Corridor Consult

Anaphylaxis

By Michael S Kaplan, MD

Report of a Case

A nurse, age 32 years, with a history of hives, angioedema of the lips and eyelids, and stridor after eating an avocado, eats a plum and within minutes experiences similar symptoms. Her condition partially responds to initial treatment with a fast-acting antihistamine and an injection of epinephrine, yet she experiences a second wave of symptoms as well as hypotension while being transported to the Emergency Department by paramedics.

This nurse has latex sensitivity that developed after several years of repeated exposure to latex gloves. She had subsequently developed a cross-sensitivity to foods associated with latex allergy, namely avocados and stone fruits (pitted) such as plums. Her anaphylaxis was compounded by the use of latex gloves and equipment during the paramedic transport. (Note: Currently the chances of this happening are low because the use of natural-rubber latex has been significantly reduced in the medical environment. However, previously sensitized health care workers need to be cautious.)

Scope

Data on the prevalence of the risk of anaphylaxis are limited. Calculations based on reported reactions in the United States range from approximately 3 million to 41 million individuals who have had a serious allergic reaction in their lifetime. Eleven million have experienced a life-threatening reaction.[1] Each year in the United States, 800 people have fatal anaphylactic reactions. This number may be an underestimate, because some cases of unexplained death or shock may in fact be due to anaphylaxis. Some patients do not present with the more obvious signs such as hives or respiratory distress, so their condition may go unrecognized and treatment may be delayed.

This review presents a working definition of anaphylaxis (See sidebar: A Working Definition of Anaphylaxis) and summarizes leading causes, emergency treatment, and prevention. Resources for clinicians and patients are listed at the end of the review.

Prevalence

The prevalence of signs and symptoms in patients presenting to Emergency Departments is in large part related to the relative distribution of mast cells in the body: skin > respiratory tract > gut. In one representative report, >90% of patients had flushing and/or hives but 5% to 10% did not. Respiratory symptoms occurred in 40%, gastrointestinal symptoms in 30%, and shock occurred in about 10% of those patients presenting to Emergency Departments with anaphylactic reactions.[5] Generally, the more rapid the onset of symptoms after exposure to the offending agent, the more severe the reaction.

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Table 1. Nonimmunoglobulin E causes of anaphylaxis (anaphylactoid reactions)

Classification	Mechanism	Example
Nonimmunoglobulin E immunologic	Complement activation Anaphylatoxin, intravenous aggregates	Cobra venom reaction, dextran, intravenous immunoglobulin
Nonimmunologic	Direct activation of mast cells (secretagogues)	Opiates Ionic contrast media: It is a misconception that this reaction is due to iodine allergy
Sensitivity to nonsteroidal anti-inflammatory drugs	Pharmacologic inhibition of cyclooxygenase, leading to increased generation of lipoxygenase products	ASA, ibuprofen, Toradol

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Mechanisms and the Most Common Causes of Anaphylaxis in the US

- IgE-mediated:
  - Foods
  - Medications
  - Insect venoms
- Non–IgE-mediated (Table 1):
  - Acetylsalicylic acid/nonsteroidal anti-inflammatory drugs
  - Ionic contrast media.

Management of Anaphylactic Reactions

Office Management

Rapid initiation of treatment can be critical. Follow these steps to treat anaphylactic reactions in the office (Table 2):

1. Assess the ABCs (airway patency, breathing effort, and circulation) and mentation.
2. Administer epinephrine intramuscularly by auto-injector (eg, EpiPen, Twinject) for serious or potentially serious reactions.
3. Administer a fast-acting antihistamine. Add an H_2-blocker, pending the reaction's course. Antihistamines relieve the acute effects of itch, flushing, and perhaps some angioedema. They are not effective for hypotension. H_2-blockers may help ameliorate the cardiovascular effects of histamine release from mast cells surrounding the coronary arteries.
4. Administer albuterol for bronchospasm.
5. Administer oxygen at 6 to 8 L/minute.

A Working Definition of Anaphylaxis[2,3]

Anaphylaxis can be defined as follows:

1. An acute, severe, or life-threatening systemic reaction caused by the release of mediators from mast cells or basophils
2. Most commonly—but not exclusively—mediated by immunoglobulin E (IgE)
3. Possibly mediated by non-IgE immune reactions or nonimmunologic direct release of mediators (anaphylactoid reaction)
4. Most often occurs within minutes of exposure to an allergy-causing agent
5. A condition that should be suspected in patients presenting with any of the following signs and symptoms; a patient may have some, all, or none in any particular category:
   - *Skin:* Flushing, urticaria with itching. In severe reactions, skin manifestations may be delayed while cardiovascular collapse is occurring. Angioedema may be present. Increased vascular permeability can allow the transfer of up to 50% of the intravascular volume into the extravascular space within ten minutes in extreme cases.
   - *Gastrointestinal:* Unexplained nausea, vomiting, diarrhea, abdominal cramps
   - *Respiratory:* Stridor, dyspnea, asphyxiation, or asthma symptoms; reduced peak expiratory flow rate
   - *Circulatory:* Unexplained hypotension or collapse. Rarely, this can occur without skin manifestations.
   - *Systemic:* A sense of impending doom. This is a valuable sign for impending shock. If asked how they feel, these patients think that they are going to die and often say, "I don't feel right."
6. Highly likely when the first of the three following criteria plus at least one of the other criteria are filled:[2]
   - Acute-onset illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both, as noted above, plus at least one of the following:
     - Respiratory compromise
     - Reduced blood pressure or weakness or syncope
   - Two or more of the following after exposure to a likely allergen for the patient:
     - Skin and/or mucosal tissue involvement
     - Respiratory compromise
     - Reduced blood pressure or weakness or syncope
     - Persistent gastrointestinal symptoms
   - Reduced blood pressure after exposure to a known allergen for the patient:
     - Infants and children: Systolic blood pressure <70 mm Hg if one month to one year old; <70 mm Hg + (2 × age) or >30% decrease in systolic blood pressure if one to ten years old
     - Adolescents and adults: Systolic blood pressure <90 mm Hg or >30% decrease from usual baseline
7. Can be confirmed by an elevated serum tryptase level:
   - Specific for mast cell–mediator release
   - Can remain elevated for three to six hours after the onset of symptoms, unlike plasma histamine, which is evanescent
   - May not be elevated in many cases of food-related anaphylaxis

6. For hypotension, place the patient in the recumbent position and elevate his or her legs.
7. Infuse normal saline or colloid volume expanders for shock or hypotension.
8. Use glucagon or dopamine for refractory hypotension.
9. Be aware that although systemic corticosteroids may decrease the intensity of late-phase or biphasic reactions and asthma symptoms, there is no evidence that they are effective for anaphylactic shock in humans.

When to Administer Epinephrine

There are no universally accepted guidelines as to the minimal reaction that requires epinephrine administration. The suggestions that follow are based on the severity of the acute reaction and the patient's past history.

These are definite indications:

- Rapidly evolving hives and angioedema even in the absence of hypotension or respiratory distress
- Hypotension
- Expression by the patient of a sense of impending doom. In this circumstance, most patients tend to say the same thing, as if they were reading from a script: "Something isn't right" or "I don't feel right."
- Angioedema in the throat manifested by altered speech quality, drooling, or difficulty swallowing
- Respiratory distress

These are probable indications:

- Generalized hives
- Any signs or symptoms of anaphylaxis in a patient with a prior history of severe allergic reaction or anaphylactic shock
- Multiple bites or stings from an insect known to have caused an allergic reaction in the past.

Precautions

Patients should be observed for an appropriate period of time before discharge from medical observation. These are some of the reasons to observe patients for an extended period:

- Prolonged severe reaction or signs and symptoms refractory to initial treatment
- Rapid recurrence of signs and symptoms after initial response to treatment
- Presentation with uncontrolled asthma
- Inadequate supervision or monitoring of patient at home, as with an elderly person living alone
- Patient who lives too far from access to emergency services
- Significant comorbidities.

Table 2. Equipment and medications for office management of anaphylaxis

Equipment	Medications
Blood pressure monitor	Epinephrine (Adrenalin) 1:1000
Intravenous supplies for fluid support	Fast-acting H_1 and H_2 antihistamine (oral and parenteral)
Oral airway and endotracheal tubes	Vasopressor agents
Oxygen, tubing, and mask	Solu-Medrol Colloid or crystalloid intravenous fluids Glucagon Albuterol

Pretreatment in High-Risk Procedures

Patients with a history of anaphylaxis who are undergoing procedures that carry a high risk for an anaphylactic reaction should be pretreated. Asthma should be stabilized with systemic corticosteroids and bronchodilators. The following represents recommended pretreatment of older children and adults before the use of ionic contrast media. (See Table 3 for pediatric doses.)

- Prednisone, 20 to 50 mg orally, 13 hours, 7 hours, and 1 hour prior to the procedure
- Diphenhydramine, 50 mg, 1 hour prior
- Orally: cimetidine, 300 mg, or ranitidine, 150 mg, 13 hours and 1 hour prior.

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Follow-Up Care

Patients should continue treatment at home with antihistamine until the reaction has subsided. Oral corticosteroids may prevent or decrease the effects of an ongoing or recurrent reaction. Patients should be discharged with enough injectable epinephrine for two emergency doses and should be able to demonstrate knowledge of how and when to use the auto-injector. In a review of 676 Emergency Department charts of patients treated for anaphylaxis, only 16% of patients were discharged with epinephrine injectors and only 12% were referred to an allergy specialist.[4]

Patients should be referred to an allergy specialist if they have had a severe reaction without an obvious or previously defined trigger; have a reaction that is thought to be due to a food, drug, insect sting, or exercise; or have a reaction that is food-dependent and exercise-induced.

The patient, the patient's family, and the primary care clinicians referring the patient should expect the allergy specialist to determine whether an anaphylactic event

Table 3. Medication doses[3]		
	Adults	**Children**
Diphenhydramine Oral, IM, or IV	 25–50 mg	 1 mg/kg, ≤50 mg
Ranitidine IV over 10–15 minutes Oral	 1 mg/kg 150–300 mg	 12.5–50 mg 2–3 mg/kg, ≤150 mg
Cimetidine IV slow drip Oral	 4 mg/kg 300–400 mg	 No established dose No established dose
Epinephrine 1:1000 IM or subcutaneous[a]	0.2–0.5 mL May be repeated in 5–10 minutes if needed May be administered via EpiPen	0.01 ml/kg, up to 0.3 mL May be repeated in 5–10 minutes if needed May be administered via EpiPen Jr for patients weighing <60 lb
Refractory hypotension		
IV dopamine 400 mg in 500 mL of NS	2–20 µg/kg/min or 0.025–0.25 mL/kg/min	
Glucagon	1–5 mg IV over 5 minutes by continuous IV, 5–15 µg/min	20–30 µg/kg; maximum 1 mg

[a] In a study of healthy children who were not experiencing shock, IM epinephrine given in the upper, outer thigh achieved higher and more rapid peak blood levels than did the same dose given subcutaneously or at other peripheral sites.

IM = intramuscular; IV = intravenous; NS = normal saline.

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occurred; determine or rule out causes of the reaction; determine whether other medications in the patient's regimen might be aggravating or interfering with treatment of the episodes, and suggest alternatives; educate the patient about how to avoid triggers; educate the patient and the patient's family about how to recognize the symptoms of an allergic reaction; create a written emergency plan for the patient and for other caretakers; and reinforce how and when to use epinephrine for emergency purposes.

Happy Ending

Fortunately for the nurse who had prolonged and recurrent anaphylaxis after eating a plum, the outcome wasn't the pits. An astute emergency medicine specialist recognized the association of latex sensitivity to stone-fruit anaphylaxis and promptly ordered the use of nonlatex materials for the care of this patient in the emergency department. Her condition responded to volume expansion, additional epinephrine, H_1 and H_2 antihistamines, and corticosteroids. Her condition stabilized after an hour in the Emergency Department, and she was discharged after overnight observation. Before discharge, she was instructed in the use of an EpiPen. A consult with an allergist confirmed her sensitivities. The allergist reinforced her knowledge of EpiPen use and provided information on avoidance of latex products and potential cross-reacting foods. ❖

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Resources

www.foodallergy.org
www.aaaai.org
www.acaai.org
www.medicalert.org (1-800-432-537)