Recognition & Management of Anaphylaxis in the Community

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Disclosures

- None

Outline

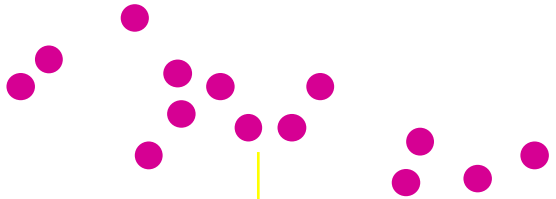
- Define anaphylaxis
- Pathophysiology
- Common causes
- Recognition and Management

Definition

- Acute, potentially life-threatening systemic/multi-organ reaction that is immunologically mediated and occurs after the likely exposure to an allergen
- Two or more of the following, following exposure to a likely allergen:
  - Involvement of skin/mucosa
  - Respiratory symptoms
  - Gastrointestinal symptoms
  - Lightheadedness / syncope
  - Hypotension
- Clinical diagnosis
  - Very little if any role for acute diagnostic testing
  - Consider allergy/immunology evaluation for long term management

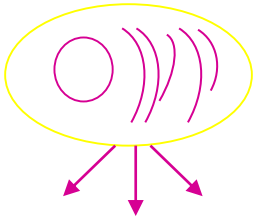
Sensitization

① Antigen (allergen) exposure



Antigen

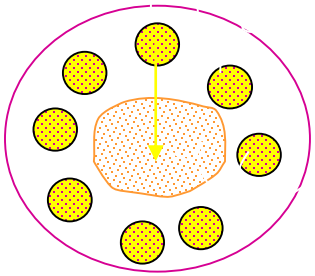
② Plasma cells produce IgE antibodies against the allergen



Plasma cell

IgE

③ IgE antibodies attach to mast cells and basophils



Mast cell with fixed IgE antibodies

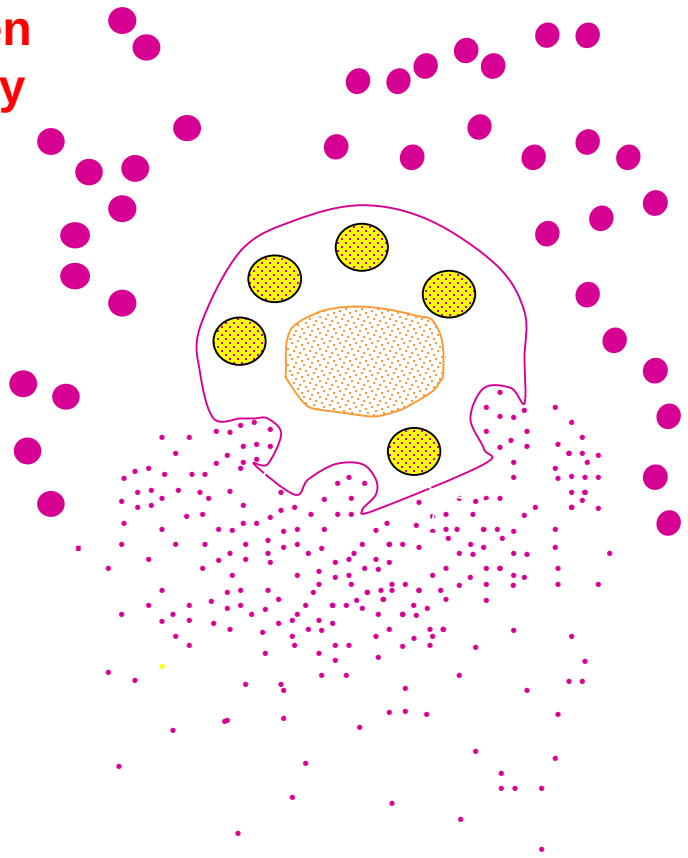
Granules containing histamine

Allergic Reaction

④ More of same allergen invades body

Antigen

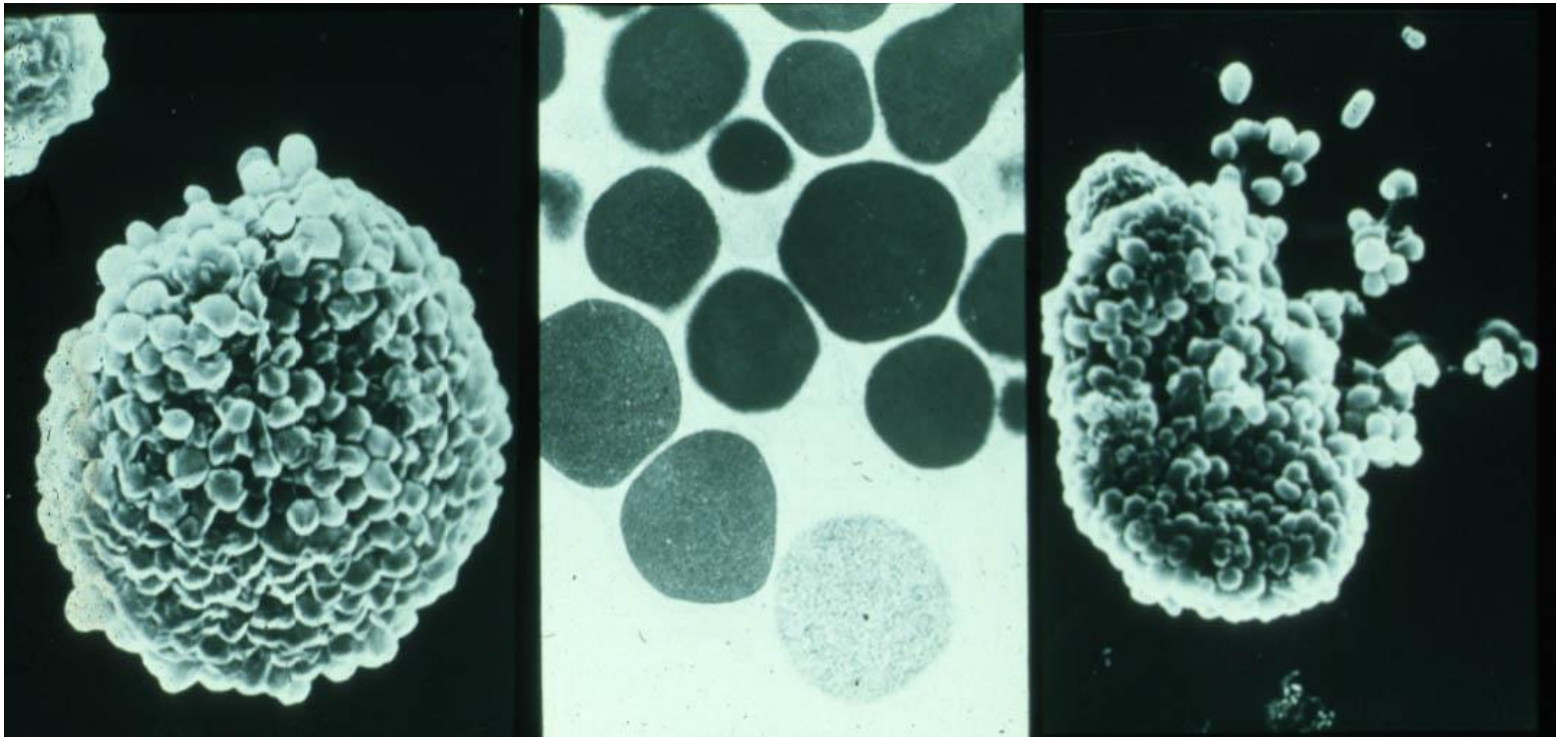
⑤ Allergen combines with IgE attached to mast cells and basophils, which triggers degranulation and release of histamine and other chemical mediators



Mast cell granules release contents after antigen binds with IgE antibodies

Histamine and other mediators

Mast Cell Degranulation



- Orr. TSC in Slide Atlas of Immunology; Roitt et al,, ed. 1991.

IgE Mediated & Non-IgE Mediated Reactions

IgE Mediated	Non-IgE Mediated
Foods	Radio-contrast material
Stinging insects	Acute viral infections
Medications Penicillin Sulfa NSAIDs	Medications Narcotics Vancomycin NSAIDs
Latex	Scromboid poisoning
Immunotherapy Aeroallergens Stinging insects	Idiopathic

IgE Versus Non-IgE Mediated Reactions

Allergy	Intolerance
Requires sensitization	Can occur in absence of sensitization
Validated diagnostic testing	Minimal validated diagnostic testing
Reproducible reactions	Reactions can occur inconsistently
Dose independent	Frequently dose dependent
Caused by an individual allergen	Can be caused by a class effect
Cannot block with pre-treatment	Validated pre-treatment regimens
Desensitization protocols	Desensitization not possible
Can lead to death	Typically very little mortality

Common Food Allergens

Pediatrics

Food	%
Cow's milk	2.5
Egg white	1.5
Peanut	1.0
Tree nuts	0.5
Wheat	0.4
Soy	0.4
Shellfish	0.1
Finned fish	0.1
Sesame	0.1*

Adults

Food	%
Peanut	0.6
Tree nuts	0.6
Shellfish	2.0
Finned fish	0.4
Sesame	0.1*

- Boyce. JACI 2010; 126: 1105.

Stinging Insects

Yellow jacket

Yellow hornet

White-faced hornet

Honeybee

Wasp

Fire ant

Anaphylaxis with Allergen Immunotherapy

- Subcutaneous immunotherapy
  - 0.1%
  - 1 per 1 million doses result in grade 3/4 systemic reaction
  - 1 confirmed death since 2008
- Sublingual immunotherapy
  - Case reports only (~6)
  - No fatality reported despite more than 1 billion doses administered

Management

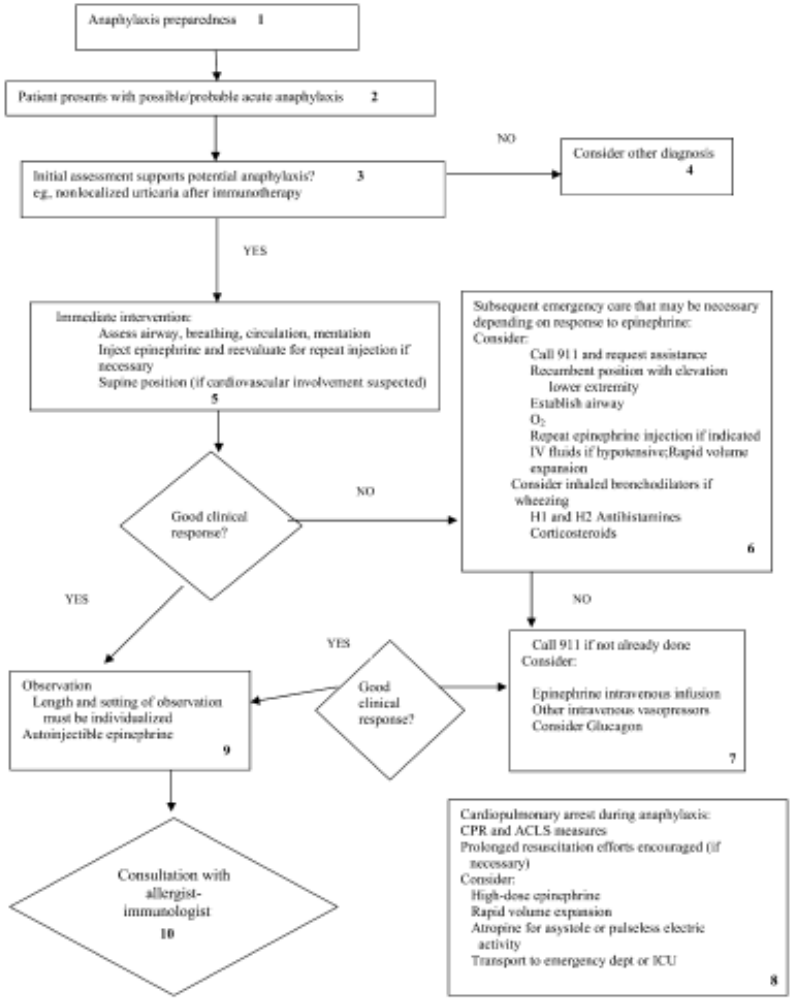
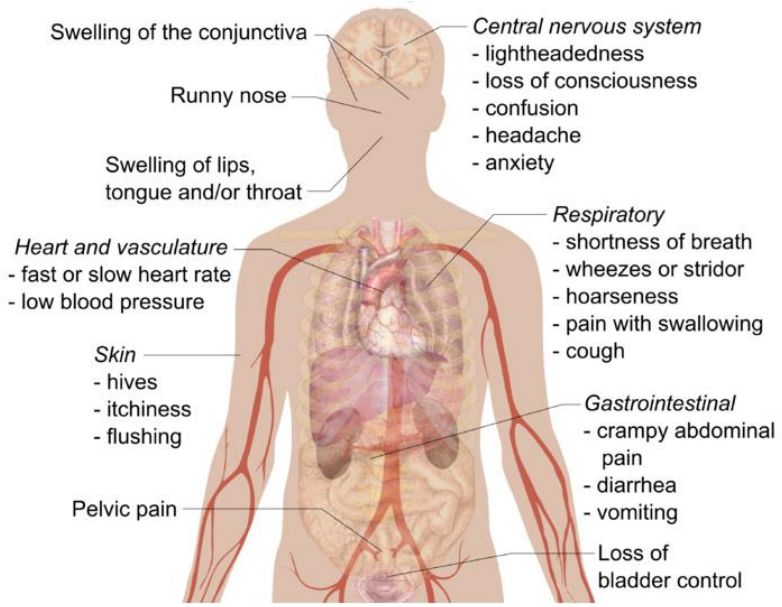


FIG E2. Algorithm for the treatment of an anaphylactic event in the outpatient setting. *IV*, Intravenous.

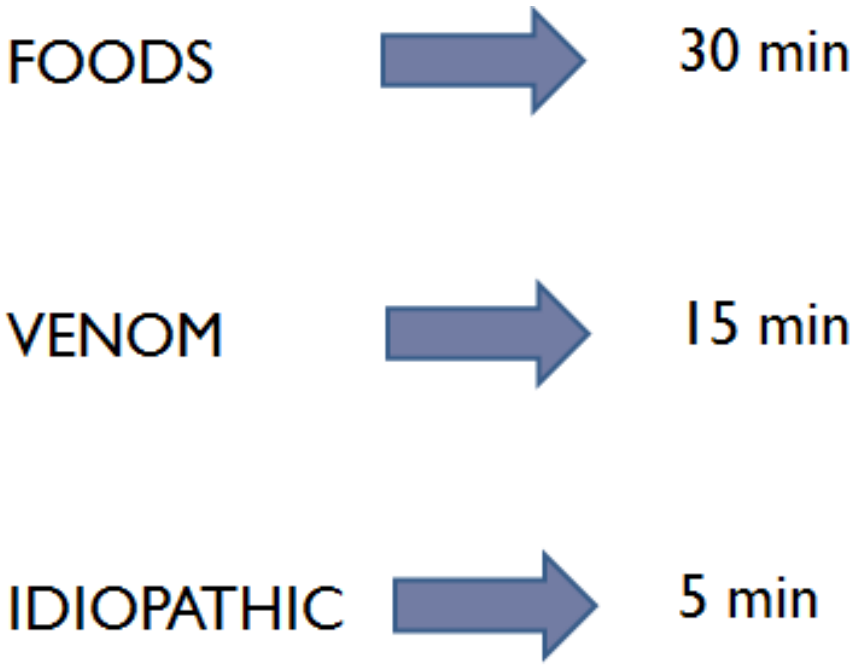
- Lieberman P. JACI 2010; 126(3): 477.

Signs and Symptoms



- Common complaints NOT suggestive of an IgE mediated mechanism
  - Isolated rhinitis
  - Isolated cough/asthma
  - Chronic abdominal discomfort
  - Isolated GERD
  - Chronic urticaria
  - Fatigue
  - Reactions occur inconsistently
  - Reactions occur only with larger doses
  - Ongoing mild to moderate atopic dermatitis

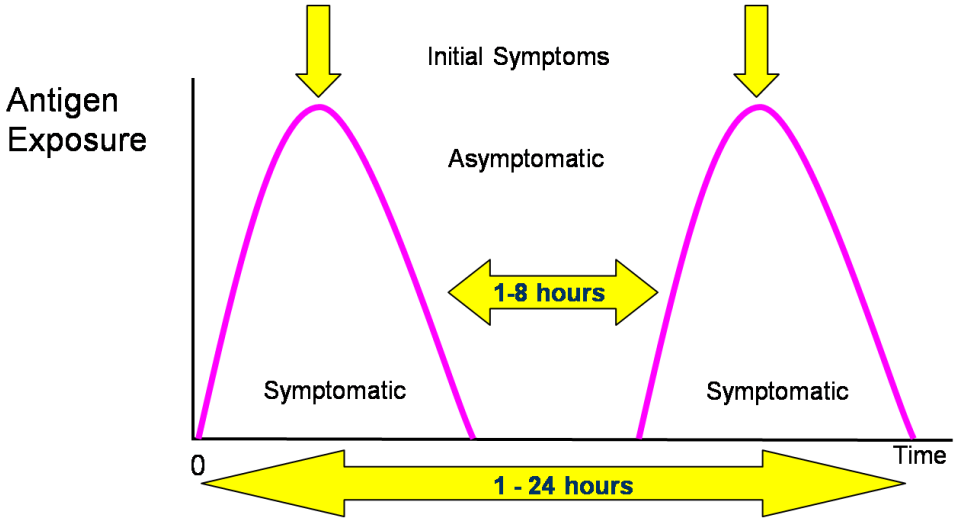
Mean Time to Respiratory or Cardiac Arrest



- Pumphrey RS. Clin Esp All 2003; 30(8): 1144.

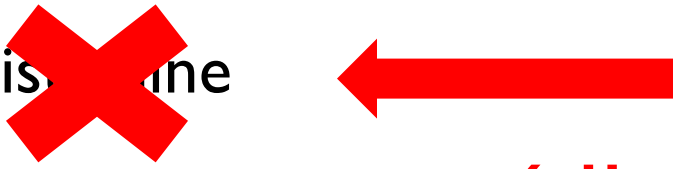
Management of Anaphylaxis

- Secure airway
- Epinephrine is the 1st line and only FDA approved therapy
- Antihistamines act as an adjunctive therapy mostly aimed at dermatologic manifestations
- Systemic steroids decrease the risk of biphasic or protracted reactions



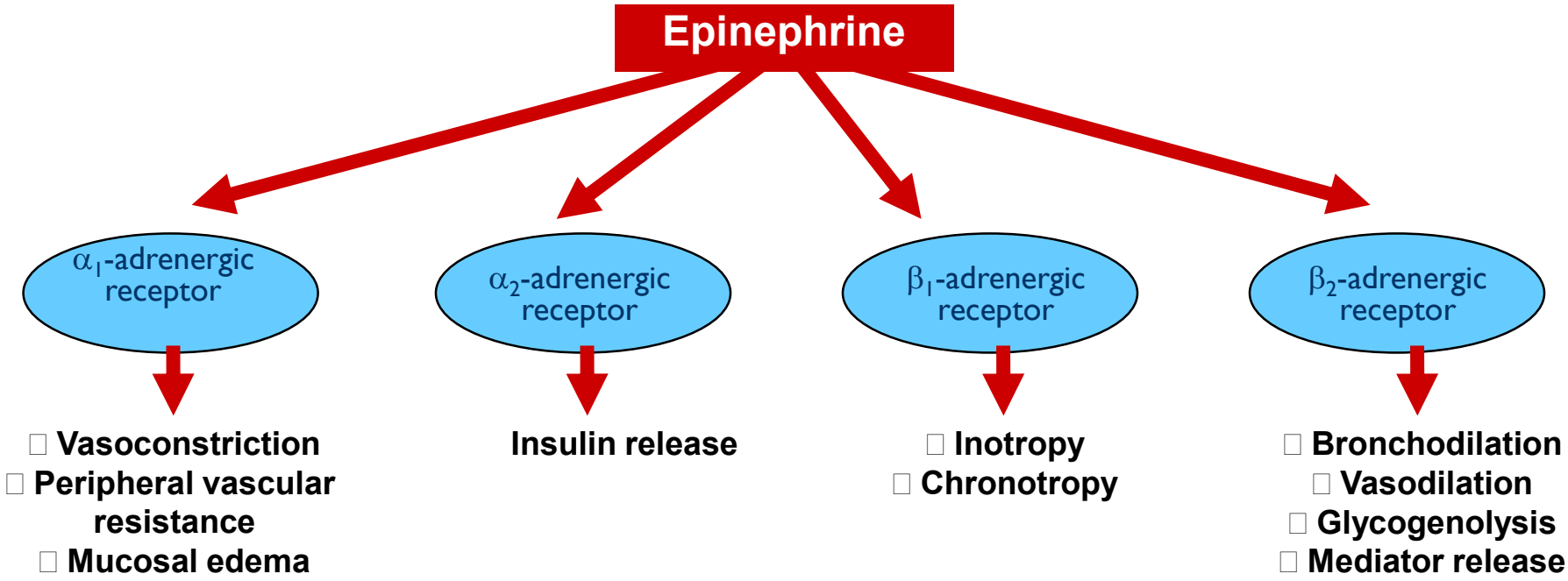
Mediators of Anaphylaxis

- Leukotrienes
- Prostaglandins
- Kinins
- Platelet activating factor
- Interleukins
- Tumor necrosis factor
- Histamine



Benadryl
(diphenhydramine)

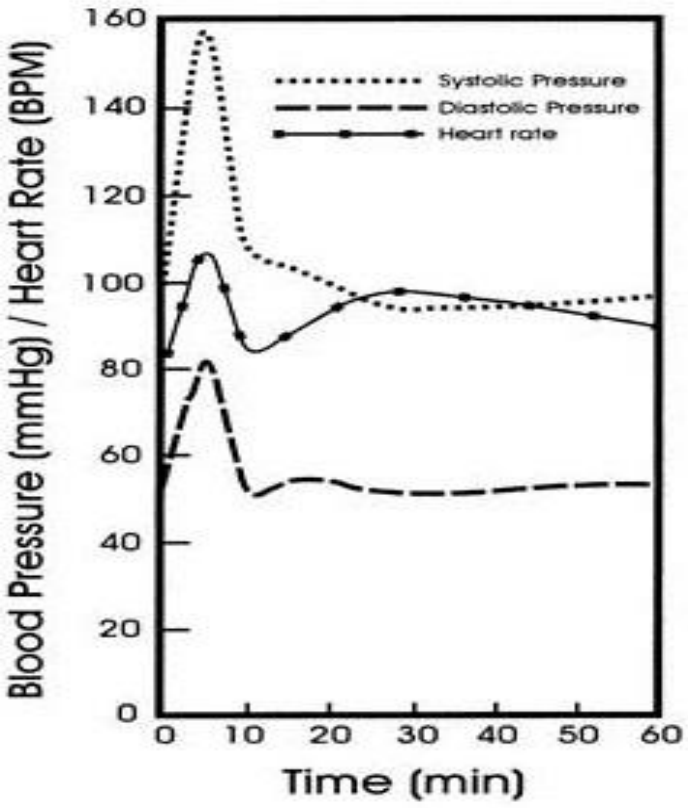
Management of Anaphylaxis



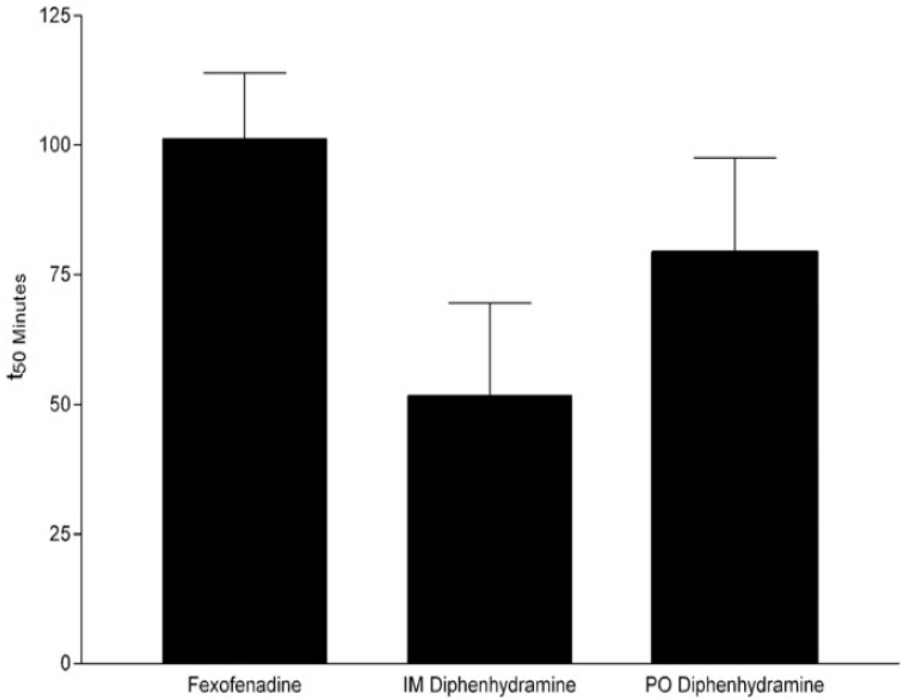
- Simons. Curr Opin All Clin Immunol 2010; 10: 354.

Management of Anaphylaxis

Epinephrine



Antihistamines



Simons. JACI 1998; 101: 33.

Jones. Ann All Asth Immunol 2008; 100(5): 458.

Medications for Anaphylaxis

TABLE 77-7 Drugs and Other Agents Used in Anaphylaxis Therapy

Drug	Dose/Route of Administration	Comment
EPINEPHRINE	Adult: 0.3-0.5 mL of 1:1000 dilution IM lateral thigh Child: 0.01 mg/kg or 0.1-0.3 mL of 1:1000 solution IM lateral thigh	Initial drug of choice for all anaphylactic episodes; should be given immediately; may repeat every 5-15 minutes
	0.1-1.0 mL (0.1-1.0 mg) of 1:1000 aqueous epinephrine diluted in 10 mL normal saline IV	
	Alternatively, epinephrine infusion prepared: 1 mg (1 mL) of 1:1000 dilution added to 250 mL D5W to yield concentration of 4.0 µg/mL. Solution infused at 1-4 µg/min (15-60 drops/min with microdrip) [60 drops/min = 1 mL = 60 mL/h], increasing to maximum 10 µg/min	If no response to IM administration and patient in shock with cardiovascular collapse
ANTIHISTAMINES		
Diphenhydramine	Adult: 25-50 mg IM or IV Child: 12.5-25 mg PO, IM, or IV	Route depends on episode severity
Cimetidine	Adult: 4 mg/kg IV	Cimetidine given slowly; rapid rate associated with hypotension
Ranitidine	Adult: 1 mg/kg IV	Child doses not well established
CORTICOSTEROIDS		
Hydrocortisone	Adult: 100 mg to 1 g IV or IM Child: 10-100 mg IV	Exact dose not established Methylprednisolone and other corticosteroids also used Prednisone, 30-60 mg, used for milder episodes
DRUGS FOR RESISTANT BRONCHOSPASM		
Aerosolized β-agonist: albuterol, metaproterenol	Dose as for asthma: 0.25-0.5 mL in 1.5-2 mL saline every 4 hours as needed	Useful for bronchospasm not responding to epinephrine
Aminophylline	Dose as for asthma	Rarely used for recalcitrant bronchospasm; β-agonist preferred
VOLUME EXPANDERS		
Crystalloids: normal saline, Ringer's lactate	Adult: 1000-2000 mL rapidly Child: 30 mL/kg in first hour	Rate titrated to BP response for IV volume expander After initial infusion, further administration requires tertiary care monitoring; larger amounts may be needed in β-blocked patients
Colloids (hydroxyethyl starch)	Adult: 500 mL rapidly, followed by slow infusion	
VASOPRESSORS		
Dopamine	400 mg in 500 mL D5W as IV infusion; 2-20 µg/kg/min	Dopamine probably drug of choice; rate titrated to BP response; continued infusion requires intensive care monitoring
DRUGS IN β-BLOCKED PATIENTS		
Atropine sulfate	Adult: 0.3-0.5 mg IV; may repeat every 10 minutes to maximum 2 mg	
Glucagon	Initial dose of 1-5 mg IV, followed by infusion of 5-15 µg/min titrated to BP response	Glucagon probably drug of choice, with atropine useful only for bradycardia
Ipratropium		As alternative or added to inhaled β-blockers for wheezing

BP, Blood pressure; *D5W*, dextrose 5% in water; *IM*, intramuscularly; *IV*, intravenously; *PO*, orally.

- Brown S. Middleton's Allergy Principle and Practice 8th Edition. Chapter 77. 2013.

Risk Factors for Poor Outcomes in Anaphylaxis

- Adolescent patients
- History of previous anaphylaxis
- History of peanut and/or tree nut allergy
- History of sub-optimally controlled asthma
- Delayed or lack of epinephrine administration

- Epinephrine is exceedingly safe and there have been few if any reports in the literature implicating epinephrine with significant adverse effects when used appropriately.

Community Survey (n =1385)

Reasons Epinephrine Not Used	
Used antihistamine	38%
Never given epinephrine rx	28%
Reaction was "mild"	13%
Used albuterol	8%
Did not have epinephrine on hand	8%
Unsure of when to administer epinephrine	8%
Previous reactions had been mild	8%
Afraid to inject epinephrine	6%

- Simons. JACI 2009; 124(2): 301., Wood. JACI 2014; 133(2): 461.

Points to Consider

- Previous reactions do NOT predict the severity of future reactions
- No diagnostic tools to predict the severity of reactions

- Absolute contraindication to epinephrine:
  - None!
- Relative contraindication to epinephrine:
  - None!
- Comorbidities to be aware of:
  - Coronary artery disease

Epinephrine Auto-Injectors

- Camargo. JACI In Prac 2013; 1(3): 266.

Patient Preference

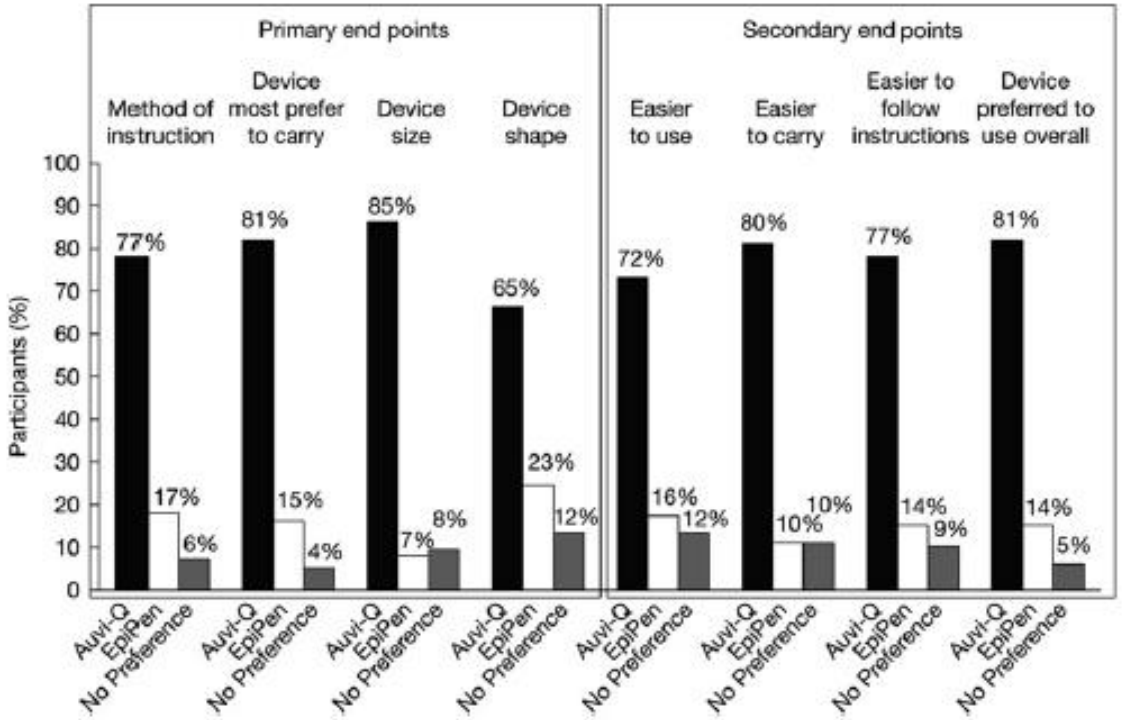


FIGURE 2. Preferences among all participants. All differences between Auvi-Q and EpiPen were significant ($P < .001$).

- Camargo. JACI In Prac 2013; 1(3): 266.

Mortality in the U.S.

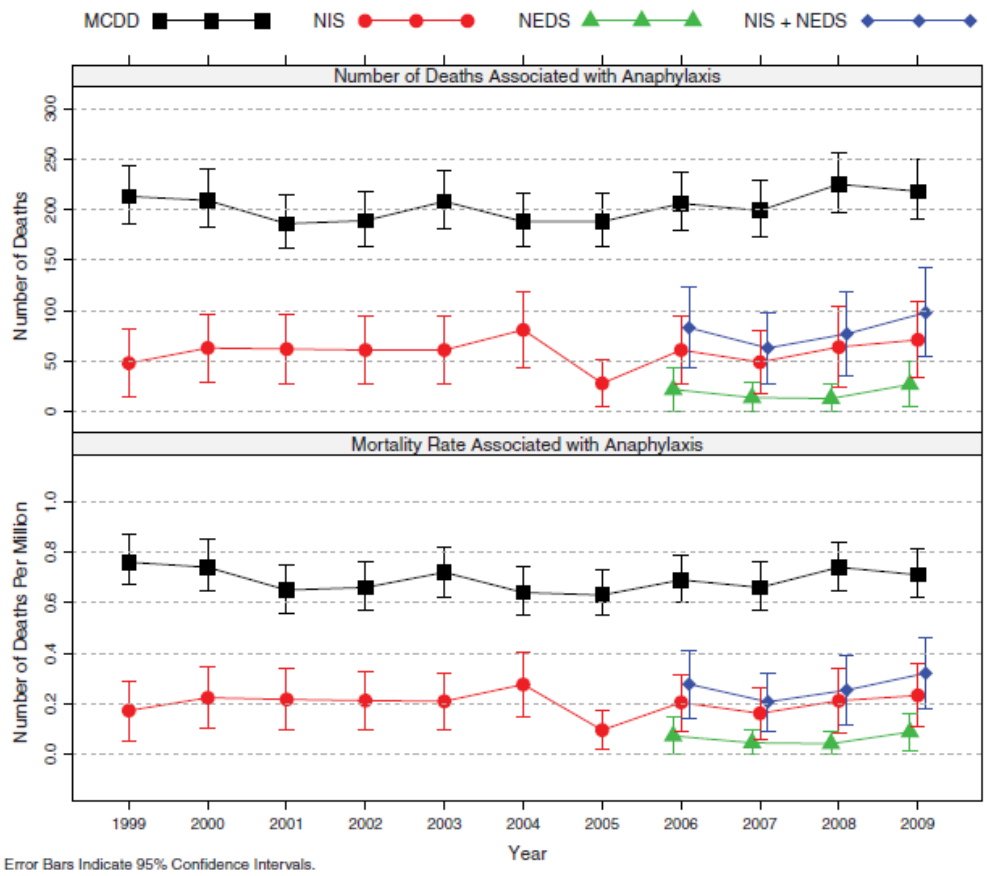


FIG 2. Mortality associated with anaphylaxis in the United States.

- Ma. JACI 2014; 133(4): 1075.

Summary

- Anaphylaxis is an acute, potentially life-threatening, systemic allergic reaction
- Common triggers include foods, stinging insects, allergen immunotherapy
- Epinephrine is the treatment of choice for anaphylaxis

Questions and Comments

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