ANNEX 2: ANAPHYLAXIS

Grey buttons list

Key symptoms *(Hover box 1)*

Clinical symptoms	Organ involvment
Generalized hives, itch-flush, swollen lips-tongue-uvula	SKIN-MUCOSAL TISSUE
Dyspnea, wheeze-bronchospasm, stridor, hypoxemia	RESPIRATORY SYSTEM
Hypotension or shock	CARDIOVASCULAR SYSTEM
Collapse, syncope, incontinence	END-ORGAN DYSFUNCTION
Crampy abdominal pain, vomiting	GASTRO-INTESTINAL SYSTEM

From *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,* Sampson et al., JACI 2006.

⚠ Special population *(Hover box 1a)*

Among these populations, anaphylaxis clinical presentation may differ from current symptoms.

- ELDERLY (>65 y.o.)

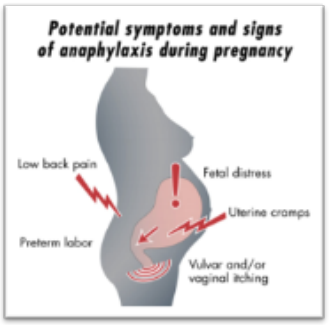
- **Neurologic symptoms**: headache, dizziness, confusion, tunnel vision.
- **Cyanosis, syncope and dizziness** suggest the present of shock
- **Paradoxical bradycardia** may occur in the presence of beta blockers and/or ACEI.

From *The difficult management of anaphylaxis in the elderly,* Gonzalez-de-Olano et al., Curr Opin Allergy Clin Immunol, 2016.

- PREGNANT WOMEN

- **Uterine cramping** that can induce labour and lead to miscarriage.

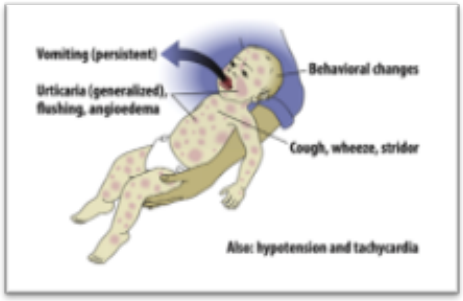
From *Anaphylaxis during pregnancy*, Simons et al., JACI 2012.



- INFANTS (<2 y.o.)

- As in other children, **cough, wheeze, stridor, lethargy/drowsiness**, **tachycardia, cardiovascular collapse**, and/or **persistent gastrointestinal symptoms**
- **Persistent vomiting** may be the only sign
- **Neurologic symptoms :** cessation of play, clinging to the caregiver, drowsiness, and persistent crying.

From *Guiding Principles for the Recognition, Diagnosis, and Management of Infants with Anaphylaxis: An Expert Panel Consensus,* Greenhawt et al., JACI 2018.



How ? *(Hover box 2)*

How ?

→ Intra-muscular adrenalin injection

Use of

Solution of adrenalin

Inject a 1:1000 (1mg/ml) solution of adrenaline
IM in the anterolateral thigh

Dose : **0,01 mg/kg body weight** (0,01 ml/kg) up to a **maximum of 0,5 mg**

OR

Adrenalin auto-injectors

- EpiPen

http://www.epipen.co.uk/demonstrationvideo/

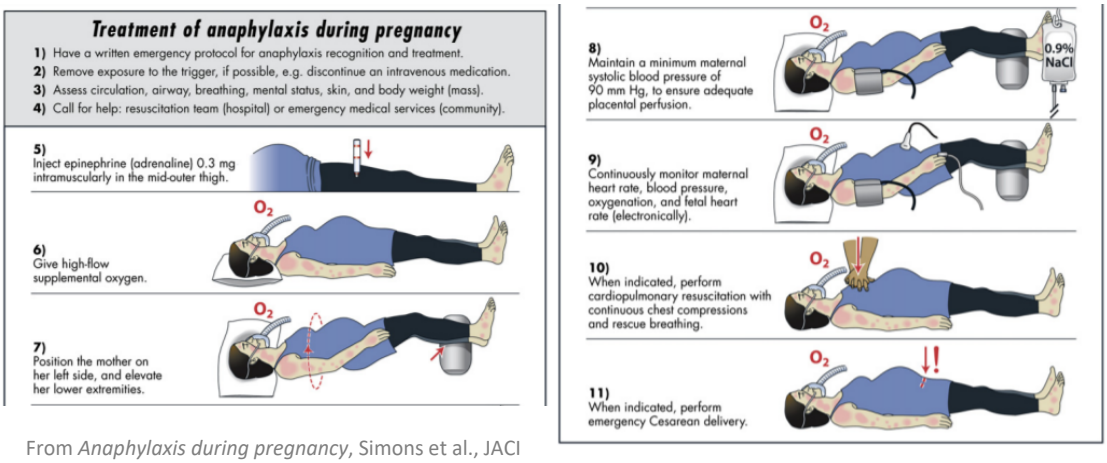
- Emerade

https://www.emerade.com/hcp/instruction-video

- Jext

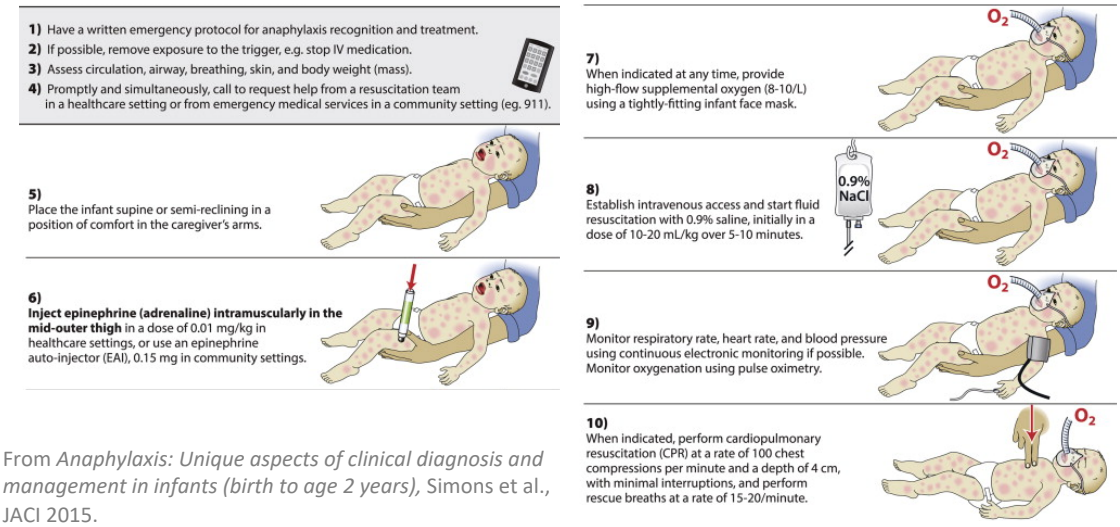
https://adults.jext.co.uk/about-jext/how-to-use/

Correct positioning *(Hover box 2q)*



From *Anaphylaxis during pregnancy*, Simons et al., JACI 2012.

- <u>Treatment for infants:</u>



From *Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years),* Simons et al., JACI 2015.

Differential diagnosis *(Hover box 3)*

Urticaria/ angioedema	Others shock's etiologies
- Chronic spontaneous urticaria - Hereditary angioedema - Angiotensin-Converting-Enzyme (ACE) inhibitor- associated angioedema	- Septic, cardiogenic, hemorrhagic
Neurologic syndromes	**Other causes of acute respiratory distress**
- Epilepsy - Stroke	- Asthma - Pulmonary embolism - Anxiety/ panic attack - Vocal cord dysfunction - Aspiration of a foreign body
Syndromes with erythema or flushing	**Others**
- Carcinoid syndrome - Peri-menopause - Alcohol	- Vasovagal reactions - Scombroidosis - Food poisoning - Sulfite hypersensitivity - Pheochromocytoma - Food protein-induced enterocolitis syndrome (FPIES)

Adapted from *Clinical Practice Guide for Anaphylaxis in Latin America,* 2019.

Known allergen exposure ? *(Hovebox 4)*

Remove trigger

Interrogatory about **where** was the patient, **what** he was doing and what exactly happened.
The emergency is to **REMOVE** the trigger from patient's environment.

Most commons triggers of anaphylaxis are :

- **FOOD:** To view the food logogram click here.
- **DRUG:** To view the drug logogram click here.
- **VENOM:** Indigenous insect populations differ from continent to continent and from region to region on the same continent. Consequently, the likelihood of exposure to different orders and families of stinging or biting insects and the risk of anaphylaxis from these insects also differs.

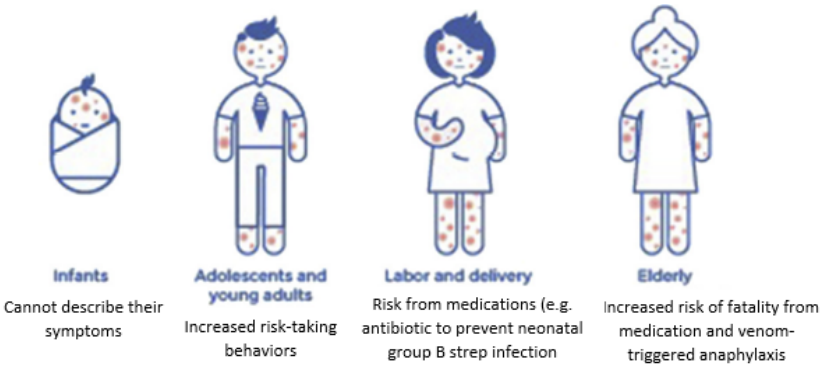
Commons anaphylaxis triggers worldwide:

FOOD	INSECT VENOM	DRUGS
celery	bee and wasp venom	analgesics
cow's milk	fire ants	antibiotics
hen's egg	horse fly	biologics
peach		chemotherapeutics
peanut		contrast media
seeds eg, sesame		proton pump inhibitors
shellfish		
tree nuts		
wheat and buckwheat		

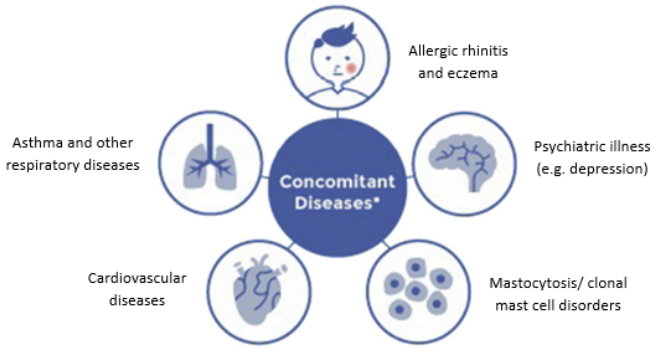
From *WAO Anaphylaxis Guidance* 2020.

Known cofactors AND/OR risk factors ? *(Hover box 5)*
Aid diagnosis

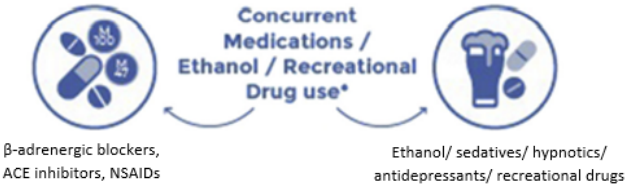
- Individual **RISK FACTORS** potentially contribute to severe or fatal anaphylaxis.
  - AGE-RELATED FACTORS



  - CONCOMITANT DISEASES



  - CONCURRENT MEDICATIONS

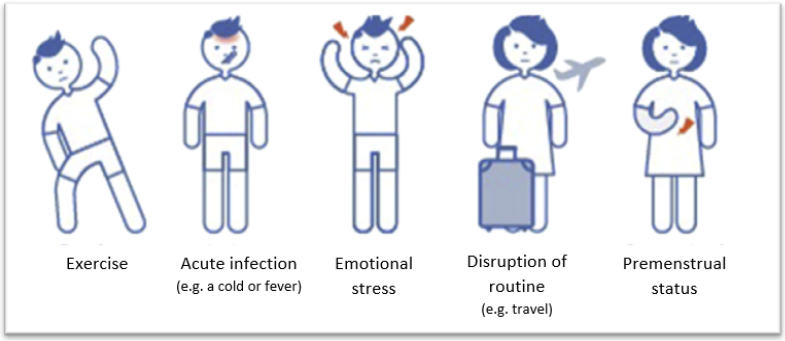


From *WAO Anaphylaxis Guidance* 2020.

- **CO-FACTORS** potentially amplify anaphylaxis.

Search for

- **NSAID :** enhances intestinal permeability and allergen absorption
- **Exercise :** often linked to food allergens such as wheat/omega-5 gliadin, celery, or shellfish.
- **Alcohol :** same as NSAID
- **Infection**



From *WAO Anaphylaxis Guidance* 2020.

When to refer ? *(Hover box 6)*

- Refer patient to an allergy specialist for a risk-assessment.
- In some countries, GPs with a special interest in allergy are trained to perform the risk-assessment in primary care.

Education *(Hover box 7)*

GPs should devise self-management plan in collaboration with the patient.

1. Immediately **administer adrenaline** auto-injector in any of the following circumstances:
   - *you think that you are having an anaphylactic reaction*
   - *your throat feels tight or you have wheezing or whistling in your chest or you are finding it difficult to breath*
   - *you feel faint or feel like you are about to collapse*
   - *you have severe gastrointestinal symptoms (eg crampy abdominal pain, vomiting) plus sudden onset skin symptoms (eg generalised hives, itch, swollen lips or tongue)*

   Via the **intramuscular route**, in the mid-anterolateral thigh, holding the EAI in place for about **3–10 seconds.**
2. **Call emergency** medical services,
3. Sit up unless you feel faint or feel you are about to collapse in which case lie down with your feet raised above your chest
4. if your breathing problems are worse or no better, or you are still feeling faint, you can use a **second adrenaline autoinjector**

Adapted from *EAACI Anaphylaxis Guideline*, 2013.

Follow-up *(Hover box 8)*

Five points' annual structured review

1. Instructions on prompt recognition of symptoms of anaphylaxis;
2. Remind patients to carry the personalized written anaphylaxis emergency action plan that illustrates how to recognize anaphylaxis symptoms;
3. Training on when and how to use an adrenaline auto-injector, where appropriate, using a dummy adrenalin auto-injector;
4. Check their understanding about calling the emergency service;
5. Remind patients to be watchful about the expiration date of the adrenaline auto-injector .

Adapted from *EAACI Anaphylaxis Guideline,* 2013.

Prevention *(Hover box 9)* = **Avoidance AND/OR be ready to treat if an accidental exposure happens**

Prescribe an adrenalin auto-injector to avoid fatal anaphylaxis for all suspected reaction of anaphylaxis.

Adrenaline is not dangerous to a person for whom it is prescribed even if taken unnecessarily (i.e.patient thought thet were having anaphylaxis but in fact they were not) and is administered correctly (i.e. intra muscularly).

Adrenalin Auto-Injector

= Device designed to be used by a nonmedical person to give a predefined dose of intramuscular adrenaline. Adrenaline is a drug with combined a- and b-agonist actions which result in

(i) peripheral vasoconstriction, thereby reversing hypotension and mucosal oedema;
(ii) increased rate and force of cardiac contractions, thereby reversing hypotension;
(iii) reversal of bronchoconstriction and reduction in the release of inflammatory mediators.

From Muraro A, Roberts G, Worm M, Bilo MB, Brockow K, et al. *Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology.Allergy2014;69: 1026–1045.*

From Muraro A, Agache I, Clark A, Sheikh A, Roberts G, et al. *EAACI Food Allergy and Anaphylaxis Guidelines: managing patients with food allergy in the community.Allergy2014;69: 1046–1057.*

1.1 When patient reporting a past history of possible anaphylaxis.

Key symptoms

Differential diagnosis

Risk factors ?

Cofactors ?

Link to the first anaphylaxis decision tree "when patients experiencing anaphylaxis" click here.

Differential diagnosis *(Hover box 3)*

- Skin or mucosal - chronic remittent or physical urticaria and angioedema - pollen-food allergy
- syndrome Respiratory diseases - acute laryngotracheitis - tracheal or bronchial obstruction (e.g. foreign substances, vocal cord dysfunction) - status asthmaticus (without involvement other organs)
- Cardiovascular diseases - vasovagal syncope - pulmonary embolism - myocardial infarction - cardiac arrhythmias - hypertensive crisis - cardiogenic shock
- Pharmacological or toxic reactions - ethanol - histamine, e.g. scombroid fish poisoning – opiates
- Neuropsychiatric diseases - hyperventilation syndrome - fright and panic disorder - somatoform disorder (e.g. psychogenic dyspnea, vocal cord dysfunction) - dissociative disorder and conversion (e.g. globus hystericus) - epilepsy - cerebrovascular event - psychoses - artifact (factitious disorder) - Hoigné's syndrome - coma, e.g. metabolic, traumatic
- Endocrinological diseases - hypoglycemia - thyrotoxic crisis - carcinoid syndrome - vasointestinal polypeptide tumours – phaeochromocytoma

Enquire about **home environment, occupation and hobbies** for any potential triggers *(Hovebox 3)*

Home environment

Search for potential hidden triggers by asking about:

- **ventilation ?**
- **humidity ?**
- **carpets?**
- **Plants?**
- **Animals ?**

Occupation

In order to evaluate patient's risk exposure.

e.g. : - bee-keepers / gardeners/ forestry workers for venom allergy
- bakers for food allergy (wheat)
- hairdressers for cosmetic products allergy (persulphates)
- caregivers for drug allergy
- healthcare workers for latex allergy

Hobbies

Where can the suspect allergen be found ?

e.g. : - beekeeping for venom allergy
- sport for exercise- induced anaphylaxis

How to establish an individualized management plan ? *(Hover box 4a)*

Give specific instructions about *when to inject epinephrine* ("action plan")

A person who is having an allergic reaction should use his/her adrenalin Auto-Injector **immediately** if he/she:

- Is having trouble breathing.
- Feels tightness or swelling in the throat.
- Feels lightheaded or thinks that he/she might pass out.

The autoinjector should also be used promptly after an allergen exposure if the person has symptoms that could progress to the life-threatening ones listed above. These may include wheezing, repetitive coughing, swelling of the lips, tongue or throat, many hives, repetitive vomiting (especially with other symptoms), having a "feeling of doom," or a combination of these symptoms. For milder symptoms like a few hives, mild abdominal discomfort, or itching, your allergist may tell you to give another medication (eg, an antihistamine) first.

If treating a child with an allergic reaction, **also** use the autoinjector if the child:

- Is not responding, seems groggy, or passes out during an allergic reaction.
- Has food allergies and is vomiting repeatedly shortly after eating, especially if these symptoms are accompanied by flushing or hives.
- Is coughing repeatedly during an allergic reaction.
- Had previous anaphylaxis and develops widespread hives after possibly eating a trigger food.
- Has definitely eaten a trigger food that previously caused very severe anaphylaxis and has any symptoms at all, even very mild symptoms.

Uptodate, Patient education: Use of an epinephrine autoinjector (Beyond the Basics). Author:Scott H Sicherer, MD, FAAAAI

⇨ Also view Education on the first anaphylaxis flow diagram untitled "*when patient is currently experiencing anaphylaxis*", click here.

How?

⇨ Provision of individualized management plan written clearly in simple, non-medical language

It should include:

- personal identification data: name and address; contact details of the parents, guardian or next of kin, allergist, family doctor and the local ambulance service; and preferably a photograph
- clear identification of the source of the allergens to be avoided and allergen avoidance advice
- clear identification of any non-allergen triggers or co-factors, such as exercise, and avoidance advice
- anaphylaxis emergency action plan
-

Copy of plan should be kept by the patient, any caregivers, school staff and family doctor.

Example of an individualized anaphylaxis emergency action plan :

1. Immediately administer adrenaline auto-injector in any of the following circumstances:
    - you think that you are having an anaphylactic reaction
    - your throat feels tight or you have wheezing or whistling in your chest or you are finding it difficult to breath
    - you feel faint or feel like you are about to collapse
    - you have severe gastrointestinal symptoms (eg crampy abdominal pain, vomiting) plus sudden onset skin symptoms (eg generalised hives, itch, swollen lips or tongue)
2. Call emergency medical services
3. Sit up unless you feel faint or feel you are about to collapse in which case lie down with your feet raised above your chest
4. If you have any swelling of your face or itching, take an antihistamine by mouth
5. After 5 minutes, if your breathing problems are worse or no better, or you are still feeling faint, you can use a second adrenaline autoinjector.

From *EAACI Anaphylaxis Guideline,* 2013

When ? *(Hover box 4b)*

Absolute indications for at least one adrenaline auto-injector:

- Previous anaphylaxis triggered by food, latex or aeroallergens
- Exercise-induced anaphylaxis
- Idiopathic anaphylaxis
- Co-existing unstable or moderate to severe, persistent asthma and a food allergy
- Venom allergy in adults with systemic reactions (not receiving maintenance VIT) and children with more than cutaneous/mucosal systemic reactions.
- Underlying mast cell disorders or elevated baseline serum tryptase concentrations together with any previous systemic allergic reactions to insect stings, even in VIT treated patients.