

Recognizing and managing acute anaphylaxis

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Anaphylaxis is a severe systemic allergic reaction resulting from exposure to an allergen. The reaction is mediated in most cases by immunoglobulin E (IgE). The reaction has a rapid

onset and can lead to death. An estimated 50 to 2,000 episodes per 100,000 persons occur (or a lifetime prevalence of 0.05 to 2%).¹ Approximately 2% of the population is affected.¹ Numerous allergy-producing substances are known to precipitate an anaphylactic response (see *Anaphylaxis triggers*). Food is the most common cause, especially in young children and accounts for 30% of fatal cases; the majority are due to peanuts, tree nuts, fish, or shellfish.²⁻⁴

Patients with asthma are at an increased risk for food allergies, especially when the asthma is severe or uncontrolled.^{3,5} Other common causative agents are medications and insect stings; penicillin is the most common medication that can pre-

cipitate an anaphylactic response.² Although the true cross-reactivity to cephalosporins is unknown, the rate appears low. Anaphylaxis after insect stings occurs in 3% of stung adults and 1% of stung children.² Reactions can be very severe; therefore, nurse practitioners' (NPs') understanding of the causes, pathophysiology, presentation, and emergent treatment is essential to manage and prevent potentially fatal events.

■ Pathophysiology

Two distinct mechanisms are responsible for the pathogenesis of anaphylaxis: the IgE-dependent reaction and the IgE-independent reaction.⁶ Most anaphylactic reactions are IgE-dependent. Exposure to the

Anaphylaxis triggers^{2,5,9,10,13,20}

IgE-dependent immunologic mechanism

- Foods (such as peanut, tree nut, seafood, milk, soy, egg, vegetable, fruit, sesame seed)
- Insect (stinging venoms or saliva from biting)
- Other venoms (such as jellyfish, scorpions, snakes)
- Natural rubber latex
- Medications (such as penicillin and cephalosporins)
- Biologic materials (such as allergens, vaccines, hormones, onabotulinumtoxinA [Botox])
- Dextran and iron dextran
- Food additives (such as spices, insect-derived colorants, and vegetable gums)
- Inhalants (such as animal dander and grass pollen)
- Seminal fluid
- Occupational allergens

IgE-independent

(formerly called anaphylactoid reactions)

- Physical factors (such as exercise, cold/heat, and sunlight/UV radiation)
- Ethanol
- Medications (such as opioids, muscle relaxants, aspirin, nonsteroidal anti-inflammatory agents)
- Immunoglobulins
- Radiographic contrast media
- Idiopathic

Diagnostic criteria for anaphylaxis¹¹

Classic anaphylaxis is likely when any 1 of the 3 criteria is present

- (1) Acute illness onset (minutes to hours with involvement of skin/mucosal tissue (hives, pruritus, swelling) **AND** Airway compromise (dyspnea, stridor, wheezing/bronchospasm, reduced peak expiratory flow) **AND/OR** Reduced blood pressure (BP) or associated symptoms (hypotonia, syncope, incontinence)
- (2) Two or more of the following after known allergen exposure (minutes to hours)
 - Skin/mucosal tissue symptoms
 - Airway compromise
 - Reduced BP or associated symptoms
 - Gastrointestinal symptoms (such as abdominal pain, vomiting)
- (3) Hypotension after known allergen exposure (minutes to hours) Infants/children: low systolic BP (age-specific*) or > 30% drop in systolic BP Adults: systolic BP < 90 mm Hg or > 30% drop from baseline

*low systolic BP for children is defined as <70 mm Hg from 1-12 months of age, <70 mm Hg + [2 x age] from 1-10 years, and <90 mm Hg from 11-17 years

Reprinted from Journal of Allergy and Clinical Immunology, 117, Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium, p 391-397, (2006), with permission from Elsevier.

allergen initiates an IgE-mediated activation of mast cells and circulating basophils. On initial exposure to the antigen, specific IgE antibodies are synthesized by lymphocytes and plasma cells. Portions of these antibodies fix themselves to mast cell surfaces and circulating basophils. The IgE-bearing mast cells reside primarily in cutaneous, mucosal, and submucosal surfaces. The antigen binds to the IgE antibodies and triggers a degranulation of mast cells and basophils. Both release mediators, such as histamine, prostaglandin, leukotrienes, platelet-activating factor (PAF), and tryptase.^{7,8} Histamine, tryptase, and bradykinins cause inflammation and increased vascular permeability. Histamine, prostaglandins, and leukotrienes cause bronchial smooth muscle contraction.^{6,9} Initial exposure to the antigen may not always produce a reaction; however, subsequent exposure will trigger the process.

Other immunologic mechanisms not involving IgE can also lead to anaphylaxis. Although not entirely understood in humans, these mechanisms may include IgG complexes and activation of coagulation and complement systems. IgG receptors can activate macrophages to release PAF, which, in turn, activates mast cells.⁶ Other proposed mechanisms may contribute, including T-cell activation, cytotoxicity, and neuropeptide release.¹⁰ Mast cells and basophils can be perturbed via nonimmune processes manifesting as an exercise-induced, cold exposure-induced, or opioid-induced episode.¹⁰ These reactions do not require previous exposure to an allergen.

■ Clinical presentation

History is critical in determining whether a patient has had anaphylaxis and the precipitating cause. Details to be gathered include time of occurrence, setting, any treatment given, duration, and all potential causes, including medications, foods, environment, and recent sexual activity. Past allergies should be elicited in addition to a history of any past anaphylactic episodes.

Classic diagnosis of anaphylaxis is highly likely when any one of 3 criteria is present.¹¹ (See *Diagnostic criteria for anaphylaxis*.) A drop in BP of more than 30% from baseline is termed anaphylactic shock.¹² The majority of anaphylactic reactions include cutaneous symptoms (pruritus, flushing, urticarial, angioedema), but these may be absent in up to 20% of cases.^{2,13} Other common manifestations include upper or lower airway obstruction (edema of the tongue, lip swelling, laryngeal edema, stridor, dyspnea, tachypnea, bronchospasm, wheezing), cardiovascular symptoms (hypotension, tachycardia, cardiac dysrhythmias, syncope, or presyncope), and

gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea). The more rapidly symptoms occur after exposure, the more likely the reaction is severe and life-threatening.² Some reactions can occur more than 30 minutes after exposure or may be biphasic. A biphasic reaction is one that can occur within 1 to 72 hours (most within 10 hours) after an initial occurrence.² Differential diagnoses, depending on symptom presenta-

sal edema.¹⁴ Additionally, epinephrine downregulates mast cell and basophil release of mediators of inflammation (histamine and tryptase).^{14,15} Initial epinephrine should be administered via the I.M. route in the lateral thigh based on evidence that this route and site produces the best absorption and shortest time to peak concentrations.^{16,17}

Fluid resuscitation is necessary—especially in patients with persistent hypotension—despite epinephrine administration. Increased vascular

Patients can experience biphasic reactions hours after an initial occurrence.² For most patients, a reasonable post-anaphylactic observation is 4 to 6 hours unless the symptoms were severe or refractory.⁹ In such cases, the patient should be hospitalized for a prolonged observation, since a biphasic reaction can occur within 1 to 72 hours.⁹ An extended observation period should be considered for patients who experience food-induced anaphylaxis, since biphasic reactions can occur in up to 25% of severe reactions from food.² Since no predictors exist for biphasic reactions, observation periods must be individualized. Factors such as home distance to emergency facilities, severity of the initial reaction, and treatment response must be considered in the decision. Data on the use of corticosteroids do not support their use acutely.^{18,19} Although no conclusive evidence exists concerning their use, a corticosteroid may be prescribed at discharge to help prevent a biphasic reaction.

Initial epinephrine should be administered via the I.M. route in the lateral thigh.

tion, include vocal cord dysfunction, panic attacks, vasovagal reactions, flushing episodes, postprandial syndromes (usually due to monosodium glutamate, sulfites, or scombroid fish) that can mimic anaphylaxis, cardiac dysrhythmias, pulmonary embolism, myocardial infarction, and acute foreign body airway obstruction.^{2,9,12,13}

■ Emergent management

A patient with confirmed or suspected anaphylaxis requires immediate management of airway, breathing, and circulation. If the patient presents to the primary care setting, immediate transport via emergency medical services (EMS) to an equipped ED should be secured. Immediate office management includes airway support, limiting allergen exposure if possible, and rapid administration of epinephrine (see *Pharmacologic management*).

Epinephrine, a direct-acting sympathomimetic agent, is considered the first-line medication of treatment and should be given as soon as possible. Epinephrine causes vasoconstriction, bronchodilation, and decreased muco-

permeability occurs and can leak up to 35% of the vascular volume into the periphery.⁶ Vasodilation leads to pooling. Adults may need rapid infusion of 1 to 2 liters of 0.9% sodium chloride, and children should receive up to 30 mL/kg during the first hour of treatment.² Supplemental oxygen should be administered, especially for patients with severe or prolonged reactions, or in patients with underlying hypoxemia or cardiac conditions.² Continuous pulse oximetry and/or arterial blood gases can be used as therapy guides, especially in high-risk patients.

Histamine₁ (H₁) receptor antihistamines and histamine₂ (H₂) receptor antagonists are second-line agents that are useful for controlling cutaneous manifestations. Although diphenhydramine is still used acutely due to route administration, second-generation H₁ non-sedating agents such as loratadine or cetirizine can also be used. These agents are particularly more tolerable to patients for use after discharge. An H₂ antagonist such as ranitidine can be added to the regimen for more effective control of symptoms.^{2,9}

■ Prevention

The patient should be counseled on treatment and to return immediately to the ED if late recurrence of symptoms occurs. If the precipitating allergen, such as food, medication, insect, or environment is known, the patient will need to be instructed to avoid exposure. In cases of food allergy, the patient needs instructions on reading food labels for ingredients and terms such as “may contain.” The importance of reporting all allergies, regardless of source, to healthcare providers at every encounter should be stressed. The Food Allergy and Anaphylaxis Network (<http://www.foodallergy.org>) has educational information and many resources for patients. The patient should be provided with a prescription for an epinephrine auto-injector (EpiPen, Adrenaclick, Auvi-Q, Twinject) and should also be instructed on its use. For pediatric

patients, the parent(s) need instructions on administration. School-age children should have a pen that is made available through the school nurse in case of any future event. A plan should be in place for accessing EMS and the nearest ED,²⁰ and the patient should be urged to carry allergy information by means of an ID card, bracelet, or engraved jewelry. The patient should follow up with the primary care provider after an occurrence. Referral to an allergist is warranted in cases of an unknown allergen, a severe reaction, or repeated episodes.

■ Moving forward

Anaphylaxis can be a life-threatening occurrence and requires early recognition, anticipation of deterioration, and aggressive treatment. Patient and family education by the NP aimed at antigen avoidance, early treatment if symptoms occur, an emergency plan, and allergy testing is important in preventing future occurrences. **NP**

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Pharmacologic management^{2,5,9,12,21,22}

Office

- Administer supplemental oxygen and maintain airway; prepare for emergency transport to ED.
- Limit further exposure to antigen if possible.
- Administer epinephrine 0.3 to 0.5 mg of 1:1,000 (pediatric dose 0.01 mg/kg—maximal dose 0.3 mg) I.M. in lateral thigh. Repeat dose every 5 to 10 minutes as needed.
- Place the patient on his or her back and elevate legs (if not in respiratory distress or vomiting).
- Treat bronchospasm with nebulized beta-agonist (albuterol) 2.5 mg/3 mL sterile 0.9% sodium chloride and inhaled anticholinergic (ipratropium bromide) if refractory.
- Administer I.V. fluids for volume replacement; 5 to 10 mL/kg (pediatric 10 mL/kg) in first 5 to 10 minutes.
- Continue monitoring vital signs and oxygenation.
- Administer H₁ antagonist diphenhydramine 25 to 50 mg (pediatric 1 to 2 mg/kg—maximal dose 50 mg) I.M., I.V., or P.O.

Tertiary care

- Support airway and continue oxygen. Prepare for intubation or emergency cricothyroidotomy.
- Epinephrine in above dosage; if persistent hypotension despite I.V. fluids and I.M. epinephrine; consider I.V. or continuous infusion.
- Aggressive fluid resuscitation with crystalloids or colloids.
- Vasopressors if refractory hypotension occurs.
- Consider glucagon if hypotensive and epinephrine ineffective or if the patient is taking a beta-blocker.
- Administer H₁ antagonist diphenhydramine 25 to 50 mg (pediatric 1 to 2 mg/kg—maximal dose 50 mg) I.M., I.V., or P.O.
- Consider H₂ antagonist; (off-label use) ranitidine 50 mg (pediatric 12.5 to 50 mg; 1 mg/kg) I.V. or I.M. (dose adjustments are needed for patients with creatinine clearance less than 50 mL/minute).

Discharge therapy

- Preloaded epinephrine auto-injector prescription (with instructions).
- H₁ antagonist (nonsedating).
- H₂ antagonist (ranitidine).
- Prednisone or methylprednisolone (if biphasic reaction anticipated).

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The author has disclosed that she has financial relationships related to this article.

DOI-10.1097/01.NPR.0000433082.01313.c2