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Outpatient Emergencies: Anaphylaxis

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Synopsis

Anaphylactic fatalities are rare and in the vast majority of instances, patients will do well. Nevertheless, fatalities do occur and reactions presenting with mild symptoms can rapidly progress to cardiovascular and respiratory arrest. At the initiation of symptoms it is not possible to know whether an episode will rapidly progress. Because the clinical course of anaphylaxis can be unpredictable, prompt and early use of epinephrine should be considered even with mild symptoms or single-system involvement. Any patient who has experienced an episode of anaphylaxis should be evaluated to determine the causative agent. Most anaphylaxis episodes have an immunologic mechanism involving immunoglobulin E (IgE). Foods are the most common cause in children, while medications and insect stings are more common causes in adults. Any patient who has experienced anaphylaxis when the cause is not completely avoidable or cannot be determined should be supplied with auto-injectable epinephrine (AIE) and should be instructed in the use of this device and told to keep their AIE with them at all times. The patient should be taught to recognize the signs and symptoms of anaphylaxis and when to administer the injection and be given an anaphylaxis action plan.

Keywords

IgE; mast cell; allergy; tryptase; anaphylaxis

INTRODUCTION

Anaphylaxis is a life-threatening reaction with respiratory, cardiovascular, cutaneous, or gastrointestinal manifestations resulting from exposure to an offending agent, usually a food, insect sting, medication, or physical factor. It causes approximately 1,500 deaths in the United States annually.^{1,2} Occasionally, anaphylaxis can be confused with septic or other forms of shock, asthma, airway foreign body, panic attack, or other entities.^{3–5} Urinary and serum histamine levels and plasma tryptase levels drawn after onset of symptoms may assist in diagnosis as well as assessment of platelet activating factor.^{3,6,7} Prompt treatment of anaphylaxis is critical, with intramuscular epinephrine, recumbent positioning and

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intravenous fluids remaining the mainstays of acute management.^{4,8} Adjunctive measures include airway protection, antihistamines, glucocorticoids and beta-agonists.⁴ Patients should be observed for delayed or protracted anaphylaxis and instructed on how to initiate urgent treatment for future episodes.^{9,10}

A significant portion of the U.S. population is at risk for anaphylaxis and these reactions are under-recognized and frequently under treated.^{2,11} Anaphylaxis is mediated by immunoglobulin E (IgE), while anaphylactoid reactions are not.⁴ Because of their clinical similarities, the term anaphylaxis will be used to refer to both conditions. In keeping with the theme of this collection, we will focus on aspects of anaphylaxis primarily related to outpatient emergencies: symptoms, treatment and management with less discussion devoted to diagnostic testing and consideration of differential diagnosis.

SYMPTOMS

Anaphylaxis may include any combination of common signs and symptoms (Table I).⁴ Cutaneous manifestations of anaphylaxis, including urticaria and angioedema, are by far the most common, occurring in 62% to 90% of reported cases.¹² Nonetheless, the absence of cutaneous symptoms speaks against a diagnosis of anaphylaxis but does not rule it out. Severe episodes characterized by rapid cardiovascular collapse and shock can occur without cutaneous manifestations.¹³ The respiratory system is also commonly involved, producing symptoms such as dyspnea, wheezing, and upper airway obstruction from edema.¹² Gastrointestinal manifestations (e.g., nausea, vomiting, diarrhea, abdominal pain) and cardiovascular manifestations (e.g., dizziness, syncope, hypotension) affect about one third of patients.¹⁴ Headache, rhinitis, substernal pain, pruritus, and seizure occur less frequently.¹² In addition, it is important to note that anaphylaxis can present with unusual manifestations, such as syncope without any further sign or symptom.¹⁵ The essentials of the history are listed in Box 1.

Symptom onset varies widely but generally occurs within seconds or minutes of exposure.^{2,5} A novel IgE antibody to a mammalian oligosaccharide has been discovered that is associated with 2 distinct forms of anaphylaxis, an immediate onset of an event to cetuximab and a delayed onset of anaphylaxis, usually occurring 3 to 6 hours after the ingestion of mammalian food products (eg, beef and pork).^{16,17} This red meat allergy has been associated with tick bites and appears to have significant and expanding regional prevalence in the southern and eastern U.S.¹⁸ Anaphylaxis can be protracted, lasting for more than 24 hours, or recur after initial resolution.¹⁰

OUTPATIENT-BASED TREATMENT

Plan for appropriate office response to anaphylaxis by (1) educating staff and patients, (2) preparing an anaphylaxis emergency cart (Table II), and (3) developing an office action plan for anaphylaxis management to maintain proficiency in anaphylaxis management.⁴ At the onset of anaphylaxis, (1) administer epinephrine intramuscularly in the mid-outer thigh; (2) remove the inciting allergen, if possible (eg, stop an infusion); (3) quickly assess airway, breathing, circulation, and mentation and summon appropriate assistance from staff

members; and (4) start, if needed, cardiopulmonary resuscitation and summon EMS.⁴ After administering epinephrine, notify EMS for patients having severe anaphylaxis and/or patients not responding to epinephrine.

Apart from the administration of medications, it is important to remember to place and maintain patients in a supine position, unless the respiratory compromise contraindicates it, to prevent or to counteract potential circulatory collapse.⁴ Place pregnant patients on their left side. As soon as possible after administering epinephrine and appropriate positioning, establishing intravenous access is essential for maintaining hemodynamic stability. Consider initiating supplemental oxygen to select patients in anaphylaxis. Rapid and ongoing assessment of the patient's airway status should be made a priority and maintain airway patency using the least invasive but effective method (eg, bag-valve-mask).^{4,19} Intravenous fluid replacement should be initiated with normal saline for patients with circulatory collapse and for patients who do not respond to intramuscular epinephrine.^{8,20} In addition to epinephrine administered for anaphylaxis, consider administering a nebulized beta₂-agonist (eg, albuterol) for signs and symptoms of bronchospasm.⁴ In patients receiving beta-adrenergic blocking agents, administer glucagon if they have not responded to epinephrine.²¹

Administration of H1 and H2 antihistamines or corticosteroids should not replace epinephrine as initial therapy for anaphylaxis.⁸ In fact, these agents are considered optional or adjunctive therapy. Individualize the duration of direct observation and monitoring after anaphylaxis but provide longer periods of observation for those patients with a history of risk factors for severe anaphylaxis (eg, asthma, previous biphasic reactions, or protracted anaphylaxis) for at least 4 to 8 hours or initiate transfer of such patients via EMS as soon as possible.^{9,10}

Staff and patients must recognize that any significant change in clinical status or the onset or increase of symptoms, however subtle, which occurs immediately after in-office immunotherapy or diagnostic or therapeutic procedures, or possible ingestion of a known food or medication allergen should be considered anaphylaxis.¹¹ Anaphylaxis must be viewed as a serious allergic reaction that is rapid in onset and may cause death for which the only treatment is epinephrine.^{8,9} The anaphylaxis cart (Table II) must be inventoried on a regular basis (eg, every 3 months) and kept up to date by using the detailed listing of medications, supplies, and equipment as a checklist.

All practice settings where there is a risk for anaphylaxis should collaborate with their nursing staff to develop a customized written protocol for the management of anaphylaxis in the office. Several action plans for anaphylaxis management in the office setting have been published and a revised office-based anaphylaxis treatment protocol is presented in Table III.⁴ The anaphylaxis action plan should follow evidence-based guidelines and should provide a detailed stepwise approach based on symptoms and the patient's response to treatment. It can take the form of an algorithm, a table, a graph, or even a combination of these, but it must be easy to read and follow during an emergency.¹⁹ Ideally, it would include assigned roles for each staff member, by position or name, to be followed during anaphylaxis management. Once developed, it should be posted in all patient care areas of the

office and with the emergency supplies for ready access. The successful management of anaphylaxis requires that office staff must immediately activate the response team and expeditiously deliver appropriate treatment. This can be accomplished with frequent (eg, periodic), organized, mock anaphylaxis drills in which all staff members, clerical and medical, are required to participate.¹⁹ Maintaining clinical proficiency with anaphylaxis management involves certification in basic cardiopulmonary resuscitation and, ideally, advanced life support to insure the proper skillset for treatment of refractory anaphylaxis, including airway management, cardiac compressions, venous and intraosseous access, and parental medication calculation and delivery.^{19,22}

The initial assessment and treatment of the patient in anaphylaxis involves several critical steps that should be started concomitantly (Table III).^{4,19,22} Urgent treatment is based on the finding that there is often a very short time (eg, 5 minutes for an iatrogenic intravenously administered allergen such as an antibiotic and 30 minutes for food-induced anaphylaxis) from the onset of mild symptoms to respiratory or cardiac arrest.^{23–27} Although removal of the inciting allergen is ideal, this will rarely apply in the office setting because parental or ingestion will usually have been completed before the onset of symptoms. However, with medication infusions or oral challenges with food or medications, the procedure should be stopped as soon as signs and symptoms of even mild anaphylaxis are noted.^{28,29}

The first member of the office staff to recognize that the patient is experiencing anaphylaxis must be prepared to evaluate the airway, breathing, circulation, and mentation.¹⁹ If the patient has moderate to severe anaphylaxis or is showing signs and symptoms of impending cardiopulmonary arrest, EMS must be summoned immediately in addition to all available office medical staff.^{4,12} Cardiopulmonary resuscitation should be started immediately in the event of cardiopulmonary arrest, with emphasis on adequate chest compressions without interruption (Table IV).^{19,22} Ventilations can be given once there are 2 medical staff members at the patient's side.²²

For imminent or established cardiopulmonary arrest, rapidly establish venous access and administer an intravenous bolus dose of epinephrine because ventricular arrhythmias have been reported after epinephrine administration.^{19,22,30} For adults, the dose is 1 mg intravenously (as a 1:10,000 dilution).^{31,32} This can be repeated every 3 to 5 minutes as cardiopulmonary resuscitation is continued.^{22,31–33} If the intravenous route is not available, epinephrine can be given by endotracheal administration if the advanced airway is in place (adult dose is 2–2.5 mg of 1:1,000 diluted in 5–10 mL of sterile water).^{19,22} The treatment of anaphylaxis is, at best, based on indirect and observational studies and primarily on consensus.¹² Observational studies and analysis of near-fatal and fatal reactions have shown that prompt and decisive treatment of any systemic reaction, even a mild one, with epinephrine prevents progression to more severe symptoms.^{5,34} In contrast, delayed administration of epinephrine is often believed to be the major contributing factor to fatalities.^{5,34} Anaphylaxis guidelines are in agreement that epinephrine should be administered intramuscularly into the lateral thigh.^{4,5,14} Published studies on epinephrine pharmacokinetics in patients not in anaphylaxis have shown that intramuscular administration in the vastus lateralis muscle produces a more rapid rate of increase in blood epinephrine levels than subcutaneous or intramuscular administration in the deltoid

muscle.^{35,36} Unfortunately, there are no studies evaluating the pharmacokinetics of a subcutaneous injection in the lateral thigh. The adult dose of 1:1,000 epinephrine is 0.2 to 0.5 mL, whereas the pediatric dose is 0.01 mg/kg, with a maximum of 0.3 mg.¹⁹ A higher dose (eg, 0.5 mL) within the recommended dose range should be considered in patients with severe anaphylaxis.^{4,12,19} If there has not been significant improvement in symptoms, then the dose can be repeated approximately every 5 to 15 minutes, as the physician deems to be necessary. It has been shown that a repeat dose is required up to 35% of the time.^{37,38} Monitor and record the patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation at frequent and regular intervals.¹⁹ Start frequent oxygen saturation measurement, start continuous noninvasive monitoring, and obtain an electrocardiogram, if available.

There is universal agreement that most patients should be placed in a supine position during anaphylaxis.^{4,5,12,14,19,39,40} However, whether to elevate the legs is controversial.^{4,41,42} Although some guidelines continue to recommend the Trendelenburg position (feet are elevated 15–30° higher than the head) for the management of shock, the American Heart Association and the American Red Cross in a 2010 consensus document concluded that there is insufficient evidence to support routine use of the Trendelenburg position in patients with shock.^{30,43} If the patient is having respiratory difficulty, consider having the patient sit up.³⁰ In a retrospective study of 10 anaphylactic fatalities, there appeared to be an association with fatality when there was a change in position from a supine to an upright or standing position during anaphylaxis.⁴⁴ Although the investigators recommended maintaining a supine position during anaphylaxis, they did not recommend the Trendelenburg position.⁴⁴

Administration of oxygen is the second most important therapeutic intervention, second only to epinephrine administration, for the treatment of anaphylaxis and should be considered for all patients experiencing anaphylaxis regardless of their respiratory status.^{4,5,12,14,20,40} It is imperative to administer oxygen for any patient with respiratory or cardiovascular compromise and to patients who do not respond to the initial treatment with epinephrine.¹⁹ Oxygen up to 100% should be administered at a flow rate of 6 to 10 L/min through a facemask. Ideally, oxygen saturation should be monitored and kept at 94% to 96% by oximetry.¹⁹ In most office settings, bag-valve-mask ventilation will be the method of choice to support ventilation in the event of respiratory failure or arrest.^{4,12} It is most effective when 2 individuals can support the airway.²² One person opens the airway with the head-tilt and chin-lift maneuver and seals the mask to the face, covering the nose and mouth.²² The second person squeezes the bag and the 2 rescuers look for adequate chest rise.²² It is recommended that approximately 600 mL of tidal volume for 1 second using an adult (1–2 L) bag be delivered.^{22,30} Supplementary oxygen at a flow rate of 10 to 12 L/min should be used.³⁰ Two breaths are delivered during a 3- to 4-second pause after every 30 chest compressions.²² An oropharyngeal airway can aid in the delivery of adequate ventilation in an unconscious patient with no cough or gag reflex.³⁰ The training, skill, and experience of the physician should guide the selection of the most appropriate airway for the patient.²² When the provider can adequately ventilate the patient using the bag-valve-mask, there is no evidence that the use of advanced airway measures improves survival rates of out-of-hospital cardiac arrest.^{22,30,43} The incidence of complications is unacceptably high when

endotracheal intubation is performed by an inexperienced provider or monitoring of the tube is inadequate.¹⁹ Use of a supraglottic airway (eg, laryngeal mask airway), esophageal-tracheal tube (Combitube), or laryngeal tube is believed to be a reasonable alternative to the endotracheal intubation and its use can be accomplished without interruption of chest compressions.³⁰ Upper airway obstruction (eg, severe laryngeal edema) is an absolute contraindication for endotracheal intubation.³⁰ It has been suggested that inhaled epinephrine or intratracheally administered epinephrine might decrease oropharyngeal edema, making airway management less difficult.¹⁹ The use of cricothyrotomy should be reserved for life-and-death situations when obstruction (eg, angioedema) above the larynx prevents adequate ventilation, even with the endotracheal tube.^{19,41}

Hypotension should be treated with rapid fluid replacement using 1 to 2 L of 0.9% normal saline, infused rapidly (eg, 5–10 mL/kg within the first 5 minutes for an adult and up to 30 mL/kg in the first hour for children).^{22,30,45} Large-bore (14- to 16-gauge for adults) intravenous catheters should be used. For the normotensive patient in anaphylaxis, starting NL saline at an appropriate maintenance rate for weight (eg, 125 mL/h for adults) to maintain venous access for medications and/or rapid fluid replacement is often unnecessary.¹⁹ Intravenous administration of epinephrine will rarely be necessary in the office setting and should be administered in a monitored setting with a programmable infusion pump to titrate appropriately.^{4,12,19,40} However, if there is no response to multiple injections of intramuscular epinephrine and intravenous fluid replacement in combination with a delay in EMS response, prolonged transport, or cardiopulmonary arrest and resuscitation, then intravenous epinephrine might be needed.^{19,30} There is no established dosage or regimen for intravenous epinephrine in anaphylaxis.^{4,8,12,20,40} However, a prospective study demonstrated the efficacy of a 1:100,000 solution of epinephrine intravenously by infusion pump at the initial rate of 2 to 10 mg/min titrated up or down depending on the clinical response or epinephrine side effects.⁴⁶ If an infusion of epinephrine is started in the office setting, then monitor by available means (eg, every-minute blood pressure and pulse and electrocardiographic monitoring, if available) and be prepared to treat ventricular arrhythmias.^{4,12,19,22,30} Other vasopressors (eg, dopamine and vasopressin) have been suggested as alternative agents to epinephrine for treatment of refractory hypotension. However, there are no controlled studies that have evaluated the efficacy of these drugs in the treatment of anaphylaxis.^{30,43}

Cases of unusually severe or refractory anaphylaxis (paradoxical bradycardia, profound hypotension, and severe bronchospasm) have been reported in patients receiving beta-adrenergic blockers.^{21,47} These systemic effects also have been documented with use of ophthalmic beta-blockers.⁴⁸ Greater severity of anaphylaxis observed in patients receiving beta-blockers might relate in part to a blunted response to epinephrine administered to treat anaphylaxis.^{4,12} Epinephrine administered to a patient taking a beta-blocker can produce unopposed alpha-adrenergic and reflex vagotonic effects, possibly leading to hypertension and the risk of cerebral hemorrhage.⁴¹ In patients receiving beta-blockers, increased propensity not only for bronchospasm but also for decreased cardiac contractility with perpetuation of hypotension and bradycardia is possible. There are no epidemiologic studies that have indicated that anaphylaxis occurs more frequently in patients receiving beta-blockers.^{49,50} Use of selective beta₁-antagonists does not lower the risk of anaphylaxis

because β_1 - and β_2 -antagonists can inhibit the beta-adrenergic receptor.¹² If epinephrine is ineffective in treating anaphylaxis in patients taking beta-blockers, then glucagon administration might be necessary. Glucagon can reverse refractory bronchospasm and hypotension during anaphylaxis in patients on beta-blockers by activating adenylyl cyclase directly and bypassing the beta-adrenergic receptor. The recommended dosage for glucagon is 1 to 5 mg administered intravenously over 5 minutes and followed by an infusion at 5 to 15 mg/min titrated to clinical response.^{4,12,30} Protection of the airway is important because glucagon can cause emesis and risk aspiration in severely drowsy or obtunded patients. Placement in the lateral recumbent position provides sufficient airway protection for most of these patients.^{4,12,19}

Antihistamines, H1 and H2, should be considered second-line drugs in the management of anaphylaxis because there is no direct evidence to support their use in the treatment of anaphylaxis.^{3–5,12,14,40} The use of the H1 antihistamines is extrapolated mainly from their use in other allergic diseases (eg, urticaria or allergic rhinitis) in which they relieve itching, urticaria, flushing, sneezing, and rhinorrhea.¹² However, they do not prevent or treat upper airway obstruction or hypotension. The frequent and at times fatal error that is made by professionals and patients is to delay the administration of epinephrine while waiting for the antihistamines to relieve symptoms.^{8,20,22,39,51–54} When administered as adjunctive treatment for severe anaphylaxis, only sedating antihistamines (eg, diphenhydramine) are available for intravenous administration. The dose for diphenhydramine is 25 to 50 mg in adults administered intravenously over 10 to 15 minutes.¹⁹ When given orally, a low or nonsedating antihistamine (eg, fexofenadine) is preferred over a sedating antihistamine (eg, diphenhydramine or chlorpheniramine) to avoid somnolence and impairment of cognitive function and the decreased ability to describe symptoms.¹⁹ If administered parentally, then the dose of the H2 antihistamine ranitidine is 1 mg/kg for adults and can be administered intramuscularly or intravenously (with slow infusion) because these administration methods have the same onset of action.^{12,19}

The use of corticosteroids has no role in the acute management of anaphylaxis.^{22,30} The purported evidence that they produce a decrease of biphasic or prolonged reactions is not supported by strong evidence.^{8–10} Their use and dosage are extrapolated from those used for acute asthma. When administered, the intravenous or oral dosage often recommended is 1 to 2 mg/kg per dose up to 125 mg of methylprednisolone or an equivalent formulation.¹⁹ Patients who have complete resolution of symptoms after treatment with epinephrine do not need to be prescribed antihistamines or corticosteroids thereafter.⁴

The duration of direct observation and monitoring after an episode of anaphylaxis must be individualized and based on the severity and duration of the anaphylactic event, response to treatment, pattern of previous anaphylactic reactions (eg, history of protracted or biphasic reactions), medical comorbidities, patient reliability, and access to medical care.^{2,4,12,19,20,40} Patients with moderate to severe anaphylaxis should be observed for a minimum of 4 to 8 hours.^{4,12,19} Mild anaphylactic symptoms that occur in a medical setting (eg, office-based allergy injection) and that rapidly resolve with treatment usually will require a relatively shorter period of observation. A longer observation, including possible hospital admission, should be considered when (1) risk factors for more severe anaphylaxis (eg, history of severe

asthma) are present, (2) the allergens have been ingested, (3) more than 1 dose of epinephrine is required, (4) pharyngeal edema is present, and (5) severe or prolonged symptoms (eg, prolonged wheezing or hypotension) are noted.^{4,12,14,19,40,55,56}

FOLLOW-UP EDUCATION

As in many diseases, patient education is vital; however, due to the potential for rapidly progressing, life-threatening reactions, proper and thorough patient education is a critical component in the management of anaphylaxis. Auto-injectable epinephrine should be prescribed for patients who have experienced an anaphylactic reaction and for those at increased risk for anaphylaxis. The patient must be instructed in the administration of epinephrine. Patients should be encouraged to fill this prescription immediately because up to 23% can experience a return of symptoms as a biphasic reaction, usually within 10 hours after the resolution of the presenting symptoms of anaphylaxis.¹⁰ Two auto-injectors should be provided because up to 30% of patients who develop anaphylaxis will require more than 1 dose of epinephrine.^{2,8,9,34} In the U.S., auto-injectors are available in only 2 doses, 0.15 and 0.30 mg. The preferred adult dose is 0.30 mg. Although the initial anaphylaxis action plan can be provided at the point of care (eg, emergency department or primary care office), the permanent anaphylaxis action plan should be developed by the allergist working with the patient, the primary care physician, other members of the interdisciplinary clinical team, and the school, when appropriate. Education on the triggers and early signs and symptoms of anaphylaxis must be a structured, reoccurring, and scheduled process for all office staff, medical and clerical, and patients. The patient's education on anaphylaxis should start at the time of the new patient visit for all patients who present with signs and symptoms of anaphylaxis and for all patients who will be undergoing a diagnostic or treatment procedure that could result in anaphylaxis (eg, chemotherapy infusion).

FUTURE CONSIDERATIONS/SUMMARY

Patients with anaphylaxis should be assessed and treated as rapidly as possible, as respiratory or cardiac arrest and death can occur within minutes. Anaphylaxis appears to be most responsive to treatment in its early phases, before shock has developed, based on the observation that delayed epinephrine injection is associated with fatalities. Epinephrine is life-saving in anaphylaxis. It should be injected as early as possible in the episode in order to prevent progression of symptoms and signs. There are no absolute contraindications to epinephrine use, and it is the treatment of choice for anaphylaxis of any severity. Patients successfully treated for anaphylaxis should be discharged with a personalized written anaphylaxis emergency action plan, an AIE, written information about anaphylaxis and its treatment, and a plan for further evaluation. Consultation with an allergist can help (1) confirm the diagnosis of anaphylaxis; (2) identify the anaphylactic trigger through history, skin testing, and RAST; (3) educate the patient in the prevention and initial treatment of future episodes; and (4) aid in desensitization and pretreatment when indicated as well as, for some allergens, immunomodulation is also available to reduce the risk.^{4,12}

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Key Points

- Anaphylaxis is a severe allergic reaction that can be rapidly progressive and fatal. In instances where the triggering allergen is not known, establishing the etiology of anaphylaxis is pivotal to long-term risk management.
- There is no current diagnostic test that will adequately predict the severity of the next episode of anaphylaxis: mild events can be followed by life-threatening reactions.
- Medications and insect stings are the most common causes of anaphylaxis in adults, while foods are more common in children.
- At the onset of anaphylaxis, (1) administer epinephrine intramuscularly in the mid-outer thigh; (2) remove the inciting allergen, if possible; (3) quickly assess airway, breathing, circulation, and mentation, and summon appropriate assistance from staff members; and (4) start, if needed, cardiopulmonary resuscitation and summon emergency medical services (EMS).

Box 1**Pertinent history taking in evaluation of a patient presenting with anaphylaxis**

- Detailed history of ingestants (foods, drinks/medications) taken within 8 h before the event
- Activity in which the patient was engaged at the time of the event
- Location of the event (home, school, work, indoors/outdoors)
- Exposure to heat or cold
- Any related sting or bite (significant tick or chigger bites within prior 4 weeks)
- Time of day or night
- Duration of event
- Recurrence of symptoms after initial resolution
- Exact nature of symptoms (eg, if cutaneous, determine whether flush, pruritus, urticaria, or angioedema)
- In a woman, the relation between the event and her menstrual cycle
- Was medical care given and what treatments were administered
- How long before recovery occurred and was there a recurrence of symptoms after a symptom-free period
- The perceived level of stress by the patient prior to the episode
- Any recent illness or infection
- Pertinent travel history
- Description of any prior similar episodes
- Return of mild symptoms with exposure to heat, exercise or alcohol ingestion

Adapted from Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis--a practice parameter update 2015. *Ann Allergy Asthma Immunol* 2015;115(5):341–84; with permission.

Table I

Signs and symptoms of anaphylaxis

Signs and Symptoms	Frequency (%)
Urticaria, angioedema	60–90
Upper airway edema	50–60
Flush	45–55
Dyspnea, wheeze	45–50
Dizziness, syncope, hypotension	30–35
Nausea, vomiting, diarrhea, cramping abdominal pain	25–35
Rhinitis	15–20
Headache	10–15
Chest pain	3–7
Pruritus without rash	2–5
*Palmar erythema and pruritus	35–45

* Specifically related to patients with IgE to galactose-alpha-1,3-galactose mammalian meat allergy.

Data from Refs^{2, 4, 12, 14, 51}

Table II

Essential elements in an outpatient office-based emergency cart to treat anaphylaxis

Stethoscope and Sphygmomanometer
Tourniquets
Syringes
IV Catheters (e.g. 14–18 gauge)
Aqueous Epinephrine HCL (1:1000 w/v) or equivalent auto-injectable epinephrine device
Airway support devices (e.g. endotracheal tubes, resuscitator bag)
Portable oxygen supply
Oral and injectable antihistamines (both H1 and H2)
Corticosteroids for intramuscular or intravenous injection
Ammonia inhalant pad or breakable capsule
IV Fluids (e.g. saline)
Glucagon kit for patients on beta-blockers
Also suggested: infusion pump, external defibrillator

Table III

Treatment of anaphylaxis in the physician's office

Immediate measures		
1	Allergen	Remove the inciting allergen, if possible
2	Airway	Assess airway, breathing, circulation, and orientation; if needed, support the airway using the least invasive but effective method (eg, bag-valve-mask)
3	Cardiopulmonary resuscitation	Start chest compressions (100/min) if cardiovascular arrest occurs at any time
4	Epinephrine	Inject epinephrine 0.3–0.5 mg intramuscularly in the vastus lateralis (lateral thigh)
5	Get help	Summon appropriate assistance in office
6	Position	Place adults and adolescents in recumbent position; place pregnant patient on left side
7a	Oxygen	Give 8–10 L/min through facemask or up to 100% oxygen as needed; monitor by pulse oximetry if available
7b	Epinephrine	Repeat intramuscular epinephrine every 5–15 min for up to 3 injections if the patient is not responding
7c	EMS	Activate EMS (call 911 or local rescue squad) if no immediate response to first dose of IM epinephrine or if anaphylaxis is moderate to severe
7d	IV fluids	Establish intravenous line for venous access and fluid replacement; keep open with 0.9 NL saline, push fluids for hypotension or failure to respond to epinephrine using 5–10 mg/kg as quickly as possible and up to 1–2 L in the first hour
Additional measures		
8	Albuterol	Consider administration of 2.5–5 mg of nebulized albuterol in 3 mL of saline for lower airway obstruction; repeat as necessary every 15 min
9	Glucagon	Patients on beta-blockers who are not responding to epinephrine should be given 1–5 mg of glucagon IV slowly over 5 min because rapid administration of glucagon can induce vomiting
10	Epinephrine (infusion)	For patients with inadequate response to IM epinephrine and IV saline, give epinephrine by continuous infusion by micro-drip in office setting (infusion pump in hospital setting); add 1 mg (1 mL of 1:1,000) of epinephrine to 1,000 mL of 0.9 NL saline; start infusion at 2 mg/min (2 mL/min = 120 mL/h) and increase up to 10 mg/min (10 mL/min = 600 mL/h); titrate dose continuously according to blood pressure, cardiac rate and function, and oxygenation
11	Intraosseous access	If IV access is not readily available in patients experiencing refractory anaphylaxis, obtain intraosseous access for administration of IV fluids and epinephrine infusion
Refractory anaphylaxis		
12	Advanced airway management	Use supraglottic airway, endotracheal intubation, or cricothyroidotomy for marked stridor, severe laryngeal edema, or when ventilation using the bag-valve-mask is inadequate and EMS has not arrived
13	Vasopressors	Consider administration of dopamine (in addition to epinephrine infusion) if patient is unresponsive to above treatment; this will likely be in the hospital setting where cardiac monitoring is available
Optional treatment (efficacy not established)		
14	H ₁ anti-histamine	Consider giving 25–50 mg of diphenhydramine intravenously; use 10 mg of cetirizine if an oral antihistamine is administered; once there is full recovery, there is no evidence that this medication needs to be continued
15	Corticosteroids	Administer 1–2 mg/kg up to 125 mg per dose, IV or PO, of methylprednisolone or an equivalent formulation; once there is full

		recovery, there is no evidence that this medication needs to be continued
Observation and monitoring		
16	Observation in hospital	Transport to emergency department by EMS for further treatment and observation for ~8 h
17	Observation in office	Observe in office until full recovery + additional 30–60 min for all patients who are not candidates for EMS transport to emergency department
Discharge management		
18	Education	Educate patient and family on how to recognize and how to treat anaphylaxis
19	Auto-injectable epinephrine	Prescribe 2 doses of auto-injectable epinephrine for patients who have experienced an anaphylactic reaction and for those at risk for severe anaphylaxis; train patient, patient provider, and family on how to use the auto-injector
20	Anaphylaxis action plan	Provide patients with an action plan instructing them on how and when to administer epinephrine

EMS - emergency medical services; IV – intravenous; IM – intramuscular; PO – oral; NL – normal

Adapted from Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis--a practice parameter update 2015. *Ann Allergy Asthma Immunol* 2015;115(5):341–84; with permission.

Table IV

Summary of adult cardiac life support recommendations

Basic cardiopulmonary resuscitation is C-A-B (compressions-airway-breathing)		
Check for pulse	Take for a maximum of 10 seconds	
Chest compressions	Push hard and push fast on the center of the chest <ul style="list-style-type: none"> • Maintain rate of 100/min • Compress chest 5 cm with each downstroke • Allow complete chest recoil between compressions • Minimize frequency and duration of any interruptions 	
Ventilations	Perform only if 2 rescuers are present <ul style="list-style-type: none"> • Avoid excessive ventilation - just enough to confirm chest rise • Deliver ventilation over 1 second • If 3 rescuers available: 1 for compressions, 2 for bag-valve-mask and rotate positions every 2 min 	
Compression/ventilation ratio	30/2	
Defibrillation	Single defibrillation using highest available energy in adults	Adult: 200 J
Phases of resuscitation in cardiac arrest	Electrical phase 0–4 min	Defibrillate, compressions
	Hemodynamic phase 4–10 min after arrest	Defibrillate, compressions
	Metabolic phase >10 min after arrest	Few patients survive

Data from Refs^{4, 12, 19, 22}