

Anaphylaxis

A review and update

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You are working in an emergency department when a 20-year-old woman presents with an "asthma attack" after eating at a Thai restaurant. She appears agitated and complains of shortness of breath, nausea, and stomach cramps. Measurement of her vital signs reveals the following: blood pressure of 100/70 mm Hg, pulse of 120 beats/min, and a respiratory rate of 30 breaths/min. Her physical examination is remarkable only for bilateral expiratory wheezes, which have not responded to 4 doses of salbutamol.

Is this patient having an anaphylactic reaction?

Anaphylaxis is the quintessential disease of emergency medicine. It is a potentially fatal illness with rapid onset that can affect young, healthy people. It must be diagnosed clinically, and is potentially curable if treated immediately. Yet, a universally accepted definition of anaphylaxis has been elusive, and it continues to be underrecognized and undertreated.¹

Diagnosis

Anaphylaxis is a severe, multisystem allergic reaction that occurs suddenly after contact with an allergen. The classic presentation includes urticaria or angioedema, hypotension, and bronchospasm. However, anaphylaxis can often be difficult to diagnose, with up to 20% of anaphylactic reactions lacking any cutaneous manifestations or signs of vasomotor instability.² Diagnostic criteria were established by a multidisciplinary task force in 2005 to aid in the recognition of atypical presentations of anaphylaxis.²

In cases of anaphylaxis, laboratory tests might show transient elevation of tryptase and histamine levels, but these are not useful diagnostically in the acute setting.³

Pathophysiology

Anaphylaxis is the result of immunoglobulin E-mediated mast cell degranulation, which releases inflammatory immune mediators. These mediators cause increased vascular permeability, peripheral vasodilation, increased mucus production, and bronchial smooth muscle contraction.⁴ Anaphylactoid reactions do not require a previous exposure to an allergen, but the clinical course and treatment are identical to those of anaphylaxis.

Causes

The primary precipitants of anaphylactic reactions are foods (eg, milk, soy, eggs, nuts, and shellfish), medications (eg, antibiotics [penicillin], nonsteroidal anti-inflammatory drugs, anesthetics), venom (Hymenoptera stings), intravenous contrast materials, and latex. Up to 20% of anaphylactic reactions are idiopathic.

Mortality

The primary cause of mortality in anaphylaxis is airway compromise or cardiovascular collapse. The median time interval between onset of symptoms and cardiopulmonary arrest in one study was less than 30 minutes.⁵ Fatal anaphylactic reactions are more common in asthmatic patients.⁵

Treatment

Treatment of anaphylaxis begins with removal of the offending agent, preparation for impending airway obstruction, and correction of vasomotor instability. The 2 most common errors associated with mortality in severe anaphylaxis are delays in intubation and delays in administration of epinephrine.

Airway edema can be rapid and dramatic. In patients with stridor, tongue swelling, or hoarseness, immediate airway protection is imperative. Rapid sequence intubation can be used, but rescue airway methods must be readily available at the bedside.

The treatment of choice for anaphylaxis is epinephrine. The recommended dose of epinephrine in anaphylaxis is 0.3 to 0.5 mg (concentration of 1:1000) intramuscularly (IM) every 5 to 10 minutes for adults (Table 1). Intramuscular injection in the anterolateral thigh is the preferred route regardless of age, as faster and higher plasma concentrations are obtained.⁶

Table 1. Recommended doses of epinephrine in anaphylaxis

INDICATION	DOSE	CONCENTRATION	ROUTE
Anaphylaxis	0.3-0.5 mg	1:1000	IM
Anaphylactic shock refractory to IM epinephrine	0.1 mg	1:10 000	IV over 5 min
Cardiac arrest	1 mg	1:10 000	IV push
Anaphylaxis in children	0.15 mg	1:1000	IM

IM—intramuscular, IV—intravenous.



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Intravenous epinephrine is reserved for cases of cardiovascular collapse that are unresponsive to IM therapy.²

Safety of epinephrine

Epinephrine is a lifesaving medication; however, because it is available in different doses, concentrations, and routes of administration (Table 1), there is frequent confusion in its use. Inadvertent overdose can cause coronary artery dissection, acute myocardial infarction, cardiomyopathy, arrhythmias, and death.⁷ The error rate of epinephrine administration causing potentially fatal adverse reactions in one study was reported to be 2.4%.⁸ One study suggested that prefilled syringes of 0.3 mg of 1:1000 epinephrine clearly labeled to be given IM for anaphylaxis would decrease the incidence of dosing errors.⁸

Special cases. There are no absolute contraindications to the use of epinephrine in anaphylaxis.⁷ Patients taking β -blockers have a decreased response to epinephrine and are at risk of unopposed α activity with treatment. A half dose of epinephrine is recommended. Cocaine, tricyclic antidepressants, or monoamine oxidase inhibitors potentiate the effects of epinephrine, which might increase the risk of cardiac arrhythmias. A half dose should again be considered.⁷

Fluid resuscitation

Anaphylaxis is a distributive form of shock. Patients with severe reactions require aggressive fluid resuscitation, frequently with up to 5 to 7 L of normal saline.⁵

Treatment adjuncts

Other treatments of anaphylaxis classically taught include histamine (H_1 or H_2) blockers and steroids. A systematic review of the literature has failed to demonstrate the effectiveness of any of these medications in the treatment of anaphylaxis.⁵ They have not been shown to relieve upper or lower airway obstruction, gastrointestinal symptoms, or shock.⁵

Steroids are unlikely to be helpful in the treatment of acute anaphylaxis. They have a delayed onset of 4 to 6 hours. Steroids are thought to play a role in preventing rebound anaphylaxis; however, this has never been proven.⁵

Bronchodilators might be used in patients with refractory wheeze, but they do not relieve bronchial smooth muscle contraction or decrease mucus production.

One study showed that patients suffering from anaphylaxis received both antihistamines and corticosteroids more frequently than epinephrine despite the lack of evidence for their use as first-line agents in anaphylaxis.⁹

Rebound anaphylaxis

Patients with severe anaphylactic reactions,

BOTTOM LINE

- Anaphylaxis is a severe, life-threatening allergic reaction. It must be diagnosed clinically and must be treated immediately. Twenty percent of patients with anaphylaxis lack cutaneous manifestations, and patients with asthma are at higher risk of undertreatment, misdiagnosis, and death.
- The cornerstone of treatment of anaphylaxis is 0.3 to 0.5 mg of epinephrine (1:1000 concentration) intramuscularly, early intubation, and aggressive fluid resuscitation. There is no evidence for the use of histamine (H_1 or H_2) blockers or steroids in anaphylaxis.
- The incidence of rebound anaphylaxis is up to 20%. Patients should be observed in the emergency department for 4 to 24 hours before discharge.

POINTS SAILLANTS

- L'anaphylaxie est une réaction allergique grave mettant la vie en danger. Elle doit être cliniquement diagnostiquée et traitée immédiatement. Chez 20% des patients en anaphylaxie, il n'y a pas de manifestations cutanées et les patients asthmatiques courent plus de risques de ne pas être traités adéquatement, ou bien diagnostiqués, et de mourir.
- Le traitement de l'anaphylaxie repose principalement sur une injection intramusculaire de 0,3 à 0,5 mg d'épinéphrine (concentration de 1 pour 1000), une intubation rapide et une réanimation proactive avec fluides. Il n'y a pas de données probantes justifiant l'utilisation de bloqueurs d'histamine (H_1 ou H_2) ou de stéroïdes dans les cas d'anaphylaxie.
- L'incidence d'une récurrence de l'anaphylaxie est à hauteur de 20%. Il faut donc garder les patients sous observation à l'urgence durant 4 à 24 heures avant d'accorder le congé.

particularly of rapid onset, are at risk of biphasic or rebound anaphylaxis. The recurrence rate is up to 20%.³ Most biphasic responses occur during the first 8 hours, but it might be delayed up to 72 hours.⁵ There is no consensus on the optimal period of observation for a patient who has been treated for anaphylaxis.⁴ In patients with moderate or severe anaphylaxis, consider admission. For patients whose symptoms resolve promptly and completely, it is recommended that they be observed for 4 to 8 hours. All patients being sent home from the emergency department should have immediate access to epinephrine injectors.

Emergency Files is a quarterly series in *Canadian Family Physician* coordinated by the members of the Emergency Medicine Committee of the College of Family Physicians of Canada. The series explores common situations experienced by family physicians doing emergency medicine as part of their primary care practice. Please send any ideas for future articles to Dr Robert Primavesi, Emergency Files Coordinator, at robert.primavesi@muhc.mcgill.ca.

Once you have ascertained that there is no evidence of biphasic anaphylaxis, it is recommended that you do a SAFE (Support; Allergen; Follow-up; Epinephrine injector) discharge (Table 2⁹).

Table 2. A SAFE discharge

SAFE STEPS	EXPLANATION
S upport	Ensure that there is someone to monitor patient at home
A llergen	Try to identify precipitating agent, avoid re-exposure
F ollow-up	Follow-up allergy testing
E pinephrine injector	Prescribe epinephrine injector on discharge; might require 2 doses ⁹

Conclusion

Yes, this patient is suffering from an anaphylactic reaction. She is successfully treated with 2 doses of 0.3 mg of epinephrine IM and steroids. She stays in the emergency department overnight and is safely discharged in the morning with a prescription for epinephrine.



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Competing interests

None declared

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