, prednisone 40 to 60 mg every morning, often supplemented with an H₁-antihistamine, such as cetirizine 10 mg at bedtime). After symptom control is achieved, the prednisone can be given on an alternate-day basis, then gradually tapered. H₂-antihistamines or leukotriene modifiers are also sometimes recommended for individuals who have idiopathic anaphylaxis [9,10]. Prophylactic medication is not recommended for individuals who have infrequent episodes of idiopathic anaphylaxis [9].

Immunomodulatory strategies

Anaphylaxis triggered by stings of insects in the order Hymenoptera (bees, wasps, hornets, yellow jackets, fire ants) can be almost entirely prevented by use of allergen-specific immunotherapy initiated by an

allergy-immunology specialist [15,16], and protection is long lasting in most individuals [16].

Desensitization strategies are effective for anaphylaxis triggered by some medications, including β -lactam antibiotics and acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs, and for seminal fluid-induced anaphylaxis [10].

Additional effective immunomodulatory strategies for long-term risk reduction in anaphylaxis are being developed [13,14,29–31]. These include allergen-specific treatment, such as “engineered” recombinant proteins in which substitution of a critical amino acid within the IgE-binding epitopes reduces IgE binding and prevents IgE-mediated reactions [29], or allergen-nonspecific treatment, such as administration of anti-CD63 antibodies [30].

Proof of principle of one allergen-nonspecific approach, regular subcutaneous injections of anti-IgE antibody to prevent anaphylaxis, has already been obtained in humans who have peanut allergy [31]. In the future, this approach might provide many at-risk individuals with an increased margin of protection against exposure to trace amounts of various allergens to which they are sensitized.

Risk reduction through emergency preparedness

Self-injectable epinephrine: medication of choice in anaphylaxis

Despite long-term preventive measures to reduce risk, anaphylaxis triggers can be accidentally encountered, and anaphylaxis can recur. Symptoms may be more severe than those noted during previous episodes [32,33]. In community settings, when no health care professionals are available to recognize and treat anaphylaxis, individuals and their caregivers must be prepared to recognize and treat it. Physicians should ensure that all at-risk individuals or their caregivers have self-injectable epinephrine and know how to use it in the context of a personalized Anaphylaxis Emergency Action Plan [2,10,34,35].

Epinephrine is the medication of choice in the first-aid treatment of anaphylaxis in the community [35,36]. Acting through cyclic adenosine monophosphate, it has broad pharmacologic effects, the most important of which are: vasoconstriction with consequent increase in systolic blood pressure and decrease in laryngeal edema, decreased release of mediators of inflammation from mast cells and basophils, and bronchodilation [35]. Albuterol and other selective β_2 -adrenergic bronchodilators cannot replace epinephrine, although they may be given as ancillary medications to relieve wheeze, cough, and shortness of breath. Likewise, H_1 -antihistamines cannot replace epinephrine, although they may be given as ancillary medications to relieve itch, hives, and nasal symptoms (Table 1) [2,35,37,38].

Death can occur within a few minutes in anaphylaxis [24,25], and therefore epinephrine should be injected promptly, preferably intramuscularly in

Table 1

Rationale for epinephrine as the first-aid treatment of choice for anaphylaxis in the community

Medications and routes of administration	Epinephrine (injection)	β_2 -adrenergic agonists (inhalation)	H ₁ -antihistamines (oral)
Grade for level of evidence	B (adults and older children) C (infants)	C in anaphylaxis; A for asthma symptom relief and for prevention of exercise-induced bronchospasm	C in anaphylaxis treatment, B-C in anaphylaxis prevention, A in allergic rhinitis, A in urticaria
Pharmacologic effects	At α_1 -receptor ↑ vasoconstriction ↑ peripheral vascular resistance ↑ blood pressure ↓ mucosal edema (eg, in larynx); At β_1 -receptor ↑ heart rate ↑ force of cardiac contraction, At β_2 -receptor ↓ mediator release ↑ bronchodilation ↑ vasodilation	At β_2 -receptor ↑ bronchodilation	At H ₁ -receptor ↓ itch (skin, mucus membranes) ↓ flush ↓ hives ↓ sneezing ↓ rhinorrhea
Potential adverse effects when given in usual doses by the routes stated above	Anxiety, pallor, tremor, palpitations, headache	Tremor, tachycardia, dizziness, jitteriness	First-generation H ₁ -antihistamines cause sedation and impaired cognitive/psychomotor function; also dry mouth, urinary retention, and other antimuscarinic effects
Current recommendations	Treatment of first choice	Asthmatics should use their albuterol or other bronchodilator inhaler in addition to epinephrine	Not life-saving; ancillary treatment for symptom relief in addition to epinephrine

In community settings, where health care professionals are not available, individuals (or for children, their caregivers) are on their own regarding recognition and first-aid treatment of anaphylaxis. Treatment of anaphylaxis in community settings therefore differs from treatment in health care settings, such as emergency departments, where continuous monitoring of vital signs and frequent reassessment of symptoms and signs is performed, and where treatment can be modified rapidly if needed. Glucocorticoids (evidence grade for use = C) and other medications are not included in the table because they are not recommended for the *first-aid* treatment of anaphylaxis in community settings.

Data from [2,35–38].

the anterolateral thigh to achieve peak concentrations rapidly in plasma and tissues [39,40]. If epinephrine is injected into subcutaneous tissue, which has poor vascularity in comparison to skeletal muscle, complete absorption occurs eventually but is slow in many individuals. The pharmacokinetic elimination half-life of epinephrine is 43 minutes in children and slightly longer in adults [39]. The pharmacodynamic half-life has never been established; however, based on retrospective studies, more than one epinephrine injection may be needed in up to 35% of individuals [41]. Although the optimal interval between injections is not known, 5 to 15 minutes is commonly recommended [10]. Many of the individuals at risk for anaphylaxis in the community are infants and children [42]. The limited range of premeasured fixed epinephrine doses, 0.15 mg and 0.3 mg, currently available in auto-injectors presents a quandary for physicians wishing to prescribe an optimal epinephrine dose for infants and many young children [34,35,43] or for large teens and adults. Lack of availability of auto-injectors with a needle length adequate to achieve intramuscular injection in overweight and obese individuals is also a concern [44].

Currently, two types of epinephrine auto-injectors are available in North America. The advantages and disadvantages of each have been recently reviewed [45]. One Twinject provides two epinephrine doses less expensively than two EpiPens do and is more than 50% lighter and smaller. The Twinject auto-injector needle is 25-gauge in contrast to the EpiPen auto-injector needle, which is 22-gauge. The second epinephrine dose from a Twinject is not an auto-injector dose; rather, it requires manipulation of the needle and syringe.

In many countries life-saving epinephrine auto-injectors are either not available, or, if available, are not affordable for at-risk individuals who need them [46]. Existing alternatives cannot be depended on to produce high concentrations of epinephrine rapidly in tissues; these include laypersons' use of a needle and syringe to draw up and measure an epinephrine dose from an ampule [47] or use of an epinephrine metered-dose inhaler [48]. Sublingual dosage formulations of epinephrine are being developed specifically for use as noninvasive first-aid treatment in the community [49].

Rarely, an individual seems to be unresponsive to epinephrine. This unresponsiveness may be due to an extremely rapid progression of the anaphylaxis episode, or failure to administer epinephrine in a timely manner. Even if epinephrine is injected promptly, the dose may be inadequate or it may be given through a suboptimal route of injection or site of injection, or by a suboptimal injection technique, such as withdrawing the auto-injector too quickly. As described previously, some individuals may be refractory to epinephrine because they are concurrently taking a medication, such as a nonselective β -blocker, that prevents optimal epinephrine effect. In rare instances, an individual may be allergic to sodium metabisulfite, an antioxidant in epinephrine solutions [35]. Moreover, epinephrine in solution is

notoriously prone to degradation. If the expiry date printed on the label has passed or if the auto-injector has been exposed to high ambient temperatures, the dose of epinephrine actually injected may be significantly lower than the dose stated on the label [50].

Epinephrine is underused in anaphylaxis for various reasons, including lack of recognition of the episode, spontaneous recovery from a previous anaphylaxis episode in which epinephrine was not injected, or fear of needles. In addition, an epinephrine auto-injector may not be readily available or may never have been prescribed or dispensed [35].

Occasionally, epinephrine is not injected because of fear of adverse effects. Individuals at risk for anaphylaxis, or their caregivers, should be advised that the transient anxiety, pallor, tremor, and palpitations that commonly occur after epinephrine injection correlate with the beneficial pharmacologic effects of epinephrine and should not be a cause for concern (see Table 1) [35]. Serious adverse effects, such as myocardial ischemia, arrhythmias, and pulmonary edema, are seldom attributable to use of epinephrine auto-injectors by individuals in the community. More commonly they are attributable to overdose of epinephrine in health care settings, such as intravenous administration of inappropriately high concentrations or an overly rapid rate of infusion. Moreover, there is increasing awareness that the heart, like the skin, airways, gastrointestinal tract, and vasculature, can be a target organ in anaphylaxis and that coronary artery spasm, myocardial injury, and cardiac arrhythmias can occur in individuals who have anaphylaxis episodes *before* they receive any epinephrine treatment [51].

Personalized Anaphylaxis Emergency Action Plan

Epinephrine should always be prescribed in the context of broader educational interventions, including a written, personalized Anaphylaxis Emergency Action Plan [2,52,53]. Such plans should list the most common symptoms and signs of anaphylaxis, emphasize prompt epinephrine injection, and state clearly that asthma puffers and oral antihistamines cannot be depended on in anaphylaxis [2,34,35].

Action plans should also make it clear that after epinephrine injection, the individual should be transported to the nearest hospital emergency department [2], preferably in the supine position [54], for additional monitoring of the episode and further treatment if necessary. Although more than 80% of anaphylaxis episodes are uniphasic, some episodes are biphasic or prolonged and involve recurrent or persistent symptoms without any additional exposure to the trigger. Factors associated with increased risk for such reactions are: history of a previous biphasic response, severity of the episode being treated, brief time elapsed from trigger exposure to onset of primary symptoms, presence of hypotension or laryngeal edema during the primary response, and administering too little epinephrine too late

[55]. In reality, there is no certain way to predict the occurrence of biphasic or prolonged anaphylaxis.

Medical identification

Individuals known to be at risk for anaphylaxis should be equipped with accurate medical identification, such as a wallet card (available at www.aaaai.org) or a medical identification bracelet or other jewelry, listing their confirmed trigger factors and their relevant comorbidities and concurrent medications [2,56]. Options with regard to medical identification jewelry include Medic Alert, Bodyguard, American Medical ID, E-health-KEY, Stay Stat, and Medi-Guard ID. These vary with regard to range of different items available, durability, initial purchase cost, annual fee, presence or absence of an embedded medical record, and reliability of worldwide confidential 24-hour access 365 days per year to the at-risk individual's medical record.

Anaphylaxis education

At-risk individuals and their families

Education sessions should provide basic information about anaphylaxis, prevention of anaphylaxis, and emergency preparedness for anaphylaxis recurrence. Education of individuals at risk for anaphylaxis and their families helps to reduce stress and instill confidence in ability to cope, not only by avoiding relevant triggers for anaphylaxis and preventing episodes but also by recognizing and treating episodes promptly if they occur.

To provide a framework for discussion, educators may find it helpful to use commonly asked, basic questions, such as: Who is at risk? When can it happen? How do we recognize it? Where can it happen? What should we do? Why is follow-up needed? [2]. In addition, anaphylaxis education may involve broaching some difficult topics. For example, at-risk individuals and their families may find it helpful to discuss the balance between maintenance of vigilance and preparedness versus overprotection and withdrawal from daily life. Educators may encounter individuals who deny the possibility that an anaphylaxis episode might recur, and the possibility that a subsequent anaphylaxis episode may be more severe than a previous episode. At the opposite end of the spectrum, some individuals who have anaphylaxis are coming to the attention of psychologists and psychiatrists because of high anxiety levels that restrict their lives beyond what is medically necessary [57].

Supervised practice with an epinephrine auto-injector trainer until technique is perfected, and review of the Anaphylaxis Emergency Action Plan, should take place at yearly intervals, or more often if needed (eg, if an anaphylaxis episode has inadvertently occurred despite preventive measures). Supervised practice with an actual epinephrine auto-injector has been recommended [58].

Anaphylaxis education may be more complex and time-consuming than asthma education is, and for the many individuals at risk for anaphylaxis who have concurrent asthma, both types of education need to be provided (Table 2).

Health care professionals

Health care professionals, including nurses, emergency medical service technicians, first responders, and pharmacists, need regular anaphylaxis education updates. Pharmacists are an underutilized resource for providing

Table 2
Management of anaphylaxis compared with management of asthma

	Anaphylaxis	Asthma
Treatment options	Limited number	Many well-studied options
Self-treatment in community settings	Medication of choice: epinephrine injection; implement action plan	Medication of choice: inhalation of albuterol or other bronchodilator (reliever); adjust dose of controller or add another controller; implement action plan
Trigger avoidance	Difficult; constant vigilance required (eg, for peanut avoidance)	Easier to institute for allergens such as house dust mites and indoor molds than for household pets, outdoor molds, or pollen; difficult to maintain
Immunomodulation: allergen-specific	Where relevant, insect venom immunotherapy provides highly effective, long-lasting protection in selected patients	Specific immunotherapy with airborne allergens may be helpful in selected patients
Immunomodulation: allergen-nonspecific	Proof of concept exists for use of an anti-IgE antibody, but further studies are needed	Anti-IgE antibody is helpful in moderate-severe asthma
Quality of the evidence base for interventions	Not optimal; the only intervention graded A is venom immunotherapy; few are graded B; most are graded C	Excellent: the level of evidence for many interventions is graded A
Guidelines for management	No widely accepted national or international guidelines	Well-accepted international and national guidelines that are regularly updated
Education programs ^a	Not formalized or validated yet	Formalized, validated education programs and certified educators are widely available and have already reached many individuals in the community

^a Anaphylaxis education is a relatively new concept [2]. Many at-risk individuals require both anaphylaxis education (level of evidence grade C) and asthma education (level of evidence grade A).

anaphylaxis education in the community at the time prescriptions for epinephrine auto-injectors are filled or refilled [59].

All physicians, including primary care physicians and emergency medicine specialists, need to be aware of the new definition of anaphylaxis and the criteria for diagnosis [1]. One of the key aspects of this definition is recognition that many individuals who die of anaphylaxis die of respiratory failure rather than cardiovascular system failure and shock; therefore, it is unwise to delay aggressive management until hypotension develops. Moreover, all physicians should also be aware of the need for prompt treatment and for implementation of long-term preventive strategies. Ideally, advanced cardiac life support instruction should introduce the concepts of prescribing self-injectable epinephrine for individuals who are treated for anaphylaxis occurring in community settings, and of referring such individuals to appropriate specialist physicians for long-term risk assessment and risk reduction. Allergy/immunology specialists need to make themselves available in their communities as providers of risk assessments and long-term risk-reduction strategies in anaphylaxis.

General public

The first episode of anaphylaxis can be fatal [24,25]. It is therefore important to increase widespread awareness of anaphylaxis as a killer allergy, especially among educators, coaches, camp directors, childcare providers, food industry workers, restaurant workers, and transportation industry workers; to provide clear aids to recognition of early symptoms and signs; and to promulgate prompt use of self-injectable epinephrine. Optimally, epinephrine auto-injectors should be available in all public places because anaphylaxis can occur anywhere in the community.

All educators, whether at the childcare, preschool, school, or college level, need to be aware that children, teens, and young adults who seem to be in robust good health can be at increased risk for anaphylaxis and that fatal anaphylaxis can occur in the educational setting [24].

The childcare system presents unique challenges regarding anaphylaxis education. Infants and preschool children are vulnerable to accidental allergen exposure because of age-related inability to recognize and avoid triggers, and in addition, anaphylaxis is more difficult to recognize in the very young because of their inability to describe symptoms [2,60]. Moreover, in many jurisdictions, childcare centers and preschools are not as well regulated by government agencies as school systems are, and may not have policies in place to facilitate prompt recognition and treatment of anaphylaxis.

Allergy/immunology specialists and their allied health colleagues have been instrumental in developing anaphylaxis programs for schools. There are ongoing attempts to ensure that children and adolescents can carry or access self-injectable epinephrine in the school environment. The need

Box 3. Anaphylaxis in schools*Student's responsibilities^a*

Avoid his/her trigger (eg, if food-allergic: do not trade food with others, do not eat anything containing unknown ingredients)

Notify an adult immediately if inadvertently exposed to trigger or if symptoms develop

Wear medical identification jewelry and/or carry wallet card

Carry self-injectable epinephrine if age-appropriate and if permitted by local regulations

Family's responsibilities^a

Notify the school in writing of the student's risk for anaphylaxis and his/her triggers

Educate student about trigger avoidance

Provide medical documentation from the student's physician, including an Anaphylaxis Emergency Action Plan

Provide a properly labeled epinephrine auto-injector

Replace epinephrine auto-injector after use or if past expiry date

Provide emergency contact information for parents or guardians

Work with the school to further develop a personalized action plan for the student

Physician's responsibilities^a

Provide accurate risk assessment

Recommend risk reduction measures (eg, allergen avoidance, venom immunotherapy, if relevant)

Prescribe self-injectable epinephrine

Recommend medical identification jewelry and/or wallet card

Provide Anaphylaxis Emergency Action Plan

Provide medical information to student and parents

Provide medical documentation to the school

If the student has concurrent asthma, achieve optimal symptom control

School's responsibilities^a

Review health records of at-risk students

Identify a team (eg, teachers, school nurse, principal) to prevent, recognize, and treat anaphylaxis

Designate school personnel who are trained to administer epinephrine injections

Rehearse the response to an anaphylaxis episode:**Give epinephrine promptly****Contact 911 or emergency medical services****Contact parents**

^a All information should be updated annually before the start of the school year and at additional intervals as needed (eg, if an episode of anaphylaxis occurs or if a student's allergen triggers change) ([61] and the Food Allergy and Anaphylaxis Network, 2007, www.foodallergy.com).

to address the significant racial and socioeconomic differences identified in providing self-injectable epinephrine for schoolchildren has been recognized. Students, families, physicians, and schools all bear responsibility for anaphylaxis risk reduction in the educational environment (Box 3). Efforts to streamline communication between parents, physicians, and schools need to be adopted; currently, numerous different forms are needed for different schools [61–64].

Many teens and young adults are at increased risk for anaphylaxis. Individuals in this age group have been reported to have a high level of risk-taking and coping behaviors and to be at increased risk for fatal food-induced anaphylaxis on college campuses and elsewhere [24,25,65]. Colleges and universities therefore offer unique opportunities for anaphylaxis education of at-risk individuals and their peers. Policies with regard to supporting these individuals vary from one institution to another, and this, too, presents unique opportunities for dialog and education.

In recent years, legislators in many countries have been receptive toward changing public policy and improving medical services for individuals who have anaphylaxis. Two examples of important legislation being implemented in the United States include: the National Food Allergy Labeling Consumer Protection Act, which mandates clear food labeling, and HR23, a bill mandating that children and teens in schools should have access to life-saving epinephrine auto-injectors. In many Canadian schools, an Act to Protect Anaphylactic Pupils (Sabrina's Law) is being implemented. This law mandates the establishment of minimum standards for education of all school personnel with regard to recognition and management of anaphylaxis in the school setting.

In summary, all time and effort spent on anaphylaxis education of at-risk individuals and their families, health care professionals, and the general public is immensely rewarding and potentially life-saving.

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