# Anaphylaxis: Triggers & Treatments

ALISON HAYNES, MD, FRCPC

OCTOBER 4TH 2015

# OBJECTIVES

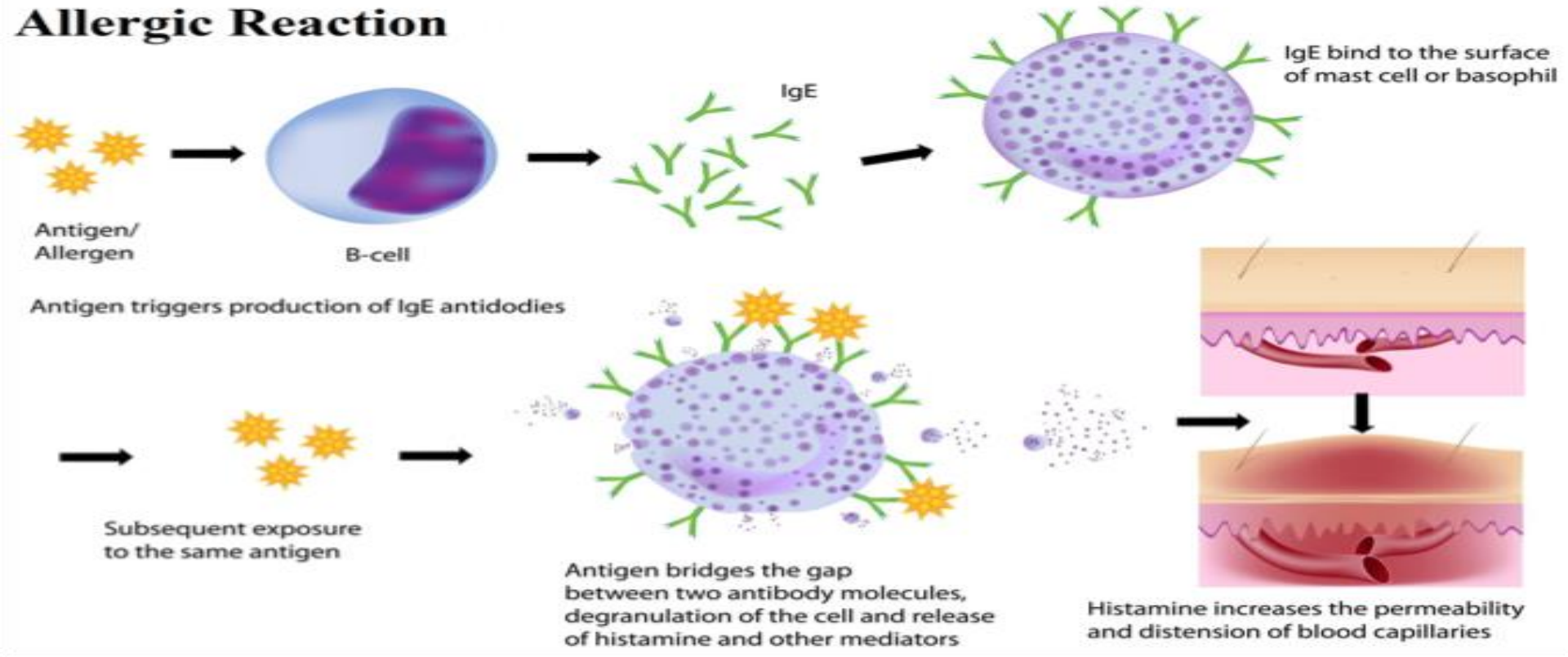
- Review common triggers for anaphylaxis presenting to the emergency department
- Discuss the evidence for treatment options commonly used to manage anaphylaxis
- Discuss key elements to include in the discharge planning for patients presenting with anaphylaxis

# CASE #1

- 6 month old male presents to the ER
  - Diffuse urticaria
  - Wheeze on auscultated
  - Vitals stable

# ANAPHYLAXIS

- Acute, potentially lethal, multisystem syndrome resulting from the release of mast cell / basophil derived mediators into the circulation



# ANAPHYLAXIS

- Lifetime prevalence of anaphylaxis from all triggers is estimated to be 0.05% to 2%

- Account for 2 to 4 per 1,000 pediatric emergency department visits in North America

Lieberman P, Camargo CA Jr, Bohlke K, Jick H, Miller RL, Sheikh A, et al. Ep- idemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. Ann Allergy Asthma Immunol 2006;97:596-602

Ben-Shoshan M, La Vieille S, Eisman H, et al. Anaphylaxis treated in a Cana- dian pediatric hospital: Incidence, clinical characteristics, triggers, and management. J Allergy Clin Immunol. 2013;132:739e741.e3

# DIAGNOSIS

- Histamine
  - 15 minutes to 1 hour of symptom onset
- Tryptase
  - 15 minutes to 3 hour of symptom onset
- Increased levels not specific for anaphylaxis
- Normal levels do not rule out anaphylaxis

# Anaphylaxis: diagnosis and treatment



## Clinical criteria for diagnosis

**Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:**

**1** **Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)**

**And at least one of the following:**

**Sudden respiratory symptoms and signs** (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)

**Sudden reduced BP or symptoms of end-organ dysfunction** (e.g. hypotonia [collapse], incontinence)

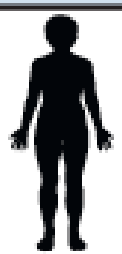
**Or** **2** **Two or more of the following that occur suddenly after exposure to a *likely allergen or other trigger* for that patient* (minutes to several hours):**

**Sudden skin or mucosal symptoms and signs** (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)

**Sudden respiratory symptoms and signs** (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)

**Sudden reduced BP or symptoms of end-organ dysfunction** (e.g. hypotonia [collapse], incontinence)

**Sudden gastrointestinal symptoms** (e.g. crampy abdominal pain, vomiting)

| | | |
|---|---|---|
| **Or** | **3** | **Reduced blood pressure (BP) after exposure to a *known allergen*** for that patient (minutes to several hours):** |
|  | **Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP***** |  **Adults: systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline** |

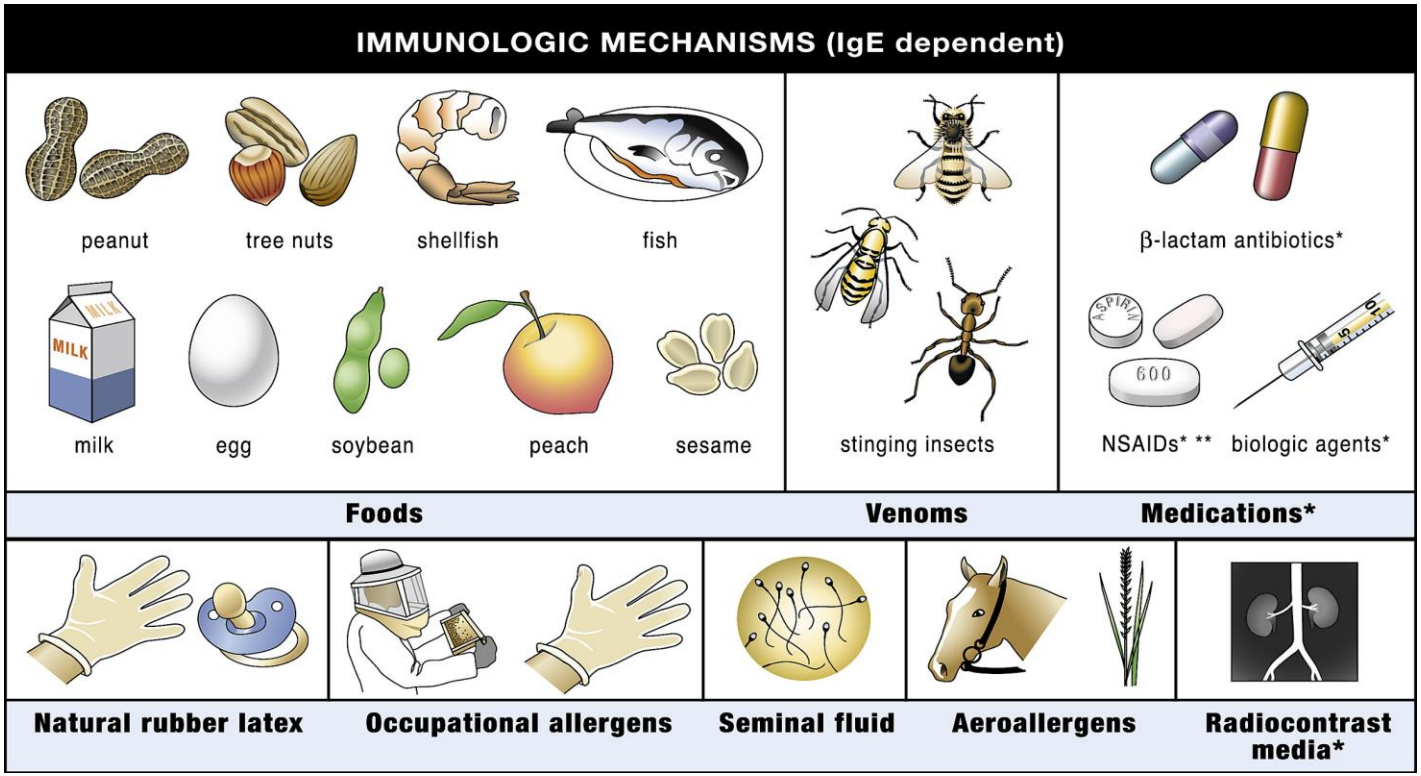

IMMUNOLOGIC MECHANISMS (IgE dependent)
peanut
tree nuts
shellfish
fish
milk
egg
soybean
peach
sesame
stinging insects
β-lactam antibiotics*
NSAIDs* **
biologic agents*
Foods
Venoms
Medications*
Natural rubber latex
Occupational allergens
Seminal fluid
Aeroallergens
Radiocontrast media*

**Table 3.** Clinical Presentation Among Children Presenting to the ED Who Met the Clinical Diagnostic Criteria for Anaphylaxis, Percentage (95% CI).[a]

| | Infants (<2 years), n = 191 | Preschool Aged (2-5 years), n = 171 | School Aged (6-11 years), n = 150 | Adolescents (12-18 years), n = 145 |
|---|---|---|---|---|
| Organ system involvement | | | | |
| Cutaneous | 98 (94-100) | 95 (90-99) | 92 (87-99) | 87 (78-96) |
| Respiratory | 59 (47-71) | 81 (72-89) | 70 (56-83) | 71 (58-83) |
| Gastrointestinal | 56 (44-67) | 50 (38-61) | 59 (45-72) | 59 (46-72) |
| Cardiovascular[b] | —[c] | —[c] | —[c] | 12 (4-20) |
| Signs and symptoms | | | | |
| Hives[b] | 89 (79-97) | 78 (69-88) | 64 (51-77) | 59 (46-72) |
| Swelling | 53 (41-65) | 56 (45-68) | 44 (30-57) | 36 (24-48) |
| Nausea/Vomiting[b] | 53 (41-65) | 34 (24-45) | 29 (17-42) | 17 (9-26) |
| Trouble breathing/ Shortness of breath | 37 (26-48) | 34 (23-45) | 39 (27-52) | 57 (44-70) |
| Wheezing[b] | 29 (20-39) | 55 (43-66) | 42 (29-56) | 23 (13-32) |
| Itching[b] | 19 (10-29) | 29 (18-40) | 54 (40-67) | 36 (24-48) |
| Stridor[b] | 5 (3-7) | 10 (2-18) | —[c] | —[c] |
| Dizziness/Fainting | 0 | 0 | —[c] | 12 (4-20) |
| Abdominal pain/Cramps | 0 | —[c] | 12 (3-21) | —[c] |
| Trouble swallowing[b] | —[c] | 18 (8-29) | 41 (27-55) | 48 (35-61) |
| Hoarse voice | —[c] | 12 (4-19) | —[c] | 13 (3-22) |
| Diarrhea | —[c] | 0 | 0 | —[c] |
| Altered mental state | —[c] | —[c] | —[c] | 0 |
| Angioedema | —[c] | —[c] | —[c] | —[c] |
| ED discharge diagnosis included the term *anaphylaxis*[b] | 6 (3-9) | 25 (14-37) | 13 (7-19) | 13 (1-24) |

Abbreviation: ED, emergency department.
[a]Reprinted from Rudders et al.[11] Copyright 2011, with permission from Elsevier.
[b]$P \leq .02$ across age groups.
[c]Not calculated because of insufficient number of observations.

# SEVERE / FATAL ANAPHYLAXIS

- Lethal anaphylaxis represents from 0.65 to 2% of cases of severe anaphylaxis
- 1 – 3 deaths per 1 million people
- 1500 deaths per year in the United States

Moneret – Vautrin et al. Epidemiology of life threatening and lethal anaphylaxis: a review. Allergy 2005:60;443-451

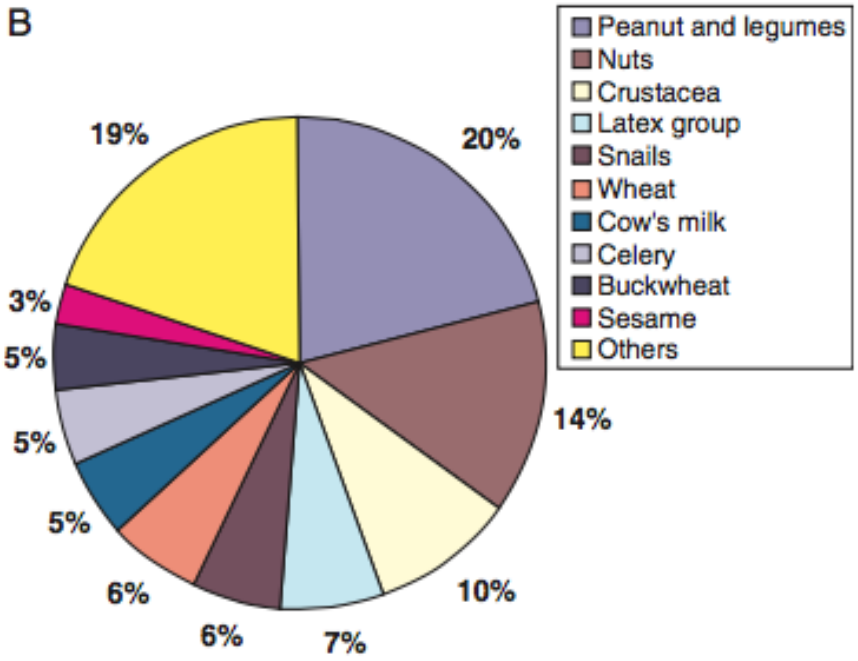
# SEVERE / FATAL ANAPHYLAXIS

- Median times to cardiac arrest
  - 5 minutes iatrogenic anaphylaxis
  - 15 minutes venom induced anaphylaxis
  - 20 minutes for medications taken outside the hospital
  - 30 minutes food induced anaphylaxis

Pumphrey, R.S. Lessons for management of anaphylaxis from a study of fatal reactions. Clin Exp Allergy. 2000;30:1144-50

# SEVERE / FATAL ANAPHYLAXIS

- Physiologic changes
  - Distributive shock from reduced total peripheral resistance and permeable capillaries
  - Angioedema of the tongue, oropharynx, or larynx
  - Arrhythmias with or without myocardial infarction
  - Severe bronchoconstriction




Moneret – Vautrin et al. Epidemiology of life threatening and lethal anaphylaxis: a review. Allergy 2005:60;443-451

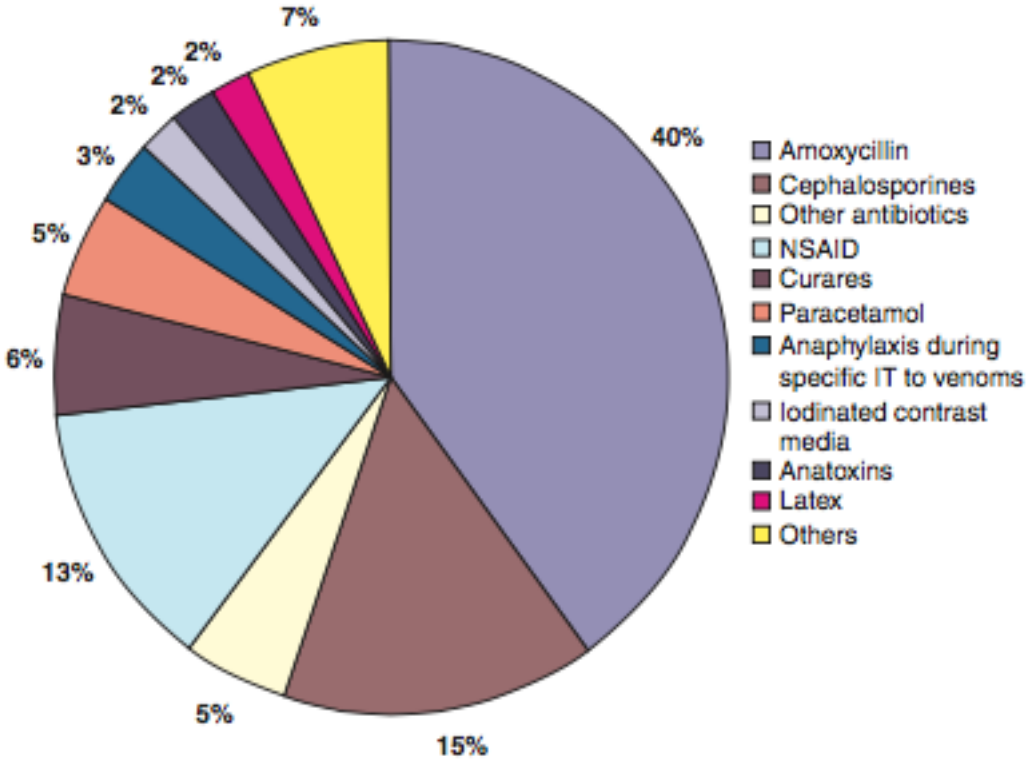



*Figure 2.* Aetiologies of 100 cases of life-threatening drug anaphylaxis registered by the Allergo Vigilance Network over 2003/2004 (%).

Moneret – Vautrin et al. Epidemiology of life threatening and lethal anaphylaxis: a review. Allergy 2005:60;443-451

# RISK OF SEVERE/ FATAL ANAPHYLAXIS

- Age
  - Infants
  - Adolescents
- Medical conditions
  - Asthma and other cardiorespiratory diseases
  - Mastocytosis
- Medications
  - B blockers
  - ACE inhibitors

# RISK OF SEVERE / FATAL ANAPHYLAXIS

- Sudden change in patient position
  - Leads to reduced blood flow back to the right ventricle and reduced cardiac output
  - Termed empty ventricle syndrome
  - Position patient with legs elevated to try to make the inferior vena cava the most dependent vessel

# RISK OF SEVERE / FATAL ANAPHYLAXIS

- Delayed use of epinephrine

**Table 3. Timing of Fatal Food-Induced Anaphylactic Reactions.**

| Patient No. | Setting | Initial Onset of Symptoms | Time of Epinephrine Dose | Onset of Severe Symptoms | Type of Symptoms | Time of Death |
|---|---|---|---|---|---|---|
| | | *min after ingestion* | | | | *min after ingestion* |
| 1 | School | 10 | 125 | 125 | Gastrointestinal, respiratory | 180 |
| 2 | School* | 20 | 80 | 65 | Gastrointestinal, respiratory | 95 |
| 3 | School | 20 | 180 | 150 | Gastrointestinal, respiratory | 300 |
| 4 | Fair | 30 | 60 | 35 | Skin, respiratory | 105 |
| 5 | School | 30 | 90 | 35 and 100† | Gastrointestinal, respiratory | 240 |
| 6 | Home | 3 | 25 | 20 | Gastrointestinal, respiratory | 120 |

*The symptoms began at home.

†The severe symptoms subsided after treatment with supplemental oxygen and then recurred.

Sampson et al. Fatal and near fatal anaphylactic reactions to food in children and adolescence. N Engl J Med 1992;327:380-4

# RISK OF SEVERE / FATAL ANAPHYLAXIS

- Delayed use of epinephrine

**Table 4. Timing of Near-Fatal Food-Induced Anaphylactic Reactions.**

| Patient No. | Setting | Initial Onset of Symptoms | Time of Epinephrine Dose | Onset of Severe Symptoms | Type of Symptoms | Time of Intubation | Duration of Intubation |
|---|---|---|---|---|---|---|---|
| | | | *min after ingestion* | | | *min after ingestion* | |
| 7 | Friend's house | 5 | 25 | 80 | Skin, respiratory | 90 | 6 hr |
| 8 | Friend's house | 2 | 130 | 130 | Gastrointestinal, respiratory, skin | 155 | 2 hr |
| 9 | Vacation home | 5 | 30 | 60 | Skin, gastrointestinal, respiratory | 70 | 3 days |
| 10 | Relative's house | 1 | 15 | 30 | Skin, respiratory | 40 | 2 wk |
| 11 | Home | 3 | 10 | 15 | Skin, respiratory | 45 | 14 hr |
| 12 | Home | 2 | 15 | 12 | Skin, gastrointestinal, respiratory | 40 | 3 wk |
| 13 | Relative's house | 5 | 30 | 25 | Respiratory, skin | 65 | 10 hr |

Sampson et al. Fatal and near fatal anaphylactic reactions to food in children and adolescence. N Engl J Med 1992;327:380-4

# Anaphylaxis: diagnosis and treatment



## Initial treatment

**1** **Have a written emergency protocol** for recognition and treatment of anaphylaxis and rehearse it regularly.

**2** **Remove exposure to the trigger** if possible, e.g. discontinue an intravenous diagnostic or therapeutic agent that seems to be triggering symptoms.

**3**

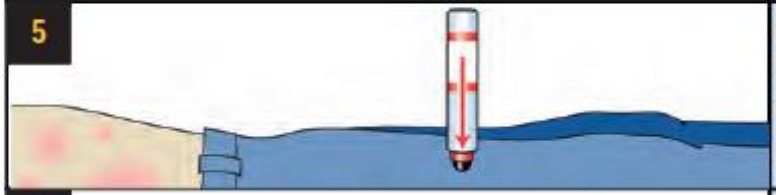
**Assess the patient's circulation, airway, breathing, mental status, skin and body weight** (mass).

**Promptly and simultaneously, perform steps 4, 5 and 6.**

**4**

**Call for help:** resuscitation team (hospital) or emergency medical services (community) if available.

**5**

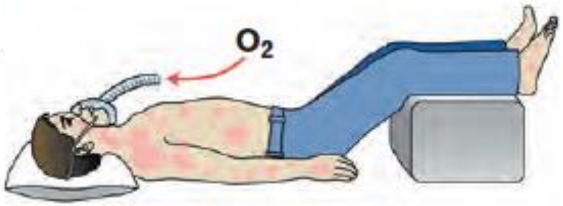


**Inject epinephrine** (adrenaline) intramuscularly in the mid-anterolateral aspect of the thigh, 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, maximum of 0.5 mg (adult) or 0.3 mg (child); **record the time of the dose and repeat it** in 5–15 minutes, if needed. Most patients respond to 1 or 2 doses.

**6**

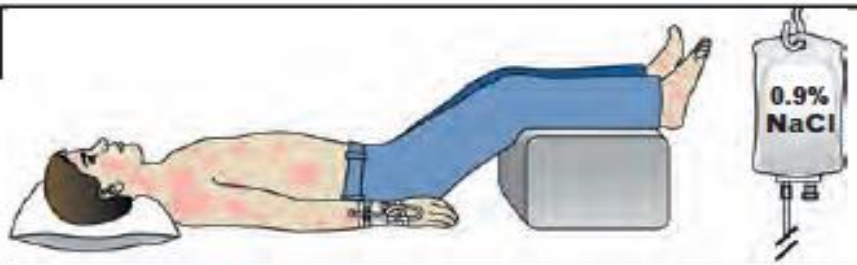
**Place patient on the back** or in a position of comfort if there is respiratory distress and/or vomiting; **elevate the lower extremities;** fatality can occur within seconds if patient stands or sits suddenly.

**7**



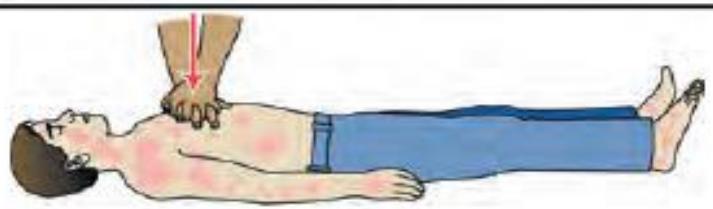

**When indicated, give high-flow supplemental oxygen** (6-8 L/minute), by face mask or oropharyngeal airway.

**8**




**Establish intravenous access** using needles or catheters with wide-bore cannulae (14 - 16 gauge): **When indicated, give 1–2 litres of 0.9% (isotonic) saline rapidly** (e.g. 5-10 ml/kg in the first 5-10 minutes to an adult; 10 ml/kg to a child).

**9**



**When indicated, at any time, perform cardiopulmonary resuscitation** with continuous chest compressions and rescue breathing.

**In addition,**

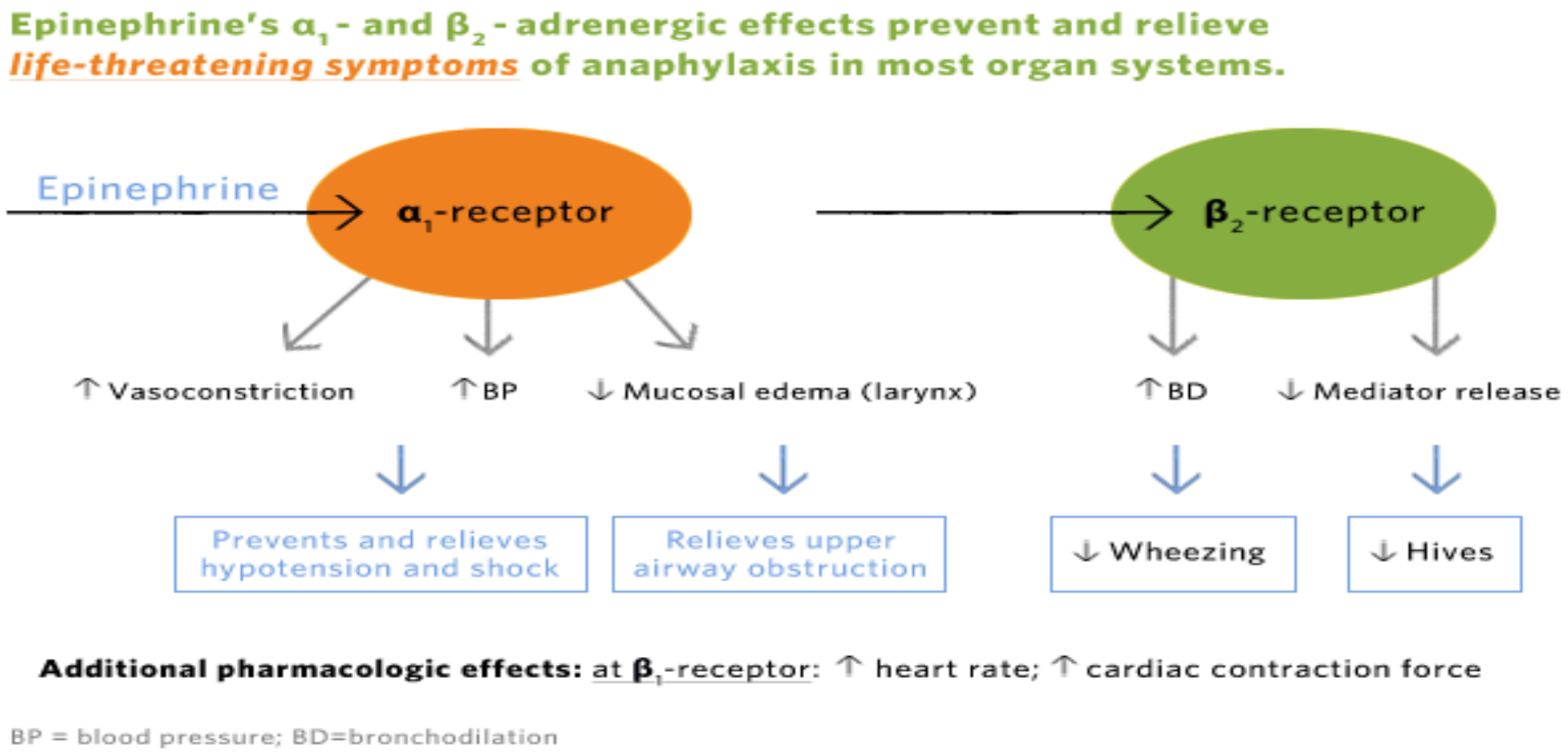
**10**

**At frequent, regular interval, monitor patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation** (monitor continuously, if possible).

*References: Simons FER et al, for the WAO. J Allergy Clin Immunol 2011;127:587-93.e22 and WAO Journal 2011;4:13-36. Illustrator: J Schaffer*

# EPINEPHRINE

- 0.01 mg/kg of 1:1,000 dilution to a max dose of 0.5 mg



# EPINEPHRINE

- Intramuscular is preferred route of delivery
- Dose can be repeated every 5 to 15 minutes, as needed
- Second dose required in 10 – 20% of patients

**TABLE II.** Setting and total number of epinephrine doses in patients presenting to the emergency department with anaphylaxis

| | Patients receiving 0 or 1 epinephrine dose (n = 537) | | Patients receiving ≥2 epinephrine doses (n = 45) | |
|---|---|---|---|---|
| **Variable** | **No. (%)** | **95% CI** | **No. (%)** | **95% CI** |
| Epinephrine doses received, No. | | | | |
| 0 | 256 (48) | 43-52 | - | - |
| 1 | 281 (52) | 48-57 | - | - |
| 2 | - | - | 36 (80) | 65-90 |
| 3 | - | - | 6 (13) | 6-27 |
| 4 | - | - | 2 (4) | 1-16 |
| 5 | - | - | 1 (2) | 0-13 |
| ≥2 doses total | - | - | 45 (100) | 90-100 |
| Setting of first epinephrine dose* | | | | |
| Home/self | 33 (12) | 8-16 | 16 (36) | 22-51 |
| EMS | 44 (16) | 12-21 | 17 (38) | 24-53 |
| ED/EDOU | 204 (73) | 67-78 | 12 (27) | 15-42 |

*ED*, Emergency department; *EDOU*, emergency department observation unit; *EMS*, emergency medical services.

*Calculations are based on 281 patients who received 1 dose of epinephrine, or 45 who received 2 or more doses.

Campbell et al. Predictors of repeat epinephrine administration for emergency department patients with anaphylaxis. J Allergy Clin Immunol Pract. 2015;3:576-84

**TABLE III.** Univariable associations among clinical features and repeat epinephrine treatment of emergency department anaphylaxis patients

| Variable | Patients receiving 0 or 1 epinephrine dose (n = 537)* | Patients receiving ≥2 epinephrine doses (n = 45)* | OR (95% CI) | *P* value† |
|---|---|---|---|---|
| Demographics | | | | |
| Age, median (IQR), y | 33 (17-52) | 41 (25-49) | 1.0 (0.9-1.2)‡ | .55 |
| Pediatric patients (<18 y) | 145 (27) | 8 (18) | 0.6 (0.3-1.3) | .18 |
| Adult patients (≥18 y) | 392 (73) | 37 (82) | 1.7 (0.8-3.8) | .18 |
| Female sex | 309 (58) | 30 (67) | 1.5 (0.8-2.8) | .24 |
| History | | | | |
| Anaphylaxis | 111 (21) | 19 (42) | 2.8 (1.5-5.3) | .001 |
| Food allergy | 189 (35) | 19 (42) | 1.3 (0.7-2.5) | .35 |
| Asthma | 128 (24) | 19 (42) | 2.3 (1.3-4.4) | .008 |
| Seasonal allergy | 84 (16) | 11 (24) | 1.7 (0.9-3.6) | .13 |
| Trigger | | | | |
| Food | 196 (36) | 13 (29) | 0.7 (0.4-1.4) | .31 |
| Medication | 102 (19) | 8 (18) | 0.9 (0.4-2.0) | .84 |
| Venom | 65 (12) | 7 (16) | 1.3 (0.6-3.1) | .50 |
| Other | 51 (9) | 4 (9) | 0.9 (0.3-2.7) | .89 |
| Unknown | 123 (23) | 13 (29) | 1.4 (0.7-2.7) | .36 |

Campbell et al. Predictors of repeat epinephrine administration for emergency department patients with anaphylaxis. J Allergy Clin Immunol Pract. 2015;3:576-84

| | | | | |
|---|---|---|---|---|
| Symptoms | | | | |
| Mucocutaneous | 532 (99) | 45 (100) | 0.6 (0.1-infinity) | 1.0‡ |
| Flushing/diaphoresis | 173 (32) | 25 (56) | 2.6 (1.4-4.9) | .002 |
| Pruritus | 244 (45) | 15 (33) | 0.6 (0.3-1.1) | .12 |
| Diffuse urticaria | 213 (40) | 18 (40) | 1.0 (0.5-1.9) | .96 |
| Throat tightness | 252 (47) | 26 (58) | 1.5 (0.8-2.9) | .16 |
| Angioedema | 289 (54) | 29 (64) | 1.6 (0.8-2.9) | .17 |
| Respiratory | 450 (84) | 42 (93) | 2.7 (0.8-8.9) | .10 |
| Dyspnea | 357 (66) | 37 (82) | 2.3 (1.1-5.1) | .04 |
| Wheezing | 130 (24) | 17 (38) | 1.9 (1.0-3.6) | .047 |
| Stridor | 18 (3) | 2 (4) | 1.3 (0.3-6.0) | .70 |
| Hypoxemia | 24 (4) | 5 (11) | 2.7 (1.0-7.4) | .058 |
| Gastrointestinal | 205 (38) | 11 (24) | 0.5 (0.3-1.1) | .07 |
| Emesis | 97 (18) | 9 (20) | 1.1 (0.5-2.4) | .75 |
| Nausea | 130 (24) | 9 (20) | 0.8 (0.4-1.7) | .53 |
| Abdominal pain | 65 (12) | 4 (9) | 0.7 (0.2-2.0) | .52 |
| Diarrhea | 30 (6) | 4 (9) | 1.6 (0.6-4.9) | .37 |
| Cardiovascular | 195 (36) | 21 (47) | 1.5 (0.8-2.8) | .17 |
| Hypotension | 43 (8) | 8 (18) | 2.5 (1.1-5.7) | .03 |
| Presyncope | 111 (21) | 9 (20) | 1.0 (0.4-2.1) | .92 |
| Syncope | 33 (6) | 4 (9) | 1.5 (0.5-4.4) | .47 |
| Incontinence | 7 (1) | 0 (0) | 1.2 (0.0-6.5) | 1.0§ |

Campbell et al. Predictors of repeat epinephrine administration for emergency department patients with anaphylaxis. J Allergy Clin Immunol Pract. 2015;3:576-84

# EPINEPHRINE

- IV infusion if symptoms continue despite 3 intramuscular injections
- Epinephrine 1:10,000
- 0.1 - 1mcg/kg/min infusion, titrated to effect on BP
- Continuous slow infusion preferred over bolus

# EPINEPHRINE

- Apparent lack of response to epinephrine
  - Error in diagnosis
  - Error in dosage
  - Suboptimal route
  - Empty ventricle syndrome
  - Medication that interferes with epinephrine

# VOLUME REPLACEMENT

- Indicated for hypotension in anaphylaxis that persists despite epinephrine
  - 35% of intravascular volume can shift into the extravascular space within 10 min of anaphylaxis
- Normal saline is preferred solution

# SECOND LINE MEDICATIONS

- H1 antihistamines
- H2 antihistamines
- Bronchodilators
- Corticosteroids

# H1 ANTIHISTAMINES

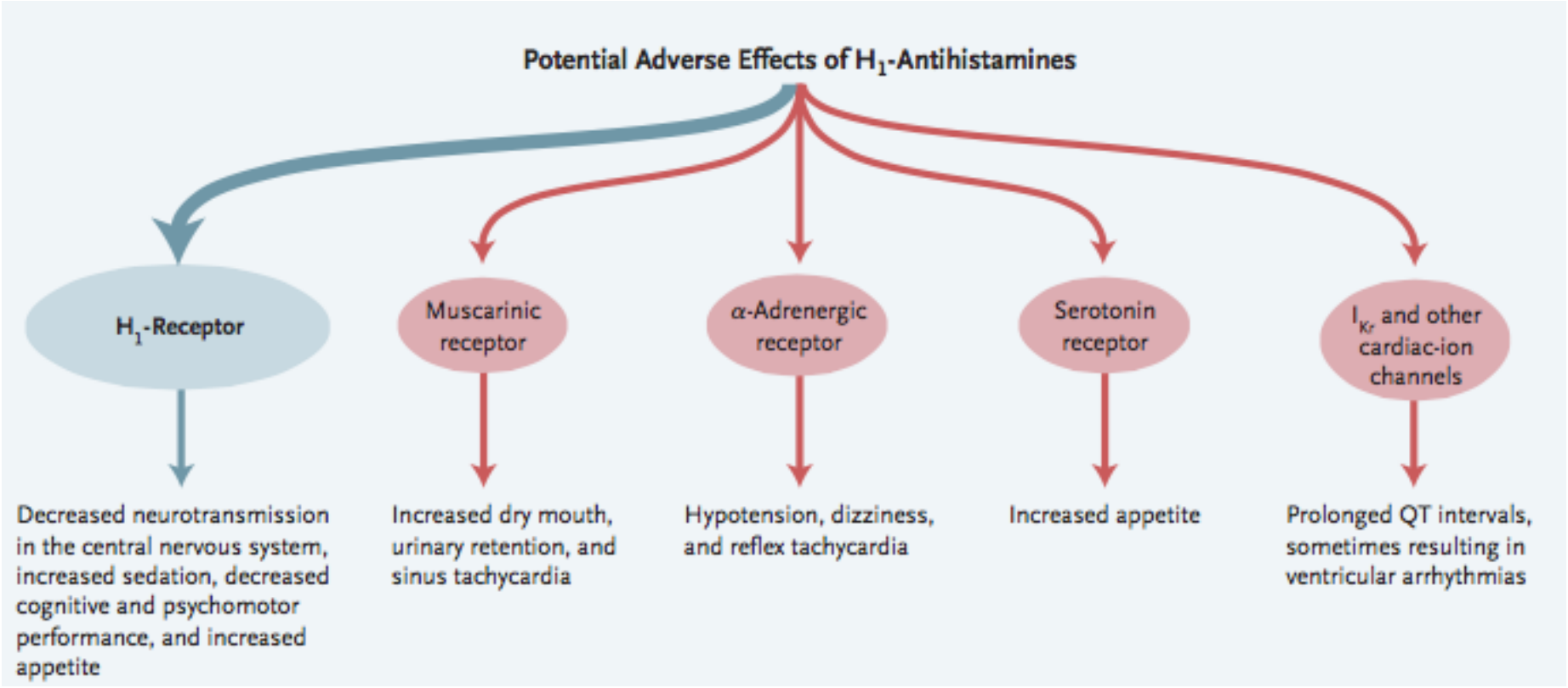
- Systematic review concluded a lack of evidence-based recommendations for the use of $H_1$-antihistamines in the treatment of anaphylaxis

- Use of antihistamines is the most common reason for nonadministration of epinephrine

Sheikh A, Ten Broek V, Brown SGA, Simons FER. H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. Allergy. 2007;62: 830-837.

# H1 ANTIHISTAMINES

- Do not prevent ongoing histamine release from mast cells and basophils
- Slow onset of action
  - Oral diphenhydramine takes up to 80 min for 50% suppression of the histamine flare and 52 min if administered intramuscularly




Simons. Advances in HI antihistamines. N Engl J Med 2004;351:2203-17

# H1 ANTIHISTAMINES

- H1- antihistamines do NOT prevent or relieve
  - Upper or lower airway obstruction
  - Hypotension or shock

- H1- antihistamines will
  - Relieve itching, hives, other cutaneous symptoms, and rhinorrhea

# H2 ANTIHISTAMINES

- Systematic review concluded that they were unable to make any evidence-based recommendations for the use of $H_2$-antihistamines in the treatment of anaphylaxis

- May provide some additional relief of hives

Nurmatov et al. $H_2$-antihistamines for the treatment of anaphylaxis with and without shock: a systematic review. Ann Allergy Asthma Immunol 2014; 112:126–131

# BRONCHODILATORS

- Adjunctive measure to relieve residual bronchospasm that has not disappeared after epinephrine injection

# CORTICOSTEROIDS

- Systematic review concluded that they were unable to make any evidence-based recommendations for the use of corticosteroids in the treatment of anaphylaxis
  - Acute management of anaphylaxis
  - Prevention of biphasic reactions

- Used in 50-97% cases of anaphylaxis

Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. Cochrane Database Syst Rev 2010

# CORTICOSTEROIDS

- Slow onset of action
  - Median time to max serum concentration is 1–2 h
- Glucocorticoids will
  - Help relieve bronchospasms
- Glucocorticoids do NOT
  - Relieve upper airway obstruction
  - Increase peripheral vascular resistance
  - Effects on preventing biphasic reactions are debatable

# BIPHASIC REACTIONS

- Recurrence of symptoms after resolution of the initial manifestations
- Typically occur within 8 to 10 hours
- Biphasic reactions up to 72hrs later reported
- 6% to 11% of children

Lee JM, Greenes DS. Biphasic anaphylactic reactions in pediatrics. Pediatrics. 2000;106:762-766

**Table 1**
Characteristics of patients who developed biphasic reactions (n = 71)

| Characteristics | |
|---|---|
| Demographics | |
| Age (y), median (IQR) | 6 (2.7–10.1) |
| Age range (y), n (%) | |
| <2 | 11 (15.5) |
| 2–5 | 24 (33.8) |
| 6–9 | 18 (25.4) |
| 10–13 | 10 (14.1) |
| ≥14 | 8 (11.3) |
| Boys, n (%) | 51 (71.8) |
| Arrival status | |
| Arrival by ambulance, n (%) | 20 (28.2) |
| Heart rate (beats/min), mean (SD) | 117.4 (27.3) |
| Respiratory rate (breaths/min), mean (SD) | 26.8 (7.7) |
| Systolic blood pressure (mmHg), mean (SD) | 108.1 (13.5) |
| Diastolic blood pressure (mmHg), mean (SD) | 61.7 (13.9) |
| $SaO_2$ by oximetry, median (IQR) | 99 (97–100) |
| Onset of biphasic reactions, n (%)[a] | |
| Before ED discharge | 53 (74.6) |
| After ED discharge | 18 (25.4) |
| Time (h) from onset of initial reaction to onset of biphasic reaction, median (IQR) | |
| Before ED discharge | 4.7 (3.3–6) |
| After ED discharge | 18.5 (9.2–25.2) |

Alqurashi et al. Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis. Ann Allergy Asthma Immunol 2015;115:217-223

| | |
|---|---|
| Clinical manifestations of biphasic reactions, n (%) | |
| Cutaneous | 59 (85.5) |
| Respiratory | 28 (40) |
| Cardiac | 21 (29.9) |
| Gastrointestinal | 8 (11.3) |
| Treatment given in ED for biphasic reactions, n (%) | |
| Oxygen | 7 (9.8) |
| Epinephrine | 35 (49.3) |
| Inhaled β-agonists | 13 (18.3) |
| $H_1$ antihistamine | 47 (66.2) |
| $H_2$ antihistamine | 16 (22.5) |
| Systemic steroids | 27 (38) |
| Intravenous fluid | 12 (16.9) |
| Magnesium sulfate infusion | 1 (1.4) |

Alqurashi et al. Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis. Ann Allergy Asthma Immunol 2015;115:217-223

**eTable 3**

Univariate correlation with biphasic reaction for variables from therapy administered for 484 anaphylaxis episodes[a]

| Variable | Biphasic (n = 71) | Uniphasic (n = 413) | *P* value |
|---|---|---|---|
| Oxygen in ED, n (%) | 8 (11.3) | 17 (4.1) | .02 |
| Bag mask ventilation/oral airway, n (%) | 2 (1.4) | 0 | 1 |
| Intubation, n (%) | 1 (0.2) | 0 | 1 |
| Epinephrine | | | |
| Administered, n (%) | 55 (77.5) | 254 (61.5) | .01 |
| Number of doses, mean (SD)[b] | 1.13 (0.34) | 1.10 (0.34) | .56 |
| >1 dose administered, n (%) | 10 (14.1) | 27 (6.5) | .03 |
| Total dose administered (mg), median (IQR) | 0.25 (0.15–0.3) | 0.20 (0.15–0.3) | .01 |
| Route of administration, n (%) | | | |
| Intramuscular | 54 (98) | 247 (97) | 1 |
| Subcutaneous | 1 (2) | 7 (3) | |
| Setting of first administered dose, n (%) | | | |
| Scene of reaction by caregiver | 24 (43.6) | 105 (41.3) | .79 |
| During transport by EMS paramedics | 5 (9.1) | 18 (7.1) | |
| ED | 26 (47.3) | 131 (51.6) | |
| Time (min) from onset of reaction to first dose, median (IQR) | 64 (25–175) | 59 (25–105) | .35 |
| Inhaled $\beta$-agonists in ED, n (%) | 23 (32.4) | 78 (18.8) | .02 |
| $H_1$ antihistamine | | | |
| Administered, n (%) | 59 (83.1) | 337 (81.6) | .87 |
| Total dose administered (mg/kg), mean (SD) | 0.80 (0.47) | 0.78 (0.51) | .76 |
| $H_2$ antihistamine in ED | | | |
| Administered, n (%) | 14 (19.7) | 67 (16.2) | .49 |
| Total dose administered (mg/kg), mean (SD) | 1.7 (0.9) | 2 (1.2) | .48 |
| Time (min) from onset of reaction to first dose, median (IQR) | 126 (99–184) | 120 (79–180) | .51 |
| Systemic steroids in ED | | | |
| Administered, n (%) | 43 (60.6) | 209 (50.6) | .13 |
| Total dose administered (mg/kg), median (IQR)[c] | 1.55 (1–2.2) | 1.85 (1–2.2) | .99 |
| Time (min) from onset of reaction to first dose, median (IQR) | 120 (87–256) | 125 (85–205) | .93 |
| Formulation, n (%) | | | |
| Dexamethasone | 18 (41.9) | 114 (54.5) | .30 |
| Hydrocortisone | 4 (9.3) | 17 (8.1) | |
| Methylprednisolone | 9 (20.9) | 24 (11.5) | |
| Prednisolone | 12 (27.9) | 54 (25.8) | |
| Intravenous fluid in ED | | | |
| Administered, n (%) | 21 (30) | 30 (7.3) | <.001 |
| Total dose administered (mL/kg), median (IQR) | 18.8 (14.4–20) | 12.6 (6.4–20) | .11 |

**Table 3**

Independent predictors of biphasic reaction as determined by stepwise logistic regression analysis for anaphylaxis episodes[a]

| Variable | β | *P* value | Odds ratio | 95% CI |
|---|---|---|---|---|
| Age 6–9 y | 1.28 | .01 | 3.60 | 1.5–8.58 |
| Delay in presentation to ED >90 min from onset of initial reaction | 0.95 | .001 | 2.58 | 1.47–4.53 |
| Wide pulse pressure at triage[b] | 1.07 | <.001 | 2.92 | 1.69–5.04 |
| Treatment of initial reaction with >1 dose of epinephrine | 0.99 | .03 | 2.70 | 1.12–6.55 |
| Administration of inhaled β-agonists in ED | 0.87 | .01 | 2.39 | 1.24–4.62 |
| Intercept | −3.36 | <.001 | 0.04 | |

Abbreviations: CI, confidence interval; ED, emergency department.

[a]Model developed for 481 patients without missing values (Hosmer-Lemeshow goodness-of-fit test 0.697, area under receiver operating characteristic curve 0.742, 95% CI 0.682–0.803).

[b]Defined as diastolic blood pressure that is lower than or equal to half the systolic blood pressure.

Alqurashi et al. Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis. Ann Allergy Asthma Immunol 2015;115:217-223

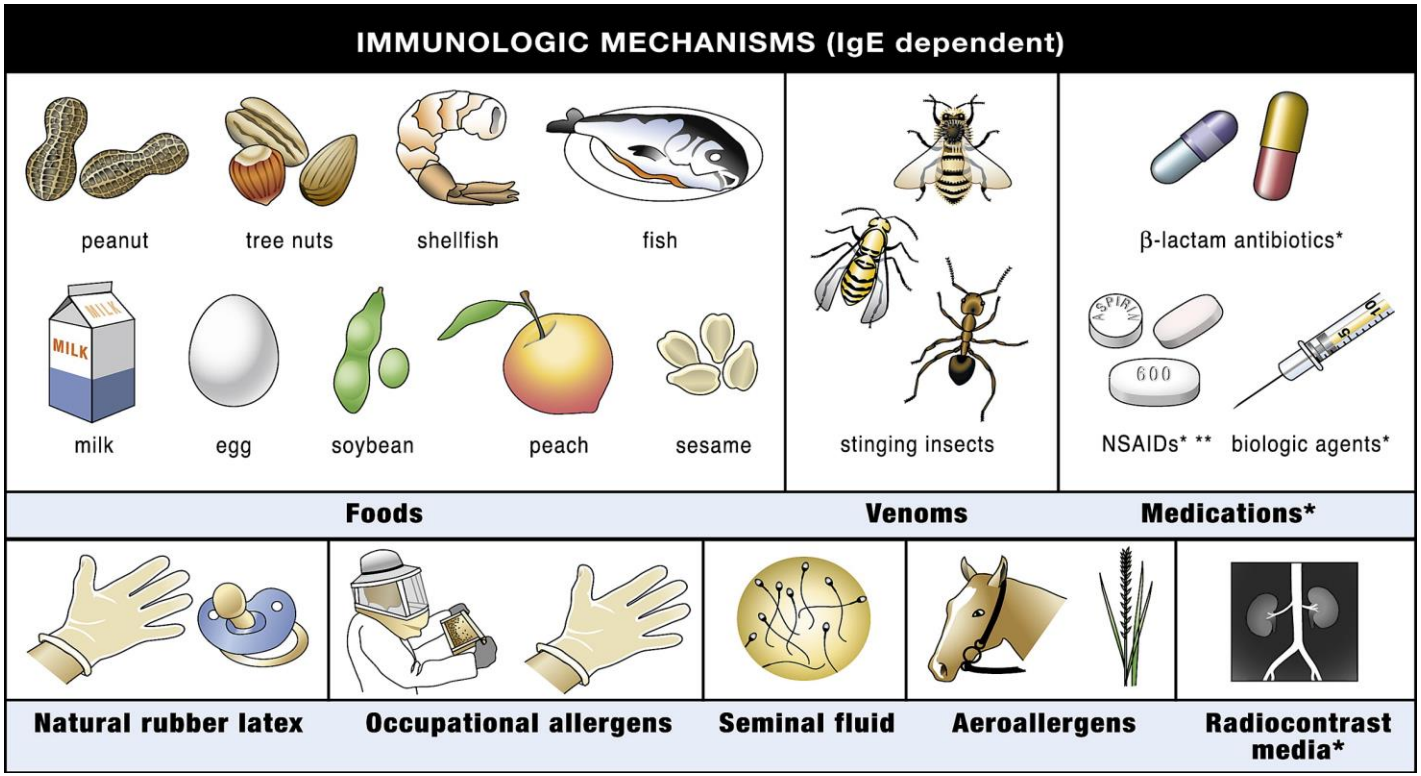
# CASE #1

- 6 month old male presents to the ER
  - First exposure to peanut 10 minutes prior to onset of symptoms
  - Managed with 1 dose of epinephrine in the ED
  - Symptoms resolved within 15 minutes

# DISCHARGE PLANNING

- Trigger avoidance
- Epinephrine autoinjector
- Written anaphylaxis plan
- Referral to certified allergist

# AVOIDANCE


IMMUNOLOGIC MECHANISMS (IgE dependent)
peanut
tree nuts
shellfish
fish
milk
egg
soybean
peach
sesame
stinging insects
β-lactam antibiotics*
NSAIDs* **
biologic agents*
Foods
Venoms
Medications*
Natural rubber latex
Occupational allergens
Seminal fluid
Aeroallergens
Radiocontrast media*

# EPINEPHRINE AUTOINJECTOR

- All patients should be discharged with an epinephrine autoinjector
- Dosing
  - Regular 0.3mg for patients > 25 kg
  - Junior 0.15mg for patients < 25kg
- Demonstrate use of the autoinjector to patients

# Anaphylaxis Emergency Plan: _____ *(name)*

## This person has a potentially life-threatening allergy (anaphylaxis) to:

PHOTO

*(Check the appropriate boxes.)*

☐ Food(s): _____

_____

_____

☐ Insect stings

☐ Other: _____

**Epinephrine Auto-Injector:** Expiry Date: _____ / _____

**Dosage:**

☐ EpiPen® Jr. 0.15 mg ☐ EpiPen® 0.30 mg ☐ Allerject™ 0.15 mg ☐ Allerject™ 0.30 mg

**Location of Auto-Injector(s):** _____

☐ **Previous anaphylactic reaction:** Person is at greater risk.

☐ **Asthmatic:** Person is at greater risk. If person is having a reaction and has difficulty breathing, give epinephrine auto-injector before asthma medication.

## A person having an anaphylactic reaction might have ANY of these signs and symptoms:

- **Skin system:** hives, swelling (face, lips, tongue), itching, warmth, redness
- **Respiratory system (breathing):** coughing, wheezing, shortness of breath, chest pain or tightness, throat tightness, hoarse voice, nasal congestion or hay fever-like symptoms (runny, itchy nose and watery eyes, sneezing), trouble swallowing
- **Gastrointestinal system (stomach):** nausea, pain or cramps, vomiting, diarrhea
- **Cardiovascular system (heart):** paler than normal skin colour/blue colour, weak pulse, passing out, dizziness or lightheadedness, shock
- **Other:** anxiety, sense of doom (the feeling that something bad is about to happen), headache, uterine cramps, metallic taste

*Early recognition of symptoms and immediate treatment could save a person's life.*

## Act quickly. The first signs of a reaction can be mild, but symptoms can get worse very quickly.

1. **Give epinephrine auto-injector** (e.g. EpiPen® or Allerject™) at the first sign of a known or suspected anaphylactic reaction. (See attached instruction sheet.)
2. **Call 9-1-1** or local emergency medical services. Tell them someone is having a life-threatening allergic reaction.
3. **Give a second dose of epinephrine** as early as 5 minutes after the first dose if there is no improvement in symptoms.
4. **Go to the nearest hospital immediately (ideally by ambulance),** even if symptoms are mild or have stopped. The reaction could worsen or come back, even after proper treatment. Stay in the hospital for an appropriate period of observation as decided by the emergency department physician (generally about 4-6 hours).
5. **Call emergency contact person (e.g. parent, guardian).**

## Emergency Contact Information

| Name | Relationship | Home Phone | Work Phone | Cell Phone |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |

*The undersigned patient, parent, or guardian authorizes any adult to administer epinephrine to the above-named person in the event of an anaphylactic reaction, as described above. This protocol has been recommended by the patient's physician.*

Patient/Parent/Guardian Signature _____ Date _____

Physician Signature ☐ On file _____ Date _____

# REFERRAL TO AN ALLERGIST

- History is the most important tool!
- Skin testing 4 – 6 weeks after anaphylaxis
- Skin testing size does not predict severity

# SUMMARY

- Anaphylaxis is a serious allergic that is rapid in onset and may cause death
- Early recognition and prompt treatment are critical in anaphylaxis
- First line therapy for anaphylaxis is IM epinephrine
- All patients should be discharged from the ER with a written anaphylaxis action plan, an epinephrine autoinjector and referral to an allergist

# REFERENCES


- Alqurashi et al. Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis. Ann Allergy Asthma Immunol 2015;115:217-223
- Ben-Shoshan M, La Vieille S, Eisman H, et al. Anaphylaxis treated in a Cana- dian pediatric hospital: Incidence, clinical characteristics, triggers, and management. J Allergy Clin Immunol. 2013;132:739e741.e3
- Campbell et al. Predictors of repeat epinephrine administration for emergency department patients with anaphylaxis. J Allergy Clin Immunol Pract. 2015;3:576-84
- Chipps et al. Update in pediatric anaphylaxis: a systemic review. Clinical pedicatrics 2013;52(5):451-461
- Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. Cochrane Database Syst Rev 2010
- Huang et al. Anaphylaxis in a New York City pediatric emergency department: Triggers, treatments and outcomes. J Allergy Clin Immunol 2012;129:162-8
- Lee JM, Greenes DS. Biphasic anaphylactic reactions in pediatrics. Pediatrics. 2000;106:762-766
- Lieberman P, Camargo CA Jr, Bohlke K, Jick H, Miller RL, Sheikh A, et al. Ep- idemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. Ann Allergy Asthma Immunol 2006;97:596-602
- Moneret – Vautrin et al. Epidemiology of life threatening and lethal anaphylaxis: a review. Allergy 2005:60;443-451
- Nurmatov et al. $H_2$-antihistamines for the treatment of anaphylaxis with and without shock: a systematic review. Ann Allergy Asthma Immunol 2014; 112:126–131
- Pumphrey, R.S. Lessons for management of anaphylaxis from a study of fatal reactions. Clin Exp Allergy. 2000;30:1144-50
- Sampson et al. Fatal and near fatal anaphylactic reactions to food in children and adolescence. N Engl J Med 1992;327:380-4
- Sheikh A, Ten Broek V, Brown SGA, Simons FER. H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. Allergy. 2007;62: 830-837
- Simons. Advances in HI antihistamines. N Engl J Med 2004;351:2203-17
- Simons. Epinephrine and its use in anaphylaxis: current issues. Current opinion in allergy and immunology. 2010;10(4):354-361

# THANK YOU