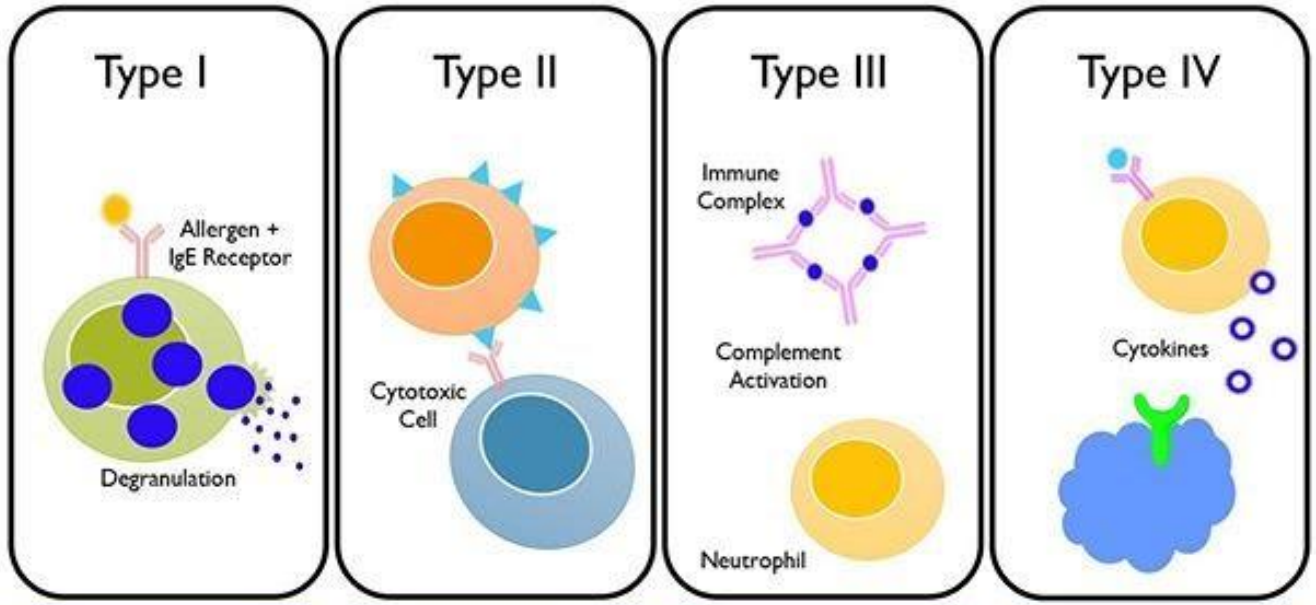
Anaphylaxis & Hypersensitivity

Harry Chen MD
Seed EM Educator
Makerere University

Anaphylaxis

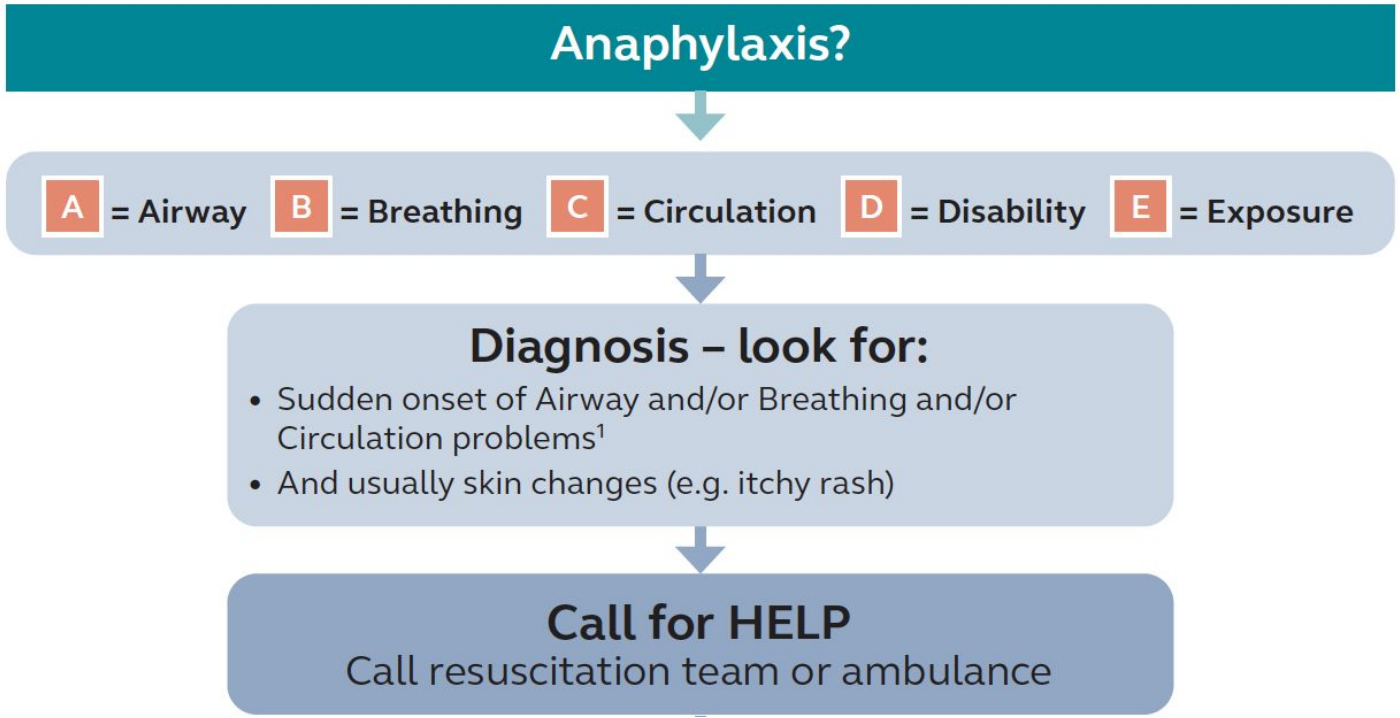
- Potentially life-threatening allergic reaction
- Recognize based on:
  - Sudden onset and rapid progression
  - Airway, Breathing and Circulation problems
  - Skin or mucosal changes (flushing, urticaria angioedema)
- Diagnosis supported by exposure to known allergen
- Treat life-threatening features using the ABCDE approach
- Adrenaline is the mainstay of treatment for Anaphylaxis

Types of Hypersensitivity Reactions



	Type I	Type II	Type III	Type IV
Mediators	IgE-Mediated	IgG or IgM Cytotoxic	Immune Complex-Mediated	T-Cell-Mediated
Onset	Within 1 Hour	Hours to Days	1-3 Weeks	Days to Weeks
Examples	Anaphylaxis	Hemolytic Anemia	Serum Sickness SLE	Rash SJS

Assess using the ABCDE approach



1. **Life-threatening problems**

Airway

hoarse voice, stridor

Breathing

 work of breathing, wheeze, fatigue, cyanosis, SpO_2 <94%

Circulation

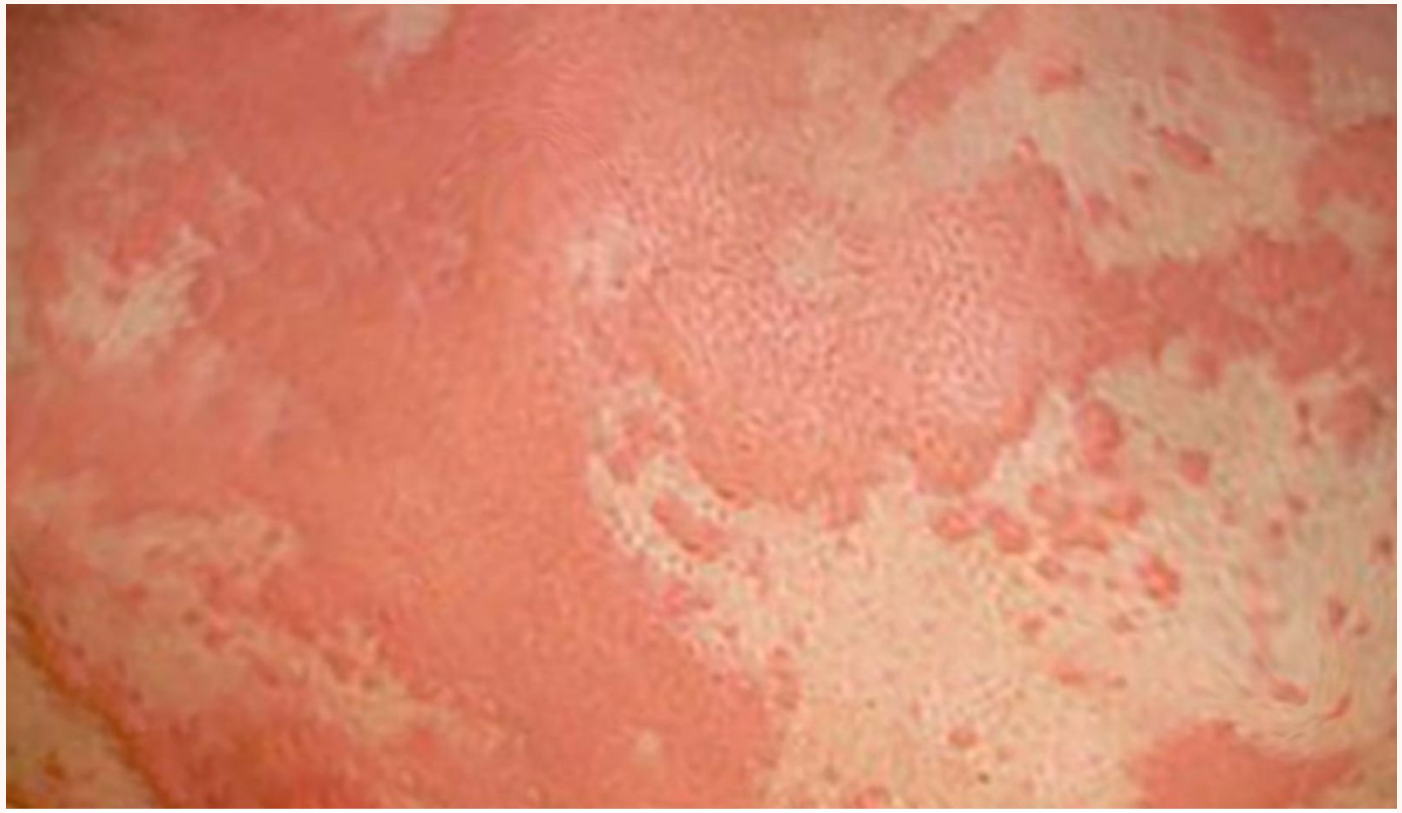
low blood pressure, signs of shock, confusion, reduced consciousness

Don't forget the history!!

Resuscitation Council UK

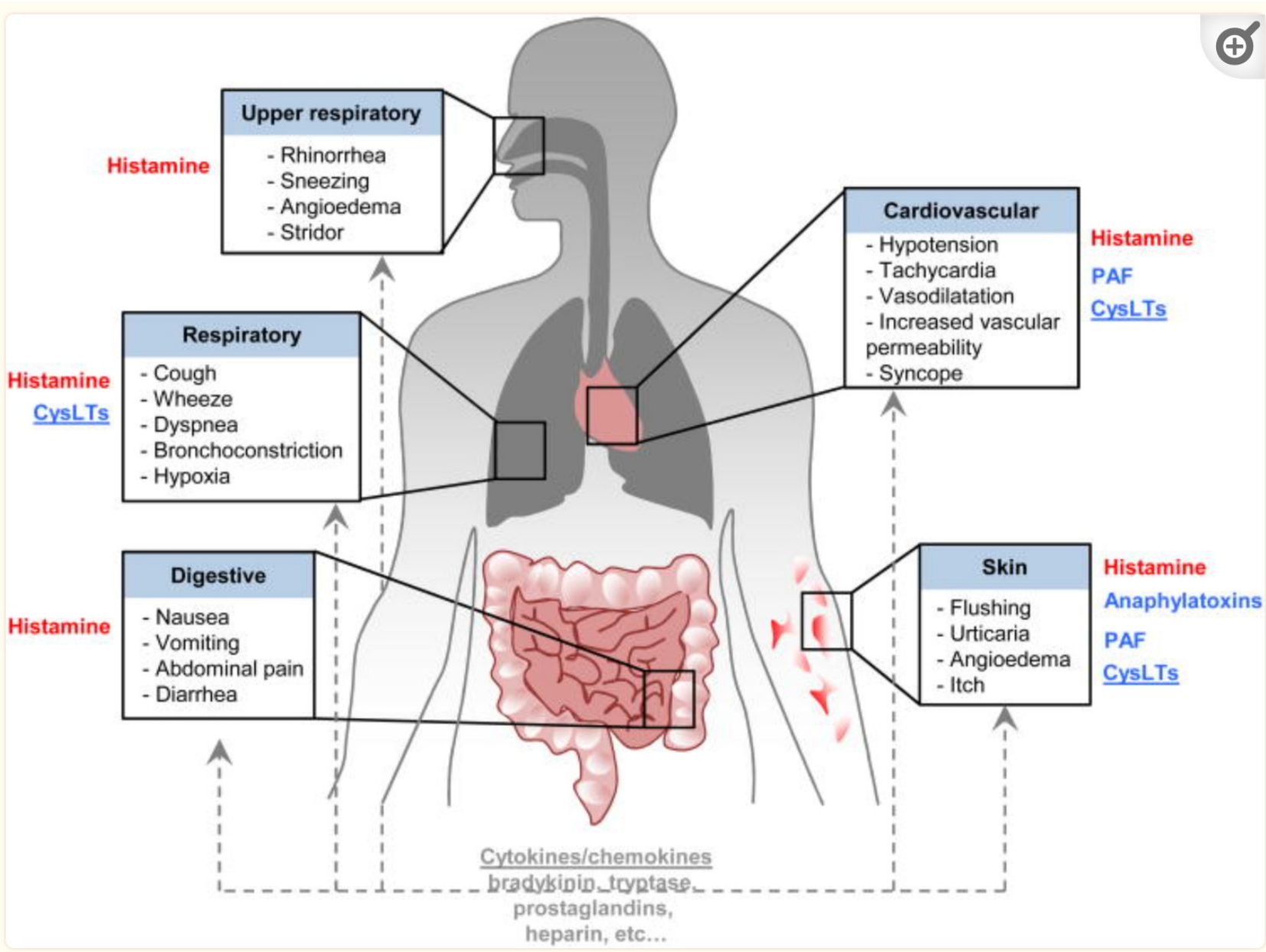
Skin Manifestations of Anaphylaxis- the “E”

Angioedema



Urticaria

Clinical Manifestations of Anaphylaxis



Anaphylaxis is highly likely when any one of the following 2 criteria are fulfilled:
1. Acute onset of an illness (minutes to several hours) with simultaneous 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, hypoxemia)
b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
c. Severe gastrointestinal symptoms (eg, severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens
2. Acute onset of hypotension[a] or bronchospasm[b] or laryngeal involvement[c] after exposure to a known or highly probable allergen[d] for that patient (minutes to several hours), even in the absence of typical skin involvement.

Table 2. Amended criteria for the diagnosis of anaphylaxis. *PEF, Peak expiratory flow; BP, blood pressure. a. Hypotension defined as a decrease in systolic BP greater than 30% from that person's baseline, OR i. Infants and children under 10 years: systolic BP less than (70 mmHg + [2 x age in years]) ii. Adults and children over 10 years: systolic BP less than <90 mmHg. b. Excluding lower respiratory symptoms triggered by common inhalant allergens or food allergens perceived to cause "inhalational" reactions in the absence of ingestion. c. Laryngeal symptoms include: stridor, vocal changes, odynophagia. d. An allergen is a substance (usually a protein) capable of triggering an immune response that can result in an allergic reaction. Most allergens act through an IgE-mediated pathway, but some non-allergen triggers can act independent of IgE (for example, via direct activation of mast cells). Adapted from ([26])*

Anaphylaxis is a clinical diagnosis; a precise definition is not important for treatment.

Anaphylaxis is characterised by:

- Sudden onset and rapid progression of symptoms.
- **A**irway and/or **B**reathing and/or **C**irculation problems.
- Usually, skin and/or mucosal changes (flushing, urticaria, angioedema).

The diagnosis is supported if a patient has been exposed to an allergen known to affect them. However, in up to 30% of cases there may be no obvious trigger.

Remember:

- Skin or mucosal changes ***alone*** are not a sign of anaphylaxis.
- **Skin and mucosal changes can be subtle or absent in 10–20% of reactions** (e.g. some patients present initially with only bronchospasm or hypotension).

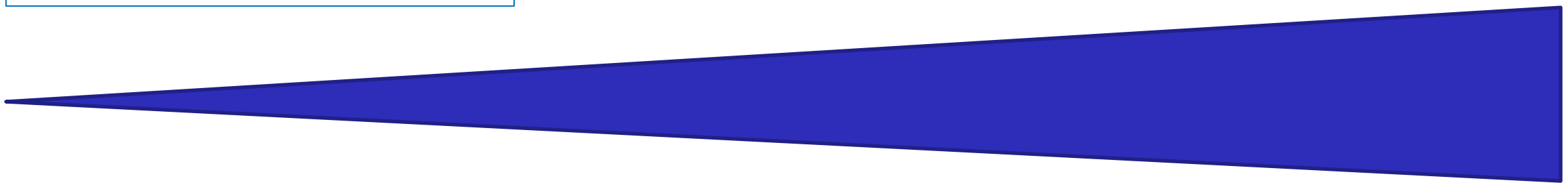
Gastrointestinal symptoms (e.g. nausea, abdominal pain, vomiting) in the absence of **A**irway and/or **B**reathing and/or **C**irculation problems do not usually indicate anaphylaxis. Abdominal pain and vomiting can be symptoms of anaphylaxis due to an insect sting or bite.

Spectrum of severity (Hypersensitivity)

Mild, localized skin symptoms and/or swelling of lips/face

Generalized skin reactions

Airway/**B**reathing/**C**irculation problems ± skin symptoms



No **A**irway/**B**reathing/**C**irculation problems:
Not Anaphylaxis

A/**B**/**C** problems:
ANAPHYLAXIS

SEVERE ANAPHYLAXIS

Resuscitation Council UK

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		

Table 4. Examples of anaphylaxis elicitors worldwide (frequency depends on age, geographical region and lifestyle) *Adapted from* ([21,53,55-57])

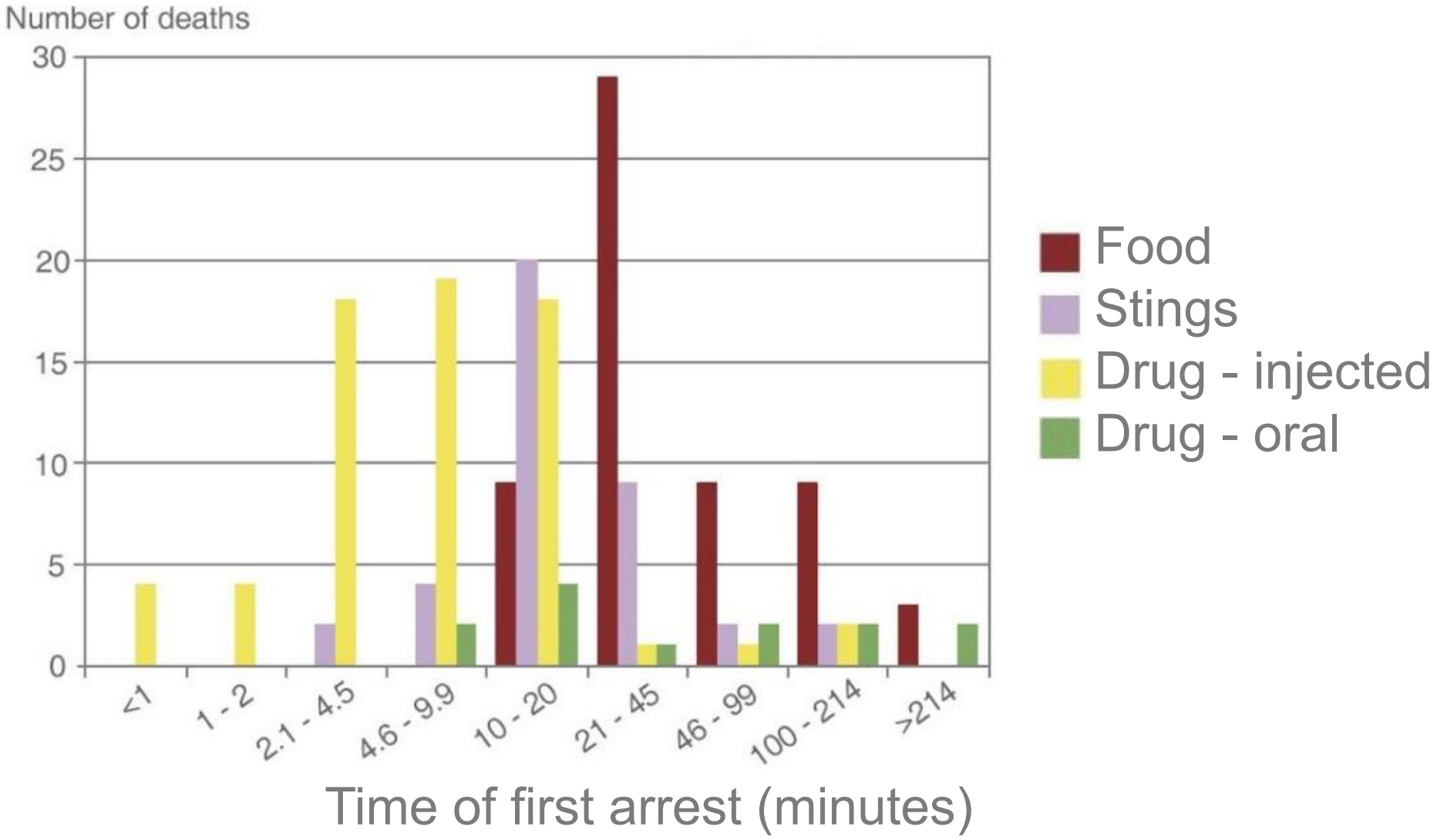
Immunologic Mechanisms (IgE Dependent)

Immunologic Mechanisms (IgE independent)

Nonimmunologic Mechanisms (Direct mast cell activation)

Idiopathic Anaphylaxis (No apparent trigger)

Time course for fatal anaphylaxis



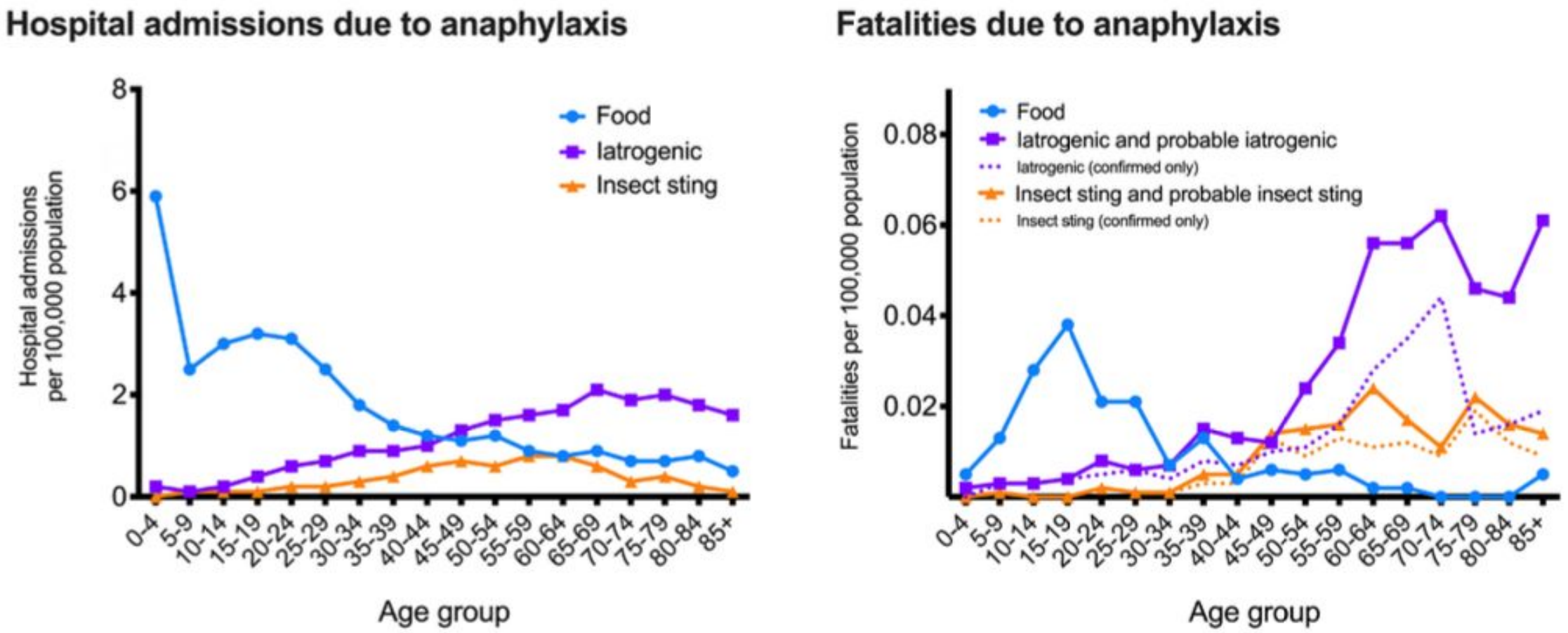


Figure 2: Age distribution for hospital admissions due to anaphylaxis (left) and fatalities (right) in the UK (1992–2012) by trigger (food, iatrogenic, insect stings)[4]

Comorbidities and concurrent medications that might impact the severity and treatment of anaphylaxis

Comorbidities
Asthma
Other pulmonary diseases (eg, COPD, interstitial lung disease)
Cardiovascular diseases (eg, ischemic heart disease, hypertensive vascular disease, cardiomyopathy)
Mast cell disorder (ie, systemic mastocytosis or mast cell activation syndrome)
Concurrently administered medications
Beta-adrenergic blockers*
Alpha-adrenergic blockers¶
Angiotensin-converting enzyme (ACE) inhibitors$^{\Delta}$
Angiotensin II receptor blockers$^{\Delta}$
Tricyclic antidepressants$^{\diamond}$
Monoamine oxidase inhibitors§
ADHD medications¥ (eg, stimulants, such as methylphenidate and amphetamines)
Recreational use of cocaine‡

Resuscitation Council UK

GUIDELINES 2021

Anaphylaxis

Anaphylaxis?

A = Airway B = Breathing C = Circulation D = Disability E = Exposure

Diagnosis – look for:

- Sudden onset of Airway and/or Breathing and/or Circulation problems[1]
- And usually skin changes (e.g. itchy rash)

Call for HELP

Call resuscitation team or ambulance

- Remove trigger if possible (e.g. stop any infusion)
- Lie patient flat (with or without legs elevated)
  - A sitting position may make breathing easier
  - If pregnant, lie on left side

Inject at **anterolateral aspect** – middle third of the thigh

Give intramuscular (IM) adrenaline[2]

- Establish airway
- Give high flow oxygen
- Apply monitoring: pulse oximetry, ECG, blood pressure

If no response:

- Repeat IM adrenaline after 5 minutes
- IV fluid bolus[3]

If no improvement in Breathing or Circulation problems[1] despite TWO doses of IM adrenaline:

- Confirm resuscitation team or ambulance has been called
- Follow REFRACTORY ANAPHYLAXIS ALGORITHM

1. Life-threatening problems

Airway
Hoarse voice, stridor

Breathing
↑work of breathing, wheeze, fatigue, cyanosis, SpO_2 <94%

Circulation
Low blood pressure, signs of shock, confusion, reduced consciousness

2. Intramuscular (IM) adrenaline
Use adrenaline at 1 mg/mL (1:1000) concentration

Adult and child >12 years:	500 micrograms IM (0.5 mL)
Child 6–12 years:	300 micrograms IM (0.3 mL)
Child 6 months to 6 years:	150 micrograms IM (0.15 mL)
Child <6 months:	100–150 micrograms IM (0.1–0.15 mL)

The above doses are for IM injection **only**.
Intravenous adrenaline for anaphylaxis to be given **only by experienced specialists** in an appropriate setting.

3. IV fluid challenge
Use crystalloid

Adults:	500–1000 mL
Children:	10 mL/kg

Resuscitation Council UK

Intramuscular Adrenaline Dosing

0.01 mg/kg of body weight, to a maximum total dose of 0.5 mg - This is equivalent to 0.5 mL of 1 mg/mL (1:1000)[a] epinephrine (adrenaline)	
Infants under 10 kg	0.01 mg/kg = 0.01 mL/kg of 1 mg/mL (1:1000)
Children aged 1–5 years	0.15 mg = 0.15 mL of 1 mg/mL (1:1000)
Children aged 6–12 years	0.3 mg = 0.3ml of 1 mg/mL (1:1000)
Teenagers and adults	0.5 mg = 0.5ml of 1 mg/mL (1:1000)

Table 6. Recommended doses for intramuscular epinephrine (adrenaline). *a. 1 mg/mL (1:1000) is recommended for intramuscular injections as this allows a more appropriate volume to be injected*

Adrenaline Concentrations

1:10,000- 1mg/10ml

1:1,000-1mg/ml

Adjunctive Therapy for Anaphylaxis

- Beta Agonists- Salbutamol via inhaler and nebulizers
- Corticosteroids: hydrocortisone, methylprednisolone
- Histamine Blockers
  - H1: diphenhydramine, chlorpheniramine maleate
  - H2: famotidine, ranitidine, cimetidine
- Glucagon for refractory anaphylaxis especially with Beta-blockers

Resuscitation Council UK

GUIDELINES 2021

Refractory anaphylaxis

No improvement in respiratory or cardiovascular symptoms despite 2 appropriate doses of intramuscular adrenaline

Establish dedicated peripheral IV or IO access

Seek expert[1] help early
Critical care support is essential

Give rapid IV fluid bolus
e.g. 0.9% sodium chloride

&

Start adrenaline infusion
Adrenaline is essential for treating all aspects of anaphylaxis

Give IM* adrenaline every 5 minutes until adrenaline infusion has been started
*IV boluses of adrenaline are not recommended, but may be appropriate in some specialist settings (e.g. peri-operative) while an infusion is set up

Give high flow oxygen
Titrate to SpO_2 94–98%

Monitor HR, BP, pulse oximetry and ECG for cardiac arrhythmia
Take blood sample for mast cell tryptase

Follow local protocol
OR
Peripheral low-dose IV adrenaline infusion:
- 1 mg (1 mL of 1 mg/mL [1:1000]) adrenaline in 100 mL of 0.9% sodium chloride
- Prime and connect with an infusion pump via a dedicated line

DO NOT 'piggy back' on to another infusion line

DO NOT infuse on the same side as a BP cuff as this will interfere with the infusion and risk extravasation

- In both adults and children, start at 0.5–1.0 mL/kg/hour, and **titrate according to clinical response**
- Continuous monitoring and observation is mandatory
- ↑↑ BP is likely to indicate adrenaline overdose

Continue adrenaline infusion and treat ABC symptoms
Titrate according to clinical response

[1]Intravenous adrenaline for anaphylaxis to be given only by experienced specialists in an appropriate setting.

A = Airway

Partial upper airway obstruction/stridor:
Nebulised adrenaline (5mL of 1mg/mL)

Total upper airway obstruction:
Expert help needed, follow difficult airway algorithm

B = Breathing

Oxygenation is more important than intubation

If apnoeic:
- Bag mask ventilation
- Consider tracheal intubation

Severe/persistent bronchospasm:
- Nebulised salbutamol and ipratropium with oxygen
- Consider IV bolus and/or infusion of salbutamol or aminophylline
- Inhalational anaesthesia

C = Circulation

Give further fluid boluses and titrate to response:
Child 10 mL/kg per bolus
Adult 500–1000 mL per bolus
- Use glucose-free crystalloid (e.g. Hartmann's Solution, Plasma-Lyte®)

Large volumes may be required (e.g. 3–5 L in adults)

Place arterial cannula for continuous BP monitoring

Establish central venous access

IF REFRACTORY TO ADRENALINE INFUSION
Consider adding a second vasopressor **in addition** to adrenaline infusion:
- Noradrenaline, vasopressin or metaraminol
- In patients on beta-blockers, consider glucagon

Consider extracorporeal life support

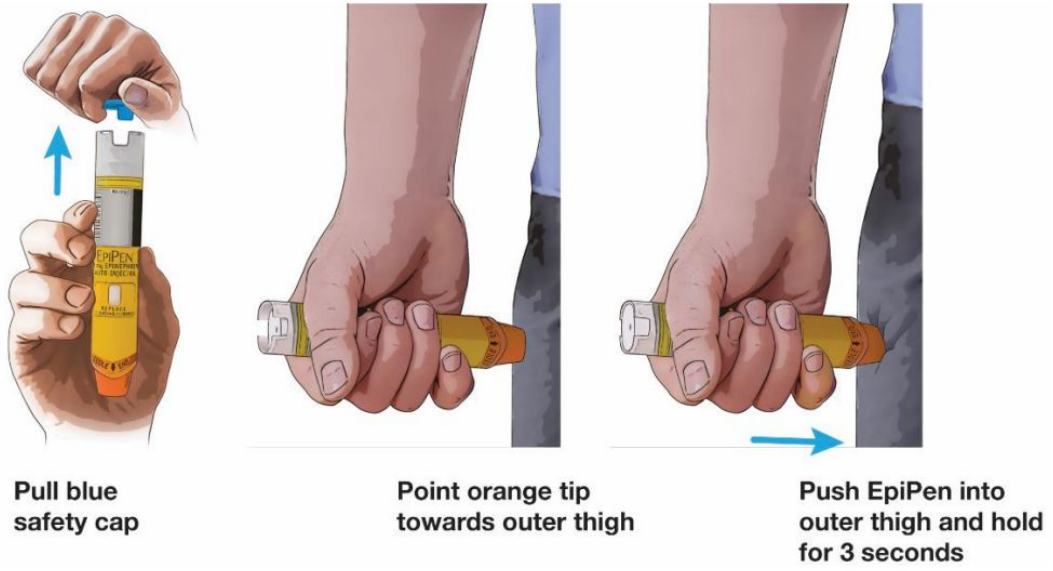
Cardiac arrest – follow ALS ALGORITHM
- Start chest compressions early
- Use IV or IO adrenaline bolus (cardiac arrest protocol)
- Aggressive fluid resuscitation
- Consider prolonged resuscitation/extracorporeal CPR

	Adult	Paediatric
Adrenaline infusion	Where a local protocol is not available, the following can be used: Mix 1 mg (1 mL of 1 mg/mL (1:1 000)) adrenaline in 100 mL of 0.9% sodium chloride. Start at 0.5 mL/kg/h (~0.1 microgram/kg/min) and titrate according to response. This dilution can be given via peripheral venous cannula. Continuous monitoring mandatory: ECG, Pulse oximetry, non-invasive BP at least every 5 min	
Adrenaline (IV bolus, until infusion is ready) **To be given only by experienced specialists.**	50 micrograms, if repeated, start an IV adrenaline infusion. Prefilled syringes of **1:10 000** adrenaline contain 100 micrograms/mL. 0.5 mL is equivalent to 50 micrograms and is the smallest dose that can be given accurately. **Do not use 1:1 000 adrenaline undiluted**	There is no evidence on which to base a dose recommendation – a child may respond to a dose as small as 1 microgram/kg. **This requires very careful dilution and checking to prevent dosing errors**.

Disposition: Anaphylaxis

Consider fast-track discharge (after 2 hours observation from resolution of anaphylaxis) if:	Minimum 6 hours observation after resolution of symptoms recommended if:	Observation for at least 12 hours following resolution of symptoms if any one of the following:
• Good response (within 5–10 minutes) to a single dose of adrenaline given within 30 minutes of onset of reaction **and** • Complete resolution of symptoms **and** • The patient already has unused adrenaline auto-injectors and has been trained how to use them **and** • There is adequate supervision following discharge	• 2 doses of IM adrenaline needed to treat reaction* **or** • Previous biphasic reaction	• Severe reaction requiring >2 doses of adrenaline. • Patient has severe asthma or reaction involved severe respiratory compromise. • Possibility of continuing absorption of allergen, e.g. slow-release medicines. • Patient presents late at night, or may not be able to respond to any deterioration. • Patients in areas where access to emergency care is difficult.
In all cases, discharge must comply with NICE Clinical Guidance CG134.[96]		

*It may be reasonable for some patients to be discharged after 2 hours despite needing two doses of IM adrenaline, e.g. following a supervised allergy challenge in a specialist setting.



EPI-Pen: Take at Home Adrenaline

Summary

- anaphylaxis poses a serious threat to life
- prompt recognition and treatment is vital
  - ABCDE approach
  - IM adrenaline
  - sit or lie them down
- **most patients respond to 1 dose of IM adrenaline, very few need 2 or more**
- follow the anaphylaxis algorithm
- consider treatment for refractory anaphylaxis
- manage appropriate investigations, discharge and follow-up

References

- https://www.worldallergyorganizationjournal.org/action/showPdf?pii=S1939-4551%2820%2930375-6
- https://www.worldallergy.org/UserFiles/Anaphylaxis_Guidance_Cards.pdf
- https://www.worldallergy.org/UserFiles/file/Anaphylaxis_Guidelines_Poster.pdf
- https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021_0.pdf
- https://www.uptodate.com/contents/anaphylaxis-emergency-treatment?csi=da2b5f4a-bc07-4d23-8515-a2f7a92494a0&source=contentShare