Anaphylaxis

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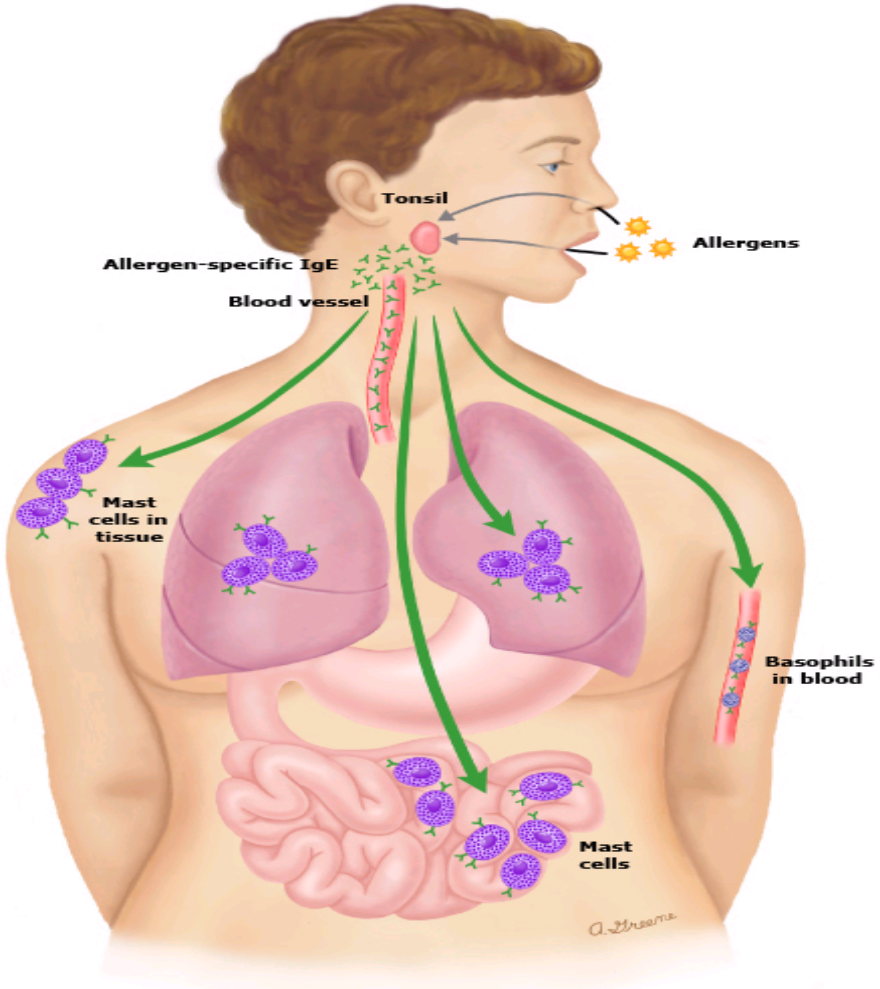
- Anaphylaxis is a serious **allergic** reaction that is rapid in onset and may cause **death**
- The rate of occurrence is **increasing** in industrialized countries
- Anaphylaxis is not always recognized as such because it can **mimic other conditions** and is variable in its presentation.

Anaphylaxis can be classified as

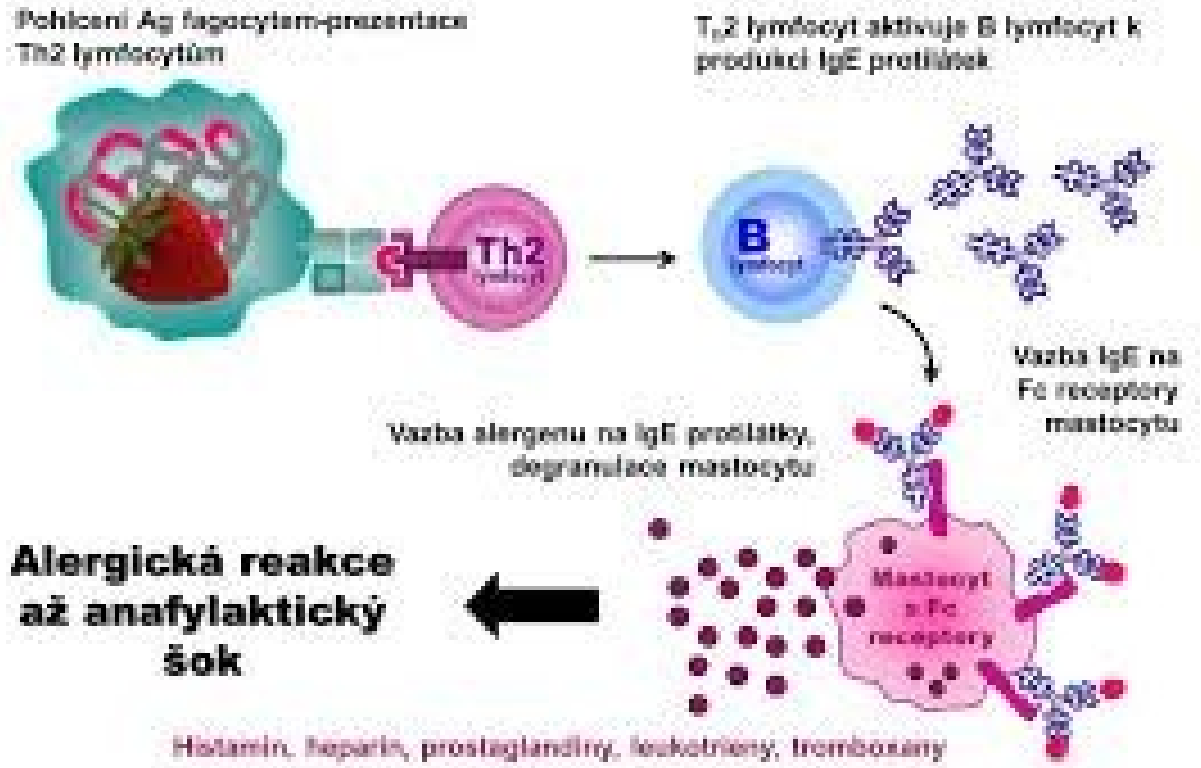
- 1.**Immunologic anaphylaxis**
  …includes both IgE-mediated and IgG-mediated reactions (which have not been identified in humans), as well as immune complex/complement-mediated mechanisms

- **2.Non-immunologic anaphylaxis**
  ……is caused by agents or events that induce sudden, massive mast cell or basophil degranulation, without the involvement of antibodies.

Allergen specific IgE production and dissemination



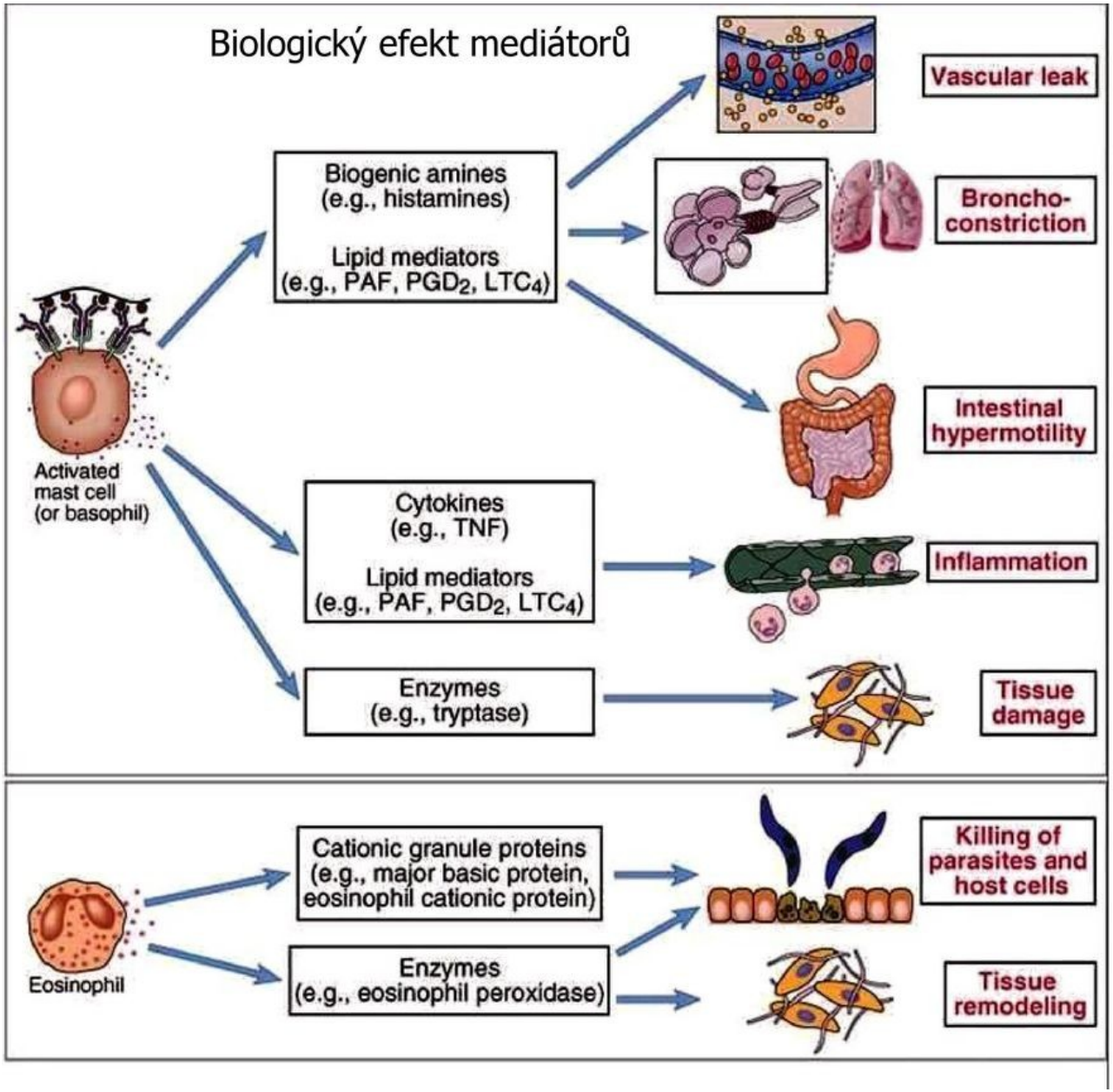
Allergens (in this figure, aeroallergens) enter the tonsils, within which they are taken up and degraded by antigen presenting cells (APC). APCs then interact with T helper cells type 2 (TH2) cells and B cells in the lymph nodes, leading to allergen-specific IgE production. The IgE enters the blood stream, and then diffuses through tissues (especially the skin and mucosal tissues of the respiratory and gastrointestinal tracts). The IgE binds to high affinity Fc receptors (FcepsilonRI) on the surface of the tissue mast cells and circulating basophils. When these IgE-coated cells encounter that specific aeroallergen subsequently, they become activated, leading to the release of inflammatory mediators, which result in the signs and symptoms of IgE-mediated allergic reactions.



1. Immunologic anaphylaxis

- In IgE-mediated anaphylaxis, the activation of mast cells, basophils, and eosinophils results in the release of preformed **inflammatory mediators**-- including histamine, tryptase, chymase, heparin, histamine-releasing factor, and PAF
- Cellular activation also stimulates the production of lipid-derived mediators such as prostaglandins and leukotrienes.

Existuje mnoho schémat…



- **Mediators** …..responsible for the main pathoph. picture of anaphylaxis
- Vasodilation
- Increasing permeability
- Myocardial depression

2.Non-immunologic anaphylaxis

- Complement-propofol
- direct mast cells-vankomycin, meperidine…

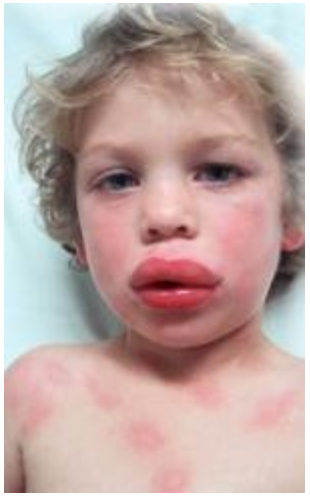
- In humans, the predominant shock organs are **the heart, lung, and vasculature,** and fatalities are divided between circulatory collapse and respiratory arrest
- Anaphylaxis is associated with **myocardial depression, arrhythmias, and myocardial ischemia.** Contributing factors include direct mediator effects on the myocardium, exacerbation of preexisting myocardial insufficiency by the hemodynamic stress of anaphylaxis, and exogenous or endogenous epinephrine.

- Anaphylaxis may affect **any part of the respiratory tract**, causing bronchospasm and mucus plugging in the smaller airways, and laryngeal edema and asphyxiation in the upper airway. Asphyxiation typically occurs rapidly after allergen exposure, with death occurring within one hour in many cases. Severe bronchospasm during anaphylaxis characteristically develops in individuals with preexisting asthma.

Symptoms and signs of anaphylaxis

Skin
Feeling of warmth, flushing [erythema], itching [may occur in areas such as external auditory canals, palms, soles, or groin], urticaria, angioedema, morbilliform rash, and "hair standing on end" [pilor erection]
Oral
Itching or tingling of lips, tongue, or palate
Edema of lips, tongue, uvula, metallic taste
Respiratory
Nose - itching, congestion, rhinorrhea, and sneezing
Laryngeal - itching and "tightness" in the throat, dysphonia, hoarseness, stridor
Lower airways - shortness of breath (dyspnea), chest tightness, deep or repetitive cough, wheezing, and cyanosis
Gastrointestinal
Nausea, abdominal pain [colic, cramps], vomiting [large amounts of "stringy" mucus], diarrhea, and dysphagia [difficulty swallowing*]
Cardiovascular
Feeling of faintness or dizziness; syncope, altered mental status, chest pain, palpitations, tachycardia, bradycardia or other dysrhythmia, hypotension, tunnel vision, difficulty hearing, urinary or fecal incontinence, and cardiac arrest
Neurologic
Anxiety, apprehension, sense of impending doom, seizures, headache•, and confusion; children may become irritable, cease to play, or have other sudden behavioral changes
Ocular
Periorbital itching, erythema and edema, tearing, and conjunctival erythema
Other
Uterine cramps and bleeding in women and girls

* Often occurs in association with throat tightness and other upper airway symptoms.
• Not common in anaphylaxis overall; however, reported in up to 30 percent of patients with exercise-induced anaphylaxis.



- The diagnosis of anaphylaxis is based primarily upon clinical symptoms and signs, as well as a detailed description of the acute episode, including antecedent activities and events occurring within the preceding minutes to hours.
- There are **three clinical criteria** for the diagnosis of anaphylaxis, which reflect the different ways in which anaphylaxis may present Anaphylaxis is highly likely when any **ONE** of the three criteria is fulfilled

Diagnostic criteria for anaphylaxis

Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:
1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF in older children and adults, hypoxemia)
B. Reduced BP* or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence)
2. TWO OR MORE OF THE FOLLOWING that occur rapidly *after exposure to a LIKELY allergen for that patient* (minutes to several hours):
A. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF in older children and adults, hypoxemia)
C. Reduced BP* or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)
D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP* *after exposure to a KNOWN allergen for that patient* (minutes to several hours):
A. Infants and children: low systolic BP (age specific)* or greater than 30 percent decrease in systolic BP
B. Adults: systolic BP of less than 90 mmHg or greater than 30 percent decrease from that person's baseline

PEF: peak expiratory flow; BP: blood pressure.
* Low systolic blood pressure for children is defined as:
- less than 70 mmHg from one month to one year,
- less than (70 mmHg + [2 x age]) from 1 to 10 years, and
- less than 90 mmHg from 11 to 17 years

Adapted with permission from: Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report-Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006; 117:391. Copyright © 2006 The American Academy of Allergy, Asthma, and Immunology.

- Recognition is not always easy, because anaphylaxis can mimic many other disorders and can be variable in its presentation. Anaphylaxis may present with various combinations of as many as 40 potential symptoms and signs
- Patients and healthcare professionals commonly fail to recognize and diagnose anaphylaxis in its early stages, when it is most responsive to treatment. In particular, there is a reluctance to diagnose anaphylaxis in the absence of hypotension, even though this sign is not required for the diagnosis and occurs late or not at all in a food-induced anaphylactic episode

Differential diagnosis of anaphylaxis

Common disorders
Acute asthma*
Acute generalized urticaria*
Acute angioedema
Syncope (faint)
Panic attack/acute anxiety attack
Aspiration of a foreign body
Cardiovascular events (myocardial infarction*, pulmonary embolus)
Neurologic events (seizure, cerebrovascular event)
Post-prandial syndromes
Scombroidosis
Pollen-food allergy syndrome
Monosodium glutamate
Sulfites
Food poisoning
Excess production of endogenous histamine
Mastocytosis and other clonal mast cell disorder
Basophilic leukemia
Flush syndromes
Peri-menopause
Carcinoid syndrome
Autonomic epilepsy
Medullary carcinoma of the thyroid
Other non-organic disease
Vocal cord dysfunction
Hyperventilation
Psychosomatic episode
Shock
Hypovolemic
Cardiogenic
Distributive•
Septic
Other
Non-allergic angioedema (hereditary angioedema types I, II, & III, ACE inhibitor-associated angioedema)
Systemic capillary leak syndrome
Red man syndrome (vancomycin)
Pheochromocytoma (paradoxical response)

The differential diagnosis in children and adults is shown. In infants, the differential diagnosis of anaphylaxis is unique.
* Acute asthma symptoms, acute generalized urticaria, or myocardial infarction symptoms can also occur *during* an anaphylactic episode.
• Distributive shock may be due to anaphylaxis or to spinal cord injury.

- Anaphylaxis most often results from an IgE-mediated allergic reaction.
- Common triggers include foods, insect stings, and medications. There is a rapidly expanding list of novel and/or unusual triggers
- The clinical diagnosis of anaphylaxis may or may not be confirmed by measurement of elevated concentrations of plasma histamine or serum or plasma total tryptase. Elevations in these mediators are transient

Triggers of anaphylaxis

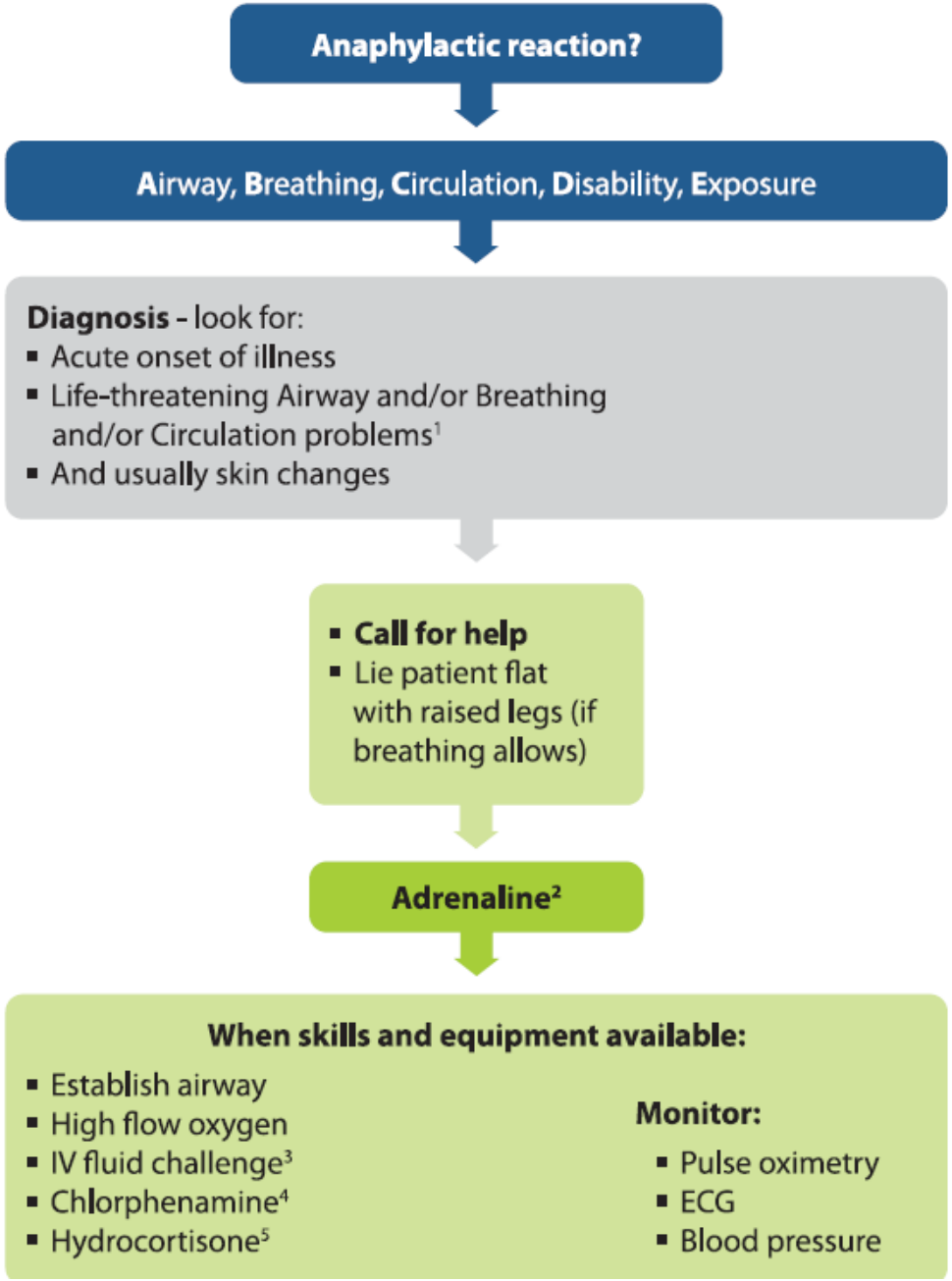
Allergen triggers (IgE-dependent immunologic mechanism)
Foods, especially peanut, tree nut, shellfish, fish, milk, egg
Insect stings (eg, Hymenoptera venom) and insect bites (eg, kissing bugs, mosquitoes)
Medications (eg, beta-lactam antibiotics, some nonsteroidal antiinflammatory drugs [NSAIDs])
Biological materials, including allergens, allergen immunotherapy, monoclonal antibodies, vaccines to prevent infectious disease, and hormones (eg, progesterone)
Natural rubber latex
Food additives, including spices, insect-derived colorants (eg, carmine), and vegetable gums
Inhalants (rare), eg, horse dander
Human seminal fluid (rare)
Occupational allergens (eg, stinging insects, natural rubber latex)
Immunologic triggers (IgE-independent mechanism)
IgG-dependent (rare) eg, to high molecular weight dextran, infliximab
Coagulation system activation
Idiopathic anaphylaxis
Consider the possibility of a hidden or previously unrecognized trigger
Consider the possibility of mastocytosis or a clonal mast cell disorder
Non-immunologic triggers (direct activation of mast cells and basophils)
Physical factors (eg, exercise*, cold, heat, sunlight/ultraviolet radiation)
Medications (eg, opioids, some NSAIDs)
Alcohol (ethanol)

Any food, insect sting or bite, or medication or biological, can potentially trigger anaphylaxis. Novel or unusual allergen triggers are frequently described. These include foods such as vegetables, fruits, lupin flour, bird's nest soup, seal, whale, and kangaroo meats, and storage mite-contaminated flour. They also include saliva from kissing bugs, mosquitoes, pigeon ticks, green ants, and pharaoh ants, and venoms from jellyfish, scorpions, and snakes. Medications include taxanes, platins, and other chemotherapy drugs; biologic agents, including monoclonal antibodies such as rituximab, cetuximab, infliximab, and uncommonly, omalizumab. Other injectants and ingestants, including Botox, bee products, and herbal formulations are also implicated.

Some triggers such as insect venoms, medications and radiocontrast media (such as nonsteroidal antiinflammatory drugs [NSAIDs]) act through more than one mechanism.

* Usually involves a co-trigger such as a food, medication (eg, an NSAID), or exposure to cold air or water.

- Prompt recognition and treatment are critical in anaphylaxis. In fatal anaphylaxis, median times to cardiorespiratory arrest are **5 minutes** in iatrogenic anaphylaxis, **15 minutes** in stinging insect venom-induced anaphylaxis, and **30 minutes** in food-induced anaphylaxis.
- Initial management is summarized in a rapid overview table


Anaphylactic reaction?
Airway, Breathing, Circulation, Disability, Exposure
Diagnosis - look for:
Acute onset of illness
Life-threatening Airway and/or Breathing and/or Circulation problems[1]
And usually skin changes
Call for help
Lie patient flat with raised legs (if breathing allows)
Adrenaline[2]
When skills and equipment available:
Establish airway
High flow oxygen
IV fluid challenge[3]
Chlorphenamine[4]
Hydrocortisone[5]
Monitor:
Pulse oximetry
ECG
Blood pressure

[1] **Life-threatening problems:**
Airway: swelling, hoarseness, stridor
Breathing: rapid breathing, wheeze, fatigue, cyanosis, SpO_2 < 92%, confusion
Circulation: pale, clammy, low blood pressure, faintness, drowsy/coma

[2] **Adrenaline** *(give IM unless experienced with IV adrenaline)*
IM doses of 1:1000 adrenaline (repeat after 5 min if no better)

▪ Adult	500 microgram IM (0.5 mL)
▪ Child more than 12 years	500 microgram IM (0.5 mL)
▪ Child 6–12 years	300 microgram IM (0.3 mL)
▪ Child less than 6 years	150 microgram IM (0.15 mL)

Adrenaline IV to be given **only by experienced specialists**
Titrate: Adults 50 mcg; Children 1 mcg kg^{-1}

[3] **IV fluid challenge (crystalloid):**

Adult 500 - 1000 mL
Child 20 mL kg^{-1}

Stop IV colloid if this might be the cause of anaphylaxis

	[4] Chlorphenamine (IM or slow IV)	[5] Hydrocortisone (IM or slow IV)
Adult or child more than 12 years	10 mg	200 mg
Child 6 - 12 years	5 mg	100 mg
Child 6 months to 6 years	2.5 mg	50 mg
Child less than 6 months	250 mcg kg^{-1}	25 mg

Fig. 4.2. Anaphylaxis treatment algorithm.[101]
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Rapid overview: Emergent management of anaphylaxis in adults

Diagnosis is made clinically:

The most common signs and symptoms are cutaneous (eg, sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20 percent of patients have no skin findings.

Danger signs: Rapid progression of symptoms, respiratory distress (eg, stridor, wheezing, dyspnea, increased work of breathing, persistent cough, cyanosis), hypotension, dysrhythmia, chest pain, collapse

Acute management:

The first and most important therapy in anaphylaxis is epinephrine. There are **NO absolute contraindications** to epinephrine in the setting of anaphylaxis.

Airway: Immediate intubation if evidence of impending airway obstruction from angioedema; delay may lead to complete obstruction; intubation can be difficult and should be performed by the most experienced clinician available; cricothyrotomy may be necessary

Promptly and simultaneously, give:

IM Epinephrine (1 mg/mL preparation): Give epinephrine 0.3 to 0.5 mg intramuscularly, preferably in the mid-anterolateral thigh; can repeat every 5 to 15 minutes as needed. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).

Place patient in recumbent position, if tolerated, and elevate lower extremities

Oxygen: Give 6 to 8 liters per minute via face mask, or up to 100 percent oxygen as needed

Normal saline rapid bolus: Treat hypotension with rapid infusion of 1 to 2 liters IV; repeat as needed; massive fluid shifts with severe loss of intravascular volume can occur

Also consider administration of:

Albuterol: For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer; repeat as needed

H1 antihistamine: Consider giving diphenhydramine 25 to 50 mg IV (for relief of urticaria and itching only)

H2 antihistamine: Consider giving ranitidine 50 mg IV

Glucocorticoid: Consider giving methylprednisolone 125 mg IV

Monitoring: Continuous non-invasive hemodynamic monitoring and pulse oximetry monitoring should be performed; urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock

Treatment of refractory symptoms:

Epinephrine infusion*: For patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion, 2 to 10 micrograms per minute by infusion pump. Titrate the dose continuously according to blood pressure, cardiac rate and function, and oxygenation.

Vasopressors*: Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according to blood pressure, cardiac rate and function, and oxygenation.

Glucagon: Patients on beta-blockers may not respond to epinephrine and can be given glucagon 1 to 5 mg IV over 5 minutes, followed by infusion of 5 to 15 micrograms per minute

* All patients receiving an infusion of epinephrine and/or another vasopressor require continuous non-invasive monitoring of blood pressure, heart rate and function, and oxygen saturation.

- **Epinephrine** is lifesaving in anaphylaxis. It should be injected as early as possible in the episode in order to prevent progression of symptoms and signs. There are no absolute contraindications to its use, and it is the treatment of choice for anaphylaxis **of any severity.** We recommend epinephrine for patients with apparently mild symptoms and signs (eg, a few hives and mild wheezing) (**Grade 1B**) and for patients with moderate to severe symptoms and signs (**Grade 1A**).

Beneficial effects and adverse effects of epinephrine in the treatment of anaphylaxis

Beneficial effects	
	At alpha-1 receptor:
	Increased vasoconstriction (at low doses)
	Increased peripheral vascular resistance
	Increased blood pressure
	Decreased mucosal edema (eg, in larynx)
	At beta-1 receptor:
	Increased heart rate (chronotropy)
	Increased force of cardiac contraction (inotropy)
	At beta-2 receptor:
	Decreased mediator release from mast cells and basophils
	Increased bronchodilation
	Increased vasodilation
Adverse effects*•Δ	
Common and transient	Anxiety, palpitations, pallor, tremor, fear, restlessness, dizziness, headache
Uncommon (typically occur after overdose)	Ventricular arrhythmias, angina, myocardial infarction, pulmonary edema, sudden sharp increase in blood pressure, intracranial hemorrhage

* Risk of adverse effects may be increased in the following conditions:
- Use of tricyclic antidepressants, monoamine oxidase inhibitors, or cocaine
- Some preexisting cardiovascular, central nervous system, or thyroid diseases

• Serious adverse effects such as those listed in the table potentially occur when epinephrine is given in overdose by any route, most commonly after an intravenous bolus injection, an overly rapid intravenous infusion, or an erroneous intravenous injection of a 1 mg/mL (1:1000) epinephrine solution instead of an appropriately diluted 0.1 mg/mL (1:10,000) or a 0.01 mg/mL epinephrine solution.

Δ Anaphylaxis can present as an acute coronary syndrome (ACS), arrhythmias, myocardial infarction, or angina, before or in the absence of epinephrine injection. This potentially occurs in patients with known coronary artery disease, patients in whom subclinical coronary artery disease is unmasked, and patients (including children) with transient coronary artery vasospasm in whom no cardiovascular abnormalities can be detected by electrocardiogram or echocardiography after recovery from anaphylaxis.

- The route of **epinephrine** administration depends upon the presenting symptoms.

  For patients who are **not** profoundly hypotensive or in shock or cardiorespiratory arrest, intramuscular (IM) injection into the mid-anterolateral thigh as the initial route of administration is advised

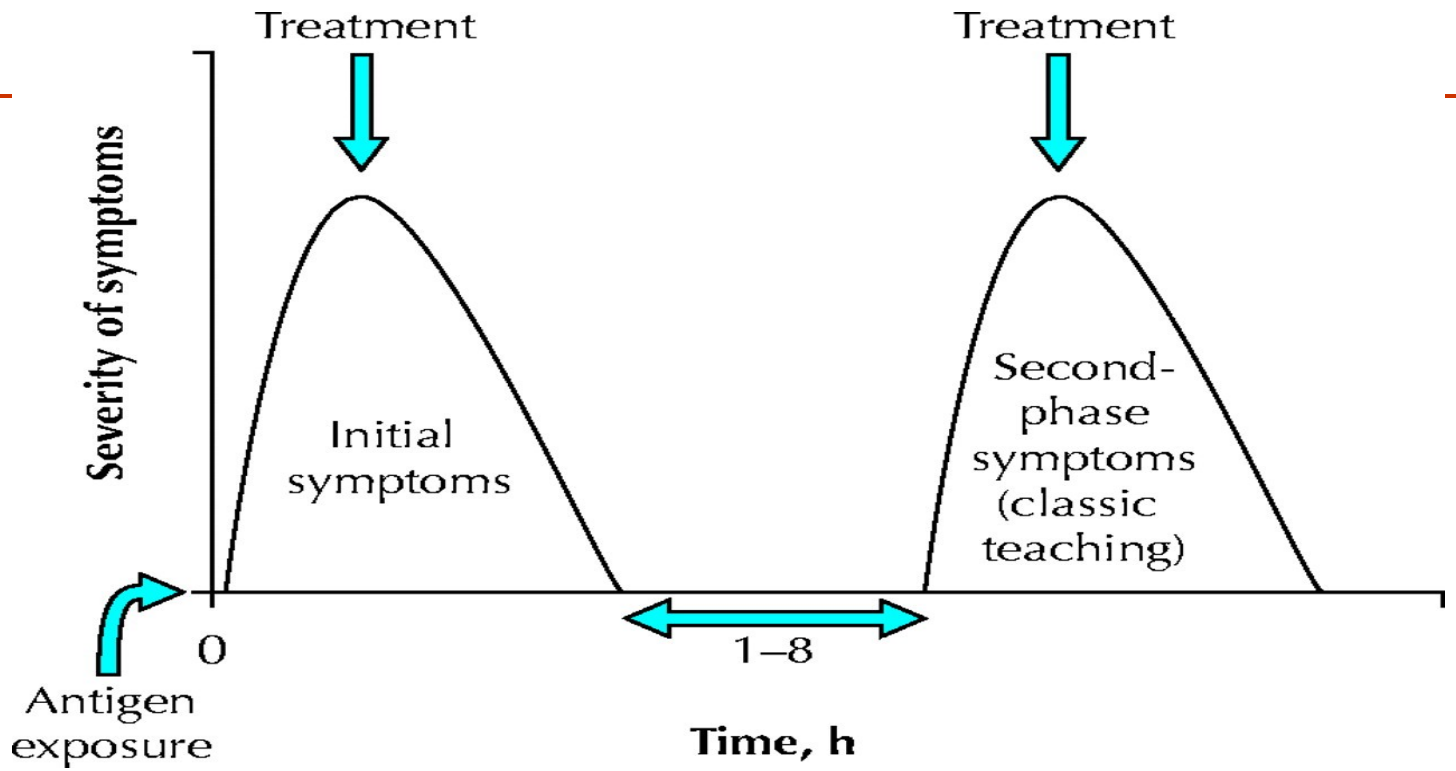
- For adults, the dose of **epinephrine** is 0.3 mg to 0.5 mg, injected intramuscularly into the mid-anterolateral thigh. This treatment may be repeated at 5 to 15 minute intervals.
- For infants and children, the dose of **epinephrine** is 0.01 mg per kilogram up to 0.5 mg per dose, injected intramuscularly into the mid-anterolateral thigh. This treatment may be repeated at 5 to 15 minute intervals.

- **Intravenous epinephrine** is indicated for patients with profound hypotension or symptoms and signs suggestive of impending shock (dizziness, incontinence of urine or stool) or those who do not respond to an initial intramuscular injection of epinephrine and fluid resuscitation. For these patients we suggest that epinephrine be administered by continuous slow intravenous infusion rather than by intermittent IV bolus

- Massive fluid shifts can occur in anaphylaxis, and all patients with orthostasis, hypotension, or incomplete response to epinephrine should receive large volume fluid resuscitation with **normal saline**. Normotensive patients should receive normal crystaloid to maintain venous access in case their status deteriorates
- Supplemental **oxygen** should be administered.

- **Glukagon** for patient taking beta-blockers- – –inotropic and chronotropic effects that are not mediated through beta-receptors
- **H1 antihistamines**- to relieving itching and hives-prometazin, cetirizine
- **H2 antihistamines**-no evidence
- **Bronchilators** inhaled, only adjunjctive to epinephrine
- **Glucocorticoids**- to prevent biphasic or protracted reactions-occur in23%

Fig. 1: Schematic representation of a biphasic anaphylactic reaction.



Schematic representation of a biphasic anaphylactic reaction. The second-phase reaction has been described as occurring between 1 and 8 hours after the initial reaction, but new evidence suggests that this second phase may occur up to 38 hours (mean 10 hours) after the initial reaction. About one-third of the second-phase reactions are more severe, one-third are as severe and one-third are less severe.

CMAJ·JAMC

- Patients successfully treated for anaphylaxis should be discharged with a personalized written anaphylaxis emergency action plan , an epinephrine autoinjector, written information about anaphylaxis and its treatment, and a plan for further evaluation

- It is critical that patients be evaluated further to confirm the trigger, as specific avoidance measures are useful in reducing the risk of recurrence. Additionally, for some allergens, immunomodulation is also available to reduce the risk

Anaphylaxis Emergency Action Plan

Patient Name: _____ **Age:** _____

Allergies: _____

Asthma ☐ Yes *(high risk for severe reaction)* ☐ No

Additional health problems besides anaphylaxis: _____

_____

Concurrent medications: _____

_____

Symptoms of anaphylaxis

Mouth	Itching, swelling of lips and/or tongue
Throat*	Itching, tightness/closure, hoarseness
Skin	Itching, hives, redness, swelling
Gut	Vomiting, diarrhea, cramps
Lung*	Shortness of breath, cough, wheeze
Heart*	Weak pulse, dizziness, passing out

Only a few symptoms may be present. Severity of symptoms can change quickly.
**** Some symptoms can be life-threatening. ACT FAST!***

Emergency action steps - DO NOT HESITATE TO GIVE EPINEPHRINE!

1. Inject epinephrine in thigh using *(check one)*: ☐ Adrenaclick (0.3 mg) ☐ Adrenaclick (0.15) mg ☐ EpiPen Jr (0.15 mg) ☐ EpiPen (0.3 mg) ☐ Twinject (0.15 mg) ☐ Twinject (0.3 mg)

Other medication/dose/route: _____

IMPORTANT: Asthma inhalers and/or antihistamines can't be depended on in anaphylaxis.

2. Call 911 or rescue squad (before calling contact)

3. Emergency contact #1: Home _____ Work _____ Cell _____

Emergency contact #2: Home _____ Work _____ Cell _____

Emergency contact #3: Home _____ Work _____ Cell _____

Comments: _____

_____

_____

_____ _____

Doctor's signature/Date/Phone **Parent's signature (for individuals under age 18 yrs)/Date**

- Alergen= trigger
- Sensibilisation

- Second exposition of alergen-mast cells, basofils
- Release of mediators
- Clinical signs-cardiovascular, respiratory, skin,GIT symptoms
- Dg. and therapy -epinephrin

Rapid overview: Emergent management of anaphylaxis in infants and children*

DIAGNOSIS IS MADE CLINICALLY:
The most common signs and symptoms are cutaneous (eg, sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20 percent of patients have no skin findings.
Danger signs: Rapid progression of symptoms, evidence of respiratory distress (eg, stridor, wheezing, dyspnea, increased work of breathing, retractions, persistent cough, cyanosis), signs of poor perfusion•, dysrhythmia, hypotension, collapse
ACUTE MANAGEMENT:
The first and most important therapy in anaphylaxis is epinephrine. There are **NO absolute contraindications** to epinephrine in the setting of anaphylaxis.
Airway: Immediate intubation if evidence of impending airway obstruction from angioedema; delay may lead to complete obstruction; intubation can be difficult and should be performed by the most experienced clinician available; cricothyrotomy may be necessary
IM Epinephrine (1 mg/mL preparation): Give epinephrine 0.01 mg per kilogram intramuscularly (maximum per dose: 0.5 mg), preferably in the mid-anterolateral thigh, can repeat every 5 to 15 minutes as needed. If signs of poor perfusion• are present or symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).
Place patient in recumbent position, if tolerated, and elevate lower extremities
Oxygen: Give 6 to 8 liters per minute via face mask, or up to 100 percent oxygen as needed
Normal saline rapid bolus: Treat poor perfusion• with rapid infusion of 20 mL per kilogram; re-evaluate and repeat fluid boluses (20 mL per kilogram) as needed; massive fluid shifts with severe loss of intravascular volume can occur; monitor urine output
Albuterol: For bronchospasm resistant to IM epinephrine, give albuterol 0.15 mg per kilogram (minimum dose: 2.5 mg) in 3 mL saline inhaled via nebulizer; repeat as needed
H1 antihistamine: Consider giving diphenhydramine 1 mg per kilogram (max 40 mg) IV
H2 antihistamine: Consider giving ranitidine 1 mg per kilogram (max 50 mg) IV
Glucocorticoid: Consider giving methylprednisolone 1 mg per kilogram (max 125 mg) IV
Monitoring: Continuous non-invasive hemodynamic monitoring and pulse oximetry monitoring should be performed; urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock
TREATMENT OF REFRACTORY SYMPTOMS:
Epinephrine infusionΔ: Patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion at 0.1 to 1 microgram per kilogram per minute, titrated to effect
VasopressorsΔ: Patients may require large amounts of IV crystalloid to maintain blood pressure; if response to epinephrine and saline is inadequate, dopamine (5 to 20 micrograms per kilogram per minute) can be given as continuous infusion, titrated to effect

* A child is defined as a prepubertal patient weighing less than 40 kg.
• See the topic "Assessment of perfusion in pediatric resuscitation".
Δ All patients receiving an infusion of epinephrine and/or another vasopressor require continuous non-invasive monitoring of blood pressure, heart rate and function, and oxygen saturation. We suggest that pediatric centers provide instructions for preparation of standard concentrations and also provide charts for established infusion rate for epinephrine and other vasopressors in infants and children.