



Systemic Allergic & Immunoglobulin Disorders

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Disclosures

- None



Objectives

- Pass the boards!
- Recognize anaphylaxis and understand the new guidelines for the treatment of anaphylaxis
- Compare and contrast anaphylactic and anaphylactoid reactions



The Patient

- 45 year old woman goes to lunch with her friends
 - While eating she develops GI upset, dizziness, shortness of breath and hives
 - Her friends drive her to your nearby clinic



Initial Evaluation

- Your nurse gets the history of sudden onset of GI upset, dizziness, shortness of breath and hives while eating a shrimp salad.
- The patient now has audible wheezing, tachycardia, and a blood pressure of 110/60
- Your initial response?
 - Take a detailed history of everything the patient had to eat for lunch
 - Ask if she has a history of any medical issues such as asthma, diabetes or heart disease
 - Give nebulized beta agonist
 - Give 50 mg of oral diphenhydramine
 - Give 0.3 ml of IM epinephrine



Anaphylaxis presentation

- Your nurse gets the history of sudden onset of GI upset, dizziness, shortness of breath and hives while eating lunch.
- The patient now has audible wheezing, tachycardia, and a blood pressure of 110/60
- Your initial response
 - Take a detailed history of everything the patient had to eat for lunch
 - Ask if she has a history of any medical issues such as asthma, diabetes or heart disease
 - Give nebulized beta agonist
 - Give 50 mg of oral diphenhydramine
 - **Give 0.3 ml of IM epinephrine**



Initial Response to anaphylaxis

- Initial treatment for anaphylaxis is IM epinephrine at a dose of 0.01 mg/kg up to a max dose of 0.5mg
 - Auto inject epinephrine comes in 0.1, 0.15 and 0.3 mg of epinephrine
 - You will typically be given the choice of using an auto injectable epinephrine, as time is of the essence, and time taken to draw up epinephrine is time wasted.
 - Old guidelines called for subcutaneous epinephrine, but data shows IM is better absorbed.



Effects of epinephrine

- Epinephrine is a mixed alpha and beta-adrenergic receptor agonist that treats anaphylaxis symptoms by alleviating allergen-induced inflammation and physiologic effects
- Alpha-adrenergic: vasoconstriction, reverses vasodilation and alleviates hypotension and reducing erythema, urticaria and angioedema
- Beta-adrenergic: activity dilates bronchial airways, increases the force of myocardial muscle contraction and heart rate



Distractors

- Beta agonist: she is wheezing!
 - While the beta agonist would help the wheezing and may be used to help breathing, it would not help the other S/S of anaphylaxis
 - Delay in providing epinephrine is a cause of increased morbidity and mortality in anaphylaxis.



Distractor 2

- If this is an allergic reaction, why not give antihistamine?
 - Like beta agonist, antihistamines are a second line therapy in the treatment of anaphylaxis.
 - Antihistamines may help with hives, but will not treat the myriad anaphylaxis symptoms
 - Longer onset of action and longer time to peak activity compared to epinephrine

Antihistamines are adjunctive treatment for anaphylaxis



Treatment of anaphylaxis

- IM Epinephrine is the treatment of choice for anaphylaxis
- Secondary treatments may include:
 - Oxygen
 - IV fluids
 - Beta Agonists
 - Antihistamines
 - Glucocorticoids
 - Glucagon for patients who are on beta blockers
- There is a focus on the fact that patients are not getting epinephrine in the ER; I would expect an anaphylaxis question



History as a distractor

- What about the more detailed history?
- Don't I want to try to identify what she ate, and thereby identify suspect foods?
- Isn't it important to know if she has other medical conditions?



Medical History is important!

- But don't delay epinephrine trying to decide what the allergen might be. It is important to get the epinephrine in quickly
- “But heart disease!” you say. “I may kill her with epi if she has CAD!”
 - The stress of the anaphylaxis is more likely to cause increased cardiac issues.
- Get your good medical history after epinephrine is given, while you are watching for clinical response to your epinephrine.



Long term care for Anaphylaxis

- When acute anaphylaxis is treated, it is then important to help the patient prepare for the possibility of a future episode.
 - Try to identify the allergen so the patient can avoid it
 - Identify cofactors: Asthma, exercise, confounding medications (beta blockers)
 - Provide auto injectable epinephrine
 - Provide written anaphylaxis action plan and education



Anaphylaxis



2014

SUPPLEMENT ARTICLE

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Food Allergy and Anaphylaxis Guidelines

Anaphylaxis: Underdiagnosed, Underreported, and Undertreated

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Translating knowledge into clinical practice



European Academy of Allergy and Clinical Immunology

ABSTRACT

Diagnostic criteria and administrative codes for anaphylaxis have evolved in recent years, partly reflecting the challenges in recognizing anaphylaxis and understanding its symptoms. Before the diagnostic criteria were disseminated by the National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network, several studies showed that a substantial proportion of anaphylaxis cases presenting to the emergency department (ED) were not recognized as such. Furthermore, epinephrine, the first-line treatment, was used in fewer than half of cases, especially if anaphylaxis was not diagnosed at the time. Although management practices may have improved since that time, anaphylaxis continues to be under-recognized and undertreated in the US. Of particular concern are findings that the majority of patients who visited the ED for an acute allergic reaction or anaphylaxis were not given a prescription for an epinephrine autoinjector, educated about avoiding the offending allergen, or advised to consult with an allergist. Improvements in the recognition and management of anaphylaxis have the potential to reduce the substantial burden that it currently places on the health care system. The articles in this supplement cover a wide range of issues surrounding anaphylaxis and seek to disseminate information helpful to health care professionals in general and primary care providers in particular.

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KEYWORDS: Allergy; Anaphylaxis; Drug utilization; Epidemiology; Epinephrine; Health care costs; Physician practice patterns

US Anaphylaxis practice parameters
updated 2015

World Allergy Organization
Anaphylaxis guidelines updated 2015

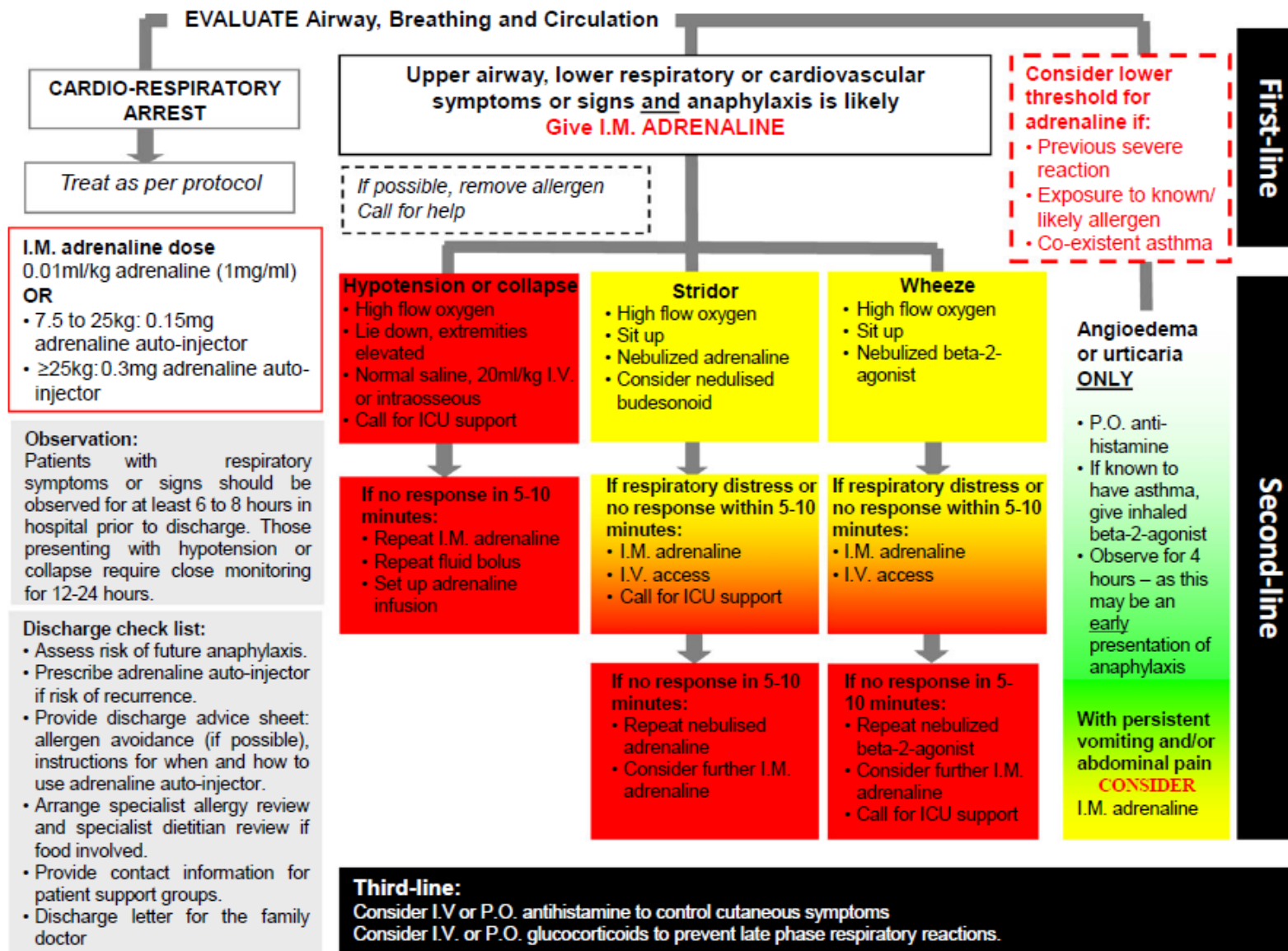


Figure 2 Schematic illustration of the initial management of anaphylaxis.

But wait...there's more:



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American Academy of Allergy, Asthma & Immunology



Five **More** Things Physicians and Patients Should Question

Don't rely on antihistamines as first-line treatment in severe allergic reactions.

Don't perform food IgE testing without a history consistent with potential IgE-mediated food allergy.

Don't routinely order low- or iso-osmolar radiocontrast media or pretreat with corticosteroids and antihistamines for patients with a history of seafood allergy, who require radiocontrast media.

Don't routinely avoid influenza vaccination in egg-allergic patients.

Don't overuse non-beta lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.

Clinical Question

- 27 year old known asthmatic presents to your office with acute onset of hives, complaining of shortness of breath, and racing heart after eating a peanut butter sandwich for lunch. He denies any known food allergy. He is wheezing and cannot speak in complete sentences. Your response?
 1. Nebulized beta-agonist
 2. IM epinephrine
 3. 50 mg benadryl
 4. Sub cutaneous epinephrine
 5. Ask him if he has his rescue inhaler and have him use it while you watch his technique



Answer

- 27 year old known asthmatic presents to your office with acute onset of hives, complaining of shortness of breath, and racing heart after eating a peanut butter sandwich for lunch. He denies any known food allergy. He is wheezing and cannot speak in complete sentences. Your response
 1. Nebulized beta-agonist
 2. **IM epinephrine**
 3. 50 mg benadryl
 4. Sub cutaneous epinephrine
 5. Ask him if he has his rescue inhaler and have him use it while you watch his technique



Asthmatic distractors

- In spite of the fact that he is a known asthmatic, his presentation is more consistent with anaphylaxis than asthma exacerbation.
 - Nebulized beta agonist could be used as an adjunctive therapy after the IM epinephrine
 - Antihistamines are also an adjunctive therapy for anaphylaxis
 - Subcutaneous Epinephrine: Epinephrine should be given IM
 - Rescue inhaler with observation: This is an emergent situation, not the best time for technique education



Clinical Criteria for Anaphylaxis

Lieberman, Amer J Med. (2014) 127, S6-S11

With unknown allergen,
acute onset of illness:

Skin and/or mucosal
involvement (e.g., hives,
angioedema, pruritus,
flushing)

and EITHER

Respiratory compromise
(e.g., dyspnea, wheeze,
bronchospasm, ↓ PEF,
stridor, hypoxemia)

OR

↓ BP or end-organ
dysfunction (e.g.,
collapse, syncope,
incontinence)

After exposure to likely
allergen, rapid occurrence of
≥2 of:

Skin and/or mucosal
involvement

Respiratory compromise

↓ BP or end-organ
dysfunction

Persistent GI Sx (e.g.,
crampy abdominal pain,
vomiting, diarrhea)

After exposure to known
allergen (minutes to hours):

Rapid occurrence
of ↓ BP (age-specific)

Figure 2 Clinical criteria for the diagnosis of anaphylaxis.¹

Anaphylaxis Signs & Symptoms

Table 1 Signs and Symptoms of Anaphylaxis

Signs and Symptoms	Frequency (%)
Urticaria, angioedema	88
Dyspnea, wheeze	47
Dizziness, syncope, hypotension	33
Nausea, vomiting, diarrhea, cramping abdominal pain	30
Flush	46
Upper airway edema	56
Headache	15
Rhinitis	16
Substernal pain	6
Pruritus without rash	5
Seizure	2

Lieberman, *Amer J Med* (2014) 127, S6-S11

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Biphasic allergic reactions

- Biphasic allergic reactions, a second reaction occurring initial recovery
 - 11% of children presenting to pediatric ED
 - 25% of fatal and near-fatal food reactions
 - 23% of drug/biologic reactions
 - 6% of anaphylaxis from mixed cause
- Time to second phase
 - 1-72 hours
 - Mean 8.13 hours
- Rarely occur without initial hypotension or airway obstruction.

Mack, Allergy, Asthma & Clinical Immunology (2014) 10:Sup 1; A10



Common Triggers

- Food 33.2-56%
 - Reportedly increasing
 - Peanut, tree nut, fish shellfish
- Insect Stings 18.5%
- Medications 13.7%
 - Beta-lactams
 - Biologic modifiers



Less Common Triggers

- Less Common
 - Latex, immunotherapy, cancer chemotherapeutics, & environmental allergens
- Nonimmunologic triggers (20%)
 - Exercise, cold exposure, radiocontrast materials and opioids
- Idiopathic anaphylaxis (20%)
 - No trigger identified



Anaphylaxis: Treatment

- Stabilize airway
- **IM Epinephrine**
 - 0.01 mg/kg
- O2
- Large gauge IV
- Benadryl 50-100 mg IV or IM
- Cimetidine 300 mg IV
- Methylprednisolone 125mg IV



Patient

- 30 year old with a benign medical history presents for a tetanus shot after stepping on a nail. Shortly after receiving the shot he becomes pale, diaphoretic and slowly slumps to the floor. Your nurse calls for your assistance.
- When you arrive his skin is cool, clammy and pale. His pulse is 58 and his blood pressure is 130/76. He begins to arouse and states he is lightheaded.
- Your first response?
 - Epinephrine 0.3 mg IM
 - Start an IV with normal saline
 - Raise his legs
 - Help him get to a chair
 - Diphenhydramine 50 mg po



First Response

- Your first response
 - Epinephrine 0.3 mg IM
 - Start an IV with normal saline
 - **Raise his legs**
 - Help him get to a chair
 - Diphenhydramine 50 mg po



Vasovagal Reaction

- Stress or fright
- Slow pulse
- Maintain blood pressure
- Pale, cold clammy skin
- Recumbancy alleviates symptoms
- No urticaria or pruritis



DDX Anaphylaxis

<u>System</u>	<u>Anaphylaxis</u>	<u>Vaso-Vagal Rxn</u>
Cutaneous	Urticaria, erythema	Pale, clammy
Respiratory	Globus, SOB wheezing, SPO2 ↓	Hyperventilation SPO2: ↑
Cardiovascular	Tachycardia, hypotension	Bradycardia, normotensive
G.I.	N, V, D	N, V, D
C.N.S.	“Feeling of impending doom”	Light headed, confused

Patient

- 63 year old patient presents with wheezing, urticaria, Nausea, and states he feels he is going to die.
- Your quick evaluation reveals an acutely ill patient with flushing and urticaria. He cannot speak in complete sentences. His blood pressure is 90/40 and his heart rate is 120
- You diagnose anaphylaxis and give the patient 0.3 mg of epinephrine IM and continue to take a more detailed history.
- You also start IV normal saline



Extended history

- The patient states he has a history of anaphylaxis to “bee stings” when he was much younger, but did not have that evaluated. He notes he was stung shortly before his symptoms began.
- He denies asthma, but states he has high blood pressure for which he takes a beta blocker.
- After approximately 10 minutes his symptoms are not improved. You give him a second IM injection of 0.3 mg epinephrine.



Anaphylaxis in patient on Beta blocker

- If he still does not improve, what is the next course of action?
 - IV fluid bolus
 - Repeat the IM epinephrine 0.3 mg
 - Start an IV epinephrine drip
 - Nebulized beta agonist
 - Glucagon



Anaphylaxis in patient on Beta blocker

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 - **Glucagon**



Refractory anaphylaxis in a patient on a beta-blocker

- If an anaphylaxis patient who is on a beta blocker is refractory to epinephrine, consider glucagon
- It is not enough to know that glucagon is the drug of choice, you may need to know dose, route of administration and side effects
- Administer 1 mg of IM or IV glucagon
- Patients require close monitoring of their blood glucose levels because glucagon elevates serum glucose.





Anaphylaxis While Receiving Beta-blocker Therapy

- Unusual severity
- Bradycardia during profound hypotension
- Severe sustained bronchospasm
- Total body angioedema
- Refractory to usual treatment
 - Glucagon is used for refractory cases



Anaphylaxis Management After Initial Assessment

- Antihistamine
- Corticosteroids
- Beta-Agonists for wheezing
- Fluids, Vasopressors
- **Glucagon**
 - Used for nonresponsive anaphylaxis in patients on beta-blockers
- Atropine





Treatment of Anaphylaxis: in presence of Beta-blockade

- Aggressive and prompt support
- Epinephrine
- Large volume IV
- **Glucagon**
- Atropine
- Increased dopamine or beta-agonist
- Antishock trousers



Mechanism of reaction



Anaphylactoid Reaction

- Anaphylaxis vs Anaphylactoid is a discussion of the mechanism of the reaction, NOT the clinical symptoms or treatment
- Resemble anaphylaxis but not immunologically mediated
 - Not IgE mediated
- **Does not require prior sensitization**
 - Reaction may occur on first exposure
- Symptoms = anaphylaxis
- Treatment = anaphylaxis





Anaphylactoid Reactions

Non IgE mediated causes

- Complement-mediated
- Direct activation of mast cell-mediator release
- Arachidonic acid metabolism
- Unknown





Complement Mediated Anaphylactoid Reactions

- Human plasma and blood products
- Dialysis membranes





Direct activation of Mast Cell mediator release

- **Opiates**
- **Radiocontrast media**
- Vancomycin
- Muscle-depolarizing drugs
- Aminoglycosides



Direct activation of Mast Cell mediator release

- Radiocontrast media
 - Increased risk with IV administration and high osmolality
 - Sensitization not required
 - Previous reaction increases probability of reaction on rechallenge
 - Pretreatment can be given to decrease risk



Modulators of Arachidonic Acid Metabolism

- Aspirin and Nonsteroidal drugs
 - Generally progresses more slowly
 - Less often hypotension
 - Bronchoconstriction, wheezing often begin within 30 minutes and progress for several hours
- Aspirin desensitization is possible





Anaphylaxis: Differential Diagnosis

- Vasodepressor Reaction
- Scromboid: exposure to histidine in poorly prepared fish
- Other forms of shock
- Endogenous overproduction of histamine
- Red-man syndrome





Good Luck



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