

Recognizing and Managing Anaphylaxis

Anaphylaxis is a severe, life-threatening systemic allergic reaction, typically rapid in onset with airway, breathing, or circulatory problems, and often associated with skin and mucosal changes (Cardona et al., 2020). Anaphylaxis is usually caused by immunoglobulin E (IgE) mediated reactions to food, insect stings, or drugs. The goal of treatment is rapid recognition and administration of epinephrine to prevent respiratory or cardiac arrest (Campbell & Kelso, 2023).

Clinical Signs and Diagnosis (Campbell & Kelso, 2023; Cardona et al., 2020)

According to the World Allergy Organization, anaphylaxis is highly likely when one of the following two criteria is present:

1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (e.g., general hives, pruritis or flushing, swollen lips-tongue-uvula), and at least one of the following:
 - a. Respiratory compromise (e.g., dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow [PEF], increased labored breathing, persistent cough, cyanosis, hypoxemia)
 - b. Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], chest pain, dysrhythmias, syncope, incontinence)
 - c. Severe gastrointestinal symptoms (e.g., severe abdominal pain, repetitive vomiting), especially after exposure to non-food allergens
2. Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement

Common Anaphylaxis Triggers (Cardona et al., 2020)

Allergens (IgE-dependent immunologic mechanisms)

- Foods: peanuts, tree nuts, eggs, soybean, fish, shellfish, milk, seeds (sesame), fruit, wheat
- Insects: bee and wasp venom, fire ants, horse flies
- Latex
- Food additives: spices, coloring, vegetable gums
- Drugs: analgesics, antibiotics, biologics, chemotherapeutics, contrast media, proton pump inhibitors

Immunologic triggers (IgE-independent):

- Radiocontrast media (can occur with first exposure)
- Non-steroidal anti-inflammatory drugs
- Dextrans such as high molecular weight iron
- Biologic agents (e.g., some monoclonal antibodies)

Nonimmunologic mechanisms (direct mast cell activation)

- Physical factors such as exercise, cold, heat, sunlight
- Ethanol

- Medications such as opioids

Idiopathic anaphylaxis (no apparent triggers)

- Previously unrecognized allergen
- Mastocytosis/clonal mast cell disorder

Emergency Treatment in Adult Patients (Campbell & Kelso, 2023)

Patients with anaphylaxis should be assessed and treated as rapidly as possible; respiratory or cardiac arrest and death can occur within minutes.

1. Remove the cause, if possible, such as stopping the infusion of a suspected medication.
2. Call for help (e.g., resuscitation team if in a hospital or 911 in the community).
3. Epinephrine (1 mg/mL) is the most critical first treatment. There are no absolute contraindications to epinephrine in the setting of anaphylaxis and it is the treatment of choice for anaphylaxis of any severity.
 - a. Give 0.3 to 0.5 mg epinephrine intramuscularly (IM), preferably in the mid-outer thigh. Repeat every 5 to 15 minutes (or more frequently), as needed.
 - i. If an exact dose can be drawn up, use 0.01 mg/kg (maximum of 0.5 mg).
 - ii. If an autoinjector is used:
 1. Children weighing less than 25 kg, give 0.15 mg.
 2. Children weighing over 25 kg, give 0.3 mg.
 - b. Most patients respond to one, two, or at most, three doses.
 - c. IM injection is preferred over IV bolus because it is faster and has a lower risk of cardiovascular complications.
 - d. If symptoms do not improve, prepare IV epinephrine for continuous infusion.
 - i. Start IV epinephrine infusion at 0.1 mcg/kg/minute (range: 0.05 to 0.2 mcg/kg/minute) and titrate as needed.
4. Assess airway, breathing, circulation, mental status, skin and body weight.
 - a. Immediate intubation is indicated in the presence of impending airway obstruction from angioedema. Intubation should be performed by the most experienced clinician available.
5. Place patient in recumbent position, if tolerated, and elevate lower extremities. If there is significant upper airway swelling, keep the patient upright. If patient is vomiting, place patient semirecumbent with lower extremities elevated.
6. Oxygen: apply 15 L/minute via nonrebreather mask or up to 100% oxygen, as needed.
7. Rapid IV fluid bolus:
 - a. Insert two large-bore IV catheters, 14 to 16 gauge.
 - b. Begin immediately in patients who present with orthostasis, hypotension, or incomplete response to IM epinephrine.
 - c. Normal saline is the preferred solution.
 - d. Rapid infusion of 1 to 2 liters IV in the first minutes of treatment; repeat as needed. Large volumes of fluid (e.g., up to 7 liters) may be needed.
 - e. In normotensive adults, infuse normal saline at 125 mL/hour to maintain IV access.

8. Albuterol (salbutamol): for bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer, or 2 to 3 puffs by metered dose inhaler. Repeat as needed.
9. Monitoring:
 - a. Continuous noninvasive hemodynamic monitoring (blood pressure, heart rate, respiratory rate)
 - b. Oxygen saturation by pulse oximetry
 - c. Urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock.
 - d. *If cardiac arrest occurs, perform cardiopulmonary resuscitation with continuous chest compressions.*

Adjunctive Therapies (Campbell & Kelso, 2023)

- H1 antihistamine for relief of urticaria and itching only; these drugs do not treat upper or lower airway obstruction, hypotension or shock.
 - Cetirizine 10 mg IV, administer over 1 to 2 minutes, or
 - Diphenhydramine 25 to 50 mg IV, administer over 5 minutes, repeat every 4 to 6 hours as necessary
- H2 antihistamine: famotidine 20 mg IV, administer over 2 minutes
- Bronchodilators: for bronchospasm not responsive to epinephrine, albuterol or salbutamol should be administered by mouthpiece (or facemask) and nebulizer/compressor, as needed
- Glucocorticoids: may be beneficial for patients with severe symptoms requiring hospitalization or for those with known asthma and significant bronchospasm that persists after other anaphylaxis symptoms have resolved. Methylprednisone 125 mg IV (or 1 to 2 mg/kg/day) for 1 to 2 days; may be stopped without a taper

Treatment of Refractory Symptoms (Campbell & Kelso, 2023)

- Patients who do not respond to initial measures should be admitted to an intensive care unit immediately.
 - Epinephrine infusion: if no response to IM epinephrine and IV saline, administer epinephrine infusion (begin at 0.1 mcg/kg/minute), titrated to maintain blood pressure, cardiac rate and function, and oxygenation.
 - Vasopressors: may be required to maintain blood pressure in addition to IV crystalloids and epinephrine. All vasopressors should be administered by infusion pump and titrated carefully. Monitor blood pressure, cardiac function and oxygenation.
 - Glucagon: if a patient taking beta-blockers appears to be refractory to epinephrine, glucagon may be administered; may produce inotropic and chronotropic effects
 - Adult dosing is 1 to 5 mg slow IV bolus over five minutes followed by an infusion of 5 to 15 mcg/minute, titrated to effect.
 - Rapid administration may cause vomiting.

- Patients who do not respond promptly to IM epinephrine, require more than one dose of epinephrine, or received epinephrine only after a significant delay (greater than 60 minutes), should be admitted to the hospital for observation due to a risk for a biphasic response.
 - Biphasic anaphylaxis reactions involve an initial reaction followed by an asymptomatic period of one hour or more, and then a subsequent return of symptoms of anaphylaxis without additional exposure to the antigen. The timeframe between reactions can range from 1 hour up to 48 hours.

Discharge Care (Campbell & Kelso, 2023)

All patients who have experienced anaphylaxis should be sent home with the following:

- Anaphylaxis emergency action plan
- At least one epinephrine autoinjector or a prescription for two epinephrine autoinjectors; up to 20% of patients require more than one dose
- Printed information about anaphylaxis and its treatment
 - List of common symptoms and signs of anaphylaxis
 - Prompt recognition and self-injection of epinephrine
- Advice to follow up with an allergist, with a referral if possible

The mnemonic “**SAFE**” reminds clinicians of the 4 basic action steps for patients leaving the emergency department or hospital.

- **Seek support**
 - Remind the patient that:
 - They have experienced a life-threatening condition.
 - Symptoms may recur up to three days after initial onset.
 - They should self-inject epinephrine and call 911.
 - They are at risk for repeat episodes of anaphylaxis.
- **Allergen identification and avoidance**
 - Tell the patient to avoid the suspected cause, or If the cause is unclear, refer the patient to an allergist for further evaluation.
- **Follow-up for specialty care**
 - Have the patient follow up with their primary care provider and obtain a referral to an allergist for allergy testing and ongoing management.
 - Tell the patient that comorbidities such as asthma, other chronic pulmonary disease, and cardiovascular disease should be controlled as they can increase the risk of fatal anaphylaxis.
- **Epinephrine for emergencies**
 - Provide the patient with a prescription for two epinephrine autoinjectors and demonstrate use.
 - Provide written information on how to use the epinephrine autoinjector and proper injection technique.
 - Emphasize the importance of carrying the epinephrine autoinjector at all times.

- Advise patient to notify all family and friends of the risks of anaphylaxis, the causes, and how to administer epinephrine.

References:

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